Furanyl Cyclic Ethers: Single and Double Diastereoselectivity in the Synthesis of 2,4-di and 2,4,5-tri-substituted tetrahydropyrans.

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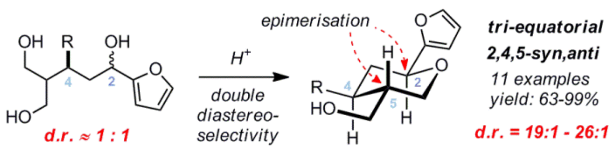
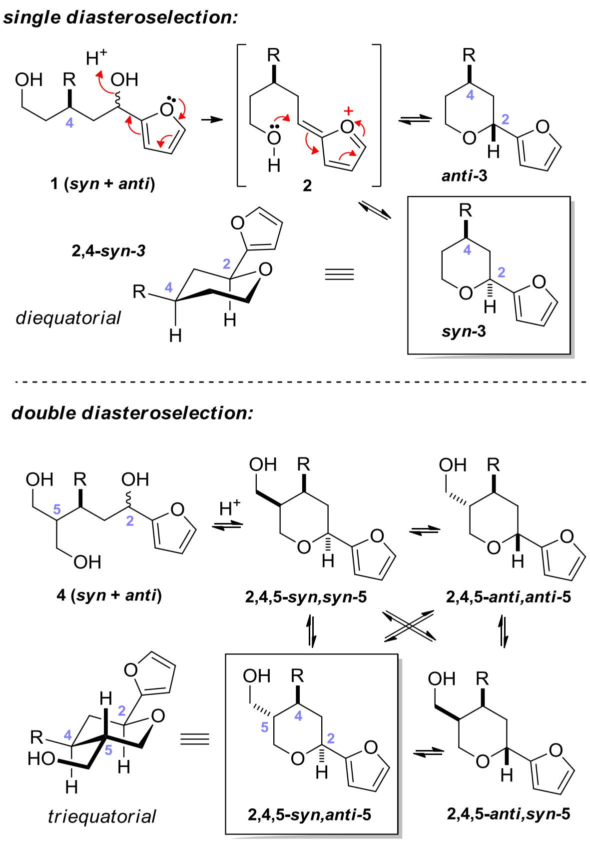


ABSTRACT: Combining the desymmetrization of a prochiral bis-hydroxymethyl group with the epimerization of a chiral furanyl ether in a single transformation, high levels of double diastereoselectivity have been achieved in a synthesis of 2,4,5-trisubstituted tetrahydropyrans which proceeds under thermodynamic control.

Introduction

The tetrahydropyran moiety is found in a large number of biologically active natural and non-natural products and can rightly be classed as a privileged scaffold.[1] Examples include zincophorin (ionophore antibiotic)[1a], sorangicin-A (antibiotic)[1b], polycarvernoside-A (algal toxin)[1c], the bryostatins (cytotoxins)[1d,e], salinomycin (coccidiostat ionophore)[1f,g], halichondrin-B (cytotoxin)[1h], eribulin (simplified synthetic analogue of halichondrin-B and clinical cancer chemotherapeutic)[1i], swinholide-A (actin-binding cytotoxin)[1j] and the tubulexins (modulators of mitosis)[1k]. Due to the importance of these and other compounds, the development of new stereoselective methodologies for tetrahydropyran construction has been, and continues to be, the focus of intense research activity.[2] Building on our previous research into the use of epimerizable furanyl ethers in cyclic scaffolds,[3] we here report the diastereoselective formation of 2,4-*syn*-disubstituted tetrahydropyrans and the doubly diastereoselective formation of 2,4,5-*syn*,*anti*-trisubstituted tetrahydropyrans. Our conceptual plan is outlined in Scheme 1.

