Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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Supplementary Information

Accessible sugars as asymmetric olefin epoxidation organocatalysts: glucosaminide ketones in the synthesis of terminal epoxides

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Supplementary Information

1. General procedures

Melting points were recorded on a Kofler hot block and are uncorrected. Proton nuclear magnetic resonance (δ_H) spectra were recorded on a Bruker DPX 200 (200 MHz), a Bruker DPX 400 (400 MHz) or a Bruker DQX 400 (400 MHz) spectrometer. 400 MHz spectra were assigned using COSY. Carbon nuclear magnetic resonance (δ_C) spectra were recorded on a Bruker DQX 400 (100 MHz) spectrometer. Spectra were assigned using HMQC and DEPT 135. All chemical shifts were quoted in the δ-scale in ppm using residual solvent as the internal standard.

Infrared spectra were recorded on a Bruker Tensor 27 Fourier Transform spectrophotometer, absorption maxima were recorded in wavenumbers (cm^{-1}).

Low resolution mass spectra were recorded on a Micromass Platform 1 spectrometer using electron spray ionisation (ES) or by Dr. J. Kirkpatrick using a Micromass LCT (Resoloution = 5000 FWHM) using a lock spray source. The calibration is corrected using a lock-mass; in positive ion this is tetraoctylammonium bromide. *M/z* values are reported in Daltons and are followed by their percentage abundance.

Analytical High Performance Liquid Chromatography (HPLC) was performed on a Waters 2795 separations module coupled to a Waters 2996 photodiode array detector. An inline degasser was used to degas all solvents used in this machine. This system was controlled by Empower 2002 software. Enantiomeric excess was measured using the following column: Chiralcel OD, Diacel Chemical Industries, Ltd, 250 mm x 2.3 mm internal diameter. A flow rate of 1 mL/min was used with an isocratic gradient as described in the relevant experimental section.

Gas Chromatography (GC) was performed on a Thermoquest Trace GC 2000. Enantiomeric excess was measured using a β-Cyclodextrin column (Cydex B), 0.25 mm x 30 m, thickness 0.25 μm, using He as a carrier gas (flow = 1.0 mL/min, injector T = 220 °C; detector: FID, T = 250 °C).

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Optical rotations were measured on a Perkin–Elmer 241 polarimeter with a path length of 1 dm and are reported with implied units of 10^{-1} deg cm^2 g^{-1}. Concentrations (c) are given in g/100 ml.

Thin layer chromatography (TLC) and semi-prep TLC were carried out on Merck Kieselgel $60F_{254}$ precoated aluminium backed plates. Visualization of TLC plates was accomplished with 254 nm UV light and/or ammonium molybdate (5 % in 2M H_2SO_4), ninhydrin (0.2 % in ethanol) or potassium permanganate (0.5 % in 1M NaOH).

Flash column chromatography was conducted using silica gel (Fluka Kiegselgel 60 220–440 mesh). DCM and THF were dried by passing through a column of Al_2O_3. Remaining anhydrous solvents were purchased from Fluka. All other solvents were used as supplied (analytical or HPLC grade), without further purification. Petrol refers to the fraction of petroleum ether boiling in the range 40–60 ^oC. Distilled water was used for chemical reactions. Reagents were purchased from Aldrich and used as supplied. All reactions using anhydrous conditions were performed using flame-dried apparatus under an atmosphere of argon.

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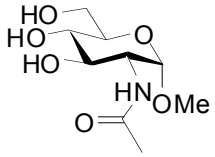
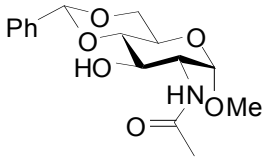
2. Synthesis of catalysts 7a–e and 8

Methyl *N*-acetyl-*α*/*β*-D-glucosaminide



N-Acetyl-D-glucosamine, **5** (100 g, 0.452 mol) was dissolved in methanol and acetyl chloride (145.2 mL, 2.034 mol) was slowly added. The mixture was then stirred for 24 hours after which the reaction progress was followed by NMR to completion. The solvent was then removed from the reaction mixture under reduced pressure affording the desired product in quantitative yield. The product was carried on without further purification.

Methyl 2-*N*-acetylamido-4,6-*O*-benzylidene-2-deoxy-*α*/*β*-D-glucopyranoside



Methyl *N*-acetyl-*α*/*β*-D-glucosaminide (106 g, 0.452 mol) was dissolved in DMF (1200 mL). Benzaldehyde dimethylacetal (136 mL, 0.904 mol) and *para*-toluene sulphonic acid (1.72 g, 9.04 mmol) were added and the reaction mixture was heated to 70 °C. The reaction progress was monitored by TLC (4:4:2, isopropanol:water:ethyl acetate). After 2.5 hours TLC showed formation of product (R_f 0.7) along with complete consumption of the starting material (R_f 0.2). The reaction mixture was concentrated to half volume under reduced pressure and then diluted with chloroform (2000 mL) and washed with water (1500 mL). The aqueous layer was extracted with chloroform (1000 mL) and the organic fractions combined. A precipitate formed in the organic fractions which was collected and dried. The remaining product was obtained by removing the solvent under reduced pressure. This afforded in total 116 g (80% yield) of the desired product as a mixture of anomers.

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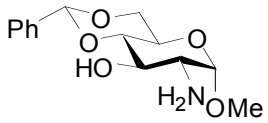
The alpha anomer was synthesised separately in the following procedure:

Methyl 2-amino-4,6-*O*-benzylidine-2-deoxy-α-D-glucopyranoside (4.0 g, 0.014 mol), sodium methoxide (0.03 g, 0.6 mmol), and acetic anhydride (2.9 g, 0.028 mol) were added to methanol (120 mL) and the solution was stirred for 24 hours. After 24 hours a TLC (4:1, ethyl acetate:methanol) indicated product formation (R_f 0.5) and the presence of no starting material (R_f 0.1). The resulting crystals were removed from the solvent under reduced pressure and the crude product was recrystallized from methanol. This afforded 3.62 g (81% yield) of the desired product.

$[\alpha]_D^{21}$ = +67.2. (c = 1.15, DMSO) {Lit.: $[\alpha]_D^{21}$ = +63.8 (c = 0.91, DMSO)[1]}. IR (KBr): ν/cm^{-1} = 3456 (NH), 3301 (OH), 3072 (Aromatic), 2992, 2949, 2920, 2876 (CH), 1647 (Amide I), 1550 (Amide II). ^{1}H NMR (400 MHz, DMSO): 7.95 (d, $J_{2,NH}$ 8.3 Hz, 1H, NH), 7.47-7.44 (m, 2H, 2 x Ar-H), 7.41-7.36 (m, 3H, 3 x Ar-H), 5.61 (s, 1H, PhCH), 5.22 (s, 1H, OH), 4.61 (d, $J_{1,2}$ 3.5 Hz, 1H, H-1), 4.17 (dd, $J_{6,6'}$ 9.9 Hz, $J_{5,6}$ 4.7 Hz, 1H, H-6'), 3.82 (m, $J_{2,3}$ 10.3 Hz, $J_{2,NH}$ 8.3 Hz, $J_{1,2}$ 3.5 Hz, 1H, H2), 3.74 (at, J 10.1 Hz, 1H, H-6), 3.64 (at, J 9.1 Hz, 1H, H-3), 3.60 (atd, J 10.0 Hz, 4.7 Hz, 1H, H-5), 3.48 (at, J = 9.2, 1H, H-4), 3.29 (s, 3H, OMe), 1.84 (s, 3H, COMe). ^{13}C NMR (100 MHz, DMSO): 170.3 (COMe), 138.6 (Quaternary Ph-C), 129.7, 128.9 & 127.3 (Aromatic C), 101.8 (Benzylic C), 99.6 (C1), 82.9 (C4), 68.9 (C6), 68.2 (C5), 63.3 (C3), 54.6 (C2), 55.0 (OCH_3), 23.4 (COCH_3). Mass *m/z* (ES$^+$) 382 (100%) [M+NH_4+MeCN]$^+$. M.p.= 279 °C (methanol). {Lit.: m.p. = 278–279 °C[2]}

Methyl 2-amino-4,6-*O*-benzylidene-2-deoxy-*α*-D-glucopyranoside (6)



Methyl 2-*N*-acetylamido-4,6-*O*-benzylidene-2-deoxy-*α*/*β*-D-glucopyranoside (10:1, *α*/*β*) (72 g, 0.22 mol) was added to a 4M solution of potassium hydroxide in ethanol (1.5 L). The solution was then refluxed for 4 hours. A TLC (1:2:7, water:isopropanol:ethyl acetate) indicated product formation (R_f 0.2) along with consumption of starting material (R_f 0.6). The reaction mixture was then cooled to room temperature and added to DCM (1 L). The solution was washed with water and the aqueous layer extracted with DCM.

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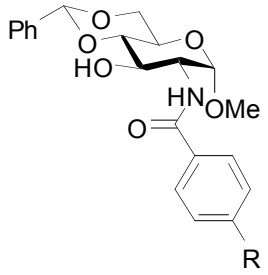
The combined organic fractions were washed with brine before being dried over magnesium sulfate, filtered, and concentrated. The crude product was purified using column chromatography (1:2:7 water:isopropanol:ethyl acetate, 1% triethylamine) to separate the anomers. This gave 48 g (76%) of the desired product.

$[\alpha]_D^{21}$ = +122 (c = 1.0, $CHCl_3$). {Lit.: $[\alpha]_D^{21}$ = +102 (c = 0.91, $CHCl_3$).[3]} IR (KBr): ν/cm^{-1} = 3376 (NH), 3300 (OH), 3088, 3073, 3036 (Aromatic), 3000, 2969, 2913, 2871, 2838 (CH), 1647. ^{1}H NMR (400 MHz, $CDCl_3$): 7.50 (m, 2H, 2 x Ar-H), 7.37 (m, 3H, 3 x Ar-H), 5.53 (s, 1H, Benzylic), 4.68 (d, $J_{1,2}$ 3.6 Hz, 1H, H-1), 4.28 (dd, $J_{6,6'}$ 9.4 Hz, $J_{5,6}$ 4.0 Hz, 1H, H-6'), 3.81 (dd, J 10.2 Hz, 4.5 Hz, 1H, H-5), 3.75 (at, J 9.8 Hz, 1H, H-6), 3.70 (at, J 9.4, 1H, H-3), 3.46 (at, J 9.1 Hz, 1H, H-4), 3.41 (s, 3H, OMe), 2.78 (dd, $J_{2,3}$ 9.6 Hz, $J_{1,2}$ 3.6 Hz, 1H, H-2). ^{13}C NMR (100 MHz, $CDCl_3$): 137.2 (Quaternary Ph-C), 129.2, 128.3 & 126.3 (Aromatic C), 101.9 (Benzylic C), 101.2 (C1), 82.0 (C4), 71.7 (C3), 69.1 (C6), 62.5 (C5), 56.6 (C2), 55.4 (OCH_3). Mass m/z (ES^+) 340 (100%) $[M+NH_4+MeCN]^+$. M.p. = 131 °C (chloroform). {Lit.: m.p. = 135 °C[3]}

Methyl 2-*N*-(*p*-R)benzoylamido-4,6-*O*-benzylidene-2-deoxy-*α*-D-glucopyranoside



General method:

Methyl 2-amino-4,6-*O*-benzylidene-2-deoxy-*α*-D-glucopyranoside, **6** (1.0 g, 3.5 mmol) was dissolved in a minimal amount of 1:1 DCM:pyridine (~8 mL) and the solution cooled to 0 °C. The appropriate benzoyl chloride (1.1 eq) was then slowly added. The reaction progress was monitored by TLC (4:1, ethyl acetate:methanol), after 30 min the formation of product (R_f ~ 0.8) was detected with complete consumption of the starting material (R_f 0.5). The product was then dissolved in chloroform (100 mL) and the solution was washed with water, 5% w/w aq. NH_4Cl (50 mL), 5% w/w aq. NaOH (50 mL), and finally water (50 mL). The organic layer was dried over anhydrous magnesium sulfate, filtered, and the solvent removed under reduced pressure. Any precipitate formed

during the work up was collected and dried. Analysis of the crude material by NMR showed the presence of the di-benzoylated product. The ester was then hydrolysed by dissolving the crude products with heating in methanol (50 mL) with NaOH (5 eq to the estimated di-benzoylated sugar). After 1.5 hours TLC (ethyl acetate) showed consumption of the di-benzoylated sugar ($R_f \sim 0.75$) and formation of the desired product was (R_f~0.7). The solvent was removed under reduced pressure and water (50 mL) added to the product which was then extracted with DCM (70 mL), washed with water (50 mL), dried with anhydrous magnesium sulfate, filtered and the solvent removed under reduced pressure.

R = CF_3, **methyl 2-*N*-(*p*-CF_3)benzoylamido-4,6-*O*-benzylidene-2-deoxy-*α*-D-glucopyranoside**. Performed on a 1.0 g scale, product obtained in 91% yield

$[\alpha]_D^{21}$ = +63 (c = 1.0, DMSO). IR (KBr): ν/cm^{-1} = 3471 (NH), 3291 (OH), 3074, 3103 (Aromatic), 2919, 2871 (CH), 1645 (Amide I), 1551 (Amide II). ^{1}H NMR (400 MHz DMSO): 8.70 (d, $J_{2,NH}$ 7.7 Hz, 1H, NH), 8.13 (d, J 8.2 Hz, 2H, 2 x *p*-CF_3-Ar-H), 7.85 (d, J 8.3 Hz, 2H, 2 x *p*-CF_3-Ar-H), 7.47 (m, 2H, 2 x Ar-H), 7.38 (m, 3H, 3 x Ar-H), 5.65 (s, 1H, PhCH), 5.29 (s, 1H, OH), 4.80 (d, $J_{1,2}$ 3.6 Hz, 1H, H-1), 4.21 (dd, $J_{6,6'}$ 9.8 Hz, $J_{5,6}$ 4.7 Hz, 1H, H-6), 4.07 (ddd, $J_{2,3}$ 10.4 Hz, $J_{2,NH}$ 7.7 Hz, $J_{1,2}$ 3.6 Hz, 1H, H-2), 3.98 (atd, J 8.9 Hz, 5.8 Hz, 1H, H-3), 3.79 (at, J 10.0 Hz, 1H, H-6'), 3.67 (atd, J 9.7 Hz, 4.6, 1H, H-5), 3.58 (at, J 9.2 Hz, 1H, H-4), 3.31 (s, 3H, OMe). ^{13}C NMR (100 MHz, DMSO): 173.7 (*C*F_3,) 166.3 (COMe), 138.6 (Quaternary Ph-C), 129.7, 129.4, 128.9, 127.3 & 126.0 (Aromatic C), 101.8 (Benzylic C), 99.3 (C1), 82.8 (C4), 68.9 (C6), 67.7 (C3), 63.4 (C5), 56.2 (C2), 55.0 (OCH_3). Mass m/z 512.37 (100%) $[M+Na]^+$. HRMS found 454.1489 $[M+H]^+$ calculated ($C_{22}H_{23}NO_6F_3$) 454.1477. M.p. = 259 °C (chloroform).

R = Cl, **methyl 2-*N*-(*p*-Cl)benzoylamido-4,6-*O*-benzylidene-2-deoxy-*α*-D-glucopyranoside.** Performed on a 1.0 g scale, product obtained in 98% yield

$[\alpha]_D^{21}$ = +72 (c = 1.0, DMSO). IR (KBr): ν/cm^{-1} = 3426 (NH), 3293 (OH), 3088 (Aromatic), 2993, 2917, 2870 (CH), 1639 (Amide I), 1547 (Amide II). ^{1}H NMR (400 MHz, $CDCl_3$): 7.76 (d, J 8.1 Hz, 2H, 2 x *p*-Cl-Ar-H), 7.51 (d, J 8.4 Hz, 2H, 2 x *p*-

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Cl-Ar-H), 7.42-7.37 (m, 5H, 5 x Ar-H), 6.51 (d, $J_{2,NH}$ 8.5 Hz, 1H, NH), 5.58 (s, 1H, PhCH), 4.84 (d, $J_{1,2}$ 3.4 Hz, 1H, H-1), 4.44 (atd, *J* 9.4 Hz, 3.4 Hz, 1H, H-2), 4.31 (dd, $J_{6,6'}$ 5.7 Hz, $J_{5,6}$ 3.1 Hz, 1H, H-6), 4.03 (at, *J* 9.6 Hz, 1H, H-3), 3.85 (atd, *J* 9.9 Hz, 4.7 Hz, 1H, H-5), 3.80 (at, *J* 9.8 Hz, 1H, H-6'), 3.64 (at, *J* 8.8 Hz, 1H, H-4), 3.43 (s, 3H, OMe). ^{13}C NMR (100 MHz, $CDCl_3$): 167.3 (COMe), 138.2, 137.0 & 123.1 (Quaternary Ph-C), 129.2, 128.9, 128.7, 128.3 & 126.3 (Aromatic C), 102.0 (Benzylic C), 98.8 (C1), 82.0 (C4), 70.5 (C3), 68.8 (C6), 62.4 (C5), 55.3 (OCH_3), 54.4(C2). Mass *m/z* (ES^+) 478. (100%) $[M+NH_4+MeCN]^+$. M.p. = 246 °C (chloroform).

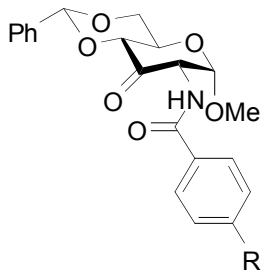
R = H, **methyl 2-*N*-benzoylamido-4,6-*O*-benzylidene-2-deoxy-*α*-D-glucopyranoside.** Performed on a 0.5 g scale, this afforded an 85% yield of the desired product. $[\alpha]_D^{21}$ = +51.5 (c = 1.0, $CHCl_3$). {Lit.: $[\alpha]_D^{21}$ = +57 (c = 2.0, $CHCl_3$).[4]} IR (KBr): *ν*/cm^{-1} = 3575 (NH), 3299 (OH), 3074 (Aromatic), 2981, 2956, 2909, 2897, 2853 (CH), 1633 (Amide I), 1538 (Amide II). ^{1}H NMR (100 MHz, $CDCl_3$): 7.83 (as, 1H, 1 x Ar-H), 7.81 (m, 1H, 1 x Ar-H), 7.54-7.51 (m, 3H, 3 x Ar-H), 7.47 (m, 2H, 2 x Ar-H), 7.38-7.36 (m, 2H, 2 x Ar-H), 6.56 (d, $J_{2,NH}$ 8.7 Hz, 1H, NH), 5.59 (s, 1H, PhCH), 4.85 (d, $J_{1,2}$ 3.8, 1H, H-1), 4.46 (atd, *J* 8.8 Hz, 3.8 Hz, 1H, H-2), 4.32 (dd, $J_{6,6'}$ 8.8, $J_{5,6}$3.9, 1H, H-6), 4.04 (at, *J* 9.6 Hz, 1H, H-3), 3.86 (atd, *J* 9.8 Hz, 4.0 Hz, 1H, H-5), 3.80 (at, *J* 9.8 Hz, 1H, H-6'), 3.66 (at, *J* 9.1 Hz, 1H, H-4), 3.44 (s, 3H, OMe). ^{13}C NMR (400 MHz, $CDCl_3$): 168.5 (COMe), 137.1 & 133.7 (Quaternary Ph-C), 131.9, 129.2, 128.6, 128.3, 127.2 & 126.3 (Aromatic C), 101.9 (Benzylic C), 98.9 (C1), 82.0 (C4), 70.8 (C5), 68.8 (C6), 62.4 (C3), 55.4 (OCH_3), 54.5 (C2). Mass *m/z* (ES^+) 444 (100%) $[M+NH_4+MeCN]^+$. M.p. = 231 °C (chloroform). {Lit.: m.p. = 239–245 °C[4]}

R = OMe, **methyl 2-*N*-(*p*-methoxy)benzoylamido-4,6-*O*-benzylidene-2-deoxy-*α*-D-glucopyranoside.** Performed on a 1.0 g scale, product obtained in 85% yield. $[\alpha]_D^{21}$ = +73.5 (c = 1.0, DMSO). IR (KBr): *ν*/cm^{-1} = 3568 (NH), 3312 (OH), 3081, 3066,3015, 3000 (Aromatic), 2985, 2971, 2956, 2890, 2853 (CH), 1627 (Amide I), 1543 (Amide II). ^{1}H NMR (400 MHz, DMSO): 8.12 (d, $J_{2,NH}$ 7.7, 1H, NH), 7.91 (d, *J* 8.8 Hz, 2H, 2 x *p*-OMe-Ar-H), 7.49-7.49 (m, 2H, 2 x Ar-H), 7.39-7.28 (m, 3H, 3 x Ar-H), 6.99 (d, *J* 8.8 Hz, 2H, 2 x *p*-OMe-Ar-H), 5.64 (s, 1H, PhCH), 4.77 (d, $J_{1,2}$ 3.5 Hz, 1H, H-1),

4.20 (dd, $J_{6,6'}$ 9.8 Hz, $J_{5,6}$ 4.6 Hz, 1H, H-6), 4.05 (ddd, $J_{2,3}$ 10.2 Hz, $J_{2,NH}$ 7.7 Hz, $J_{1,2}$ 3.5 Hz, 1H, H-2), 3.95 (at, *J* 9.5 Hz, 1H, H-3), 3.81 (s, 3H, *p*-OMe), 3.78 (at, *J* 10.0 Hz, 1H, H-6'), 3.66 (atd, *J* 9.7 Hz, 4.6 Hz, 1H, H-5), 3.56 (at, *J* 9.1 Hz, 1H, H-4), 3.30 (s, 3H, OMe). ^{13}C NMR (100 MHz, DMSO): 166.8 (COMe), 162.4 & 138.7 (Quaternary Ph-C), 130.3, 129.7, 128.9, 127.3 & 114.2 (Aromatic C), 101.8 (Benzylic C), 99.5 (C1), 82.9 (C4), 68.9 (C6), 67.8 (C3), 63.4 (C5), 56.2 (*p*-O$\underline{C}H_3$) 56.0 (C2), 55.7 (O$\underline{C}H_3$). HRMS found 416.1701 $[M+H]^+$ calculated ($C_{22}H_{26}NO_7$) 416.1709. M.p. = 261 °C (chloroform).

