Supplementary Material (ESI) for Organic and Biomolecular Chemistry

The enantioselective synthesis of APTO and AETD: polyhydroxylated β-amino acid constituents of the microsclerodermin cyclic peptides

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General Experimental

Melting points were determined using a Reichert heating stage with microscope and are uncorrected.

Optical rotations were measured using an Optical Activity PolAAr 2001 Automatic polarimeter set at the 589.3 nm sodium D line, in a 0.25 dm cell, at the indicated temperature in the indicated solvent and concentration (*c*), reported as g solute / 100 mL. Specific rotations, $[\alpha]_D$, are quoted in 10^{-1}.deg.cm^2.g^{-1}.

Infra-red absorption spectra were obtained using a Perkin Elmer 1600 series Fourier Transform Infra-Red (FTIR) spectrometer or a Shimadzu 8400 series FTIR spectrometer and were processed using Shimadzu IRsolution 1.04 software. Compounds were prepared as thin films between 0.5 cm sodium chloride plates seated on a custom made perch in the apparatus. Absorption maxima are expressed as wavenumbers (cm^{-1}) and the appearance of bands are described by the abbreviations: br = broad, s = strong, m = medium, w = weak.

^{1}H Nuclear magnetic resonance spectra were recorded using a Bruker Avance 200 (200.13 MHz), or a Bruker Avance 300 (300.13 MHz) or a Bruker DPX 400 (400.21 MHz) spectrometer at 300 K unless otherwise specified and were processed using XWIN-NMR version 3.5. Samples were analysed as a solution in the specified solvent. Data is expressed as parts per million (ppm) downfield shift from tetramethylsilane ($\delta_{TMS} = 0$) using either tetramethylsilane or residual chloroform solvent (7.26 ppm) as an internal reference and is reported as chemical shift (δ), relative integral, multiplicity (s = singlet, br = broad, d = doublet, t = triplet, m = multiplet, q = quartet, quin = quintet, dd = doublet of doublets, dt = doublet of triplets), coupling constant (*J* in Hz) and assignment. All coupling constants and multiplicities reported are apparent.

^{13}C Nuclear magnetic resonance spectra were recorded using a Bruker Avance 200 (50.0 MHz), or a Bruker Avance 300 (75.5 MHz) or a Bruker DPX 400 (100.6 MHz) spectrometer with complete proton decoupling at 300 K unless otherwise specified and were processed using XWIN-NMR version 3.5. Samples were analysed as a solution in the specified solvent. Data is expressed as parts per million (ppm) downfield shift from tetramethylsilane ($\delta_{TMS} = 0$) using deuterated chloroform (77.0 ppm) as an internal reference and is reported as chemical shift (δ). When coupling between a carbon and phosphorus was observed the data is reported as chemical shift (δ), multiplicity (d = doublet), coupling constant ($^xJ_{PC}$ in Hz, where x denotes the number of bonds between the coupled atoms) and assignment. All coupling constants and multiplicities are apparent.

Low resolution mass spectra were recorded by the Mass Spectrometry Unit at University of Sydney using positive electron impact (+EI) on a Finnigan Polaris Q ion trap mass spectrometer operated at 40 or 70 eV or using electrospray ionization (ESI) in positive (+ESI) or negative mode (-ESI) on a Finnigan LCQ ion trap mass spectrometer. High resolution mass spectra were recorded by the Mass Spectrometry Unit at University of Queensland using +EI on a Kratos MS25 RFA mass spectrometer operated at 70 eV in magnetic scan using perfluorokerosene (PFK) as standard or by the Mass Spectrometry Unit at Australian National University, Canberra using ESI on a 4.7T Bruker Apex II Fourier Transform Ion Cyclotron Resonance (FT-ICR) mass spectrometer or by the Mass Spectrometry Unit at University of New South Wales using ESI on a 7T Bruker Apex FTICR. Major fragments are quoted as mass to charge ratio (assignment where possible and relative intensity).

Analytical high performance liquid chromatography (HPLC) was carried out using a Waters Associates system consisting of a Millipore 510 pump, a Millipore U6K injector, a 2487 dual wavelength absorbance detector at 254 and 270 nm and a 410 differential refractometer. Data was acquired and processed using Empower software. Separation was carried out using the indicated solvents at a flow rate of 0.5 mL min^{-1} on a Daicel Chiralcel OD-H chiral analytical column with a length of 250 mm, and an internal diameter of 4.6 mm.

Preparative HPLC was carried out using a Waters Associates system consisting of a Model 510 pump, a Millipore U6K injector, a 490E programmable multi-wavelength detector at 254 nm and a Millipore R403 differential refractometer. Data was recorded and processed using Empower software. Separation was carried out using the indicated solvents with a flow rate of 13.5 mL / min and pressure of 1000 psi on a RTI Zorbax Sil preparative column with a length of 250 mm, an internal diameter of 21.2 mm and particle size of 7 μm. Retention time (t_R) is reported as the time corresponding to the maximum absorbance for the peak detected at 254 nm.

Analytical thin layer chromatography (TLC) was performed using 0.2 mm thick, aluminium-backed, pre-coated silica gel plates (Merck Silicagel 60 F_{254}). Compounds were visualised by short and long wavelength ultra-violet fluorescence and by staining with a mixture of phosphomolybdic acid and ceric sulfate in sulfuric acid or a solution of ninhydrin in sulfuric acid or an acidified ethanolic solution of anisaldehyde.

Flash chromatography was performed using Merck Silicagel 60 (230 – 400 mesh ASTM), under a positive pressure of nitrogen, with the indicated solvents. Solvent compositions were mixed volume per volume (v/v) as specified.

Evaporation or concentration under reduced pressure refers to evaporation using a rotary evaporator connected to a water aspirator. Removal of residual solvent when necessary was achieved by evacuation (0.1 – 0.01 mm Hg) with a high stage oil sealed vacuum pump.

All solvents and reagents were dried and purified when necessary according to procedures outlined by Perrin and Armarego[1] or Leonard, Lygo and Proctor.[2] Commercial *n*-butyl lithium in hexanes was titrated against isopropanol in tetrahydrofuran using 2,2'-bipyridyl as an indicator. "Hexanes" refers to hexanes (b.p. 65 – 69 °C) and "brine" refers to saturated aqueous sodium chloride solution.

Moisture sensitive reactions were carried out in oven dried glassware under a dry inert atmosphere of nitrogen or argon. Powdered, 5 Å molecular sieves were activated in a muffler oven at 500 °C for 3 days and allowed to cool under desiccation before use. Reaction temperatures were controlled using dry ice:acetone (-78 °C), ice:water (0 – 5 °C) cooling baths or sand, oil heating baths (> room temperature).

Experimental

(*E*)-4-Methoxy-4-oxobut-2-enyl 4-methoxybenzoate 9

Method 1 – Cross metathesis olefination: A solution of alkene **10**[3] (0.50 g, 2.6 mmol) in dichloromethane (6.0 mL) was transferred *via cannula*, to a stirring solution of tricyclohexylphosphine[1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene][benzylidene]ruthenium(IV) dichloride **11** (160 mg, 0.19 mmol) and methyl acrylate (0.57 mL, 6.3 mmol) in dichloromethane (10 mL), washing with dichloromethane (2 x 1.4 mL). The solution was heated at reflux under an atmosphere of nitrogen for the 36 h, allowed to cool and concentrated under reduced pressure to give the crude product (0.91 g). Flash chromatographic purification (20% ethyl acetate:hexanes) gave pure alkene **9** as a white crystalline solid (0.42 g, 65%); R_f 0.24 (20% ethyl acetate:hexanes); mp 48.5–49.5 °C; ν_{max}(thin film)/cm^{-1} 1722, 1668 (s, C=O), 1607, 1581, 1512 (s, Ar(C=C)); δ_H(200 MHz; $CDCl_3$) 8.03–7.95 (2H, m, Ar-H), 7.03 (1H, dt, *J* 15.8, 4.5 Hz, C_3-H), 6.93–6.86 (2H, m, Ar-H), 6.09 (1H, dt, *J* 15.8, 2.0 Hz, C_2-H), 4.92 (2H, dd, *J* 4.5, 2.0 Hz, C_4-H), 3.82 (3H, s, Ar-OCH_3), 3.72 (3H, s, C_1-OCH_3); δ_C(50 MHz; $CDCl_3$) 166.1, 165.4, 163.6, 141.8, 131.6, 121.8, 121.5, 113.6, 62.5, 55.3, 51.5; HRMS(+EI) calc. for $C_{13}H_{14}O_5$ 250.0841, found 250.0841; *m/z*(+EI) 250 (M^+, 2%), 135 (100), 77 (16).

Method 2 – Horner-Wadsworth-Emmons olefination: Water (0.11 L) was added to a solution of alkene **10** (22 g, 0.11 mol) in diethyl ether (0.33 L). Osmium tetroxide solution (4% wt aq., 7.2 mL, 1.1 mmol) was added and the biphasic reaction was stirred for 10 min. Sodium periodate (91 g, 0.42 mol) was added over 20 min and the reaction was stirred vigorously at room temperature for 15 h, after which, water (0.10 L) was added, to re-suspend the white solid, and the reaction was stirred vigorously at room temperature for 24 h. Water (0.50 L) was added, the organic layer was collected and the aqueous layer was extracted with ethyl acetate (3 x 0.50 L). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give crude aldehyde **12**[4] as an olive green liquid (22 g, quant.) which was used without further purification in the subsequent reaction.

To a solution of methyl diethylphosphonoacetate **13** (36 g, 0.17 mol) in tetrahydrofuran (0.60 L) at -78 °C, was added a solution of *n*-butyl lithium (72 mL, 1.6 M in hexanes, 0.11 mol). The reaction was stirred at -78 °C for 30 min. A solution of aldehyde **12** (22 g, 0.11 mol) in tetrahydrofuran (0.60 L) was added drop-wise, *via cannula*, and the reaction was stirred at room temperature for 5 h. Ammonium chloride solution (sat. aq., 0.50 L) was added and the crude product was extracted into ethyl acetate (3 x 0.50 L). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give the crude product as a yellow liquid (42 g). The ratio of (*E*)-alkene **9** to (*Z*)-alkene was determined to be 25:1 from integration of the C_2-H signals in the 200 MHz ^{1}H NMR spectrum. Flash chromatographic purification (10% ethyl acetate:hexanes graded to 30% ethyl acetate:hexanes) gave pure alkene **9** as a white solid (26 g, 91% over 2 steps).