Scheme 1: Conceptual Outline

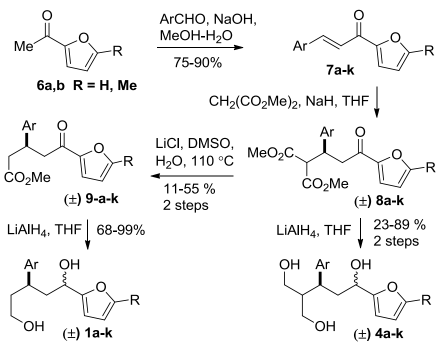


Using the ability of 2-furanyl ethers to epimerize under acidic conditions (via furanyl cations, **2**),[4] we reasoned that a suitably placed substituent at the 4 position of a tetrahydropyran formed through the reversible cyclization of either diastereisomer of diol **1** would favor formation of the 2,4-*syn* product ***syn*-3**. This would place both the 4-substituent and the furanyl group in favored equatorial positions on a chair conformation. Each diastereisomer of diol **1**, present as a diastereisomeric mixture, would thus be converted to the same product diastereisomer, irrespective of the original C-2/C-4 stereochemical relationship. Building on this basic idea, the inclusion of a second hydroxymethyl group at C-5 would provide a prochiral bis(hydroxymethyl) center in **4** that would undergo desymmetrization[5] upon cyclization by the same reversible mechanism. The primary alcohol selected for inclusion in the tetrahydropyran ring would be such that the remaining uncyclized hydroxymethyl group at C-5 was left in an equatorial position.

Under thermodynamic conditions, ***syn-anti*-5**, in which all substituents are in equatorial positions, would accordingly be favored. The chiral center at C-4 would thus control the configuration at both C-2 and C-5 (Scheme 1). In addition to facilitating the key cyclization/epimerization mechanism, the furan moiety is also synthetically versatile and can be converted into a number of useful functional motifs (e.g. oxidative cleavage to the carboxylic acid[6a], Achmatowicz-type oxidations[6b], hydrogenation[6c] to the tetrahydrofuran, Diels-Alder cycloadditions[6d], [4+3] cycloadditions[6e] etc).

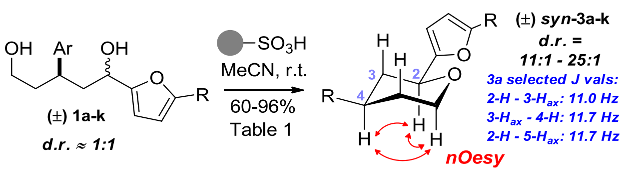
Results and Discussion

Scheme 2: Synthetic Route to Diol and Triol Substrates



Our investigation began with the synthesis of diol substrates **1a-k** (Scheme 2). Claisen-Schmidt aldol condensation of either 2-acetylfuran **6a** or 5-methyl-2-acetyl furan **6b** with a series of substituted benzaldehydes (which avoid self-aldol condensation) afforded the enones **7a-k**, from which Michael addition of dimethylmalonate furnished the keto-diesters **8a-k**. Subsequent Krapcho decarboxylation led to the ketoesters **9a-k**, which were purified by column chromatography. $LiAlH_4$ reduction provided the diols **1a-k** (formed as approximately 1:1 diastereisomeric mixtures) which were used without chromatographic purification.

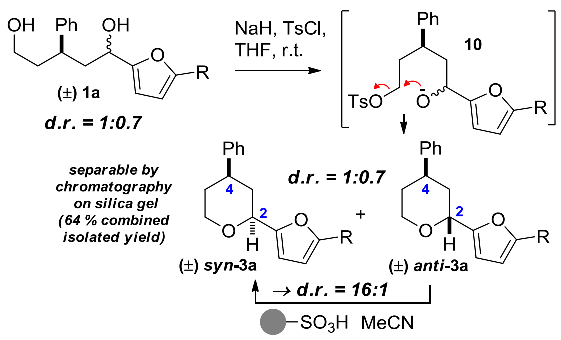
Table 1: Diol Cyclization Results.