R = NMe_2, **methyl 2-*N*-(*p*-dimethylamine)benzoylamido-4,6-*O*-benzylidene-2-deoxy-*α*-D-glucopyranoside.** Performed on a 1.4 g scale, product obtained in 67% yield. $[\alpha]_D^{21}$ = +59 (c = 1.1, $CHCl_3$). IR (KBr): ν/cm^{-1} = 3472 (NH), 3350 (OH), 3061, 3019, 2961 (Aromatic), 2902, 2833, 2725 (CH), 1617 (Amide I), 1516 (Amide II). ^{1}H NMR (400 MHz, DMSO): 7.91 (d, $J_{2,NH}$ 7.7 Hz, 1H, NH), 7.80 (d, *J* 8.7 Hz, 2H, 2 x *p*-NMe_2-Ar-H), 7.49-7.47 (m, 2H, 2 x Ar-H), 7.40-7.38 (m, 3H, 3 x Ar-H), 6.71 (d, *J* 8.7 Hz, 2H, 2 x *p*-NMe_2-Ar-H), 5.64 (s, 1H, PhCH), 4.76 (d, $J_{1,2}$ 3.4 Hz, 1H, H-1), 4.20 (dd, $J_{6,6'}$ 9.8 Hz, $J_{5,6}$ 4.6 Hz, 1H, H-6), 4.03 (m, 1H, H-2), 3.94 (at, *J* 9.6 Hz, 1H, H-3), 3.77 (at, *J* 10.1 Hz, 1H, H-6'), 3.66 (atd, *J* 9.7 Hz, 4.6 Hz, 1H, H-5), 3.55 (at, *J* 9.1 Hz, 1H, H-4), 3.29 (s, 3H, OMe), 2.97 (s, 6H, $N\underline{Me}_2$). ^{13}C NMR (100 MHz, DMSO): 166.6 (COMe), 145.8 (Quaternary Ph-C), 129.8, 129.7, 128.9, 127.6 & 111.6 (Aromatic C), 101.8 (Benzylic C), 99.7 (C1), 82.9 (C4), 69.0 (C6), 67.9 (C3), 63.4 (C5), 55.9 (O$\underline{C}H_3$), 55.7 (C2), 40.6 (*p*-$N\underline{Me}_2$). HRMS found 429.2029 $[M+H]^+$ calculated ($C_{23}H_{29}N_2O_6$) 429.2029. M.p. = 246 °C (chloroform).

Methyl 2-*N*-(*p*-R)benzoylamido-4,6-*O*-benzylidene-2-deoxy-3-ulose -*α*-D-*ribo* hexapyranoside (7a–e)



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General method:

Oxalyl chloride (4 eq) was added to dry DCM (20 mL) and the mixture cooled to –78 ^{o}C. Dry DMSO (8 eq) was added dropwise over 5 min and the mixture left to stir for 1 hour. Methyl 2-*N*-(*p*-R)benzoylamido-4,6-*O*-benzylidene-2-deoxy-*α*-D-glucopyranoside, (1 eq) was dissolved with heating in dry THF (30 mL). This solution was slowly added to the reaction mixture over 30 min. Stirring was continued for 2 hours before the addition of Et_3N (16 eq). The reaction mixture was allowed to warm to room temperature and stirred for a further hour. DCM was added to the reaction mixture until all precipitate had dissolved. The reaction mixture was washed with water and the aqueous layer extracted with DCM and the combined organic fractions washed with brine. The solution was dried over anhydrous magnesium sulfate, filtered, and the solvent removed under reduced pressure. The crude product was purified using column chromatography (7:93 acetone:toluene) where needed.

In the case of methyl 2-*N*-(*p*-methoxy)benzoylamido-4,6-*O*-benzylidine-2-deoxy-D-glucopyranoside, initial conversion was poor (~45%) so the procedure was repeated before purification to afford 53% of the product.

R = CF_3, **Methyl 2-N-(p-CF_3)benzoylamido-4,6-*O*-benzylidene-2-deoxy-3-ulose-*α*-D-ribo-hexapyranoside (7a).** 1.28 g scale of starting material, this afforded 1.2 g (94% yield) of the desired product.

$[\alpha]_D^{21}$ = +108 (c = 1.1, $CHCl_3$). IR (KBr): ν/cm^{-1} = 3269 (NH), 3084 & 3056 (Aromatic), 2986, 2934, 2832 & 2860 (CH), 1749 (CO), 1644 (Amide I), 1539 (Amide II). ^{1}H NMR (400 MHz, DMSO): 8.72 (d, $J_{2,NH}$ 7.9 Hz, 1H, NH), 8.10 (d, J 8.1 Hz, 2H, 2 x *p*-CF_3-Ar-H), 7.85 (d, J 8.3 Hz, 2H, 2 x *p*-CF_3-Ar-H), 7.47-7.40 (m, 5H, 5 x Ar-H), 5.73 (s, 1H, PhCH), 5.28 (d, $J_{1,2}$ 4.2 Hz, 1H, H-1), 5.24 (dd, $J_{2,NH}$ 7.8 Hz, $J_{1,2}$ 4.3 Hz, 1H, H-2), 4.88 (d, $J_{4,5}$ 10.5 Hz, 1H, H-4), 4.39 (dd, $J_{6,6'}$ 9.5 Hz, $J_{5,6}$ 4.3 Hz, 1H, H-6), 4.01 (at, J 9.9 Hz, 1H, H-6'), 3.94 (atd, J 9.9 Hz, 4.3 Hz, 1H, H-5), 3.38 (s, 3H, OMe). ^{13}C NMR (100 MHz, DMSO): 196.7 (C3), 156.8 (COMe), 138.0 & 137.9 (Quaternary Ph-C), 130.0, 129.7, 129.1, 127.2 & 126.1 (Aromatic C), 102.5 (C2), 101.5 (Benzylic C), 82.1 (C4), 69.2

(C6), 66.3 (C5), 60.2 (C2), 56.0 (O<u>C</u>H$_3$). HRMS found 452.1325 $[M+H]^+$ calculated ($C_{22}H_{21}NO_6F_3$) 452.1321. M.p. = 184 ^oC (chloroform).

R = Cl, **Methyl 2-*N*-(*p*-Cl)benzoylamido-4,6-*O*-benzylidene-2-deoxy-3-ulose-*α*-D-*ribo*-hexapyranoside (7b).** 1.46 g scale of starting material, product obtained in 99% yield (1.44 g)

$[\alpha]_D^{21}$ = +73.0 (c = 1.0, $CHCl_3$). IR (KBr): ν/cm^{-1} = 3271 (NH), 3050 & 3036 (Aromatic), 2986, 2945, 2881 & 2860 (CH), 1747 (CO), 1637 (Amide I), 1542 (Amide II). ^{1}H NMR (400 MHz, $CDCl_3$): 8.47 (d, $J_{2,NH}$ 7.9 Hz, 1H, N<u>H</u>), 7.95 (d, *J* 8.5 Hz, 2H, 2 x *p*-Cl-Ar-H), 7.54 (d, *J* 8.5 Hz, 2H, 2 x *p*-Cl-Ar-H), 7.46 (m, 3H, 3 x Ar-H), 7.40 (m, 2H, 2 x Ar-H), 5.73 (s, 1H, PhC<u>H</u>), 5.26 (d, $J_{1,2}$ 4.2 Hz, 1H, H-1), 5.22 (dd, $J_{2,NH}$ 7.8 Hz, $J_{1,2}$ 5.1 Hz, 1H, H-2), 4.87 (d, $J_{4,5}$ 9.5 Hz, 1H, H-4), 4.38 (dd, $J_{6,6'}$ 9.5 Hz, $J_{5,6}$ 4.2 Hz, 1H, H-6), 4.01 (at, *J* 9.9 Hz, 1H, H-6'), 3.94 (atd, *J* 9.8 Hz, 4.2 Hz, 1H, H-5), 3.37 (s, 3H, O<u>Me</u>). ^{13}C NMR (100 MHz, $CDCl_3$): 196.8 (C3), 166.6 (<u>C</u>OMe), 137.9, 137.3 & 133.0 (Quaternary Ph-C), 130.7, 130.0, 129.2, 129.0 & 127.2 (Aromatic C), 102.5 (C1), 101.5 (Benzylic C), 82.1 (C4), 69.2 (C6), 66.3 (C5), 60.2 (C2), 56.0 (O<u>C</u>H$_3$). HRMS found 418.1508 $[M+H]^+$ calculated ($C_{21}H_{21}NO_6Cl$) 418.1057. M.p. = 168 ^oC (chloroform).

R = H, **Methyl 2-*N*-benzoylamido-4,6-*O*-benzylidene-2-deoxy-3-ulose-*α*-D-*ribo*-hexapyranoside (7c).** 0.44 g scale of starting material, this afforded 0.3 g (69% yield) of the desired product.

$[\alpha]_D^{21}$ = +106 (c = 0.9, $CHCl_3$). {Lit.: $[\alpha]_D^{21}$ = +114.[5]} IR (KBr): ν/cm^{-1} = 3629 (NH), 3072 & 3014 (Aromatic), 2971, 2921, 2888 & 2860, (CH), 1742, (CO), 1637 (Amide I), 1533 (Amide II). ^{1}H NMR (400 MHz, $CDCl_3$): 7.86 (d, 2H, 2 x Ar-H), 7.60-7.44 (m, 5H, 5 x Ar-H), 7.41-7.34 (m, 3H, 3 x Ar-H), 6.95 (d, $J_{2,NH}$ 7.5 Hz, 1H, N<u>H</u>), 5.63 (s, 1H, PhC<u>H</u>), 5.38 (d, $J_{1,2}$ 4.1 Hz, 1H, H-1), 5.17 (dd, $J_{1,NH}$ 7.1 Hz, $J_{1,2}$ 4.2 Hz, 1H, H-2), 4.47 (m, 1H, H-4), 4.44 (m, 1H, H-6), 4.16 (atd, *J* 9.9 Hz, 4.8 Hz, 1H, H-5), 4.01 (at, *J* 10.2 Hz, 1H, H-6'), 3.42 (s, 3H, O<u>Me</u>). ^{13}C NMR (100 MHz, $CDCl_3$): 195.0 (C3), 167.1 (<u>C</u>OMe), 136.3 & 133.4 (Quaternary Ph-C), 132.1, 129.4, 128.7, 128.4, 127.3 & 126.4 (Aromatic C), 102.0 (benzylic C), 102.3 (C1), 82.6 (C4), 69.5 (C6), 66.1 (C5), 59.3 (C2),

55.7 (O<u>C</u>H$_3$). Mass *m/z* (ES$^+$) 442.41 (100%) [M+NH$_4$+MeCN]$^+$. M.p.= 207 ^{o}C. (toluene) {Lit.: m.p. = 204–206 °C[5]}

R = OMe, **Methyl 2-*N*-(*p*-OMe)benzoylamido-4,6-*O*-benzylidene-2-deoxy-3-ulo-*α*-D-*ribo*-hexapyranoside (7d).** 1.25 g scale of starting material, product obtained in a 53% yield (0.61 g).

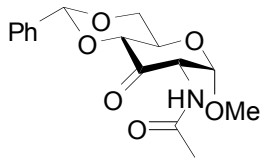
$[\alpha]_D^{21}$ = +124 (c = 1.1, $CHCl_3$). IR (KBr): ν/cm^{-1} = 3300 (NH), 3070, 3028 & 3000 (Aromatic), 2938, 2916, 2874 & 2846 (CH), 1747 (CO), 1627 (Amide I), 1535 (Amide II). ^{1}H NMR (400 MHz, DMSO): 8.09 (d, $J_{2,NH}$ 7.9 Hz, 1H, N<u>H</u>), 7.90 (d, *J* 8.7 Hz, 2H, 2 x *p*-OMe-Ar-H), 7.45-7.40 (m, 5H, 5 x Ar-<u>H</u>), 7.00 (d, *J* 8.7 Hz, 2H, 2 x *p*-OMe-Ar-H), 5.72 (s, 1H, PhC<u>H</u>), 5.24 (d, $J_{1,2}$ 4.1 Hz, 1H, H-1), 5.22 (dd, $J_{2,NH}$ 7.9 Hz, $J_{1,2}$ 4.2 Hz, 1H, H-2), 4.86 (d, $J_{4,5}$ 9.6 Hz, 1H, H-4), 4.38 (dd, $J_{6,6'}$ 9.6 Hz, $J_{5,6}$ 4.3 Hz, 1H, H-6), 4.01 (at, *J* 9.9 Hz, 1H, H-6'), 3.93 (atd, *J* 9.8 Hz, 4.3 Hz, 1H, H-5), 3.38 (s, 3H, O<u>Me</u>), 3.37 (s, 3H, Aromatic O<u>Me</u>). ^{13}C NMR (100 MHz, DMSO): 197.1 (C3), 166.9 (<u>C</u>OMe), 138.7 & 137.9 (Quaternary Ph-C), 130.6, 130.1, 129.0, 128.9, & 127.2 (Aromatic C), 114.3 (C2), 102.7 (benzylic C), 82.9 (C4), 69.2 (C6), 66.4 (C5), 60.1 (C2), 56.3 (Ar-O<u>C</u>H$_3$), 56.0 (O<u>C</u>H$_3$). HRMS found 414.1552 [M+H]$^+$ calculated ($C_{22}H_{24}NO_7$) 414.1552. M.p. = 188 ^{o}C (chloroform).

R = NMe$_2$, **Methyl 2-*N*-(*p*-NMe$_2$)benzoylamido-4,6-*O*-benzylidene-2-deoxy-3-ulo-*α*-D-*ribo*-hexapyranoside (7e).** 1.36 g scale of starting material, this afforded 1.3 g (96% yield) of the desired product.

$[\alpha]_D^{21}$ = +114 (c = 1.1, DMSO). IR (KBr): ν/cm^{-1} = 3286 (NH), 3012, 2946, 2909 (Aromatic), 2920, 2772 & 2545, (CH), 1743, (CO), 1624 (Amide I), 1518 (Amide II). ^{1}H NMR (400 MHz, DMSO): 7.81 (d, *J* 8.7 Hz, 2H, 2 x *p*-NMe$_2$-Ar-H), 7.76 (d, $J_{2,NH}$ 7.9 Hz, 1H, N<u>H</u>),7.46-7.40 (m, 5H, 5 x Ar-<u>H</u>), 6.70 (d, *J* 8.8 Hz, 2H, 2 x *p*-NMe$_2$-Ar-H), 5.71 (s, 1H, PhC<u>H</u>), 5.23 (d, $J_{1,2}$ 4.2 Hz, 1H, H-1), 5.20 (dd, $J_{2,NH}$ 7.7 Hz, $J_{1,2}$ 4.4 Hz, 1H, H-2), 4.85 (d, $J_{4,5}$ 9.7 Hz, 1H, H-4), 4.38 (dd, $J_{6,6'}$ 9.8 Hz, $J_{5,6}$ 4.4 Hz, 1H, H-6), 4.00 (at, *J* 9.9 Hz, 1H, H-6'), 3.92 (atd, *J* 9.9 Hz, 4.3 Hz, 1H, H-5), 3.36 (s, 3H, O<u>Me</u>), 2.08 (s, 6H, Aromatic N<u>Me$_2$</u>). ^{13}C NMR (100 MHz, $CDCl_3$): 197.4 (C3), 153.3 (<u>C</u>OMe), 130.0, 129.77 & 129.1 (Quaternary Ph-C), 129.1, 127.2, 126.2 & 120.5 (Aromatic C), 111.5

(C1) 102.8 (benzylic C), 82.1 (C4), 69.2 (C6), 66.4 (C5), 59.9 (C2), 55.9 (OMe), 46.3 (NMe_2). HRMS found 427.1869 $[M+H]^+$ calculated ($C_{23}H_{27}N_2O_6$) 427.1869. M.p. = 156 °C (chloroform).

Methyl 2-*N*-acetylamido-4,6-*O*-benzylidene-2-deoxy-3-ulose-*α*-D-*ribo*-hexapyranoside (8)

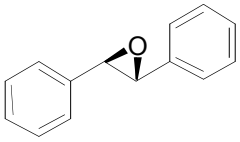


Oxalyl chloride (2.2 mL, 0.025 mol) was added to dry DCM (20 mL) and the mixture cooled to –78 °C. Dry DMSO (3.6 mL, 0.05 mol) was added dropwise over 5 min and the mixture left to stir for 2 hours. Methyl 2-*N*-acetylamido-4,6-*O*-benzylidene-2-deoxy-*α*-D-glucopyranoside (2.00 g, 0.00623 mol), was then dissolved with heating in dry THF (30 mL). This solution was slowly added to the reaction mixture over 30 min. The reaction mixture was stirred for a further 2 hours before the addition of Et_3N (13.06 mL, 0.093 mol). The reaction mixture was then allowed to warm to room temperature and stirred for a further hour. The product was dissolved in DCM (150 mL) and washed with water (100 mL) and the aqueous layer extracted with DCM (100 mL). The combined organic fractions were washed with brine, dried over magnesium sulfate, filtered, and the solvent removed under reduced pressure. The crude product was recrystallized from DCM and then chloroform. This afforded 49% of the desired product.