(2*R*,3*S*)-2-(*tert*-Butoxycarbonylamino)-3-hydroxy-4-methoxy-4-oxobutyl 4-methoxybenzoate 8

Method 1 – Using $(DHQD)_2PHAL$ ligand **14**: A solution of sodium hydroxide (4.7 g, 0.12 mol) in water (0.27 L) was added to a solution of *tert*-butyl carbamate (13 g, 0.11 mol) in 1-propanol (0.11 L). 1,3-dichloro-5,5-dimethylhydantoin (15 g, 0.076 mol) was added and the suspension was stirred until clear. A solution of $(DHQD)_2PHAL$ **14** (2.0 g, 2.6 mmol) in 1-propanol (85 mL) was added followed by a solution of alkene **9** (9.3 g, 37 mmol) in 1-propanol (85 mL). Potassium osmate(VI) dihydrate (0.68 g, 1.8 mmol) was added and the resulting cloudy brown solution was stirred at room temperature for 2 days. Sodium sulfite (anhydrous, 39 g, 0.31 mol) was added and the reaction was stirred for 1 h. Brine (0.30 L) was added and the crude product was extracted into ethyl acetate (3 x 0.40 L). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to afford a beige residue (40 g). Excess *tert*-butyl carbamate was removed by sublimation under high vacuum. Flash chromatographic purification (40% ethyl acetate:hexanes) of the crude product afforded pure β-amino alcohol **8** as a white crystalline solid (12 g, 84%); R_f 0.23 (40% ethyl acetate:hexanes); mp 80.0–82.0 °C; $[\alpha]_D^{24}$ +37.3 (*c* 1.7, CH_2Cl_2); ν_{max}(thin film)/cm^{-1} 3364 (br, m, O-H), 1715 (br, s, C=O), 1606, 1581, 1512 (m, Ar(C=C)); δ_H(300 MHz; $CDCl_3$) 8.00–7.97 (2H, m, Ar-H), 6.92–6.89 (2H, m, Ar-H), 4.94 (1H, br d, *J* 8.9 Hz, N-H), 4.49–4.40 (4H, m, C_2-H, C_3-H, C_4-H), 3.86 (3H, s, Ar-OCH_3), 3.81 (3H, s, C_1-OCH_3), 1.39 (9H, s, $OC(CH_3)_3$), O*H* not observed; δ_C(50 MHz; $CDCl_3$) 173.4, 166.0, 163.6, 155.2, 131.8, 122.1, 113.6,

80.0, 69.7, 63.2, 55.4, 53.0, 51.7, 28.2; HRMS(+ESI) calc. for $C_{18}H_{25}NO_8$+Na 406.1478, found 406.1482; *m/z*(ESI) 789 ($[2M+Na]^+$, 91%), 406 ($[M+Na]^+$, 100).

Method 2 – Using $(DHQ)_2PHAL$ ligand: A solution of sodium hydroxide (0.051 g, 1.3 mmol) in water (3.0 mL) was added to a solution of *tert*-butyl carbamate (0.14 g, 1.2 mmol) in 1-propanol (1.2 mL). 1,3-dichloro-5,5-dimethylhydantoin (0.16 g, 0.81 mmol) was added and the suspension was stirred until clear. A solution of $(DHQ)_2PHAL$ (0.022 g, 0.028 mmol) in 1-propanol (0.80 mL) was added followed by a solution of alkene **9** (0.10 g, 0.40 mmol) in 1-propanol (1.0 mL). Potassium osmate(VI) dihydrate (7.3 mg, 0.020 mmol) was added and the resulting cloudy brown solution was stirred at room temperature for 6 h. Sodium sulfite solution (sat. aq., 10 mL) was added and the reaction was stirred for 1 h. Brine (10 mL) was added and the crude product was extracted into ethyl acetate (3 x 30 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to afford a beige residue (0.40 g). Excess *tert*-butyl carbamate was removed by sublimation under high vacuum. Flash chromatographic purification (40% ethyl acetate:hexanes) of the crude product afforded pure β-amino alcohol *ent*-**8** as a white crystalline solid (0.11 g, 72%).

(2*R*,3*S*)-2-(*tert*-Butoxycarbonylamino)-3-(*tert*-butyldimethylsilyloxy)-4-methoxy-4-oxobutyl 4-methoxybenzoate 16

2,6-Lutidine (0.22 mL, 1.9 mmol) was added to a solution of β-amino alcohol **8** (0.36 g, 0.94 mmol), in dichloromethane (0.95 mL), under an atmosphere of nitrogen. The mixture was cooled to -78 °C and *tert*-butyldimethylsilyl triflate (0.32 mL, 1.4 mmol) was added drop-wise. The reaction was stirred at -78 °C for 15 min and the resulting solid melted as the reaction was allowed to warm to room temperature. The reaction was stirred for 22 h. Water (15 mL) was added and the crude product was extracted into ethyl acetate (3 x 30 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give a clear, colourless, viscous liquid (0.57 g). Flash chromatographic purification (20% ethyl acetate:hexanes graded to 40% ethyl acetate:hexanes) gave pure TBDMS protected β-amino alcohol **16** as a viscous clear, colourless liquid (0.35 g, 75%); R_f 0.55 (40% ethyl acetate:hexanes); $[\alpha]_D^{24}$ +28.8 (*c* 2.2, CH_2Cl_2); ν_{max}(thin film)/cm^{-1} 3445, 3364 (w, N-H), 1759, 1719, (s, C=O), 1606, 1581, 1512 (m, Ar(C=C)); δ_H(300 MHz; $CDCl_3$) 8.02–7.96 (2H, m, Ar-H), 6.93–6.90 (2H, m, Ar-H), 4.97 (1H, br d, *J* 9.4 Hz, N-H), 4.49–4.40 (2H, m, C_2-H, C_3-H), 4.35 (1H, dd, *J* 10.6, 6.0 Hz, C_4-H_A), 4.21 (1H, dd, *J* 10.5, 7.7 Hz, C_4-H_B), 3.86 (3H, s, Ar-OCH_3), 3.72 (3H, s, C_1-OCH_3), 1.41 (9H, s, $OC(CH_3)_3$), 0.91 (9H, s, Si-$C(CH_3)_3$), 0.10 (3H, s, Si-CH_3), 0.03 (3H, s, Si-CH_3); δ_C(75 MHz; $CDCl_3$) 172.0, 165.8, 163.5, 155.2, 131.7, 122.2, 113.7, 79.8, 70.8, 62.9, 55.4, 52.4, 52.1, 28.2, 25.7, 18.3, -4.9, -5.6; HRMS(+ESI) calc. for $C_{24}H_{39}NO_8Si$+Na 520.2343, found 520.2348; *m/z*(+ESI) 1017 ($[2M+Na]^+$, 45%), 520 ($[M+Na]^+$, 100). A second fraction gave pure recovered β-amino alcohol **8** as a white solid (0.021 g, 10%).

(2*S*,3*R*)-Methyl 3-(*tert*-butoxycarbonylamino)-2-(*tert*-butyldimethylsilyloxy)-4-hydroxybutanoate 17 and (3*R*,4*S*)-*tert*-Butyl 4-(*tert*-butyldimethylsilyloxy)-5-oxo-tetrahydrofuran-3-ylcarbamate

Caesium carbonate (0.40 g, 1.2 mmol) and *p*-methoxybenzoyl ester **16** (0.74 g, 1.5 mmol) were combined and dissolved in dry methanol (30 mL). The reaction was stirred for 15 h at room temperature, under an atmosphere of nitrogen. Additional caesium carbonate (0.11 g, 0.34 mmol) was added and the reaction was stirred for 24 h. Ammonium chloride solution (sat. aq., 30 mL) was added and the crude product was extracted into ethyl acetate (3 x 80 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give a viscous yellow liquid (0.91 g). Flash chromatographic purification (20% ethyl acetate:hexanes) gave pure alcohol **17** as a viscous clear, colourless liquid (0.35 g, 64%); R_f 0.33 (40% ethyl acetate:hexanes); ν_{max}(thin film)/cm^{-1} 3445 (br, s, N-H and O-H), 1759, 1700, (br, s, C=O); δ_H(300 MHz; $CDCl_3$) 5.03 (1H, d, *J* 8.8 Hz, N-H), 4.49 (1H, d, *J* 2.5 Hz, C_2-H), 4.07–4.00 (1H, m, C_3-H), 3.77 (1H, dd, *J* 10.8, 5.4 Hz, C_4-H_A), 3.73 (3H, s, C_1-OCH_3), 3.59 (1H, dd, *J* 10.8, 7.0 Hz, C_4-H_B), 1.43 (9H, s, $OC(CH_3)_3$), 0.92 (9H, s, Si-$C(CH_3)_3$), 0.11 (3H, s, Si-CH_3), 0.07 (3H, s, Si-CH_3), O*H* not observed; δ_C(75 MHz; $CDCl_3$) 172.5, 155.9, 79.9, 71.0, 62.3, 54.9, 52.1, 28.3, 25.7, 18.3, -5.0, -5.6. Alcohol **17** decomposed on standing to give the corresponding γ-butyrolactone as a viscous clear, colourless liquid; R_f 0.48 (40% ethyl acetate:hexanes); $[\alpha]_D^{21}$ -44.1 (*c* 0.4, CH_2Cl_2); ν_{max}(thin film)/cm^{-1} 3354 (br, m, N-H), 1793 (br, s, C=O(lactone)), 1701 (br, s, C=O(carbamate)); δ_H(200 MHz; 320 K; $CDCl_3$) 4.69 (1H, s, N-H), 4.55–4.42 (2H, m, CH), 4.20–4.03 (2H, m, CH), 1.46 (9H, s, $OC(CH_3)_3$), 0.93 (9H, s, Si-$C(CH_3)_3$), 0.20 (3H, s, Si-CH_3), 0.17 (3H, s, Si-CH_3); δ_C(50 MHz; $CDCl_3$) 173.6, 154.8, 80.7, 71.7, 67.5, 55.7, 28.3, 25.6, 18.2, -4.6, -5.2; HRMS(+ESI) calc. for $C_{15}H_{29}NO_5Si$+Na 354.1713, found 354.1716; *m/z*(+ESI) 685 ($[2M+Na]^+$, 5%), 354 ($[M+Na]^+$, 100).