$[\alpha]_D^{21}$ = +116 (c = 1, DMSO). {Lit.: $[\alpha]_D^{21}$ = +128.[6]} IR (KBr): ν/cm^{-1} = 3290 (NH), 3066 (Aromatic), 2985, 2933, 2890, 2885 (CH), 1739 (Ketone), 1646 (Amide I), 1547 (Amide II). ^{1}H NMR (400 MHz, DMSO): 8.12 (d, $J_{2,NH}$ 8.3 Hz, 1H, NH), 7.41 (m, 5H, 5 x Ph-H), 5.69 (s, 1H, PhCH), 5.11 (d, $J_{1,2}$ 4.1 Hz, 1H, H-1), 4.96 (dd, $J_{2,NH}$ 8.3 Hz, $J_{1,2}$ 4.2 Hz, 1H, H-2), 4.78 (d, $J_{4,5}$ 9.8 Hz, 1H, H-4), 4.35 (dd, $J_{6,6'}$ 9.8 Hz, $J_{5,6}$ 4.5 Hz, 1H, H-6), 3.96 (at, J 10 Hz, 1H, H-6'), 3.86 (atd, J 9.9 Hz, 4.5 Hz, 1H, H-5), 3.34 (s, 3H, OMe), 1.93 (s, 3H, COMe). ^{13}C NMR (100 MHz, DMSO): 197.8 (C3), 170.6 (COMe), 137.8 (Quaternary Ph-C), 130.0, 129.0, 127.2 (Aromatic C), 102.7 (C1), 101.4 (Benzylic C), 82.1 (C4), 69.2 (C6), 66.5 (C5), 55.9 (C2), 55.8 (OCH_3), 23.0 ($COCH_3$). Mass *m/z* (ES^+) 344 (72%) $[M+Na]^+$. M.p. = 220–221 °C (chloroform). { Lit.: m.p. = 222 °C[6]}

3. Epoxidation reactions

Trans-stilbene oxide (10)



General Epoxidation Procedure:

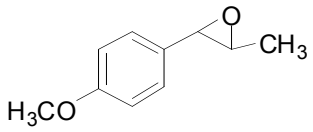
Trans-stilbene, **9** (54 mg, 0.3 mmol) and the chosen ketone catalyst (0.3 mmol) were dissolved in the chosen solvent system (4.5 mL). The phase transfer agent, NBu_4HSO_4 (TBAHS), (5 mg, 0.1 mmol) and chosen buffer solution (3 mL in 4 x 10^{-4} M Na_2EDTA) were added to the solution. Oxone® (254 mg, 0.41 mmol) in aqueous Na_2EDTA (4 x 10^{-4} M, 2 mL) and a solution of K_2CO_3 in water[a] (2 mL) were added dropwise over a period of 30 min using two separate plastic syringes with teflon needles. The mixture was stirred at room temperature for 2.5 hours. The reaction progress was followed by TLC (20:1 petrol: diethyl ether) showing consumption of the starting material (R_f 0.7) and formation of product (R_f 0.5). The reaction was quenched with water (10 mL) and the resulting precipitate was filtered off and washed with 5:1 petrol:diethyl ether solution (30 mL). The remaining precipitate was found to be the pure ketone (40–95%). The epoxide and corresponding olefin were found to be entirely within the petrol solution. The epoxide was separated from the olefin using column chromatography (97:2:1, petrol:diethyl ether:triethylamine) after conversion had been determined by crude ^{1}H NMR (calculated from the integration of the olefinic and oxiranic protons of the crude reaction mixture). In the cases where a low conversion was observed a small portion was purified using semi-prep TLC (97:3, petrol:diethyl ether). The enantiomeric excess was measured using chiral HPLC solvent A= EtOH, solvent B = hexane, t = 0, 20% A, t = 10, 20% A. Retention time = 4.7 min (minor peak), 5.6 min (major peak). In all cases it was the *R,R* epoxide that was created in enantiomeric excess.

IR (KBr): ν/cm^{-1} = 3416 (Epoxide), 3059, 3029 (Aromatic), 3000, 2927, 2949, 2853 (CH). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.41–7.36 (m, 10H, Ar), 3.89 (s, 2H, CH). ^{13}C NMR ($CDCl_3$, 100 MHz):137.1 (Quaternary Ph-C), 128.6, 128.3, 125.5 (Aromatic C), 62.8

(Epoxide C). LRMS (TOF ES+) for (M+NH_4/CH_3CN) $C_{16}H_{19}N_2O$ (*m/z*): calc. 255.1; found 255.5. Spectroscopic data are in agreement with those reported in the literature.[7]

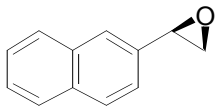
[a]Reactions at pH 10.6 were carried out using buffer 0.05 M $Na_2B_4O_7 \cdot 10H_2O$ (3 mL in 4 x 10^{-4} M Na_2EDTA) and K_2CO_3 (240 mg, 1.74 mmol) in water (2 mL) as base solution.

***Trans*-anethole oxide (15)**



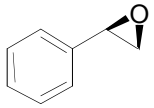
Trans-anethole, **11** (44 mg, 0.3 mmol) was treated according to the general epoxidation procedure. The enantiomeric excess was measured using chiral HPLC solvent A= EtOH, solvent B = hexane, t = 0, 0.2% A, t = 45, 0.2% A. Retention time = 28.7 min (major peak), 32.9 min (minor peak). In all cases the (+) enantiomer was created in excess.
^{1}H NMR ($CDCl_3$, 400 MHz): 7.18 (d, *J* = 8.6 Hz, 2H, Ar), 6.85 (d, *J* = 8.6 Hz, 2H, Ar), 3.79 (s, 3H, OCH_3), 3.52 (d, *J* = 2.1 Hz, 1H), 3.04 (dq, *J* = 5, 2.1 Hz, 1H), 1.43 (d, *J* = 5 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz):159.6, 129.7, 126.9, 113.8, 59.5, 58.8, 55.2, 17.8. Spectroscopic data are in agreement with those reported in the literature.[8]

2-Vinylnaphthalene oxide (16)



2-Vinylnaphthalene, **12** (46 mg, 0.3 mmol) was treated according to the general epoxidation procedure. The enantiomeric excess was measured using chiral HPLC solvent A= EtOH, solvent B = hexane, t = 0, 5% A, t = 15, 5% A. Retention time = 8.5 min (major peak), 9.2 min (minor peak). In all cases it was the *R* epoxide that was created in enantiomeric excess.
^{1}H NMR ($CDCl_3$, 400 MHz): 7.83–7.33 (m, 7H, Ar), 4.03 (dd, *J* = 4, 2.5 Hz, 1H), 3.24 (dd, *J* = 5.5, 4 Hz, 1H), 2.92 (dd, *J* = 5.5, 2.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): 135.0, 133.4, 133.3, 128.9, 127.9, 126.5, 126.2, 125.2, 122.7, 53.1, 51.0. Spectroscopic data are in agreement with those reported in the literature.[9]

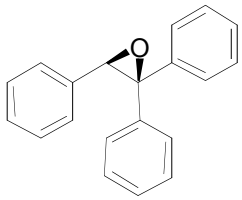
Stryrene oxide (17)



Styrene, **13** (31 mg, 0.3 mmol) was treated according to the general epoxidation procedure, however the reaction was quenched with pentane (10 mL) rather than water. The organic and aqueous layers were separated and the aqueous layer extracted further with pentane (3 x 10 mL) and the combined organic fractions were washed with water (3 x 10 mL), dried over magnesium sulfate, filtered, and the solvent removed under reduced pressure. The enantiomeric excess was measured using chiral HPLC solvent A= EtOH, solvent B = hexane, t = 0, 5% A, t = 15, 5% A. Retention time = 5.4 min (minor peak), 7.0 min (major peak). In all cases it was the *R* epoxide that was created in enantiomeric excess.[10]

LRMS (TOF CI+) for (M^+) C_8H_8O (*m/z*): calc. 220.1; found 120.1. ^{1}H NMR ($CDCl_3$, 400 MHz): 7.38–7.27 (m, 5H, Ar), 3.87 (m, 1H), 3.16 (dd, *J* = 5.3, 4.4 Hz, 1H), 2.81 (dd, *J* = 5.3, 2.5 Hz, 1H).

Triphenylethylene oxide (18)

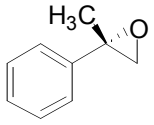


Triphenylethylene, **14** (77 mg, 0.3 mmol) was treated according to the general epoxidation procedure. The enantiomeric excess was measured using chiral HPLC solvent A= EtOH, solvent B = hexane, t = 0, 5% A, t = 15, 5% A. Retention time = 5.9 min (minor peak), 12.1 min (major peak). In all cases it was the *R* epoxide that was created in enantiomeric excess.

IR (KBr): ν/cm^{-1} = 3059 (Epoxide), 3083, 3067, 3028 (Aromatic), 2972, 2916, 2587 (CH). ^{1}H NMR ($CDCl_3$, 400 MHz): 7.45–7.16 (m, 15H, Ar), 4.38 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): 141.0, 135.8, 135.4, 129.2, 128.4, 127.9, 128.7, 127.8, 127.7, 127.6,

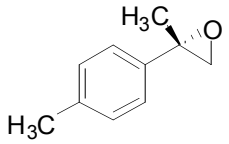
126.8, 126.3, 68.7, 68.1. Spectroscopic data are in agreement with those reported in the literature.[10]

α-Methylstyrene oxide (24)



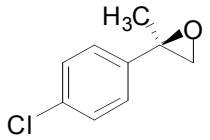
α-Methylstyrene, **19** (35 mg, 0.3 mmol) was treated according to the general epoxidation procedure. The enantiomeric excess was measured using chiral HPLC solvent A= EtOH, solvent B = hexane, t = 0, 0.4% A, t = 20, 0.4% A. Retention time = 6.5 min (major peak), 7.3 min (minor peak). In all cases the *S* enantiomer was created in excess.
^{1}H NMR ($CDCl_3$, 400 MHz): 7.40–7.24 (m, 5H, Ar), 2.98 (d, J = 5.4 Hz, 1H), 2.80 (dq, J = 5.4, 0.7 Hz, 1H), 1.71 (d, J = 0.7 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): 128.5, 127.5, 125.5, 57.2, 56.9, 22.0. Spectroscopic data are in agreement with those reported in the literature.[10]

***p*-Methyl-α-methylstyrene oxide (25)**



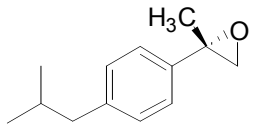
p-Methyl-α-methylstyrene, **20** (10.3 mg, 0.078 mmol) was treated according to the general epoxidation procedure. The enantiomeric excess was measured using Chiral GC: β-cyclodextrin column, 90–120 °C (1 °C/min), retention time = 19.29 min (minor peak), 21.80 min (major peak). In all cases the *S* enantiomer was created in excess. R_f (1:4 EtOAc/petrol): 0.58. ^{1}H NMR ($CDCl_3$, 200 MHz) δ in ppm: 7.25 (d, J = 8.1 Hz, 2H, Ar), 7.15 (d, J = 8.1 Hz, 2H, Ar), 2.96 (d, J = 5.4 Hz, 1H, OCH_2), 2.80 (d, J = 5.4 Hz, 1H, OCH_2), 2.34, 1.70 (s, 6H, $2CH_3$). ^{13}C NMR ($CDCl_3$, 100 MHz): 138.1, 137.1, 129.0, 125.2, 57.0, 56.7, 21.9, 21.0. Spectroscopic data are in agreement with those reported in the literature.[11]

_p_-Chloro-_α_-methylstyrene oxide (26)



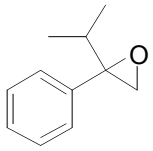
_p_-Chloro-_α_-methylstyrene, **21** (12.2 mg, 0.078 mmol) was treated according to the general epoxidation procedure. The enantiomeric excess was measured using Chiral GC: β-cyclodextrin, 90 °C (isotermic), retention time = 33.38 min (major peak), 36.28 min (minor). In this case the *R* enantiomer was created in excess.[14] R_f (1:4 EtOAc/petrol): 0.48. ^{1}H NMR ($CDCl_3$, 200 MHz) δ in ppm: 7.29 (s, 4H, Ar), 2.97 (d, *J* = 5.4 Hz, 1H, OCH_2), 2.76 (d, *J* = 5.4 Hz, 1H, OCH_2), 1.69 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): 139.7, 133.2, 128.4, 126.7, 57.0, 56.2, 21.6. Spectroscopic data are in agreement with those reported in the literature.[11]

_p_-Isobutyl-_α_-methylstyrene oxide (27)



_p_-Isobutyl-_α_-methylstyrene, **22** (13.6 mg, 0.078 mmol) was treated according to the general epoxidation procedure. The enantiomeric excess was measured using Chiral GC: β-cyclodextrin column, 90–120 °C (1 °C/min), retention time = 61.24 min (minor peak), 62.17 min (major peak). In all cases the *S* enantiomer was created in excess. R_f (1:4 EtOAc/petrol): 0.61. ^{1}H NMR ($CDCl_3$, 200 MHz) δ in ppm: 7.3 (d, *J* = 8.4 Hz, 2H, Ar), 7.2 (d, *J* = 8.4 Hz, 2H, Ar), 2.95 (d, *J* = 5.4 Hz, 1H, OCH_2), 2.80 (d, *J* = 5.4 Hz, 1H, OCH_2), 2.45 (d, *J* = 7.0 Hz, 2H, CH_2), 1.80 (nonet, *J* = 7.0 Hz, 1H, CH), 1.70 (s, 3H, CH_3),0.90 (d, *J* = 7.0 Hz, 6H, $2CH_3$). ^{13}C NMR ($CDCl_3$, 50.3 MHz): 141.0, 138.3, 129.1, 125.1, 57.1, 56.7, 45.0, 30.2, 22.3, 21.8. Spectroscopic data are in agreement with those reported in the literature.[12]

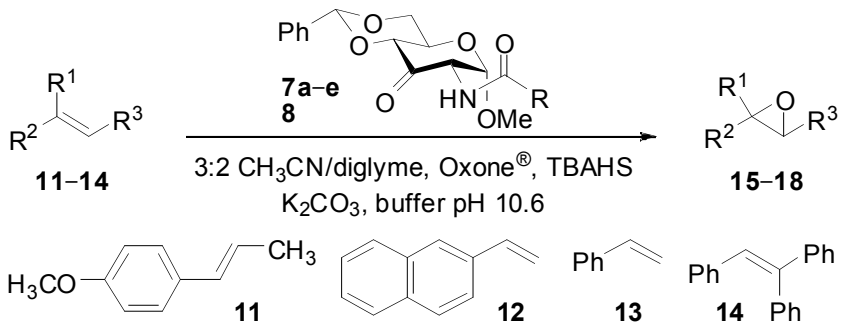
_α_-Isopropylstyrene oxide (28)



α-Isopropylstyrene, **23** (11.4 mg, 0.078 mmol) was treated according to the general epoxidation procedure. The enantiomeric excess was measured using Chiral GC: β-cyclodextrin column, 110 °C (isotermic), retention time = 27.35 min (major peak), 27.89 min (minor). In all cases the (+) enantiomer was created in excess. R_f (1:4 EtOAc/petrol): 0.61. ^{1}H NMR ($CDCl_3$, 200 MHz) δ in ppm: 7.44–7.30 (m, 5H, Ar), 3.05 (d, J = 5.2 Hz, 1H, OCH_2), 2.77 (d, J = 5.2 Hz, 1H, OCH_2), 2.14 (m, 1H, CH), 1.02 (d, J = 6.9 Hz, 3H, CH_3), 1.00 (d, J = 6.9 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): 139.3, 127.9, 127.3, 127.2, 64.4, 53.13, 33.1, 18.5, 17.8. Spectroscopic data are in agreement with those reported in the literature.[13]

Supplementary Information

4. Other asymmetric epoxidations with ketones 7a–e and 8[a] (Table ESI 1)



Entry	Ketone	R	Substrate	Conv. [%][b]	ee [%][c]
1	**7c**	C_6H_5	*trans*-anethole **11**	34	49
2	**7d**	*p*-$MeOC_6H_4$	*trans*-anethole **11**	60	35
3	**7c**	C_6H_5	vinylnaphthalene **12**	6	nd
4	**7d**	*p*-$MeOC_6H_4$	vinylnaphthalene **12**	35	18 (*R*)
5	**8**	Me	vinylnaphthalene **12**	76	2 (*R*)
6[d]	**8**	Me	vinylnaphthalene **12**	91	2 (*R*)
7[e]	**7d**	*p*-$MeOC_6H_4$	styrene **13**	39	10 (*R*)
8[e,f]	**7d**	*p*-$MeOC_6H_4$	styrene **13**	39	12 (*R*)
9[e,g]	**7d**	*p*-$MeOC_6H_4$	styrene **13**	38	15 (*R*)
10[h]	**7d**	*p*-$MeOC_6H_4$	styrene **13**	41	24 (*R*)
11[e]	**8**	Me	styrene **13**	81	15 (*R*)
12[e,i]	**8**	Me	styrene **13**	81	15 (*R*)
13	**7a**	*p*-$CF_3C_6H_4$	triphenylethene **14**	8	56 (*R*)
14[j]	**7a**	*p*-$CF_3C_6H_4$	triphenylethene **14**	9	nd
15[j]	**7b**	*p*-ClC_6H_4	triphenylethene **14**	17	53 (*R*)
16	**7b**	*p*-ClC_6H_4	triphenylethene **14**	29	43 (*R*)
17	**7d**	*p*-$MeOC_6H_4$	triphenylethene **14**	26	56 (*R*)
18	**7e**	*p*-$Me_2NC_6H_4$	triphenylethene **14**	6	59 (*R*)
19[j]	**7e**	*p*-$Me_2NC_6H_4$	triphenylethene **14**	8	nd

[a] *General conditions*: 3:2 CH_3CN/diglyme, Oxone® (1.4 equiv) added over 30 min, TBAHS (0.1 equiv), K_2CO_3 (5.8 equiv), buffer pH 10.6, ketone (1 equiv), 2.5 h, rt. [b] Determined by ^1H NMR analysis. [c] Determined by chiral HPLC (Chiralcel OD column). [d] 0.3 equiv of ketone used. [e] 0.06 equiv of ketone used. [f] Reaction conducted at 0 ºC for 2.5 h. [g] Reaction conducted at 0 ºC for 8 h. [h] 0.2 equiv of ketone used. [i] Reaction conducted at 0 ºC for 5 h. [j] 3 equiv of Oxone® used.