(4*R*,5*S*)-3-*tert*-Butyl 5-methyl 4-((4-methoxybenzoyloxy)methyl)-2,2-dimethyloxazolidine-3,5-dicarboxylate 18, (2*R*,3*S*)-2-(*tert*-Butoxycarbonylamino)-4-methoxy-3-(2-methoxypropan-2-yloxy)-4-oxobutyl 4-methoxybenzoate 19 and (4*R*,5*S*)-3-*tert*-Butyl 5-methyl 4-((4-methoxybenzoyloxy)methyl)-2-methyl-2-(2-methylprop-1-enyl)oxazolidine-3,5-dicarboxylate 20

Method 1 – Using 2,2-dimethoxypropane and TsOH: To a solution of alcohol **8** (0.40 g, 1.0 mmol) in benzene (1.0 mL) was added 2,2-dimethoxypropane (0.39 mL, 3.2 mmol) followed by *p*-toluenesulfonic acid hydrate (0.076 g, 0.40 mmol). The solution was heated at 95 °C for 32 h adding additional aliquots of 2,2-dimethoxypropane (0.50 mL, 4.1 mmol) at 2 h, 9 h, 10 h and 23 h. The reaction was allowed to cool to room temperature and was poured into sodium hydrogen carbonate solution (sat. aq., 50 mL). The organic layer was collected and the aqueous layer was extracted with ethyl acetate (3 x 100 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give a viscous orange liquid (0.41 g). Flash chromatographic purification (20% ethyl acetate:hexanes graded to 40% ethyl acetate:hexanes) gave pure oxazolidine **18** as a viscous clear, colourless liquid (0.16 g, 36%); R_f 0.49 (40% ethyl acetate:hexanes); $[\alpha]_D^{19}$ +4.8 (*c* 0.5, CH_2Cl_2); ν_{max}(thin

film)/cm^{-1} 1713 (br s, C=O), 1607, 1581, 1512 (m, Ar(C=C)) 1258 (br, s, N-CO-O); δ_H(200 MHz; 340K, $CDCl_3$) 8.01–7.96 (2H, m, Ar-H), 6.93–6.88 (2H, m, Ar-H), 4.65 (1H, d, *J* 2.8 Hz, C_2-H), 4.58–4.47 (3H, m, C_3-H, C_4-H), 3.85 (3H, s, Ar-OCH_3), 3.77 (3H, s, C_1-OCH_3), 1.62 (3H, s, $C(CH_3)_2$), 1.58 (3H, s, $C(CH_3)_2$), 1.49 (9H, s, $OC(CH_3)_3$); δ_C(50 MHz; 340K, $CDCl_3$) 171.3, 165.8, 163.9, 151.5, 131.8, 122.6, 113.9, 96.8, 81.0, 76.3, 63.5, 59.1, 55.4, 52.3, 28.5, 27.5, 26.5; HRMS(+ESI) calc. for $C_{21}H_{29}NO_8$+Na 446.1791, found 446.1779; *m/z*(+ESI) 869 ([2M+Na]$^+$, 23%), 446 ([M+Na]$^+$, 100), 390 (18), 346 (8). A second fraction gave pure intermediate acetal **19** as a viscous clear colourless liquid (0.0070 g, 1.5%); R_f 0.38 (40% ethyl acetate:hexanes); $[\alpha]_D^{21}$ +32.6 (*c* 3.6, CH_2Cl_2); ν_{max}(thin film)/cm^{-1} 3445, 3373 (br m, N-H), 1755, 1713, (s, C=O), 1607, 1581, 1514 (m, Ar(C=C)); δ_H(200 MHz; $CDCl_3$) 8.01–7.94 (2H, m, Ar-H), 6.92–6.88 (2H, m, Ar-H), 5.06 (1H, d, *J* 8.5 Hz, N-H), 4.53–4.52 (1H, m, C_2-H), 4.38–4.22 (3H, m, C_3-H, C_4-H), 3.84 (3H, s, Ar-OCH_3), 3.70 (3H, s, C_1-OCH_3), 3.19 (3H, s, $C_{2'}$-OCH_3), 1.40 (9H, s, $OC(CH_3)_3$), 1.37 (3H, s, $C(CH_3)_2$), 1.32 (3H, s, $C(CH_3)_2$); δ_C(50 MHz; $CDCl_3$) 171.8, 165.8, 163.5, 155.2, 131.7, 122.0, 113.6, 102.1, 79.8, 68.6, 63.0, 55.4, 52.1, 51.7, 50.0, 28.2, 24.5, 24.5; HRMS(+ESI) calc. for $C_{22}H_{33}NO_9$+Na 478.2053, found 478.2041; *m/z*(+ESI) 933 ([2M+Na]$^+$, 28%), 478 ([M+Na]$^+$, 100), 406 (7), 350 (10). A third fraction gave recovered-alcohol **8** as a white crystalline solid (0.16 g, 40%).

Method 2 – Using 2-methoxypropene and TsOH: To a solution of alcohol **8** (1.8 g, 4.7 mmol) in benzene (20 mL) at 0 °C, was added 2-methoxypropene (1.5 mL, 16 mmol) followed by *p*-toluenesulfonic acid (0.20 g, 1.1 mmol). The resulting dark red solution was stirred at 0 °C for 2 h and an additional aliquot of 2-methoxypropene (1.6 mL, 17 mmol) was added. The reaction was allowed to warm to room temperature and was stirred for 5h adding additional aliquots of 2-methoxypropene (2.0 mL, 21 mmol) at 2h, 4h and an additional aliquot of *p*-toluenesulfonic acid (0.20 g, 1.1 mmol) at 3 h. Sodium hydrogen carbonate solution (sat. aq., 50 mL) was added, the organic layer was collected and the aqueous layer was extracted with ethyl acetate (3 x 100 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give a viscous bright yellow liquid (3.9 g). Flash chromatographic purification (20% ethyl acetate:hexanes graded to 40% ethyl acetate:hexanes) gave pure oxazolidine **18** as a viscous clear, colourless liquid (1.2 g, 60%). A second fraction gave recovered-alcohol **8** as a white crystalline solid (0.39 g, 22%).

Method 3 – Using 2-methoxypropene and PPTS: To a solution of alcohol **8** (0.66 g, 1.7 mmol) in toluene (17 mL) was added 2-methoxypropene (3.3 mL, 34 mmol) followed by pyridinium *p*-toluenesulfonate (0.039 g, 0.16 mmol). The clear colourless solution was stirred at room temperature for 1 h, heated at 110 °C for 3 h and allowed to cool to room temperature. Sodium hydrogen carbonate solution (sat. aq., 100 mL) was added, the organic layer was collected and the aqueous layer was extracted with ethyl acetate (3 x 150 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give a viscous yellow liquid (1.4 g). Flash chromatographic purification (5% ethyl acetate:hexanes graded to 40% ethyl acetate:hexanes) gave pure oxazolidine **18** as a viscous clear, colourless liquid (0.56 g, 77%). A second fraction gave pure by-product **20** as viscous clear colourless liquid (0.16 g, 20%); R_f 0.50 (40% ethyl acetate:hexanes); $[\alpha]_D^{21}$ -68.9 (*c* 3.4, CH_2Cl_2); ν_{max}(thin film)/cm^{-1} 1701 (br, s, C=O), 1607, 1581, 1512 (m, Ar(C=C)); δ_H(200 MHz; 320K, $CDCl_3$) 8.02–7.95 (2H, m, Ar-H), 6.94–6.87 (2H, m, Ar-H), 5.42 (1H, s, $C_{3'}$-H), 4.64–4.54 (4H, m, C_2-H, C_3-H, C_4-H), 3.85 (3H, s, Ar-OCH_3), 3.70 (3H, s, C_1-OCH_3), 1.79–1.79 (3H, m, $C_{1'}$-H_3), 1.69 (6H, s, $C(CH_3)_2$), 1.47 (9H, s, $OC(CH_3)_3$); δ_C(50 MHz; 320K, $CDCl_3$) 170.4, 165.8, 163.6, 151.6, 137.3, 131.8, 126.2, 122.3, 113.7, 95.3, 80.7, 76.2, 62.9, 57.6, 55.4, 52.2, 28.4, 27.1, 26.7, 18.9; HRMS(+ESI) calc. for $C_{24}H_{33}NO_8$+Na 486.2104, found 486.2110; *m/z*(+ESI) 949 ([2M+Na]$^+$, 13%), 486 ([M+Na]$^+$, 100); *m/z*(+EI) 348 (68%), 135 (100).

Method 4 – Using 2-methoxypropene and PPTS: To a solution of alcohol **8** (4.2 g, 11 mmol) in toluene (0.11 L) was added 2-methoxypropene (21 mL, 0.22 mol) followed by pyridinium *p*-toluenesulfonate (0.25 g, 0.99 mmol). The clear colourless solution was stirred at room temperature for 1.5 h and then the low boiling point volatiles were removed under reduced pressure. The reaction mixture was returned to atmospheric pressure and was heated at 110 °C for 3 h and allowed to cool to room temperature. Sodium hydrogen carbonate solution (sat. aq., 0.15 L) was added, the organic layer was collected and the aqueous layer was extracted with ethyl acetate (3 x 0.20 L). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give a viscous yellow liquid (4.0 g). Flash chromatographic purification (15% ethyl acetate:hexanes graded to 40% ethyl acetate:hexanes) gave pure oxazolidine **18** as a viscous clear, colourless liquid (3.9 g, 84%). A second fraction gave recovered alcohol **8** as a white crystalline solid (0.63 g, 15%).

(4*R*,5*S*)-3-*tert*-Butyl 5-methyl 4-(hydroxymethyl)-2,2-dimethyloxazolidine-3,5-dicarboxylate 21

Caesium carbonate (0.41 g, 1.3 mmol) and *p*-methoxybenzoyl ester **18** (0.88 g, 2.1 mmol) were combined and dissolved in dry methanol (40 mL). The reaction was stirred for 16 h at room temperature, under an atmosphere of nitrogen. Ammonium chloride solution (sat. aq., 30 mL) was added and the crude product was extracted into ethyl acetate (3 x 0.10 L). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give a viscous orange liquid (1.0 g). Flash chromatographic purification (30% ethyl acetate:hexanes) gave pure alcohol **21** as a viscous clear, colourless liquid (0.49 g, 81%); R_f 0.22 (40% ethyl acetate:hexanes); $[\alpha]_D^{19}$ +13.5 (*c* 0.7, CH_2Cl_2); ν_{max}(thin film)/cm^{-1} 3460 (br m, O-H), 1742, 1697 (s, C=O); δ_H(200 MHz; 340K, $CDCl_3$) 4.46 (1H, d, *J* 4.9 Hz, C_2-H), 4.27 (1H, dt, *J* 5.0, 4.9 Hz, C_3-H), 3.86–3.78 (2H, m, C_4-H), 3.80 (3H, s, C_1-OCH_3), 1.62 (3H, s, $C(CH_3)_2$), 1.57 (3H, s, $C(CH_3)_2$), 1.50 (9H, s, $OC(CH_3)_3$), O*H* not observed; δ_C(50 MHz; 340K, $CDCl_3$) 171.2, 152.9, 96.6, 81.3, 75.8, 64.1, 62.3, 52.3, 28.5, 27.4, 26.8; HRMS(+ESI) calc. for $C_{13}H_{23}NO_6$+Na 312.1423, found 312.1415; *m/z*(+ESI) 312 ([M+Na]$^+$, 100), 256 (12).

(4*S*,5*S*)-3-*tert*-Butyl 5-methyl 4-formyl-2,2-dimethyloxazolidine-3,5-dicarboxylate 7.

Dess-Martin periodinane (2.2 g, 5.2 mmol) was added to a solution of alcohol **21** (1.2 g, 4.1 mmol) in dichloromethane (40 mL). The white suspension was stirred at room temperature for 1 h. A mixture of sodium hydrogen carbonate solution (sat. aq., 40 mL) and sodium thiosulfate solution (sat. aq., 10 mL) was added and the reaction was stirred vigorously for 1 h. The crude product was extracted into dichloromethane (3 x 100 mL) and the combined organic layers were washed with a mixture of sodium hydrogen carbonate solution (sat. aq., 20 mL) and sodium thiosulfate solution (sat. aq., 5 mL), dried (Na_2SO_4), filtered and concentrated under reduced pressure to give a cloudy, yellow liquid (1.2 g, quant.) which was used without further purification in subsequent reactions. For the purpose of characterization, flash chromatographic purification (20% ethyl acetate:hexanes) of a sample of crude product gave pure aldehyde **7** as a viscous, clear, colourless liquid; R_f 0.40–0.15 (40% ethyl acetate:hexanes); ν_{max}(thin film)/cm^{-1} 1744, 1717, (s, C=O), 1367 (s, C-H(aldehyde)); δ_H(200 MHz; 340K, $CDCl_3$) 9.59 (1H, s, CHO), 4.61–4.60 (2H, m, C_2-H, C_3-H), 3.77 (3H, s, C_1-OCH_3), 1.60 (3H, s, $C(CH_3)_2$), 1.55 (3H, s, $C(CH_3)_2$), 1.43 (9H, s, $OC(CH_3)_3$); δ_C(50 MHz; 340K, $CDCl_3$) 196.3, 169.9, 151.3, 97.0, 81.6, 73.6, 66.8, 52.5, 28.2, 26.6, 26.1; HRMS(+ESI) calc. for $C_{13}H_{21}NO_6$+Na 310.1267, found 310.1265; *m/z*(+ESI) 902 ([3M+Na+H_2O]$^+$, 100%), 615 ([2M+Na+H_2O]$^+$, 70), 310 ([M+Na]$^+$, 14).

2-(3-(4-Methoxyphenoxy)propylthio)benzo[*d*]thiazole

To a solution of alcohol **22**[5] (0.10 g, 0.55 mmol) in tetrahydrofuran (6.0 mL) under a nitrogen atmosphere, was added 2-mercaptobenzothiazole (0.11 g, 0.66 mmol) followed by triphenylphosphine (0.17 g, 0.65 mmol). The yellow solution was cooled to 0 °C and diisopropyl azodicarboxylate (0.20 mL, 1.0 mmol) was added drop-wise. The reaction was stirred at 0 °C for 40 min, allowed to warm to room temperature and stirred for 14 h. The bright yellow reaction was diluted with ethyl acetate (30 mL) and brine (20 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (40 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give a viscous yellow liquid (0.62 g). Flash chromatographic purification (10% ethyl acetate:hexanes graded to 20% ethyl acetate:hexanes) gave the title compound as a beige crystalline solid (0.15 g, 82%); R_f 0.37 (20% ethyl acetate:hexanes); mp 50.0–51.5 °C; ν_{max}(thin film)/cm^{-1} 1506 (s, Ar(C=C)); δ_H(300 MHz; $CDCl_3$) 7.95–7.69 (2H, m, BTAr-H), 7.48–7.25 (2H, m, BTAr-H), 6.87–6.80 (4H, m, Ar-H), 4.07 (2H, t, *J* 5.9 Hz, C_7-H), 3.76 (3H, s, Ar-OCH_3), 3.54 (2H, t, *J* 7.0 Hz, C_5-H), 2.30 (2H, quin, *J* 6.4 Hz, C_6-H); δ_C(75 MHz; $CDCl_3$): 166.6, 153.9, 153.2, 152.8, 135.2, 126.0, 124.2, 121.5, 120.9, 115.4, 114.6, 66.5, 55.7, 30.2, 29.1; HRMS(+EI) calc. for $C_{17}H_{17}NO_2S_2$ 331.0701, found 331.0696; *m/z*(+EI) 331 (M$^+$, 10%), 284 (15), 281 (13), 211 (11), 210 (15), 209 (36), 208 (100), 180 (32), 167 (21), 136 (19), 109 (12).

2-(3-(4-Methoxyphenoxy)propylsulfonyl)benzo[*d*]thiazole 23

To a suspension of 2-(3-(4-methoxyphenoxy)propylthio)benzo[*d*]thiazole (0.28 g, 0.84 mmol) in absolute ethanol (10 mL) at 0 °C was added drop-wise, a solution of ammonium molybdate tetrahydrate (0.13 g, 0.11 mmol) in hydrogen peroxide (30% (w/w), 1.4 g, 12 mmol). The reaction was allowed to warm to room temperature and was stirred for 30 h. Water (20 mL) was added and the crude product was extracted into ethyl acetate (3 x 40 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give a pale brown crystalline solid (0.31 g). Flash chromatographic purification (20% ethyl acetate:hexanes graded to 30% ethyl acetate:hexanes) gave pure sulfone **23** as a bright-yellow crystalline solid (0.30 g, 98%); R_f 0.37 (40% ethyl acetate:hexanes); mp 84.0–85.0 °C; ν_{max}(thin film)/cm^{-1} 1508 (s, Ar(C=C)), 1327 (m, SO_2), 1144 (s, SO_2); δ_H(300 MHz; $CDCl_3$) 8.21–8.18 (1H, m, BTAr-H), 8.01–7.99 (1H, m, BTAr-H), 7.66–7.56 (2H, m, BTAr-H), 6.76 (4H, s, PMPAr-H), 4.03 (2H, t, *J* 5.8 Hz, C_7-H), 3.78–3.72 (2H, m, C_5-H), 3.74 (3H, s, Ar-OCH_3), 2.38–2.33 (2H, m, C_6-H); δ_C(75 MHz; $CDCl_3$) 165.5, 154.0, 152.6, 152.3, 136.7, 128.0, 127.6, 125.4, 122.3, 115.4, 114.6, 65.8, 55.6, 51.9, 22.8; HRMS(+EI) calc. for $C_{17}H_{17}NO_4S_2$ 363.0599, found 363.0596; *m/z*(+EI) 363 (M$^+$, 12%), 299 (10), 283 (17), 282 (17), 281 (57), 269 (19), 267 (22), 265 (21), 242 (15), 241 (15), 240 (100), 229 (16), 227 (30), 226 (10), 225 (40), 213 (11), 211 (50), 210 (19), 209 (78), 207 (17), 191 (11), 182 (42), 176 (13), 151 (15), 149 (12), 134 (16), 109 (16).

5-(3-(4-Methoxyphenoxy)propylthio)-1-phenyl-1*H*-tetrazole

To a solution of alcohol **22**[5] (1.0 g, 5.5 mmol) in tetrahydrofuran (60 mL) under a nitrogen atmosphere, was added 1-phenyl-1*H*-tetrazole-5-thiol (1.3 g, 7.3 mmol) followed by triphenylphosphine (1.9 g, 7.2 mmol). The yellow solution was cooled to 0 °C and diisopropyl azodicarboxylate (2.0 mL, 10 mmol) was added drop-wise. The reaction was stirred at 0 °C for 30 min, allowed to warm to room temperature and stirred for 2 h. The bright yellow reaction was diluted with ethyl acetate (0.30 L) and brine (0.20 L). The layers were separated and the aqueous layer was extracted with ethyl acetate (0.40 L). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give a viscous cloudy yellow liquid (7.8 g). Flash chromatographic purification (15% ethyl acetate:hexanes) gave the title compound as an off-white crystalline solid (1.3 g, 69%); R_f 0.42 (40% ethyl acetate:hexanes); mp 101.0–102.5 °C; ν_{max}(thin film)/cm^{-1} 1597 (w, Ar(C=C)), 1508 (s, Ar(C=C)), 1501 (w, Ar(C=C)); δ_H(200 MHz; $CDCl_3$) 7.56–7.54 (5H, m, PTAr-H), 6.82 (4H, s, PMPAr-H), 4.04 (2H, t, *J* 5.8 Hz, C_7-H), 3.75 (3H, s, Ar-OCH_3), 3.58 (2H, t, *J* 7.0 Hz, C_5-H), 2.38–2.26 (2H, m, C_6-H); δ_C(50 MHz; $CDCl_3$) 154.1, 153.9, 152.7, 133.6, 130.1, 129.7, 123.7, 115.4, 114.6, 66.2, 55.7, 30.0, 28.9; HRMS(+EI) calc. for $C_{17}H_{18}N_4O_2S$ 342.1150, found 342.1144; *m/z*(+EI) 342 (M$^+$, 2%), 219 (66), 191 (10), 164 (12), 163 (100), 155 (15), 124 (12), 123 (16), 119 (38), 109 (19), 95 (13), 77 (19), 65 (16), 51 (11).

5-(3-(4-Methoxyphenoxy)propylsulfonyl)-1-phenyl-1*H*-tetrazole 24

To a suspension of 5-(3-(4-methoxyphenoxy)propylthio)-1-phenyl-1*H*-tetrazole (0.64 g, 1.9 mmol) in absolute ethanol (40 mL) at 0 °C, was added drop-wise, a solution of ammonium molybdate tetrahydrate (0.23 g, 0.19 mmol) in hydrogen peroxide (30% (w/w), 2.1 g, 19 mmol). The reaction was allowed to warm to room temperature and was stirred for 20 h. Water (40 mL) was added and the crude product was extracted into ethyl acetate (3 x 80 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give a viscous, cloudy yellow liquid (0.77 g). Flash chromatographic purification (crude product was absorbed onto silica (dichloromethane), 20% ethyl acetate:hexanes) gave pure sulfone **24** as a white crystalline solid (0.69 g, 99%); R_f 0.39 (40% ethyl acetate:hexanes); mp 82.5–83.0 °C; ν_{max}(thin film)/cm^{-1} 1508 (s, Ar(C=C)), 1499 (m, Ar(C=C)), 1339, 1150 (m, SO_2); δ_H(300 MHz; $CDCl_3$) 7.71–7.60 (5H, m, PTAr-H), 6.83 (4H, s, PMPAr-H), 4.08 (2H, t, *J* 5.7 Hz, C_7-H), 4.00–3.95 (2H, m, C_5-H) 3.77 (3H, s, Ar-OCH_3), 2.48–2.39 (2H, m, C_6-H); δ_C(75 MHz; $CDCl_3$) 154.2, 153.4, 152.3, 133.0, 131.5, 129.7, 125.0, 115.5, 114.7, 65.7, 55.7, 53.3, 22.7; HRMS(+EI) calc. for $C_{17}H_{18}N_4O_4S$ 374.1049, found 374.1043; *m/z*(+EI) 374 (M^+, 15%), 281 (13), 251 (30), 225 (13), 223 (51), 211 (10), 209 (21), 159 (20), 137 (46), 132 (14), 131 (100), 124 (12), 123 (19), 118 (11), 117 (55), 109 (43), 107 (11), 95 (23), 94 (10), 92 (13), 91 (14), 81 (17), 79 (23), 77 (66), 65 (41), 63 (17).

(4*R*,5*S*,*E*)-3-*tert*-Butyl 5-methyl 4-(4-(4-methoxyphenoxy)but-1-enyl)-2,2-dimethyloxazolidine-3,5-dicarboxylate (*E*)-6 and (4*R*,5*S*,*Z*)-3-*tert*-Butyl 5-methyl 4-(4-(4-methoxyphenoxy)but-1-enyl)-2,2-dimethyloxazolidine-3,5-dicarboxylate (*Z*)-6.

Method 1 – Julia olefination – BT-sulfone, LDA: A solution of sulfone **23** (0.12 g, 0.33 mmol) and crude aldehyde **7** (0.091 g, 0.32 mmol) in tetrahydrofuran (10 mL) under an atmosphere of argon, was cooled to -78 °C. A solution of lithium diisopropylamide (0.53 M in tetrahydrofuran, 0.65 mL, 0.34 mmol) was added drop-wise and the reaction was stirred at -78 °C for 15 min. The reaction was allowed to warm to room temperature and was stirred for 17 h. Ammonium chloride solution (sat.aq., 30 mL) was added and the crude product was extracted into ethyl acetate (3 x 40 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give a viscous, clear, yellow liquid (0.088 g). The ratio of (*E*)-alkene (*E*)-**6** to (*Z*)-alkene (*Z*)-**6** was determined to be 1.2:1 by integration of the C_3-H signals in the 200 MHz ^{1}H NMR spectrum. Flash chromatographic purification (5% ethyl acetate:hexanes) gave a mixture of (*E*)-alkene (*E*)-**6** and (*Z*)-alkene (*Z*)-**6** as a viscous, yellow liquid (0.058 g, 42%).