5. Epoxide HPLC and GC traces with racemic references

Trans-stilbene oxide **10** racemic reference (HPCL)

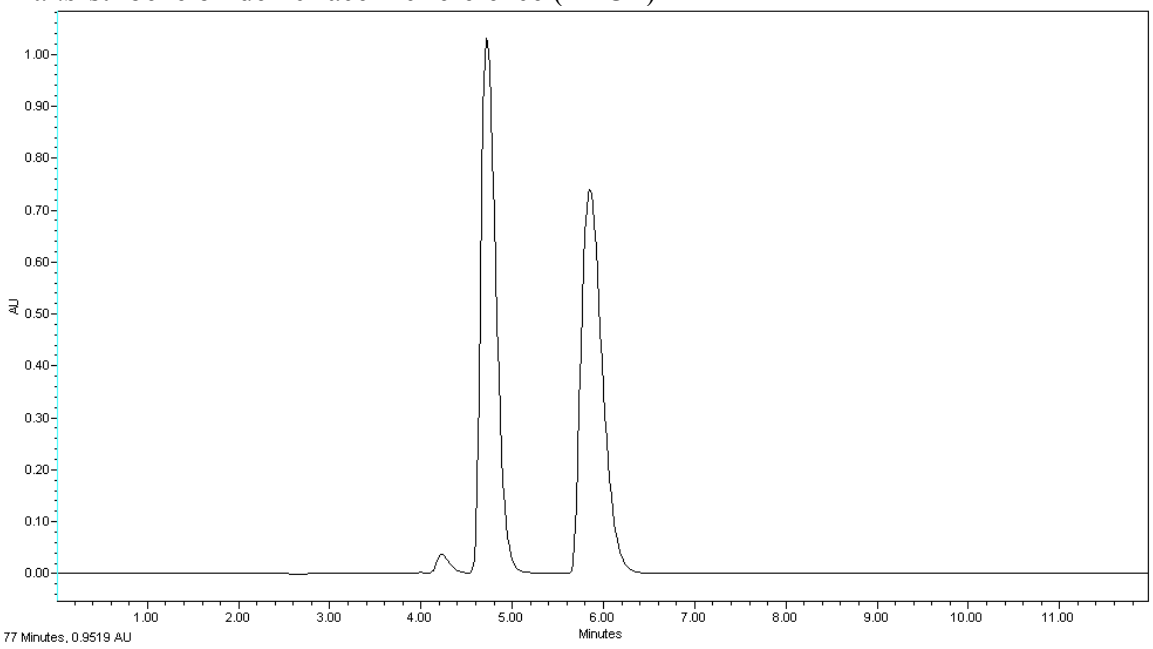
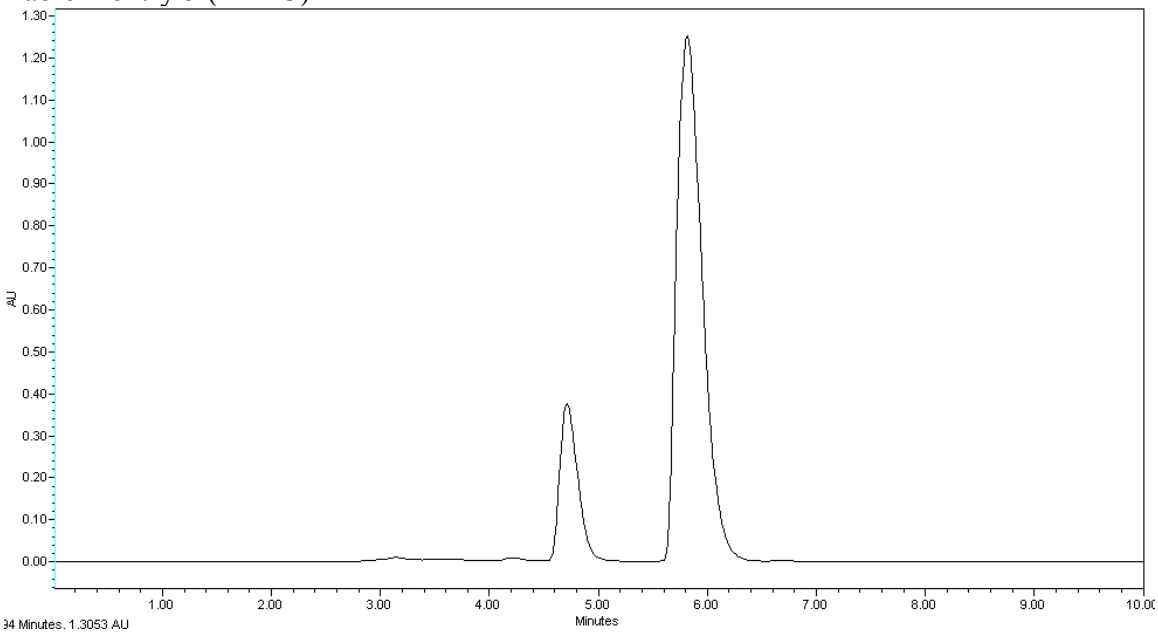


Table 1 entry 5 (HPLC)



Supplementary Information

Trans-anethole oxide **15** racemic reference (HPLC)

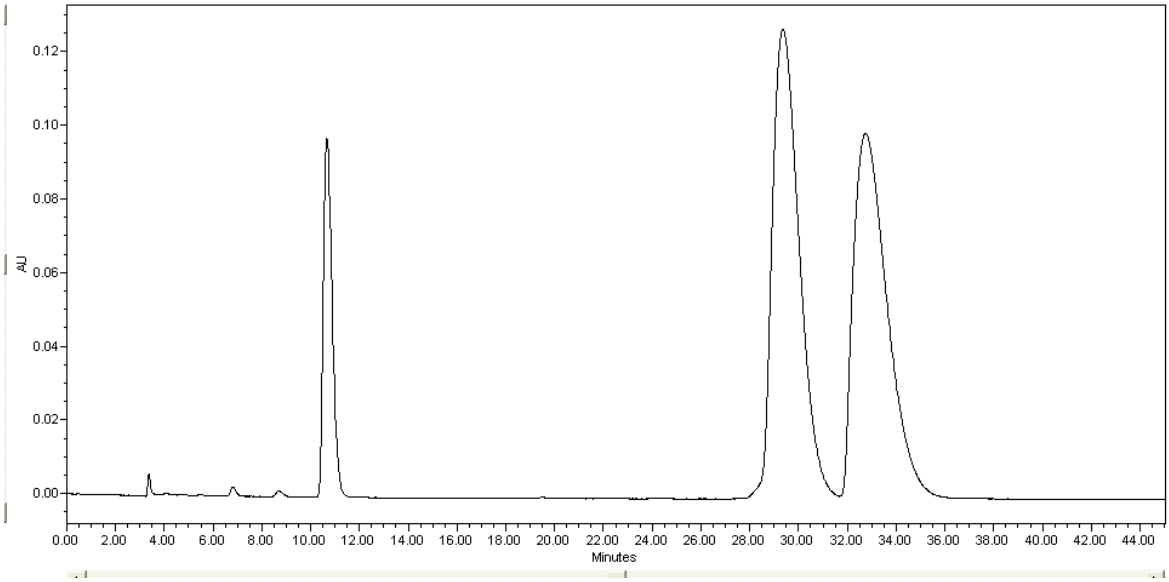
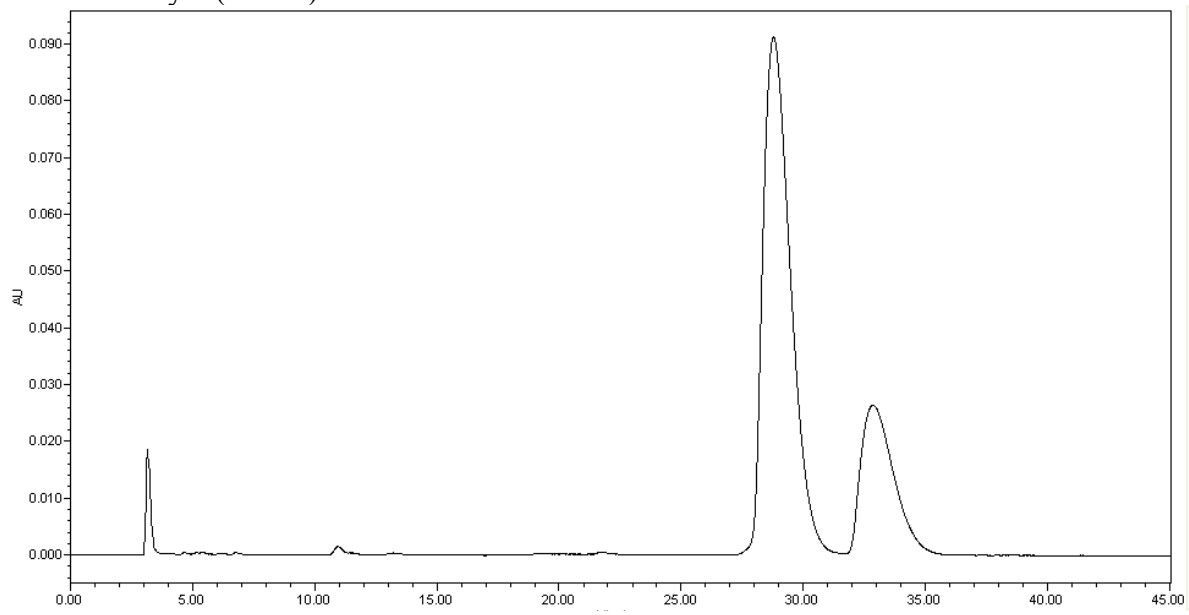
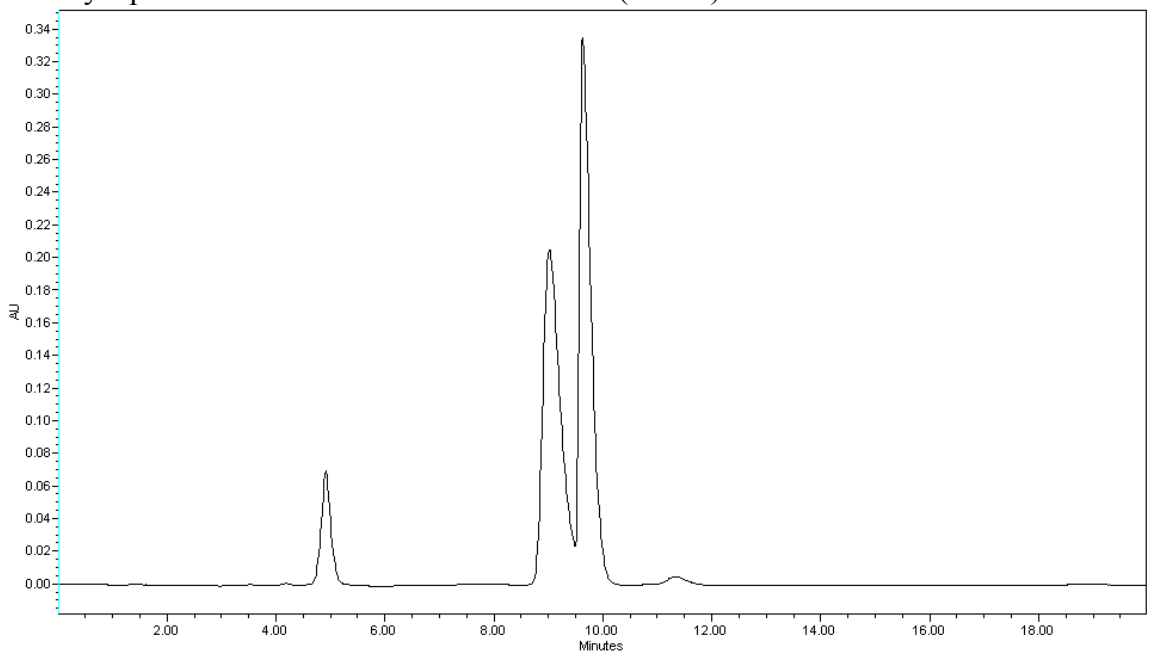


Table 2 entry 1 (HPLC)



Supplementary Information

2-Vinynaphthalene oxide **16** racemic reference (HPLC)



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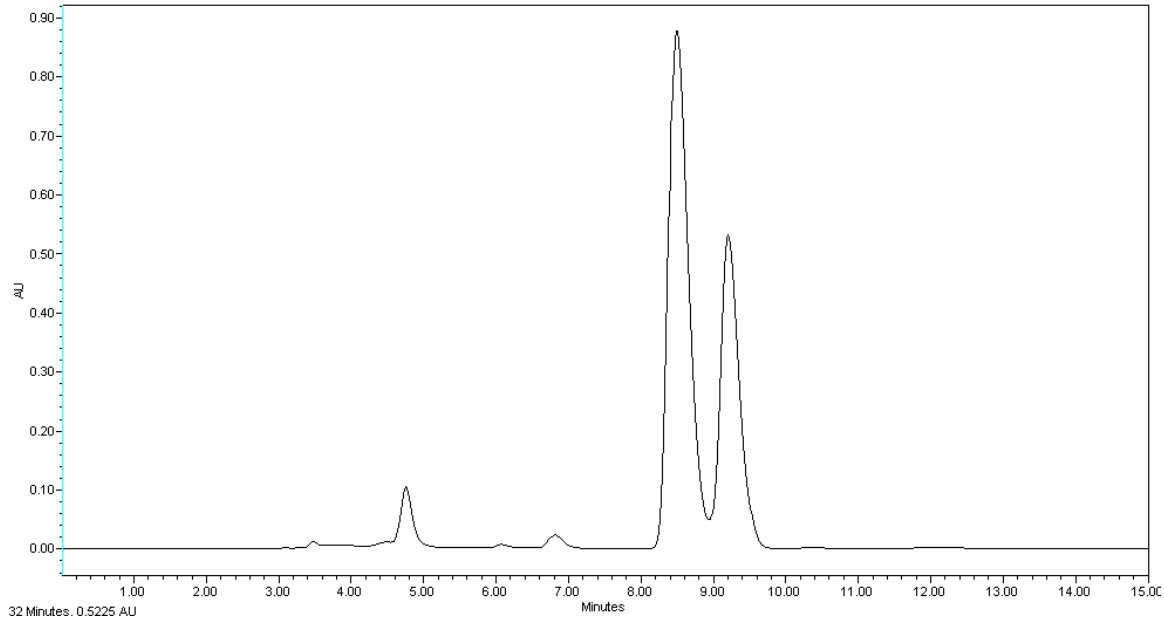


Supplementary Information

Styrene oxide **17** racemic reference (HPLC)

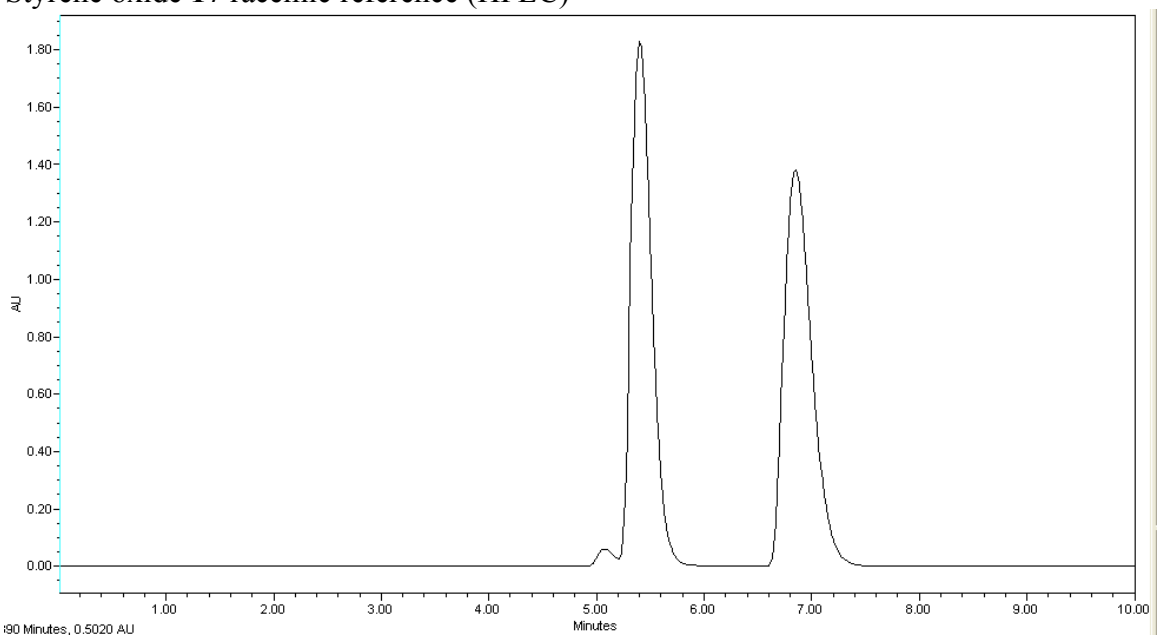
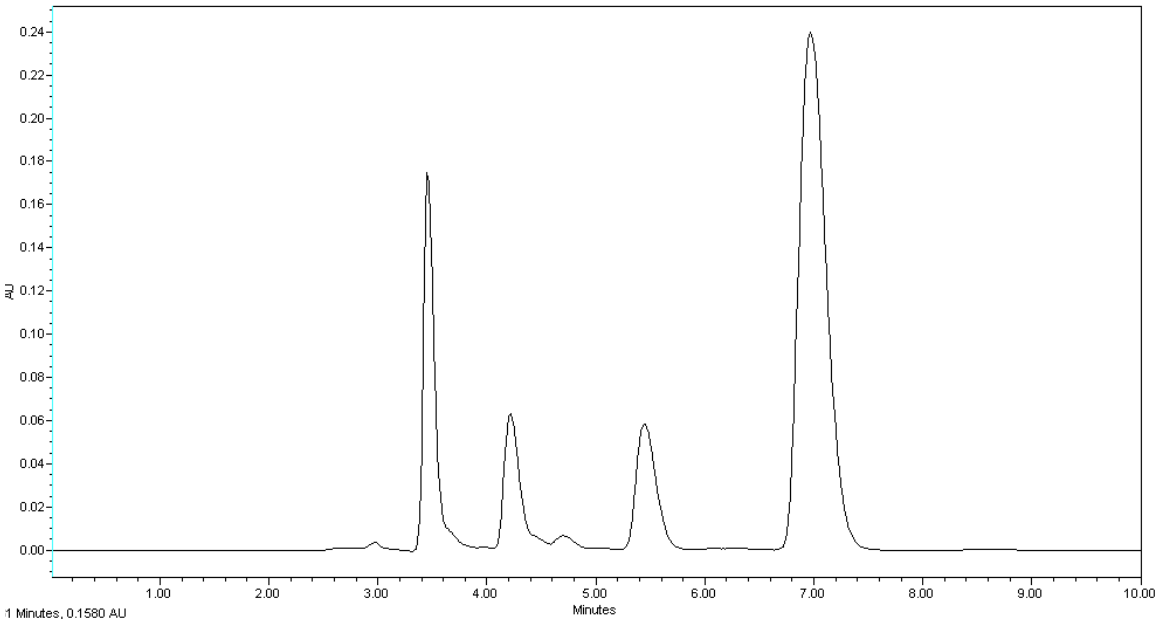


Table 2 entry 9 (HPLC)



Supplementary Information

Triphenylethene oxide **18** racemic reference (HPLC)