Method 2 – Julia olefination – PT-sulfone, LDA: A solution of sulfone **24** (0.11 g, 0.29 mmol) and crude aldehyde **7** (0.074 g, 0.26 mmol) in tetrahydrofuran (2.0 mL) under an atmosphere of argon, was cooled to -78 °C. A solution of lithium diisopropylamide (0.57 M in tetrahydrofuran, 0.50 mL, 0.29 mmol) at -78 °C was added drop-wise and the reaction was stirred at -78 °C for 15 min. The reaction was allowed to warm to room temperature and was stirred for 17 h. Ammonium chloride solution (sat.aq., 20 mL) was added and the crude product was extracted into ethyl acetate (3 x 30 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give an orange residue (0.17 g). The ratio of (*E*)-alkene (*E*)-**6** to (*Z*)-alkene (*Z*)-**6** was determined to be 1.6:1 by integration of the C_3-H signals in the 200 MHz ^{1}H NMR spectrum. Flash chromatographic purification (30% ethyl acetate:hexanes) gave a mixture of (*E*)-alkene (*E*)-**6** and (*Z*)-alkene (*Z*)-**6** as a viscous, yellow liquid (0.040 g, 35%).

Method 3 – Julia olefination – PT-sulfone, NaHMDS: A solution of sulfone **24** (0.15 g, 0.40 mmol) and crude aldehyde **7** (0.11 g, 0.38 mmol) in 1,2-dimethoxyethane (5.0 mL) under an atmosphere of argon, was cooled to -60 °C. A solution of sodium bis(trimethylsilyl)amide (1.0 M in tetrahydrofuran, 0.58 mL, 0.58 mmol) was added drop-wise and the yellow solution was stirred at -55 °C for 30 min. The reaction was allowed to warm to room temperature and was stirred for 1 h 40 min. Ammonium chloride solution (sat. aq., 40 mL) was added and the crude product was extracted into ethyl acetate (3 x 100 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give an off-white solid (0.20 g). The ratio of (*E*)-alkene (*E*)-**6** to (*Z*)-alkene (*Z*)-**6** was determined to be 1.8:1 by integration of the C_3-H signals in the 200 MHz ^{1}H NMR spectrum. Flash chromatographic purification (15% ethyl acetate:hexanes) gave a mixture of (*E*)-alkene (*E*)-**6** and (*Z*)-alkene (*Z*)-**6** as a viscous, yellow liquid (0.096 g, 58%).

Method 4 – Julia olefination – PT-sulfone, KHMDS: A solution of sulfone **24** (1.7 g, 4.5 mmol) and crude aldehyde **7** (1.2 g, 4.1 mmol) in 1,2-dimethoxyethane (40 mL) under an atmosphere of argon, was cooled to -60 °C. A solution of potassium bis(trimethylsilyl)amide (0.50 M in toluene, 12 mL, 6.0 mmol) was added drop-wise and the dark orange solution was stirred at -55 °C for 45 min. The reaction was allowed to warm to room temperature and was stirred for 30 min. Ammonium chloride solution (sat. aq., 50 mL) was added and the crude product was extracted into ethyl acetate (3 x 80 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give an orange residue (2.6 g). The ratio of (*E*)-alkene (*E*)-**6** to (*Z*)-alkene (*Z*)-**6** was determined to be 2.7:1 by integration of the C_3-H signals in the 200 MHz ^{1}H NMR spectrum. Flash chromatographic purification (5% ethyl acetate:45% dichloromethane:hexanes) afforded pure (*E*)-alkene (*E*)-**6** as a viscous, clear colourless liquid (0.53 g, 29%); R_f 0.21 (5% ethyl acetate:45% CH_2Cl_2:hexanes); $[\alpha]_D^{17}$ +46.7 (*c* 4.0, CH_2Cl_2); ν_{max}(thin film)/cm^{-1} 1759, 1735, 1701 (s, C=O); δ_H(200 MHz; $CDCl_3$) 6.68 (4H, s, Ar-H), 5.67 (1H, dt, *J* 15.3, 6.6 Hz, C_5-H), 5.45 (1H, dd, *J* 15.3, 7.5 Hz, C_4-H), 4.51–4.47 (1H, m, C_3-H), 4.22 (1H, d, *J* 3.6 Hz, C_2-H), 3.82 (2H, t, *J* 6.6 Hz, C_7-H), 3.64 (3H, s, Ar-OCH_3), 3.62 (3H, s, C_1-OCH_3), 2.39 (2H, q, *J* 6.5 Hz, C_6-H), 1.50 (3H, s, $C(CH_3)_2$), 1.45 (3H, s, $C(CH_3)_2$), 1.29 (9H, s, $OC(CH_3)_3$); δ_C(50 MHz; $CDCl_3$) 171.1, 153.8, 152.9, 151.4, 130.5, 129.6, 115.5, 114.6, 96.1, 80.2, 78.6, 67.7, 61.7, 55.6, 52.4, 32.1, 28.3, 27.3, 26.4; HRMS(+ESI) calc. for $C_{23}H_{33}NO_7$+Na 458.2155, found 458.2140; *m/z*(+ESI) 458 ([M+Na]$^+$, 100), 402 (18), 358 (4), 336 (9). A second fraction gave a mixture of (*E*)-alkene (*E*)-**6** and (*Z*)-alkene (*Z*)-**6** in a 1.1:1 ratio (determined by integration of the C_2-H and C_3-H signals in the 200 MHz ^{1}H NMR spectrum) as a viscous, yellow liquid (0.68 g, 38%). For the

purposes of characterization, flash chromatographic purification (15% ethyl acetate : hexanes) of the mixed fraction gave pure (*Z*)-alkene (*Z*)-**6** as a viscous, clear, pale yellow liquid: R_f 0.22 (5% ethyl acetate:45% CH_2Cl_2:hexanes); $[\alpha]_D^{17}$ +105.5 (*c* 0.7, CH_2Cl_2); ν_{max}(thin film) 1759, 1738, 1697 (s, C=O) cm^{-1}; δ_H(300 MHz, 320 K, $CDCl_3$) 6.83 (4H, s, Ar-H), 5.69 (1H, dt, *J* 7.2, 4.9 Hz, C_5-H), 5.53 (1H, dd, *J* 7.1, 6.2 Hz, C_4-H), 4.98 (1H, dd, *J* 6.0, 2.6 Hz, C_3-H), 4.33 (1H, d, *J* 2.8 Hz, C_2-H), 4.00-3.94 (2H, m, C_7-H_2), 3.77 (6H, s, 2 x OCH_3), 2.67–2.63 (2H, m, C_6-H), 1.64 (3H, s, $C(CH_3)_A(CH_3)_B$), 1.61 (3H, s, $C(CH_3)_A(CH_3)_B$), 1.45 (9H, s, $OC(CH_3)_3$); δ_C(75 MHz, 320 K, $CDCl_3$) 170.9, 154.1, 153.2, 151.6, 131.3, 128.5, 115.7, 114.8, 96.3, 80.4, 79.2, 68.0, 57.5, 55.8, 52.4, 28.5, 27.9, 27.4, 26.6.

Method 5 – Alkene isomerisation: To a solution of a mixture of (*E*)-alkene (*E*)-**6** and (*Z*)-alkene (*Z*)-**6** in a 1:8 ratio (0.44 g, 1.0 mmol) in benzene (26 mL) was added thiophenol (0.10 mL, 0.97 mmol) and AIBN (0.034 g, 0.21 mmol). The reaction was heated at 85 °C for 10 days with additional aliquots of AIBN (0.034 g, 0.21 mmol) added every day. The reaction was allowed to cool and was stirred at room temperature for 2 h. The reaction was concentrated under reduced pressure to give an oily residue (0.99 g). The ratio of (*E*)-alkene (*E*)-**6** to (*Z*)-alkene (*Z*)-**6** was determined to be 6.5:1 from integration of the C_4-H signals in the 200 MHz ^{1}H NMR spectrum. Flash chromatographic purification (5% ethyl acetate:45% dichloromethane:hexanes) gave a mixture of (*E*)-alkene (*E*)-**6** and (*Z*)-alkene (*Z*)-**6** as a viscous, clear, colourless liquid (0.43 g, 98%).

(4*R*,5*S*)-3-*tert*-Butyl 5-methyl 4-((1*S*,2*S*)-1,2-dihydroxy-4-(4-methoxyphenoxy)butyl)-2,2-dimethyloxazolidine-3,5-dicarboxylate (4*S*,5*S*)-5 and (4*R*,5*S*)-3-*tert*-Butyl 5-methyl 4-((1*R*,2*R*)-1,2-dihydroxy-4-(4-methoxyphenoxy)butyl)-2,2-dimethyloxazolidine-3,5-dicarboxylate (4*R*,5*R*)-5

Method 1 – No ligand: To a solution of alkene (*E*)-**6** (0.010 g, 0.023 mmol) in tetrahydrofuran (0.070 mL) and water (0.010 mL), was added a solution of osmium tetroxide (2.5% wt in *tert*-butanol, 0.030 mL, 0.0024 mmol). To the grey reaction mixture was added a solution of 4-methylmorpholine *N*-oxide (0.0090 g, 0.077 mmol) in water (0.015 mL). The reaction was stirred at room temperature (~ 28 °C) for 2 h. Sodium sulfite solution (sat. aq., 10 mL) was added, the reaction was stirred for 1 h and the crude product was extracted into ethyl acetate (3 x 50 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give a yellow residue (0.052 g). The ratio of diol (4*S*,5*S*)-**5** to its diastereomer (4*R*,5*R*)-**5** was determined to be 2:1 from integration of the C_2-H and C_3-H signals in the 300 MHz ^{1}H NMR spectrum. Flash chromatographic purification (40% ethyl acetate:hexanes) gave an inseparable mixture of diol (4*S*,5*S*)-**5** and diol (4*R*,5*R*)-**5** as a viscous, pale yellow liquid (0.0051 g, 48%).

General Asymmetric Dihydroxylation: Potassium hexacyanoferrate(III) (3.0 mmol), potassium carbonate (3.2 mmol) and sodium hydrogen carbonate (3.2 mmol) were combined and added to a mixture of *tert*-butanol (5.5 mL) and water (6.1 mL). The mixture was stirred until homogeneous. Ligand (0.060 mmol) was added followed by potassium osmate(VI) dihydrate (0.010 mmol) and methanesulfonamide (3.2 mmol). The mixture was stirred until homogeneous and was cooled to 0 °C. The biphasic reaction mixture was added to a solution of alkene (1.0 mmol) in *tert*-butanol (0.60 mL) at room temperature. The reaction mixture was stirred at room temperature (17 °C) for 17 h. Sodium sulfite solution (sat. aq., 20 mL) was added and the reaction was stirred for 2 h. The crude product was extracted into ethyl acetate (3 x 30 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give the crude product. Purification was performed as specified.

Method 2 – DHQ-IND ligand: The general AD procedure was followed using DHQ-IND ligand and alkene (*E*)-**6** (0.23 g, 0.53 mmol). The reaction was stirred at room temperature (approx. 17 °C) for 10 h and was heated at 27 °C for 4 h. The crude product was an orange residue (0.51 g). Flash chromatographic purification (40% ethyl acetate:hexanes) gave an inseparable mixture of diol (4*S*,5*S*)-**5** and diol (4*R*,5*R*)-**5** in a 7.4:1 ratio (determined by integration of the C_2-H and C_3-H signals in the 300 MHz ^{1}H NMR spectrum) as a viscous, clear, pale yellow liquid (0.21 g, 85%). Data for the major isomer only is quoted where appropriate; R_f 0.17 (40% ethyl acetate:hexanes); $[\alpha]_D^{21}$ +9.6 (*c* 3.4, CH_2Cl_2); ν_{max}(thin film)/cm^{-1} 3427 (s, O-H), 1759, 1740, 1666 (s, C=O); δ_H(300 MHz; $CDCl_3$) 6.80 (4H, s, Ar-H), 4.79 (1H, s, C_2-H), 4.35 (1H, d, *J* 9.1 Hz, C_3-H), 4.24 (1H, s, C_5-OH), 4.13–4.01 (2H, m, C_7-H), 3.90–3.86 (1H, m, C_5-H), 3.78 (3H, s, C_1-OCH_3), 3.75 (3H, s, Ar-OCH_3), 3.36 (1H, br d, *J* 9.5 Hz, C_4-H), 2.63 (1H, s, C_4-OH), 2.16–2.07 (1H, m, C_6-H_A), 1.99–1.90 (1H, m, C_6-H_B), 1.61 (3H, s, $C(CH_3)_2$), 1.48 (3H, s, $C(CH_3)_2$), 1.47 (9H, s, $OC(CH_3)_3$); δ_C(75 MHz; $CDCl_3$) 171.8, 153.8, 153.7, 153.0, 115.5, 114.6, 96.2, 82.1, 76.6, 74.4, 65.6, 65.3, 61.6, 55.7, 52.5, 32.4, 28.6, 28.3, 27.2; HRMS(+ESI) calc. for $C_{23}H_{35}NO_9$+Na 492.2210, found 492.2203; *m/z*(+ESI) 961 ($[2M+Na]^+$, 30%), 492 ($[M+Na]^+$, 100), 463 (9), 370 (15), 103 (9).

Method 3 – DHQD-IND ligand: The general AD procedure was followed using DHQD-IND ligand and alkene (*E*)-**6** (0.020 g, 0.046 mmol). The crude product was a brown residue (0.015 g). Flash chromatographic purification (40% ethyl acetate:hexanes) gave an inseparable mixture of diol (4*S*,5*S*)-**5** and diol (4*R*,5*R*)-**5** in a 1:5.1 ratio (determined by integration of the C_2-H and C_3-H signals in the 300 MHz ^{1}H NMR spectrum) as a viscous, clear, pale yellow liquid (0.0042 g, 19%). Data for the major isomer only is quoted; δ_H(200 MHz; $CDCl_3$) 6.83 (4H, s, Ar-H), 4.67 (1H, dd, *J* 7.9, 2.2 Hz, C_3-H), 4.56 (1H, d, *J* 2.2 Hz, C_2-H), 4.17–4.07 (2H, m, C_7-H), 4.02–3.92 (1H, m, C_5-H), 3.79 (3H, s, OMe), 3.77 (3H, s, OMe), 3.68 (1H, t, *J* 7.0 Hz, C_4-H), 2.16–1.94 (2H, m, C_6-H), 1.64 (3H, s, $C(CH_3)_2$), 1.61 (3H, s, $C(CH_3)_2$), 1.49 (9H, s, $OC(CH_3)_3$), two O*H* not observed.

Method 4 – DHQ-CLB ligand: The general AD procedure was followed using DHQ-CLB ligand and alkene (*E*)-**6** (0.020 g, 0.046 mmol). The crude product was an off-white solid (0.037 g). Flash chromatographic purification (40% ethyl acetate:hexanes) gave an inseparable mixture of diol (4*S*,5*S*)-**5** and diol (4*R*,5*R*)-**5** in a 3.3:1 ratio (determined by integration of the C_2-H and C_3-H signals in the 300 MHz ^{1}H NMR spectrum) as a viscous, clear, pale yellow liquid (0.0023 g, 11%).

Method 5 – DHQD-CLB ligand: The general AD procedure was followed using DHQD-CLB ligand and alkene (*E*)-**6** (0.020 g, 0.046 mmol). The crude product was an off-white solid (0.036 g). Flash chromatographic purification (40% ethyl acetate:hexanes) gave an inseparable mixture of diol (4*S*,5*S*)-**5** and diol (4*R*,5*R*)-**5** in a 1:2.5 ratio (determined by integration of the C_2-H and C_3-H signals in the 300 MHz ^{1}H NMR spectrum) as a viscous, clear, pale yellow liquid (0.0010 g, 5%).

(4*R*,5*S*)-3-*tert*-Butyl 5-methyl 4-((4*S*,5*S*)-5-(2-(4-methoxyphenoxy)ethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyloxazolidine-3,5-dicarboxylate (4*S*,5*S*)-25 and (4*R*,5*S*)-3-*tert*-Butyl 5-methyl 4-((4*R*,5*R*)-5-(2-(4-methoxyphenoxy)ethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyloxazolidine-3,5-dicarboxylate (4*R*,5*R*)-25

To a solution of diol (4*S*,5*S*)-**5** and diol (4*R*,5*R*)-**5** ((4*S*,5*S*)-**5**:(4*R*,5*R*)-**5** = 7:1, 0.053 g, 0.11 mmol) in dichloromethane (1.0 mL) was added 2,2-dimethoxypropane (0.028 mL, 0.23 mmol) followed by (1*S*)-(+)-10-camphorsulfonic acid (0.0053 g, 0.023 mmol). The reaction was stirred at room temperature for 10 min. An additional aliquot of 2,2-dimethoxypropane (0.050 mL, 0.41 mmol) was added and the reaction was stirred for 25 min. A solution of sodium hydrogen carbonate (sat. aq., 10 mL) was added and the crude product was extracted into dichloromethane (3 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give a pale yellow residue (0.063 g). Flash chromatographic purification (20% ethyl acetate:hexanes) gave an inseparable mixture of acetal (4*S*,5*S*)-**25** and acetal (4*R*,5*R*)-**25** in a 7:1 ratio (determined by integration of the C_2-H signals in the 200 MHz ^{1}H NMR spectrum.) as a viscous, clear, colourless liquid (0.057 g, 99%). Data for the major isomer only is quoted where appropriate: R_f 0.50 (40% ethyl acetate:hexanes); $[\alpha]_D^{23}$ +0.8 (*c* 6.4, CH_2Cl_2); ν_{max}(thin film)/cm^{-1} 1759, 1738, 1704 (s, C=O), 1510 (Ar(C=C)); δ_H(200 MHz; 340 K; $CDCl_3$) 6.88–6.77 (4H, m, Ar-H), 4.72 (1H, d, *J* 2.2 Hz, C_2-H), 4.47 (1H, dd, *J* 4.9, 2.2 Hz, C_3-H), 4.19–3.98 (4H, m, C_5-H, C_7-H, C_4-H), 3.75 (3H, s, Ar-OCH_3), 3.74 (3H, s, C_1-OCH_3), 2.19–1.89 (2H, m, C_6-H), 1.63 (3H, s, $NC(CH_3)_2O$), 1.59 (3H, s, $NC(CH_3)_2O$), 1.49 (9H, s, $OC(CH_3)_3$), 1.41 (3H, s, $OC(CH_3)_2O$), 1.4 (3H, s, $OC(CH_3)_2O$); δ_C(50 MHz; 340 K; $CDCl_3$) 172.0, 154.2, 153.4, 151.8, 115.9, 114.9, 109.0, 96.8, 80.9, 80.7, 75.8, 75.1, 65.8, 61.2, 55.8, 52.2, 33.6, 28.4, 27.7, 27.4, 27.2, 27.1; HRMS(+ESI) calc. for $C_{26}H_{39}NO_9$+Na 532.2523, found 532.2494; *m/z*(+ESI) 532 ([M+Na]$^+$, 100%), 410 (18).

(4*R*,5*S*)-3-*tert*-Butyl 5-methyl 4-((4*S*,5*S*)-5-(2-hydroxyethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyloxazolidine-3,5-dicarboxylate (4*S*,5*S*)-26 and (4*R*,5*S*)-3-*tert*-Butyl 5-methyl 4-((4*R*,5*R*)-5-(2-hydroxyethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyloxazolidine-3,5-dicarboxylate (4*R*,5*R*)-26

To a solution of acetal (4*S*,5*S*)-**25** and acetal (4*R*,5*R*)-**25** ((4*S*,5*S*)-**25**:(4*R*,5*R*)-**25** = 7:1, 0.065 g, 0.13 mmol) in acetonitrile (1.3 mL) at 0 °C, was added drop-wise a solution of ammonium cerium(IV) nitrate (0.16 g, 0.29 mmol) in water (1.3 mL). The solution was stirred at 0 °C for 18 min. The reaction was diluted with chloroform (20 mL) and water (10 mL) and the layers were separated. The aqueous layer was extracted with chloroform (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give a viscous yellow liquid (0.078 g). Flash chromatographic purification (40% ethyl acetate:hexanes) gave an inseparable mixture of alcohol (4*S*,5*S*)-**26** and alcohol (4*R*,5*R*)-**26** in a 7:1 ratio (determined by integration of the C_2-H and C_3-H signals in the 200 MHz ^{1}H NMR spectrum) as a clear, viscous, pale yellow liquid (0.049 g, 95%). Data for the major isomer only is quoted where appropriate; R_f 0.23 (40% ethyl acetate:hexanes); $[\alpha]_D^{23}$ -5.9 (*c* 0.7, CH_2Cl_2); ν_{max}(thin film)/cm^{-1} 3458 (br, s, O-H), 1760, 1734, 1690 (br, s, C=O); δ_H(200 MHz; 320 K; $CDCl_3$) 4.70 (1H, d, *J* 2.1 Hz, C_2-H), 4.44–4.42 (1H, m, C_3-H), 4.21–4.08 (1H, m, C_5-H), 3.96 (1H, dd, *J* 8.3, 5.2 Hz, C_4-H), 3.82–3.78 (2H, m, C_7-H), 3.77 (3H, s, C_1-OCH_3), 2.10 (1H, s, C_7-OH), 1.93–1.78 (2H, m, C_6-H), 1.60 (3H, s, $NC(CH_3)_2O$), 1.56 (3H, s, $NC(CH_3)_2O$), 1.47 (9H, s, $OC(CH_3)_3$), 1.40 (6H, s, $OC(CH_3)_2O$); δ_C(50 MHz; 320 K; $CDCl_3$) 172.1, 151.9, 109.1, 96.7, 81.1, 80.4, 77.6, 75.0, 60.9, 60.6, 52.4, 35.5, 28.4, 27.7, 27.3, 27.1, 27.0; HRMS(+ESI) calc. for $C_{19}H_{33}NO_8$+Na 426.2104, found 426.2095; *m/z*(+ESI) 426 ([M+Na]$^+$, 100%), 387 (55).