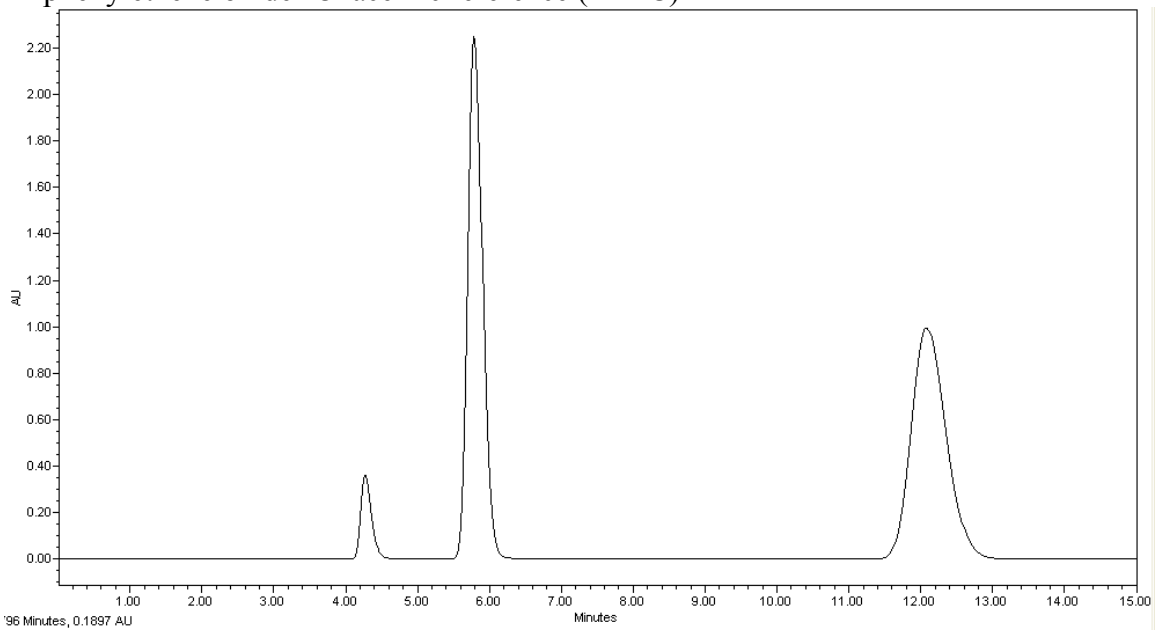
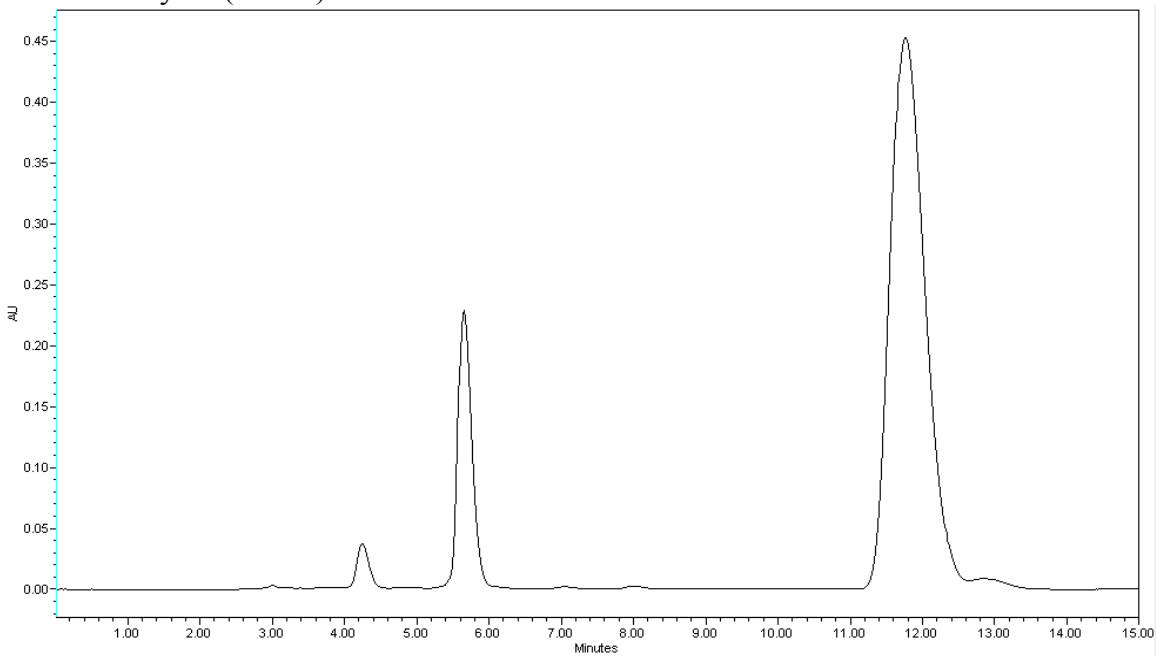


Table 2 entry 11 (HPLC)



Supplementary Information

α-Methylstyrene oxide **24** racemic reference (HPLC)

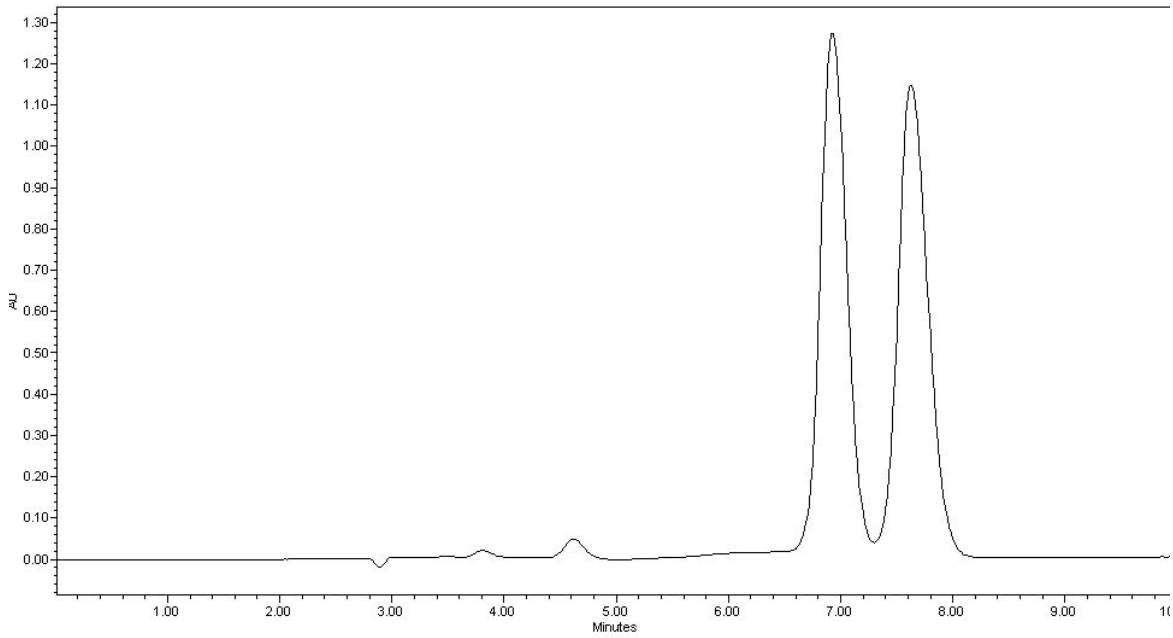
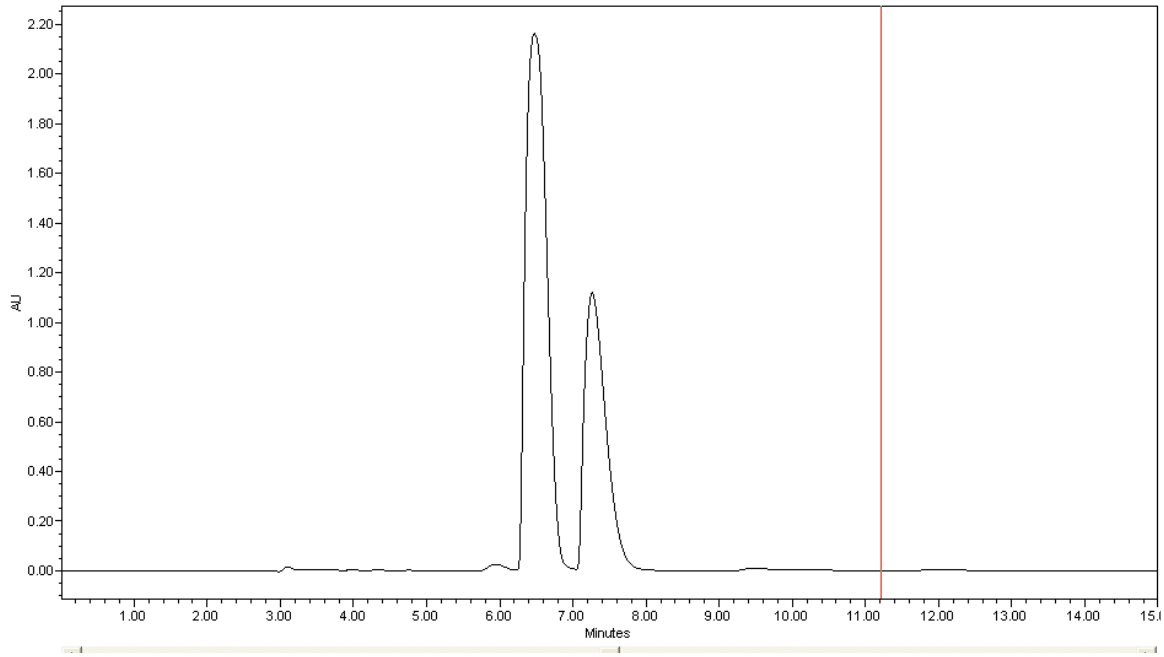


Table 3 entry 5 (HPLC)



Supplementary Information

p-Methyl-*α*-methylstyrene oxide **25** racemic reference (GC)

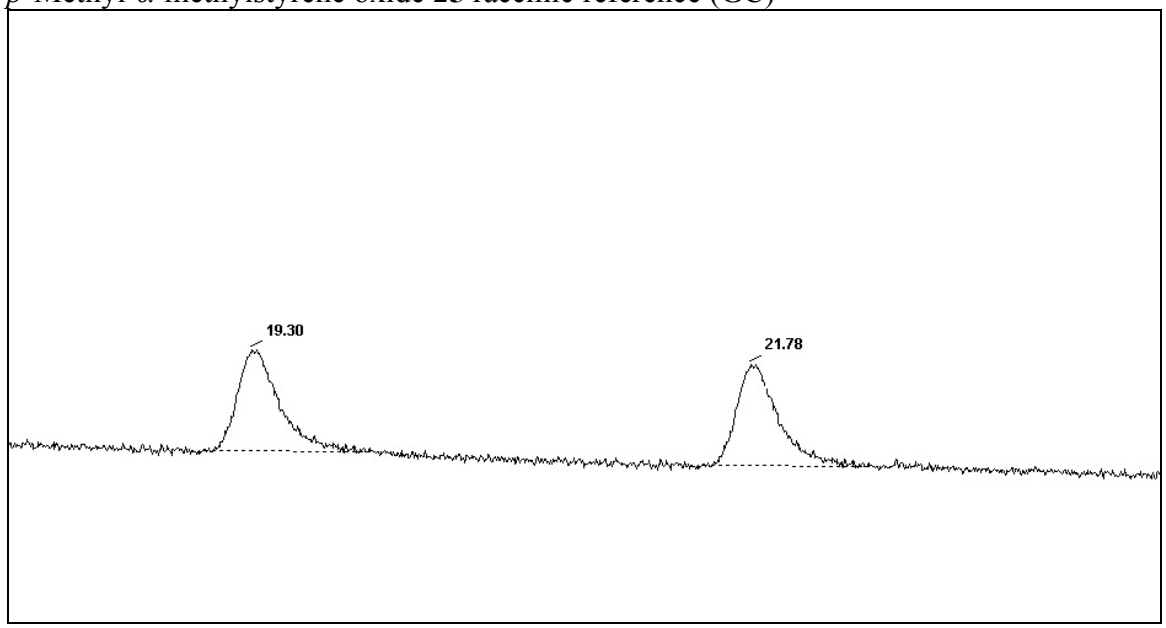
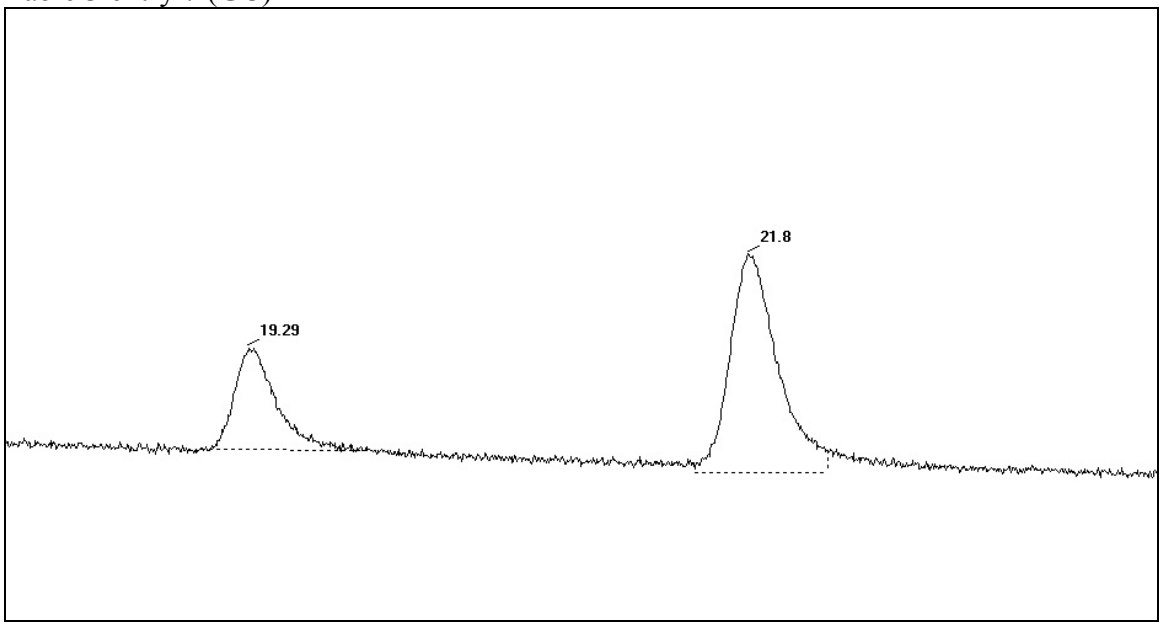


Table 3 entry 7 (GC)



Supplementary Information

p-Chloro-*α*-methylstyrene oxide **26** racemic reference (GC)

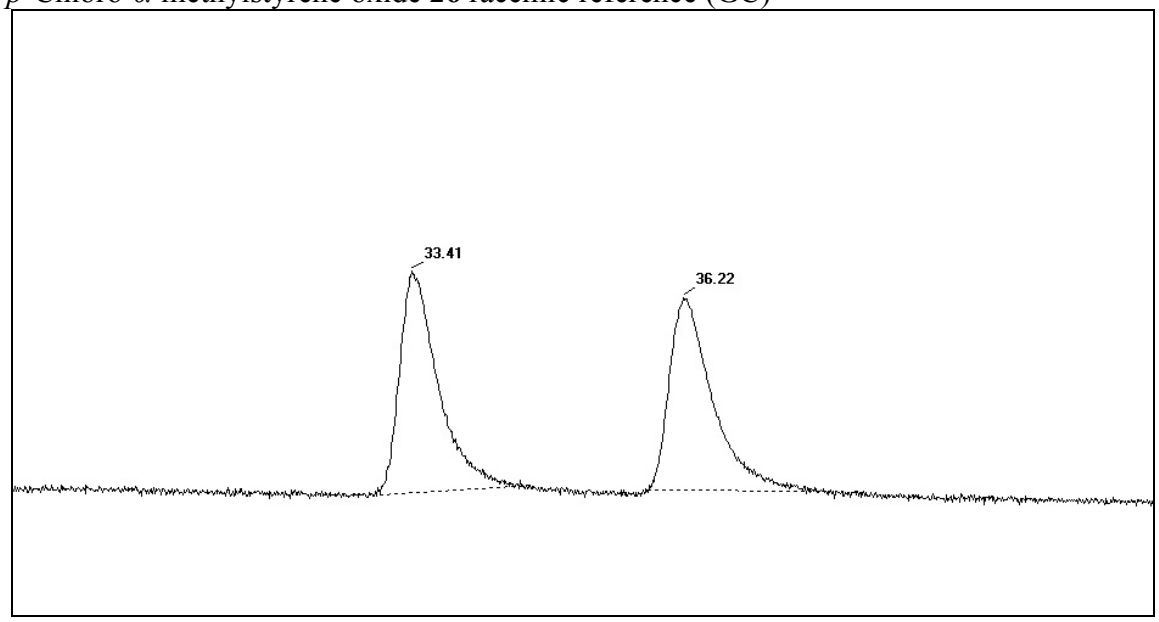
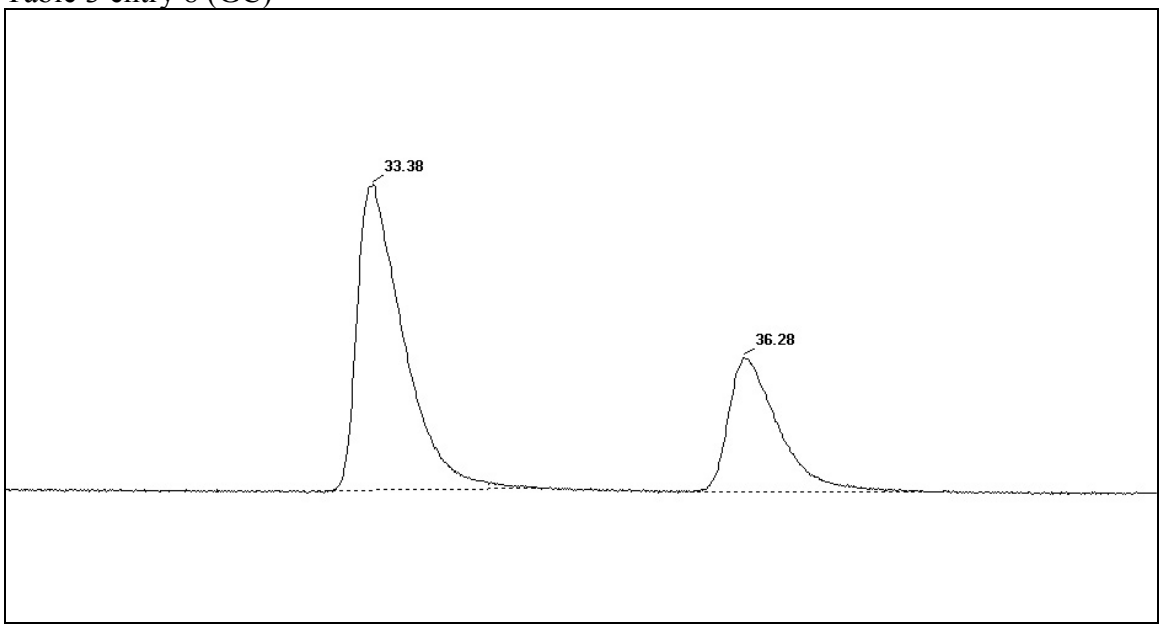


Table 3 entry 8 (GC)



Supplementary Information

p-Isobutyl-*α*-methylstyrene **27** racemic reference (GC)

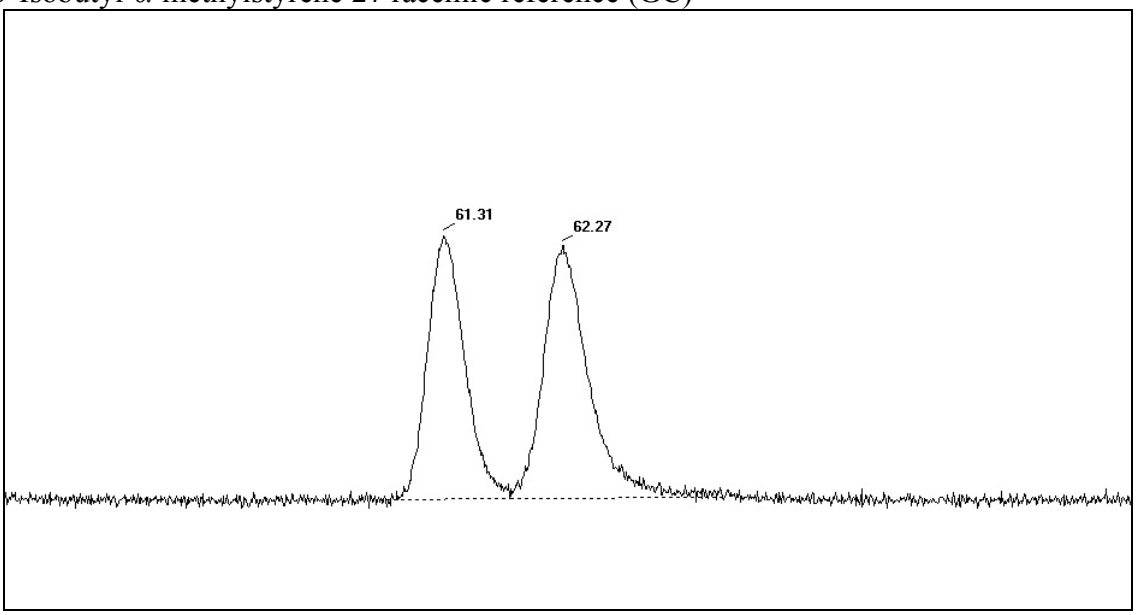
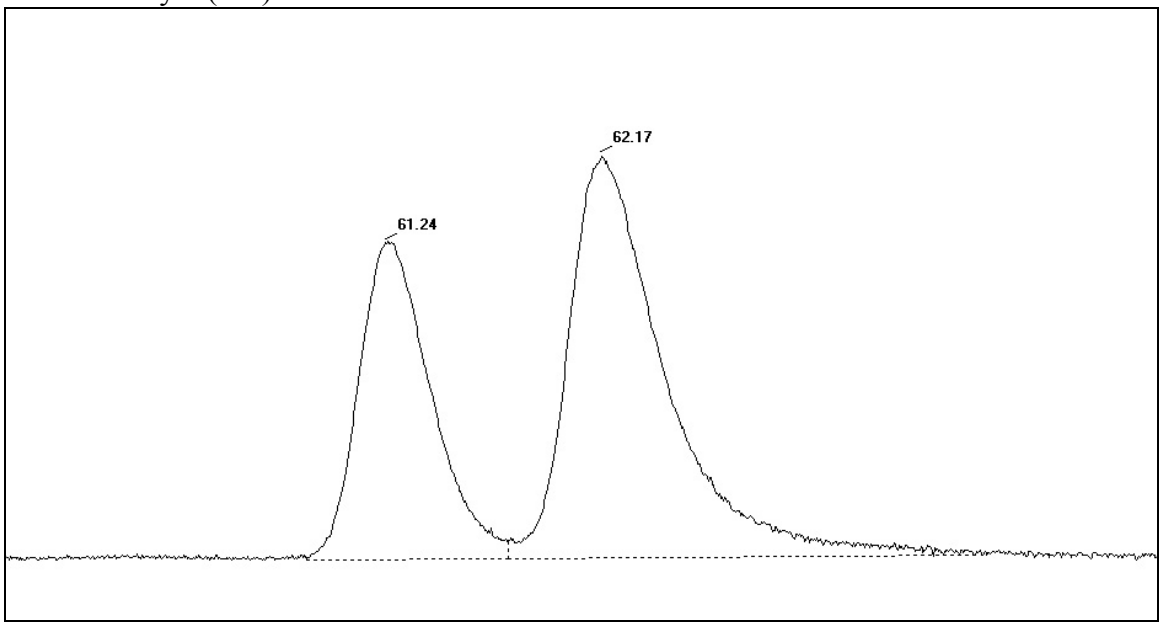