(4*R*,5*S*)-3-*tert*-Butyl 5-methyl 4-((4*S*,5*S*)-2,2-dimethyl-5-(2-oxoethyl)-1,3-dioxolan-4-yl)-2,2-dimethyloxazolidine-3,5-dicarboxylate (4*S*,5*S*)-4 and (4*R*,5*S*)-3-*tert*-Butyl 5-methyl 4-((4*R*,5*R*)-2,2-dimethyl-5-(2-oxoethyl)-1,3-dioxolan-4-yl)-2,2-dimethyloxazolidine-3,5-dicarboxylate (4*R*,5*R*)-4

Dess-Martin periodinane (0.15 g, 0.35 mmol) was added to a solution of a mixture of alcohol (4*S*,5*S*)-**26** and alcohol (4*R*,5*R*)-**26** ((4*S*,5*S*)-**26:**(4*R*,5*R*)-**26** = 7:1, 0.11 g, 0.27 mmol) in dichloromethane (3.0 mL). The white suspension was stirred at room temperature for 45 min. A mixture of sodium hydrogen carbonate solution (sat. aq., 4.0 mL) and sodium thiosulfate solution (sat. aq., 1.0 mL) was added and the reaction was stirred vigorously for 1 h. The crude product was extracted into dichloromethane (3 x 20 mL) and the combined organic layers were washed with a mixture of sodium hydrogen carbonate solution (sat. aq., 8.0 mL) and sodium thiosulfate solution (sat. aq., 2.0 mL), dried (Na_2SO_4), filtered and concentrated under reduced pressure to give a yellow residue (0.11 g, quant.) which was used without further purification in subsequent reactions. For the purpose of characterization, flash chromatographic purification (20% ethyl acetate:hexanes) of a sample of crude product gave an inseparable mixture of aldehyde (4*S*,5*S*)-**4** and aldehyde (4*R*,5*R*)-**4** in a 7:1 ratio (determined by integration of the C_2-H and C_3-H signals in the 200 MHz ^{1}H NMR spectrum). Data is reported for the major isomer only where appropriate; R_f 0.32 to 0.50 (40% ethyl acetate:hexanes); $[\alpha]_D^{26}$ -5.9 (*c* 1.2, CH_2Cl_2); ν_{max}(thin film)/cm^{-1} 1763, 1732, 1693 (s, C=O); δ_H(200 MHz; 320 K; $CDCl_3$) 9.80 (1H, t, *J* 2.1 Hz, CHO), 4.73 (1H, d, *J* 2.0 Hz, C_2-H), 4.51–4.47 (2H, m, C_3-H , C_5-H), 3.94 (1H, dd, *J* 8.1, 6.0 Hz, C_4-H), 3.79 (3H, s, C_1-OCH_3), 2.67–2.61 (2H, m, C_6-H), 1.61 (3H, s, $NC(CH_3)_2O$), 1.56 (3H, s, $NC(CH_3)_2O$), 1.48 (9H, s,

$OC(CH_3)_3$), 1.42 (3H, s, $OC(CH_3)_2O$), 1.40 (3H, s, $OC(CH_3)_2O$); δ_C(50 MHz; 320 K; $CDCl_3$) 199.4, 171.9, 151.9, 109.5, 96.7, 81.3, 80.3, 75.2, 73.7, 61.0, 52.5, 46.7, 28.4, 27.9 (2C broad), 27.2, 26.9.

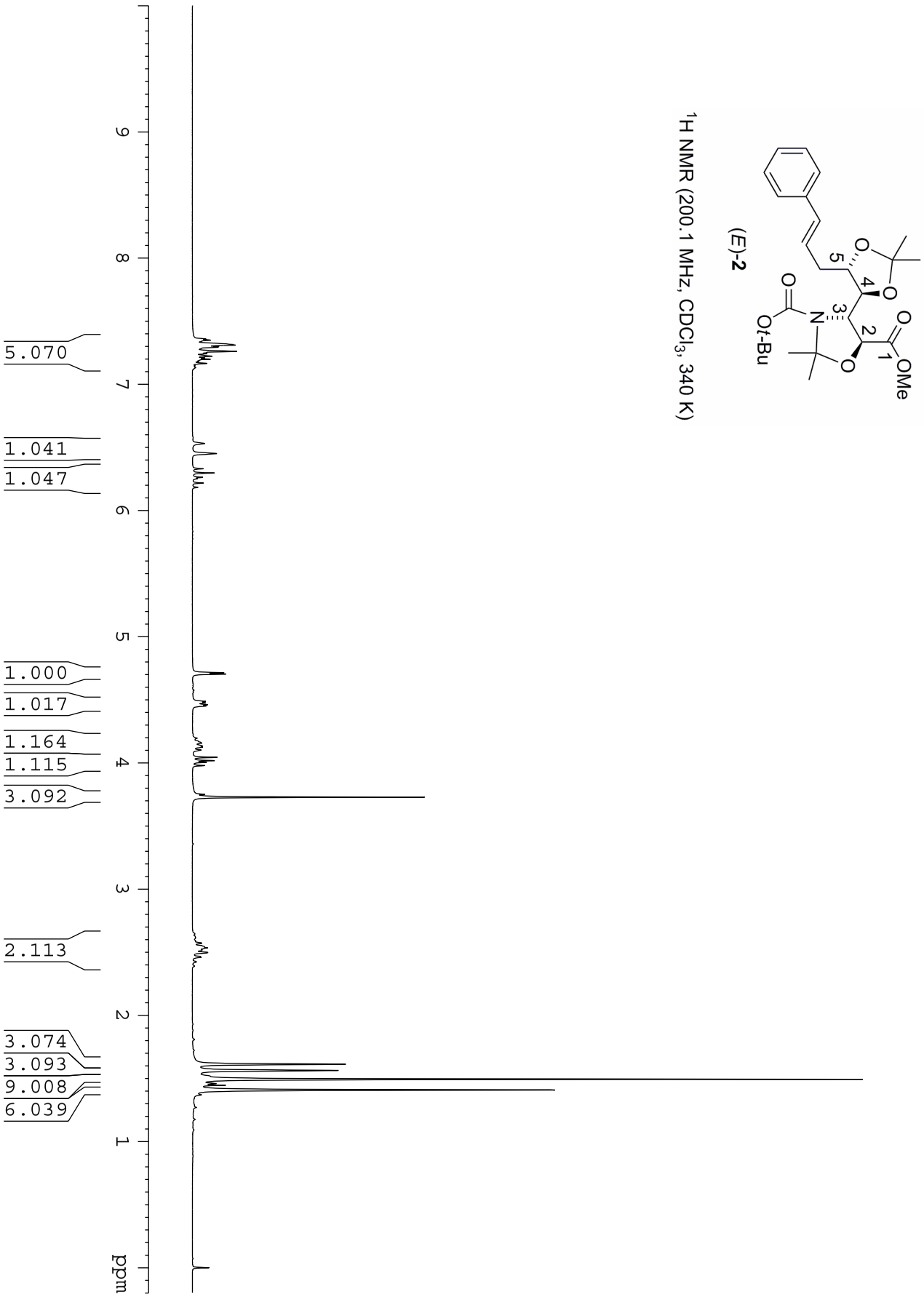
(*E*)-3-(4-Ethoxyphenyl)prop-2-enyl)triphenylphosphonium bromide 27

To a stirring white suspension of alcohol **28**[6] (0.83 g, 4.7 mmol) in diethyl ether (4.2 mL) at 0 °C, was added drop-wise via cannula a solution of phosphorus tribromide (0.22 mL, 2.3 mmol) in diethyl ether (4.2 mL). The suspension was allowed to slowly warm to 20 °C over 1 h 20 min. Water (10 mL) was added to the pale brown solution and the crude product was extracted into dichloromethane (3 x 30 mL). The combined organic layers were washed with sodium hydrogen carbonate solution (sat. aq., 15 mL), dried (Na_2SO_4), filtered and concentrated under reduced pressure to afford pure bromide **29** as a pale yellow crystalline solid (1.0 g, 89%), which was used without further purification in the subsequent reaction.

To a solution of bromide **29** (0.85 g, 3.5 mmol) in benzene (6.0 mL) was added triphenylphosphine (0.90 g, 3.4 mmol). The pale yellow solution was stirred at room temperature for 15h. The white precipitate was collected by filtration, washed with diethyl ether (3 x 5.0 mL) and dried under reduced pressure to afford pure phosphonium salt **27** as a white powder (1.5 g, 87%); R_f baseline (40% ethyl acetate:hexanes); mp 98–99 °C; ν_{max}(thin film)/cm^{-1} 1605, 1510 (s, Ar(C=C)), 1250 (s), 1043 (m), 723 (s, P-C); δ_H(200 MHz; $CDCl_3$) 7.92–7.63 (15H, m, PPh_3), 7.13 (2H, m, Ar-H), 6.76 (2H, m, ArH), 6.76–6.66 (1H, m, C_{10}-H), 5.90–5.72 (1H, m, C_9-H), 4.93 (2H, dd, $^2J_{PH}$ 15.0 Hz, *J* 7.4 Hz, C_8-H), 3.99 (2H, q, *J* 7.0 Hz, OCH_2CH_3), 1.38 (3H, t, *J* 7.0 Hz, OCH_2CH_3); δ_C(50 MHz; $CDCl_3$) 159.3, 139.8 (d, $^3J_{PC}$ 13.5 Hz, C_{10}), 135.0 (d, $^4J_{PC}$ 2.3 Hz, PPh-C), 134.1 (d, $^2J_{PC}$ 9.7 Hz, PPh-C), 130.4 (d, $^3J_{PC}$ 12.5 Hz, PPh-C), 128.5 (d, $^4J_{PC}$ 3.6 Hz, Ar-C), 127.9, 118.2 (d, $^1J_{PC}$ 85.4 Hz, PPh-C), 114.6, 110.8 (d, $^2J_{PC}$ 11.0 Hz, C_9), 63.5, 28.4 (d, $^1J_{PC}$ 48.7 Hz, C_8), 14.8; HRMS(+ESI) calc. for $C_{29}H_{28}OP$ 423.1878, found 423.1873; *m/z*(+ESI) 423 ($[M-Br]^+$, 34%), 161 (78), 133 (100) 105 (19); *m/z*(-ESI) 81 (Br(81), 83%), 79 (Br(79), 100).