Table 3 entry 9 (GC)



Supplementary Information

α-Isopropylstyrene oxide **28** racemic reference (GC)

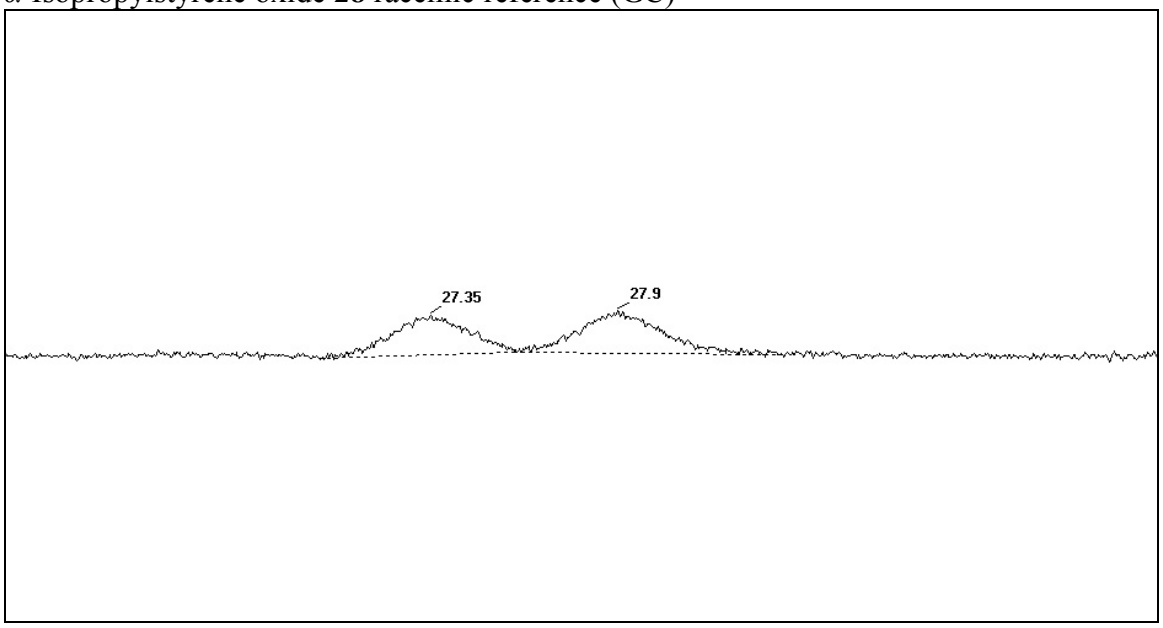
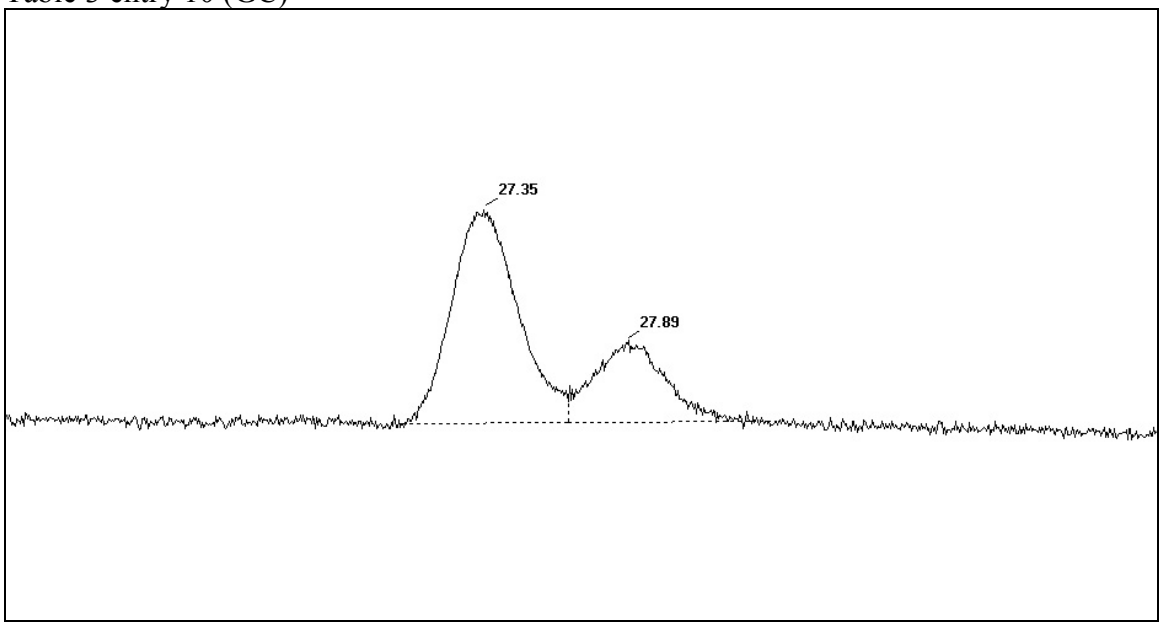
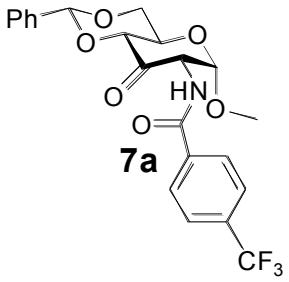


Table 3 entry 10 (GC)



6. NMR spectra



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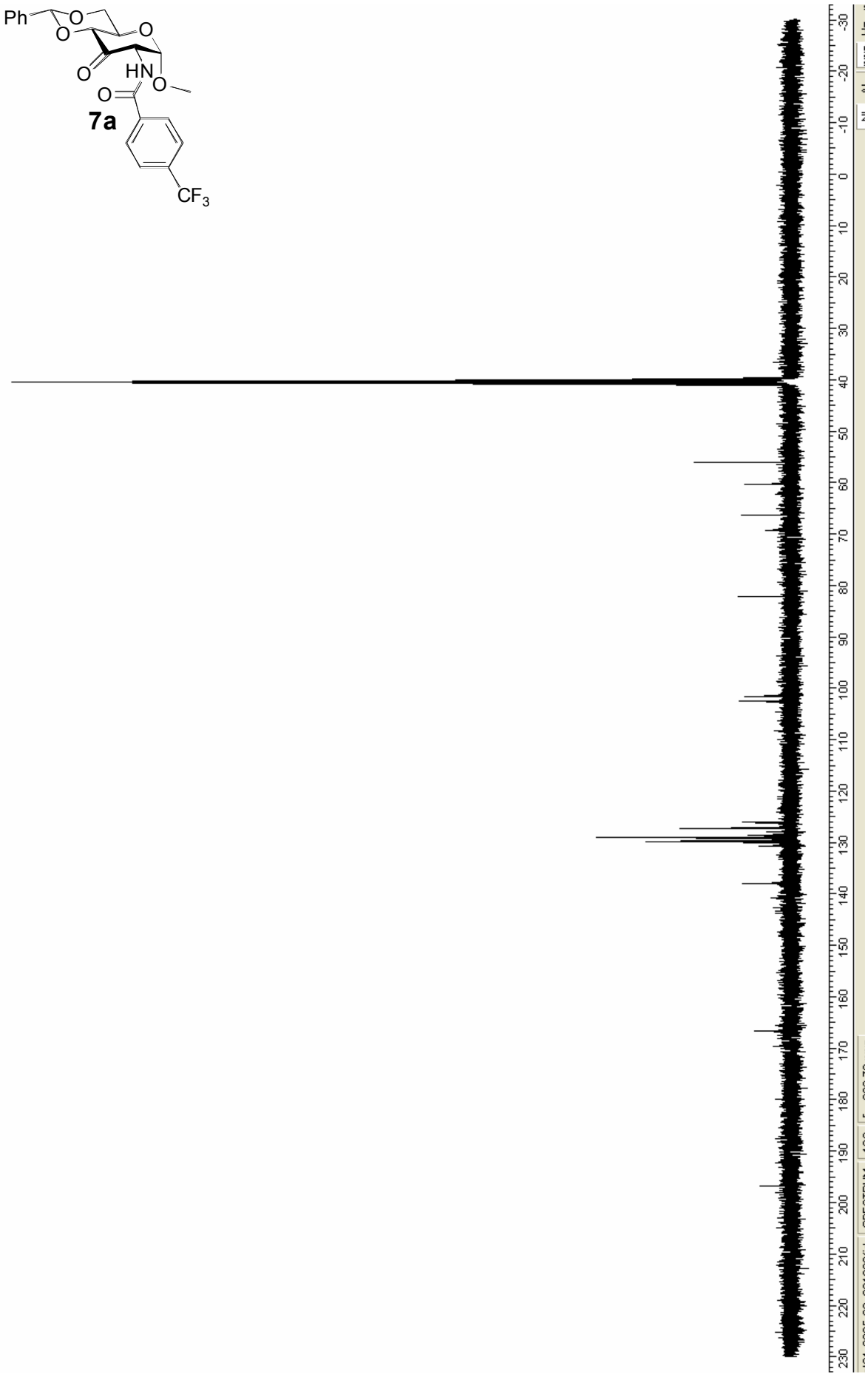
Supplementary Information



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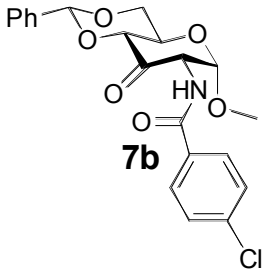
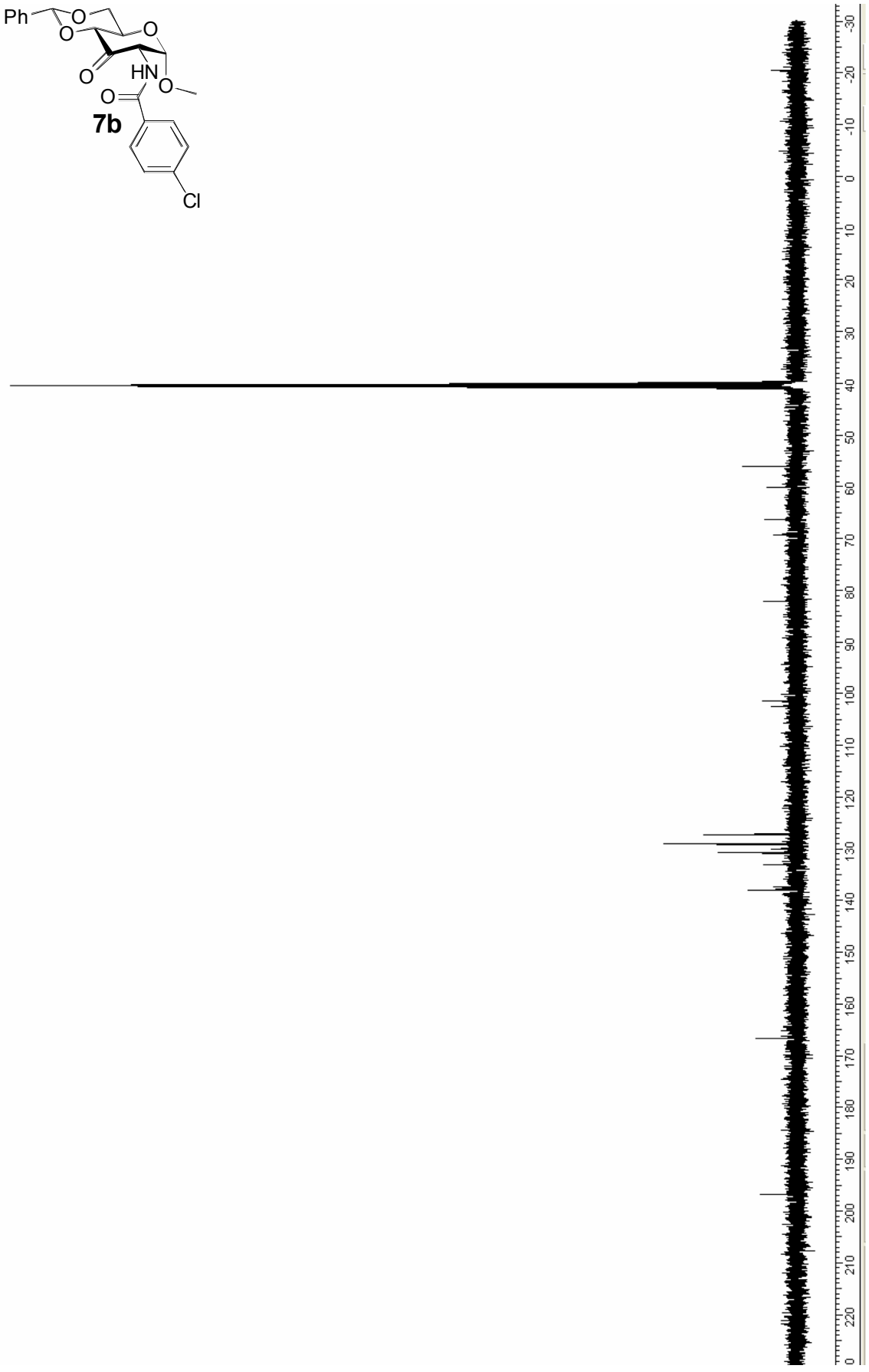


7b

Supplementary Information



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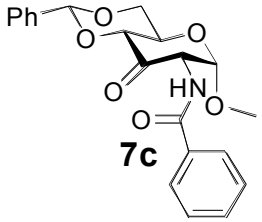

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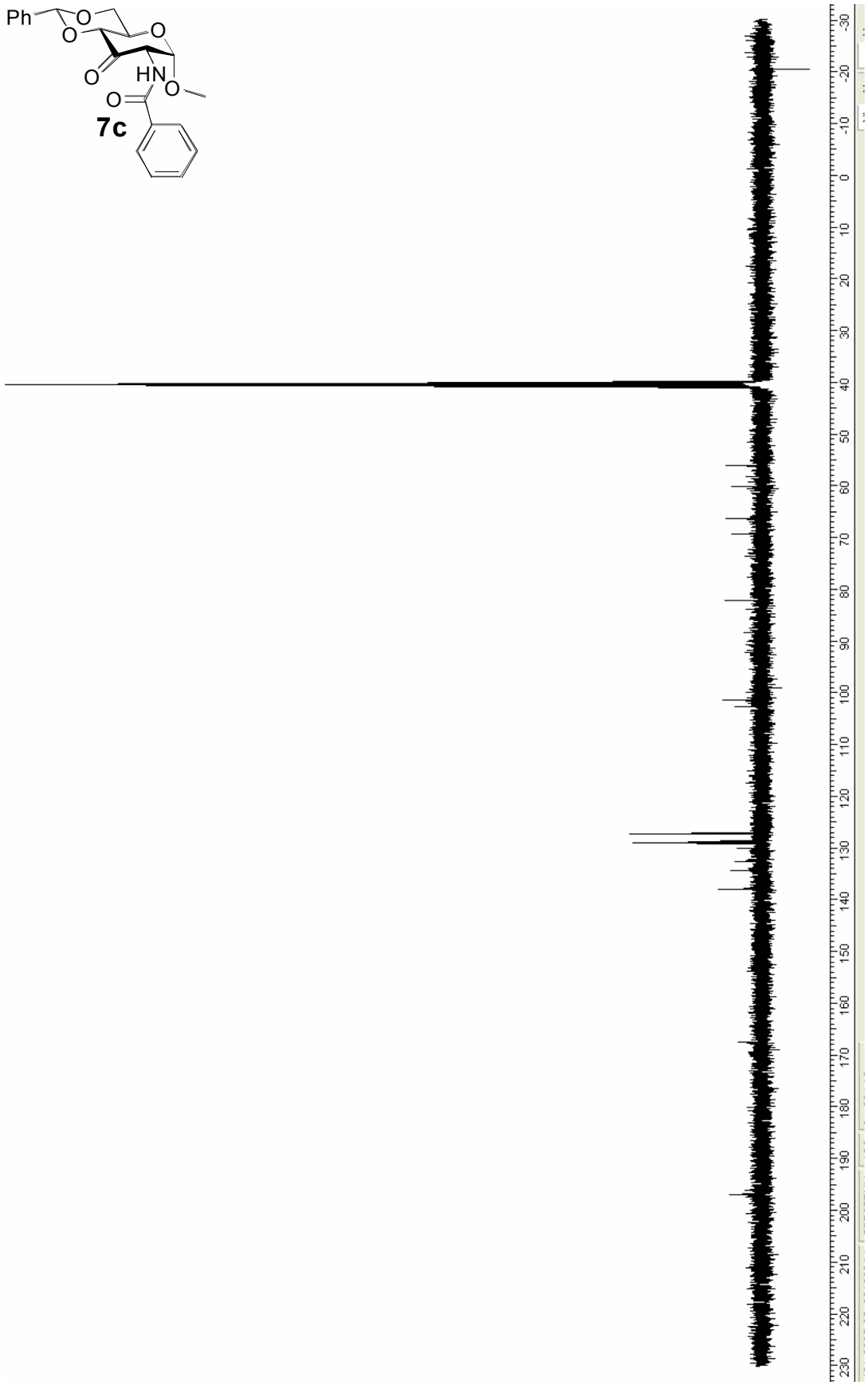

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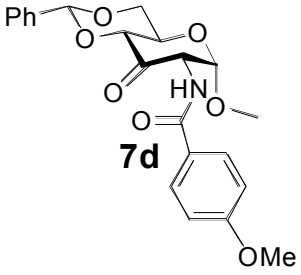