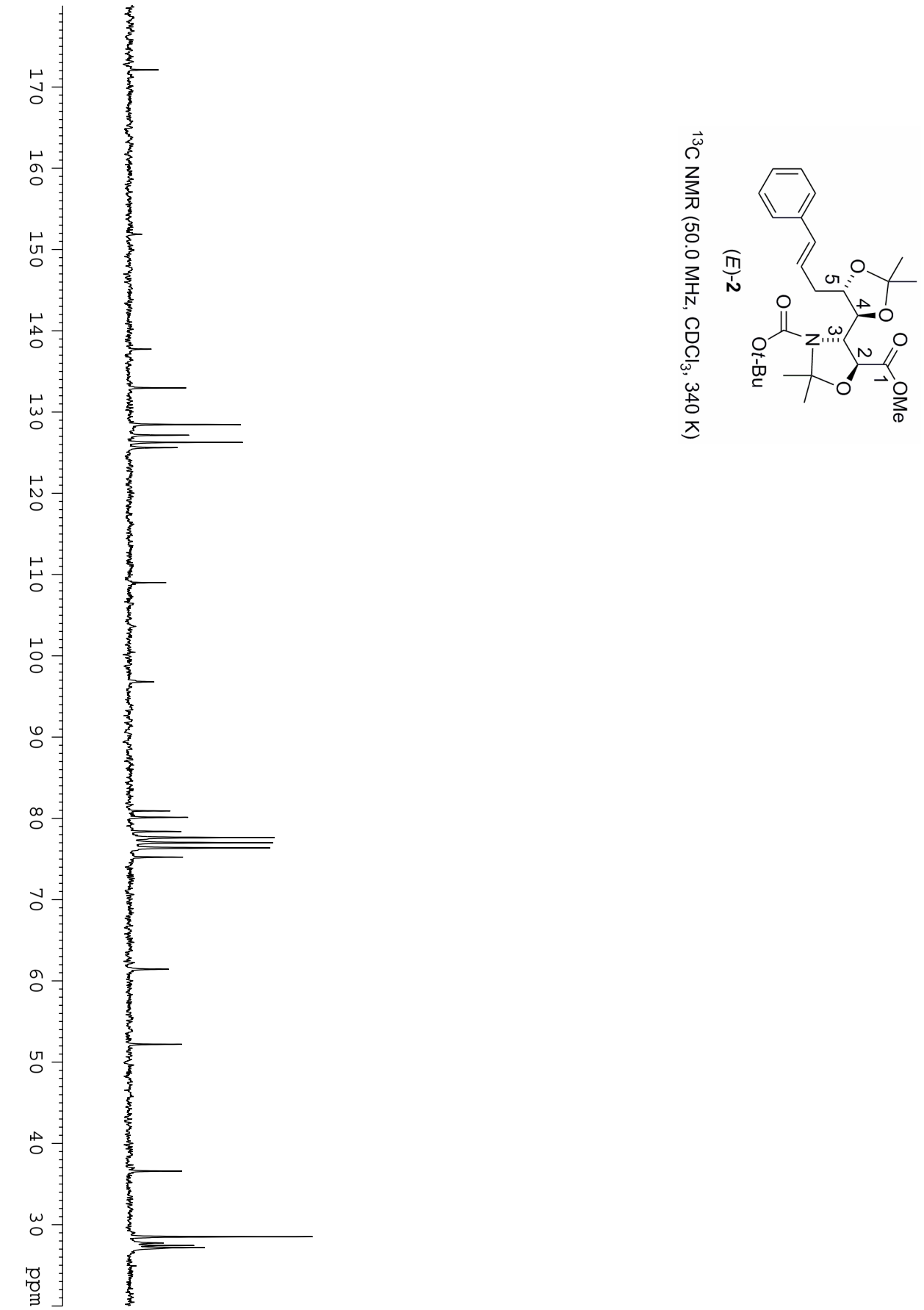
Notes and references

1. D. D. Perrin and W. L. F. Armarego, *Purification of Laboratory Chemicals*. 3rd ed.; Permagon Press Ltd: New York, **1988**.
2. J. Leonard, B. Lygo and G Proctor, *Advanced Practical Organic Chemistry*. 2nd ed.; Blackie Academic & Professional: London, **1995**.
3. E. J. Corey, A. Guzman-Perez and M. C. Noe, *J. Am. Chem. Soc.* 1995, **117**, 10805.
4. C.-Y. Chuang, V. C. Vassar, Z. Ma, R. Geney and I. Ojima, *Chirality* 2002, **14**, 151.
5. A. J. Schvartzapel, L. Zhong, R. Docampo, J. B. Rodriguez and E. G. Gros, *J. Med. Chem.* 1997, **40**, 2314.
6. G. Cignarella, E. Occelli and Testa, E., *J. Med. Chem.* 1965, **8**, 326.



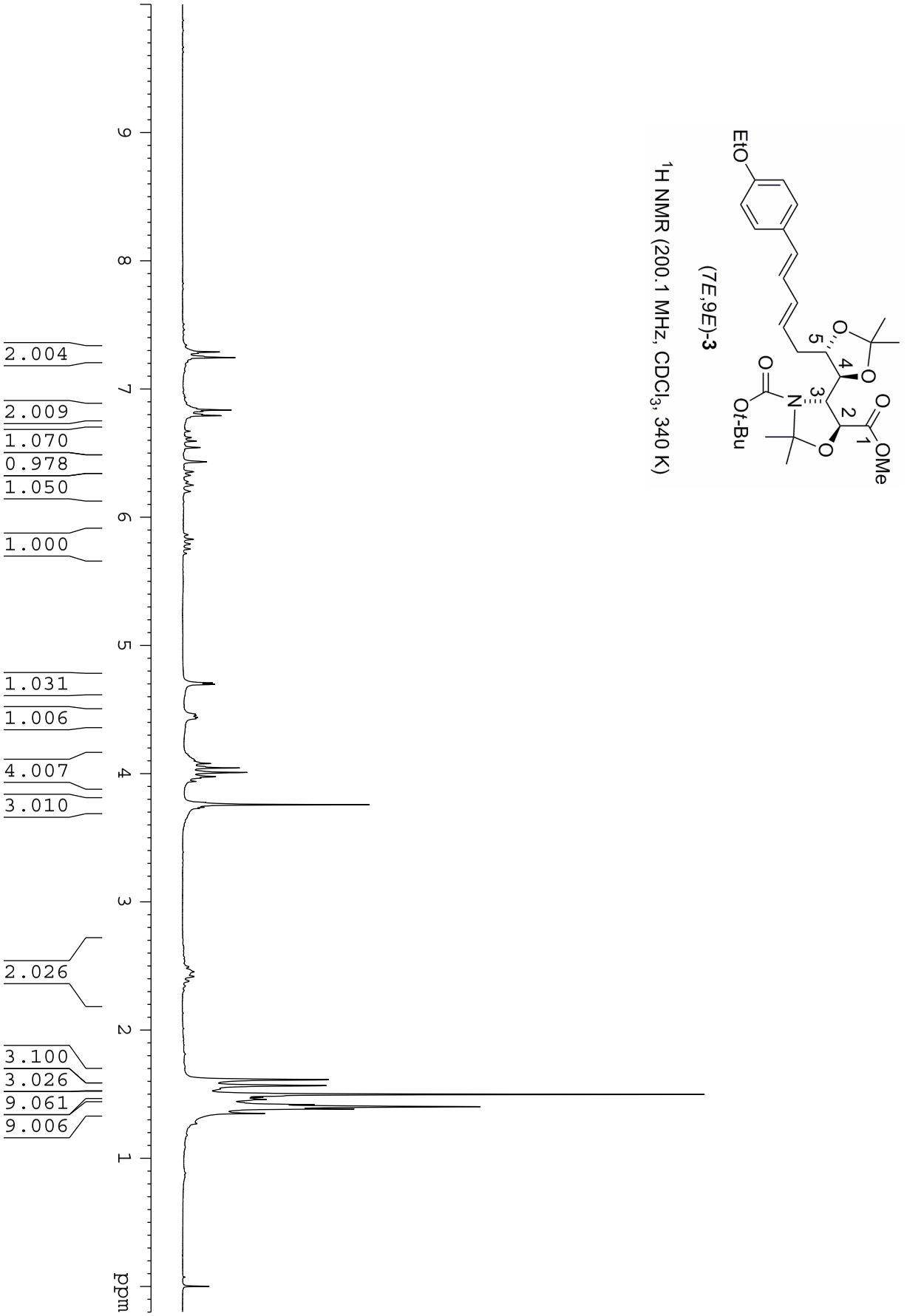
^{1}H NMR (200.1 MHz, $CDCl_3$, 340 K)

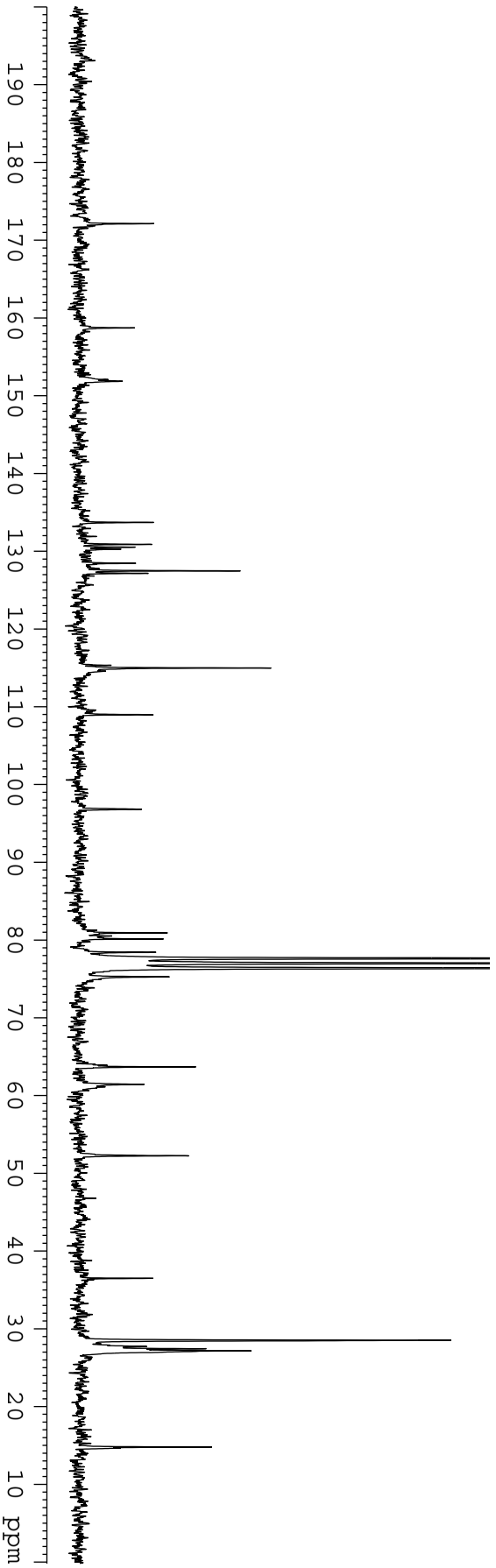
(*E*)-**2**

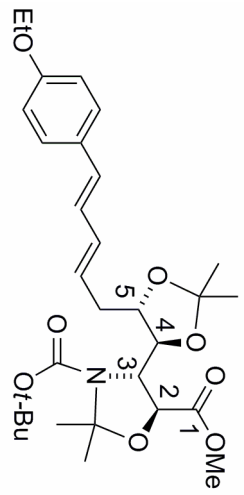


^{13}C NMR (50.0 MHz, $CDCl_3$, 340 K)

(*E*)-**2**







(*7E*,*9E*)-**3**

^{13}C NMR (50.0 MHz, $CDCl_3$, 340 K)