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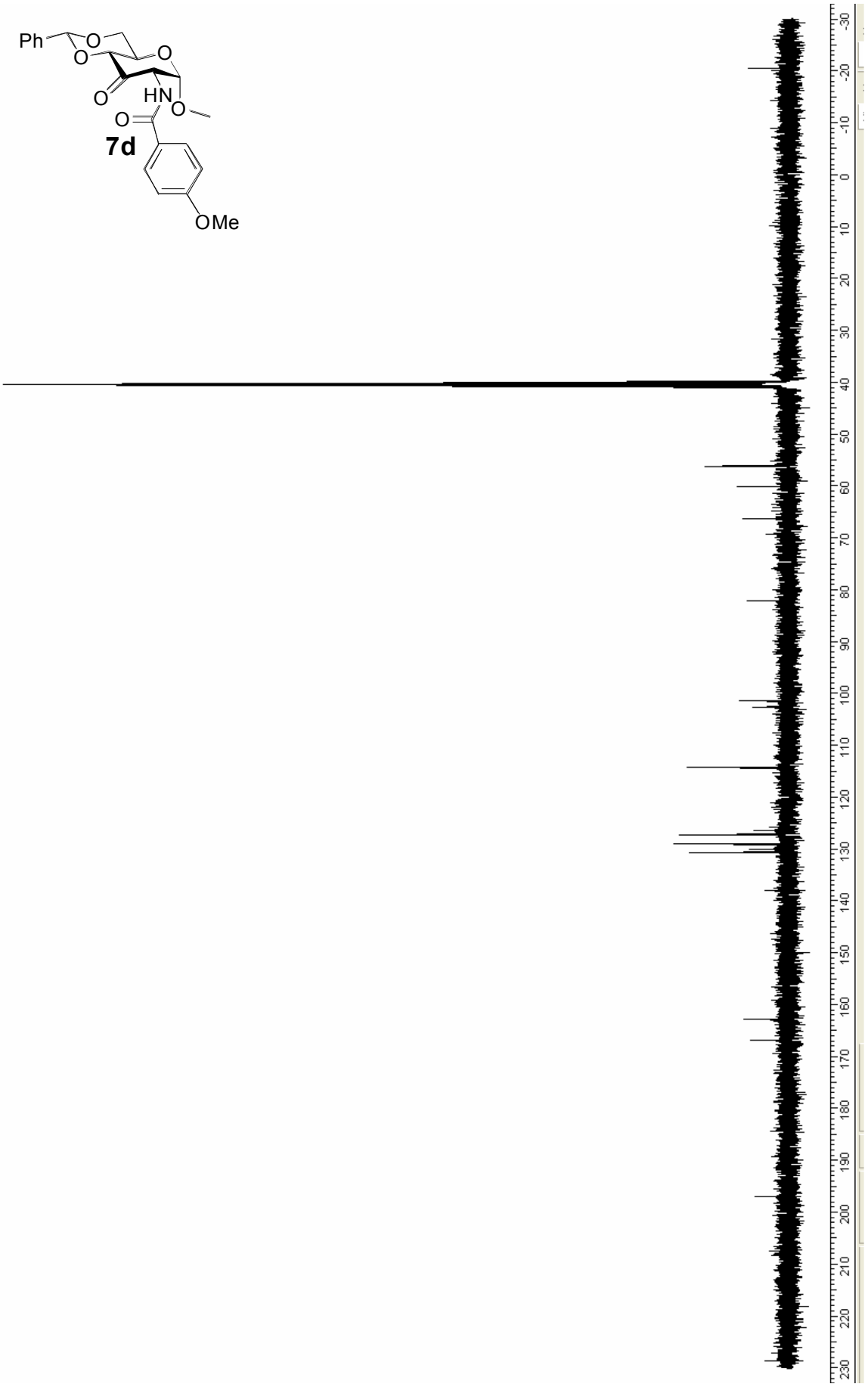

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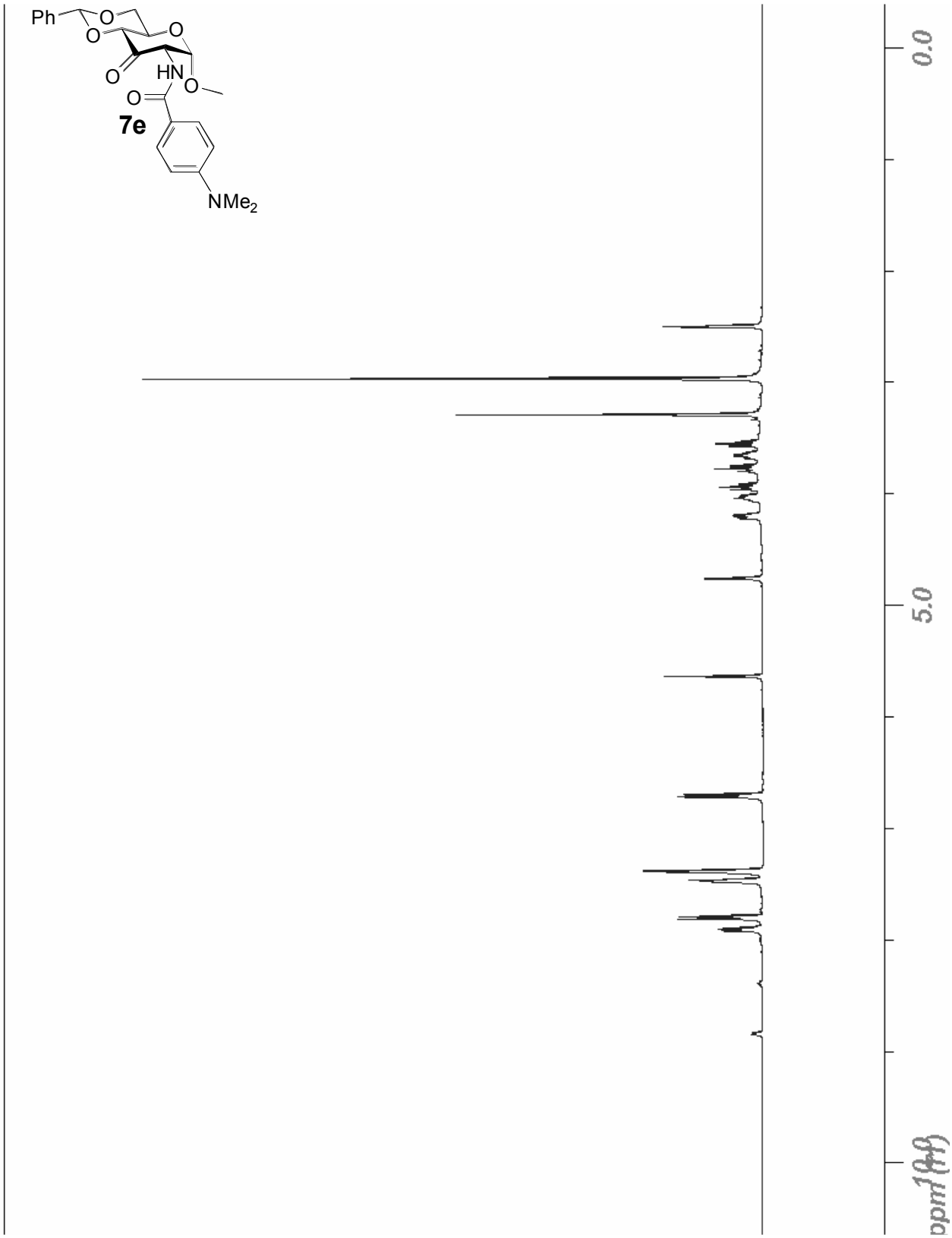

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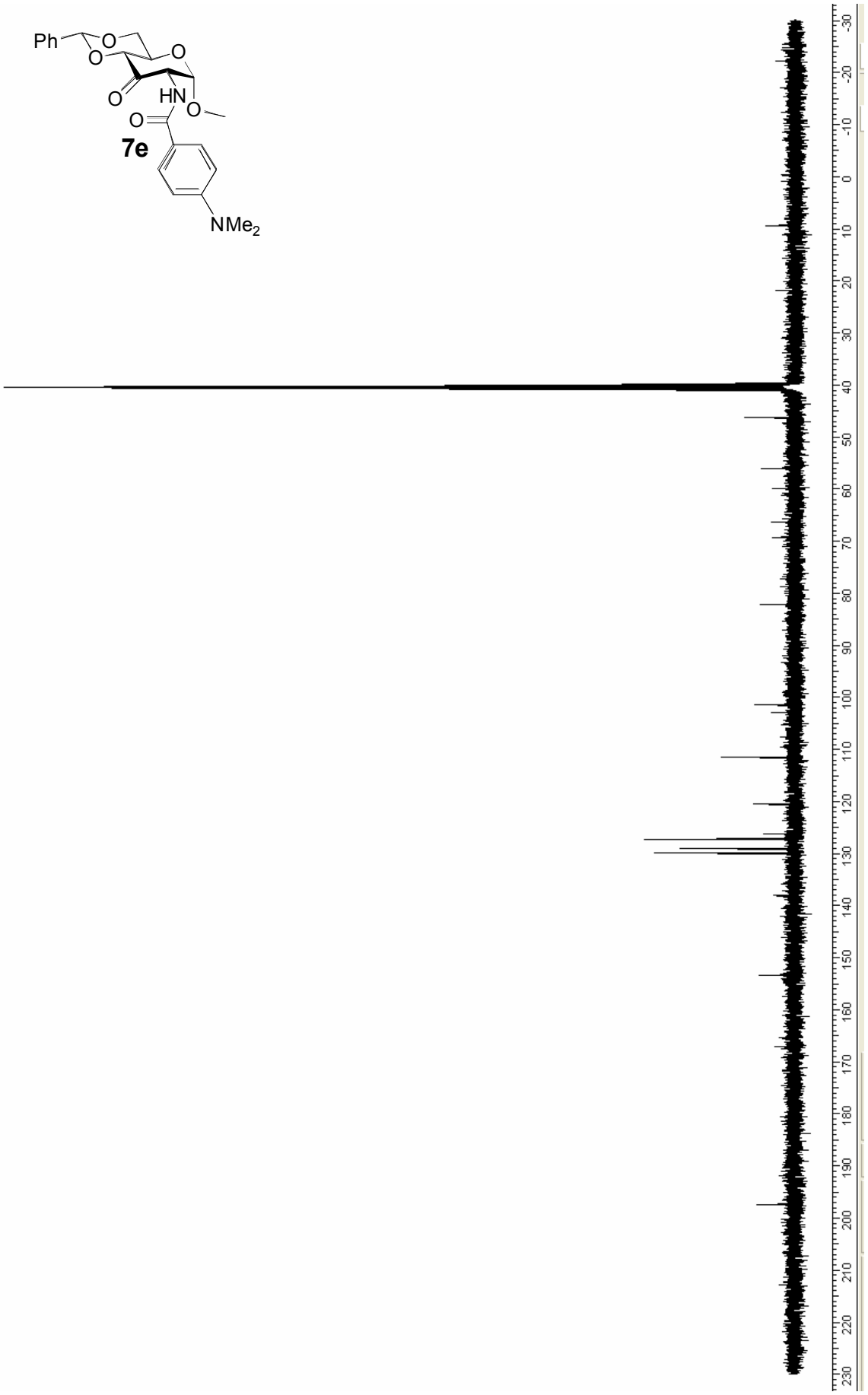

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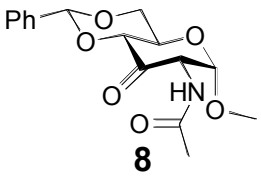

8

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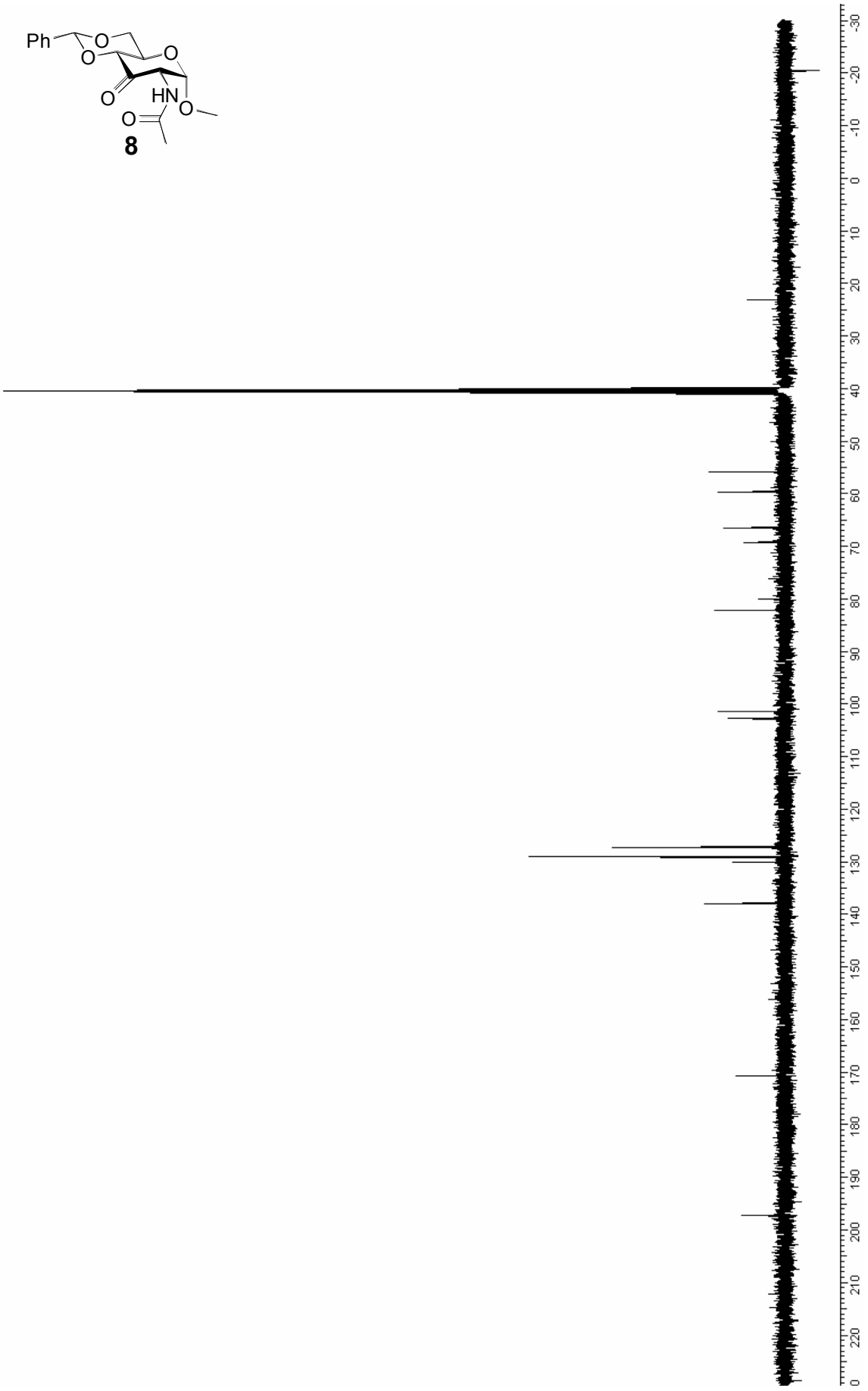

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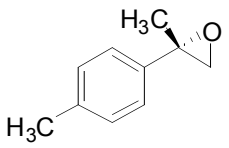

25

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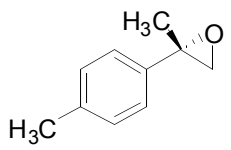

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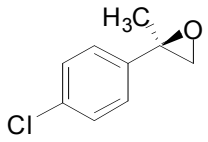

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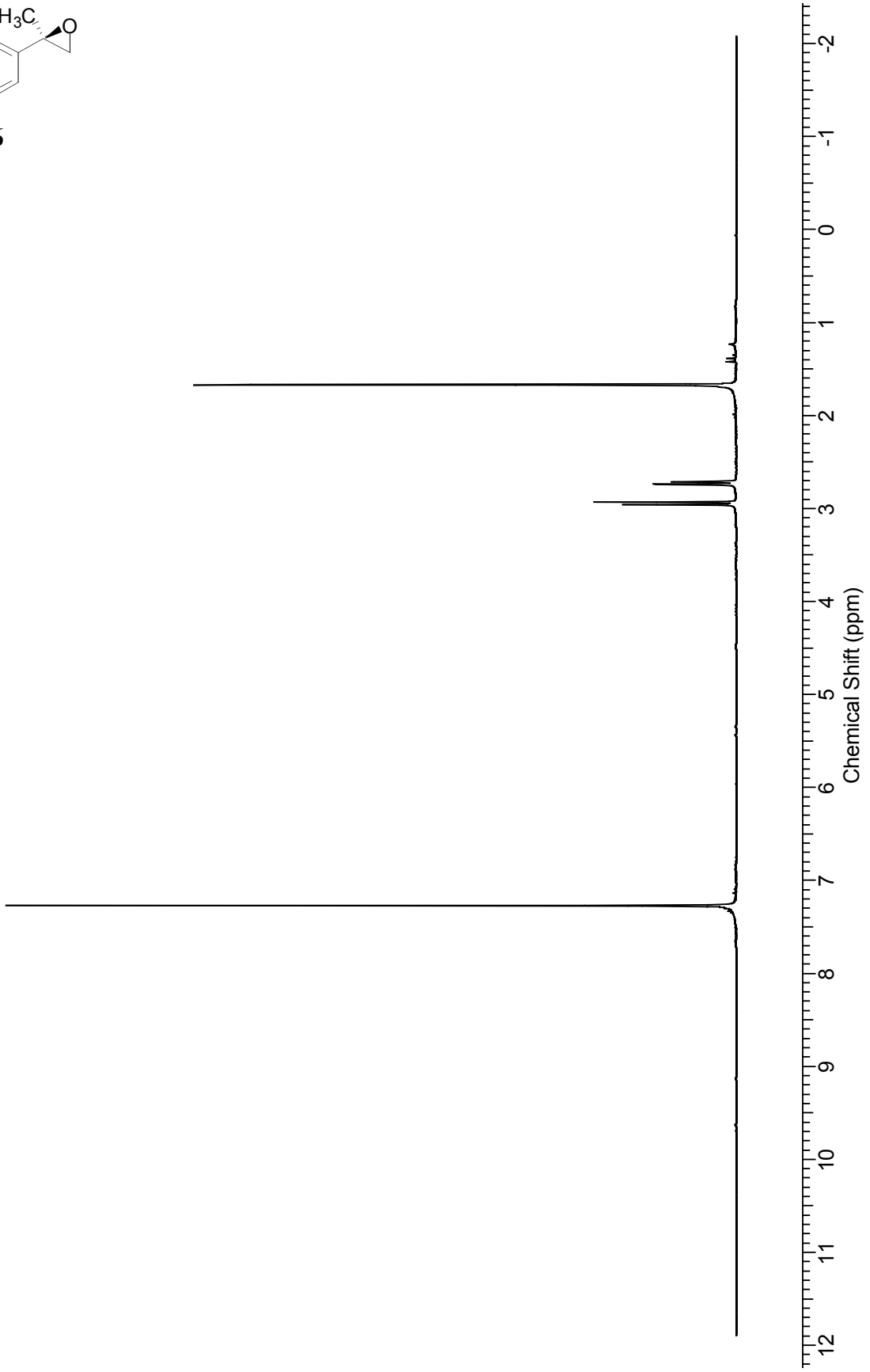

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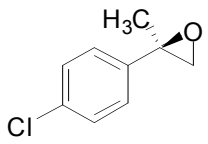

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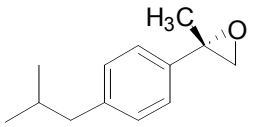

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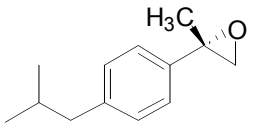
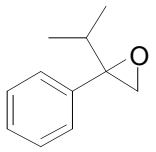


27

Supplementary Information



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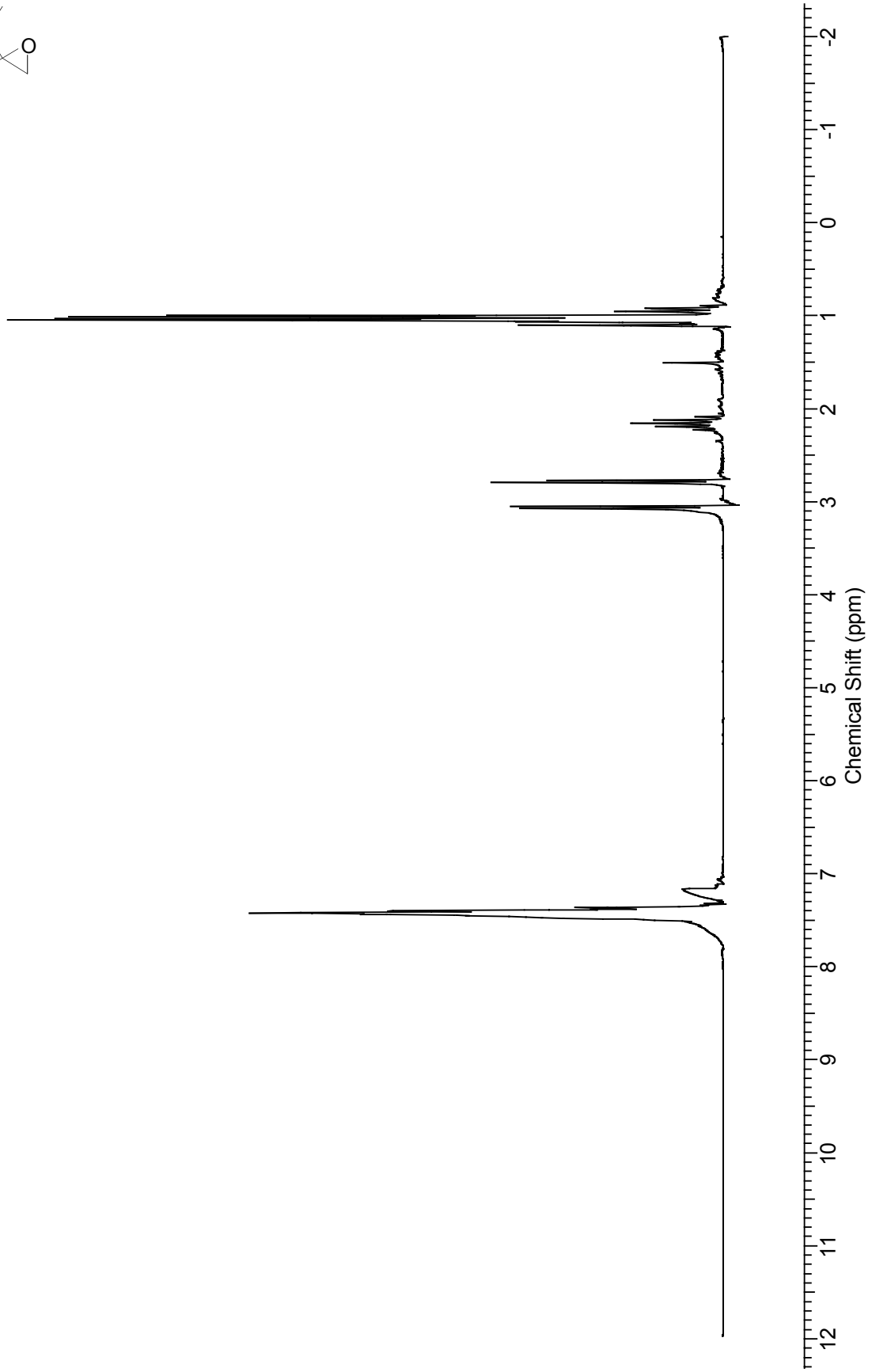

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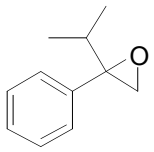

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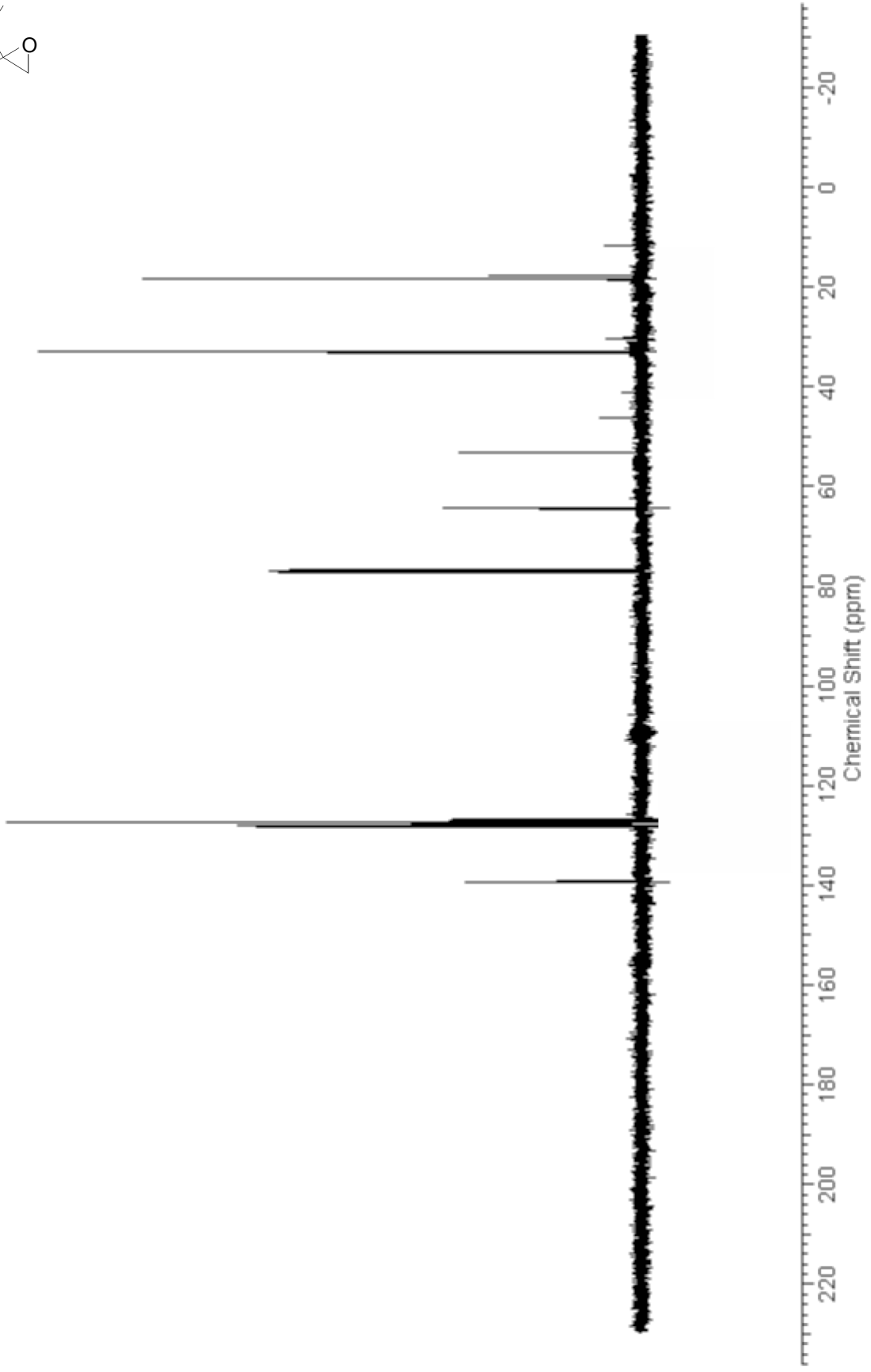

Supplementary Information

7. The origin of enantioselectivity in the epoxidation of 2,2-disubstitued terminal olefins

In order to rationalise the enantioselectivity observed in the epoxidation of 2,2-disubstituted terminal olefins with ketones **7a**–**e** and **8**, and in particular the switch of the *p*-chloro-*α*-methylstyrene oxide configuration (*R*-enantiomer) when compared with the other *p*-substituted derivatives (*S*-enantiomer in all cases), we proposed a qualitative model based on the transition state theory developed by Shi.[15] The analysis of the stereoselectivity of the product epoxides would provide the opportunity for further understanding of the interactions occurring in the hypothetical transition state that is commonly proposed for those types of oxygen transfer reactions. Key aspects of the origin of the enantioselectivity can be summarized as follows:

(1) The chiral dioxirane derived from *N*-acetyl-D-glucosamine has two diastereomeric oxygens (Figure ESI 1). The alkene would approach the least-hindered equatorial oxygen (in red) of the dioxirane due to the presence of an *α*-OMe group which would prevent the attack on the axial oxygen (in blue).

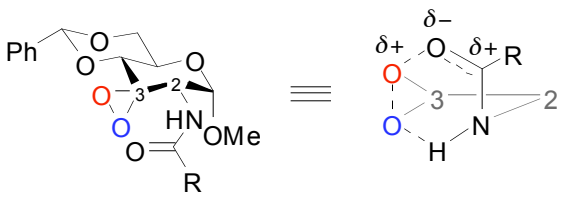

Figure ESI 1 Putative dioxirane catalyst derived from *N*-acetyl-D-glucosamine and its interactions between dioxirane at C-3 and carboxamide at C-2.

(2) In our choice of dioxirane catalyst, we considered that the use of an *α*-substituent with the potential to act as Lewis base (C-2 carboxamide) would allow scope for wide-ranging tuning of a putative dioxirane at C-3 through substituent (R) alteration (Figure ESI 1). A Hammet study of the selectivity further revealed an electrophilic character consistent with differential development of greater partial positive charge within the amide during the more diastereoselective epoxidation modes as predicted in the model.

Supplementary Information

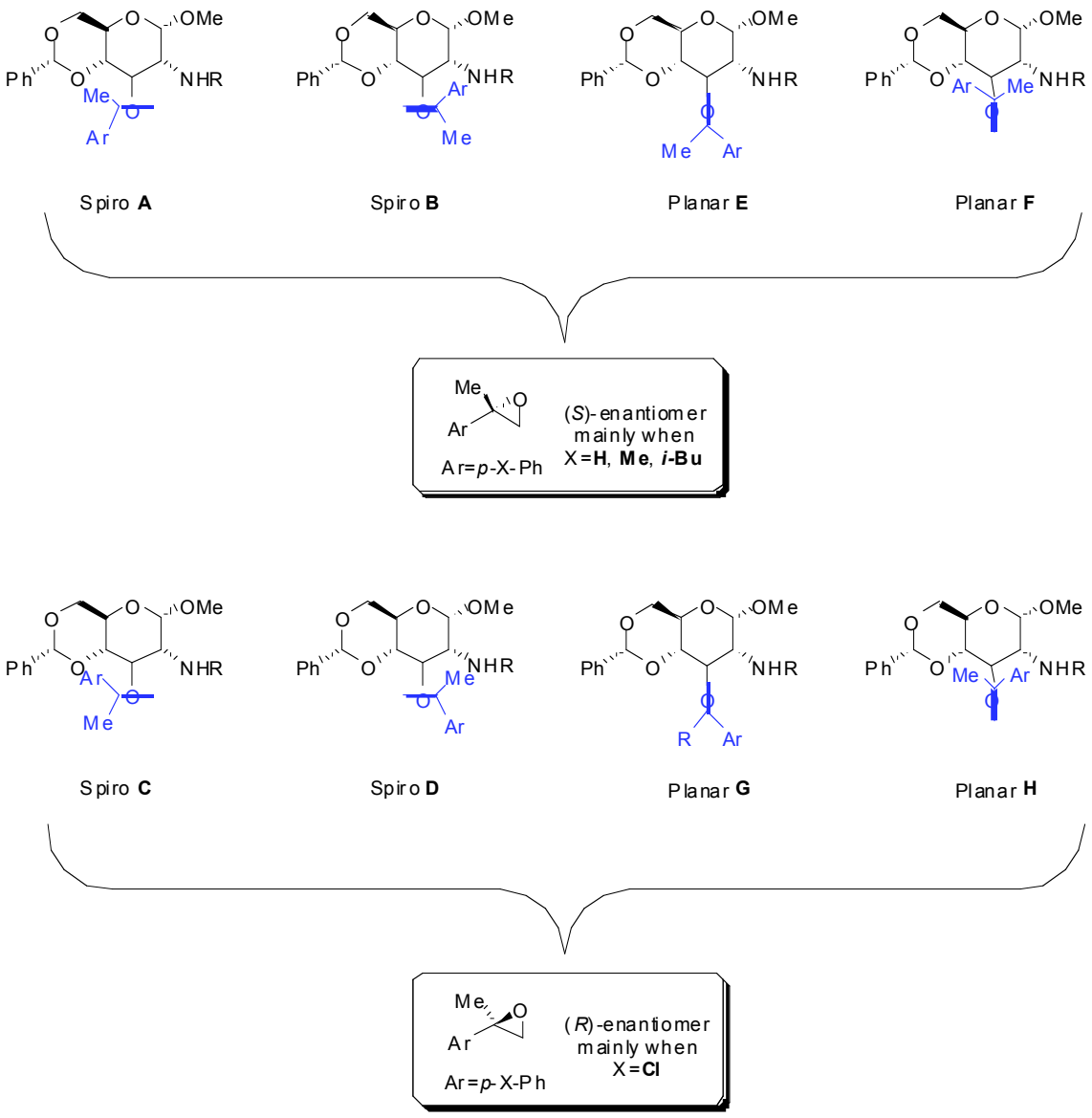

Figure ESI 2 Proposed spiro and planar transition states for the epoxidation of 2,2-disubstituted terminal olefins.

(3) In analogy to the model reported by Shi,[16] the proposed spiro **A**–**D** and planar **E**–**F** transition states for the epoxidation of 2,2-disubstituted terminal olefins with ketones **7a**–**e** and **8** are shown in Figure ESI 2. Spiro and planar are the two transition state geometries proposed for dioxirane-mediated epoxidations. Recent experimental and theoretical mechanistic studies[17] on the origin of high enantioselective epoxidation reactions with carbohydrate-based ketones have consistently supported a preference for a

spiro transition state over the planar transition state. Moreover, these studies predict that the observed major enantiomer results from an asynchronous spiro transition state, whereas the minor enantiomer arises from a different transition state geometry than a pure spiro or planar disposition, which is twisted from the plane of the dioxirane, therefore increasing its asynchronicity.

(4) The preference of the spiro transition state can be rationalized by using the frontier molecular orbital theory (FMOT). Although the primary frontier orbital interaction for both spiro and planar approaches is between the highest occupied molecular orbital (HOMO) of the alkene (π of C=C) and the lowest unoccupied molecular orbital (LUMO) of the dioxirane (σ* of O–O), the large spiro preference is attributed to the stabilizing secondary orbital interaction between the oxygen non bonding orbital (n) and the π^* orbital of the alkene in the spiro transition state structure.[8,18] This stabilizing orbital interaction cannot be achieved geometrically in the planar transition state.

(5) Based on the above model, a detailed analysis of the transition states geometries (Figure ESI 2) showed that among possible spiro and planar transition states for the epoxidation with ketone **8**, spiro transition states **A**–**D** might be electronically favored over the planar transition states **E**–**F**. Because spiro transition states **A** and **B** result in opposite configurations of the epoxide product when compared with **C** and **D**, factors influencing the competition of these two transition states would consequently affect the enantioselectivity of the epoxidation.

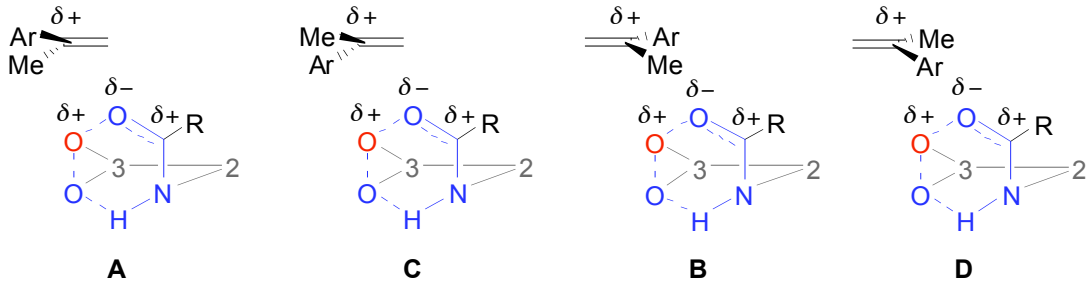

Figure ESI 3 Putative dipolar interactions between the dioxirane catalyst and the olefinic system in the spiro transition state for the epoxidation of 2,2-disubstituted terminal olefins.

(6) Another factor that might be contributing to the enantioselectivity is a putative dipolar interaction between the dioxirane catalyst and the olefinic system due to the partially positive charge developed in the C=C at the transition state (Figure ESI 3). This interaction would probably force the olefin to adopt the conformation that favours spiro transition states **B** and **D** over **A** and **C** or vice versa, depending on the electronic variations on aryl substituents of the olefin. In addition, these substituents also modify the energetic potential of the HOMO which decreases the energy gap between the LUMO of the electrophile and the HOMO of the nucleophile, thus facilitating the reaction between the two systems.[19] However, none of the spiro transition states **A**–**D** might be discarded by assuming pure electrostatic interactions since other nonbonding interactions such as van der Waals and hydrophobic repulsions/interactions between the olefinic system and the group at C-2 (R) may also occur in the transition state.[20]

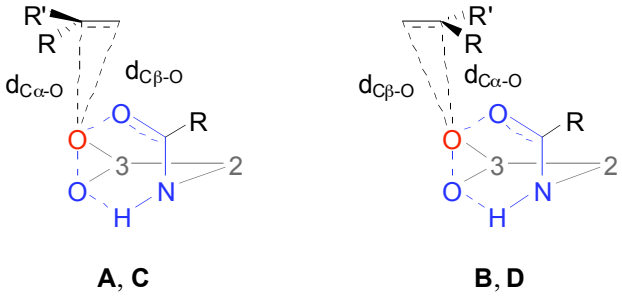

Figure ESI 4 Model for the correlation of transition state geometries with electronic parameters on the olefinic system for the epoxidation of 2,2-disubstituted terminal olefins.

(7) As already mentioned before, epoxidations with dioxiranes have spiro transition states which involve asynchronous oxygen transfer where $d_{C\alpha-O} \neq d_{C\beta-O}$ (Figure ESI 4). The asynchronicity increases with greater electron-withdrawal or electro-donation by the aryl substituent on the olefin. Furthermore, systems with electron-withdrawing groups (EWG) react in an earlier (educt-like) transition state, whereas systems with electron-donating substituents (ED) react in a later (product-like) transition state. These arguments directly correlate with distance (d_{C-O}) between the atoms involved in the formation of the new C–O bond and, ultimately, enantioselectivity.[17b,21] A late transition state (*e.g.* with ED groups such as Me, *i*-Bu) requires a certain proximity between the olefin and the chiral

environment of the dioxirane catalyst. This leads to a reduction of the distance (d_{C-O}) between olefin and catalyst and therefore, an enhanced differentiation of diastereomeric transition structures (ee increases). The opposite situation occurs in an early transition state (*e.g.* with EWG groups such as Cl) in which the proximity between the two reacting species decreases leading to a diminished interaction between the olefinic system and the chiral environment of the catalyst (ee decreases and eventually changes to the opposite enantiomer). Therefore, the asynchronicity of transition states for unsymmetrical reactants has a significant impact on steric interactions at the transition state.[17b] The steric interactions due to proximity to the catalyst increases either in one direction (*R*-enantiomer) or in the opposite one (*S*-enantiomer) depending on the asynchronicity which directly correlates with the substituents present on the olefinic system.

Finally, in view of the above arguments, we hypothesized that spiro **A**–**D** might be the major transition states for the epoxidation of α-methylstyrene derivatives based on the *S* configuration (X=H, Me, *i*-Pr) and the *R* configuration (X=Cl) of the resulting epoxides. However, this is only a qualitative model which attempts to rationalize experimental data and the origin of this enantioselectivity switch[22] is still unclear.

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[20] Previous studies have shown that the enantioselectivity afforded by carbohydrate-derived ketones results from an apparent attractive interaction between the R_π

group of the olefin and the spiro-oxazolidinone of the ketone catalyst, see: ref.[15].

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