Entry	Ar	R	Diol (d.r.)	Yld	Prod (d.r.)
1	C_6H_5	H	**1a** (1:0.7)	76 %	**3a** (16:1)
2	4-C_6H_4-Cl	H	**1b** (1:0.75)	80 %	**3b** (21:1)
3	4-C_6H_4-Cl	H	**1b** (4:1)	76 %	**3b** (19:1)
4	4-C_6H_4-Cl	H	**1b** (1:6)	78 %	**3b** (20:1)
5	4-C_6H_4-OMe	H	**1c** (1:0.75)	60 %	**3c** (11:1)
6	4-C_6H_3-Me	H	**1d** (1:0.74)	83 %	**3d** (20:1)
7	3,4-C_6H_3-$(OMe)_2$	H	**1e** (1:0.8)	95 %	**3e** (20:1)
8	4-C_6H_4-Br	H	**1f** (1:0.76)	96 %	**3f** (12:1)
9	2,4,5-C_6H_2-$(OMe)_3$	H	**1g** (1:0.65)	93 %	**3g** (25:1)
10	4-C_6H_4-Br	Me	**1h** (1:0.67)	70 %	**3h** (21:1)
11	C_6H_5	Me	**1i** (1:0.65)	88 %	**3i** (18:1)
12	4-C_6H_4-CH_3	Me	**1j** (1:0.7)	86 %	**3j** (19:1)
13	4-C_6H_4-Cl	Me	**1k** (1:0.75)	68 %	**3k** (20:1)

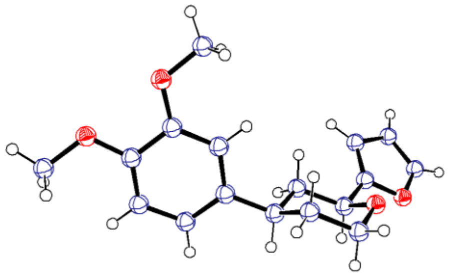
With these diols in hand we investigated their acid catalyzed cyclizations. A brief screen of solvents and acids identified acetonitrile and polymer supported sulfonic acid as satisfactory, combining clean and rapid cyclization/epimerization with ease of workup (Table 1). Initial investigation focused on phenyl substrate **1a**. The cyclization reaction itself was relatively rapid. Loss of starting material was almost complete after 10 minutes (as judged by TLC and NMR analysis of an aliquot). The initial ratio of *syn* and *anti* diastereomers ***syn*-3a** and ***anti*-3a** at this time was 2.2:1. After 10 hours, a diastereomeric ratio of 16:1 was obtained. Analysis of chemical shifts, coupling constants and NOESY correlations in the ^{1}H NMR spectra indicated that the major product was the ***syn*-3a** diastereomer. Using the same conditions, the cyclization reaction was carried out on a series of diol substrates **1a-k** to afford the 2,4-*syn* tetrahydropyran products **3a-k** in high yields and with diastereoselectivities ranging from 11:1 to 25:1 (Table 1). Adventitiously, we found that careful chromatography of *para*-chloro diol **1b** afforded diastereomerically enriched samples, both of which cyclized to essentially the same ratio of tetrahydropyran diastereisomers as the original 1:0.75 mixture (Table 1, entries 2-4). Pleasingly, tetrahydropyrans ***syn*-3e** and ***syn*-3g** formed crystals from which we were able to obtain X-ray structures, confirming the stereochemistry (Figure 1, ***syn*-3g** structure in *Supp Info*.) To explore our mechanistic hypothesis, and to obtain more of the minor diastereisomer for NMR analysis, we carried out the cyclization under base mediated conditions (Scheme 3). Treatment of the 1:0.7 *syn/anti* diastereisomeric mixture of diols **1a** with NaH and toluenesulfonyl chloride led to the formation of tetrahydropyrans ***syn*-3a** and ***anti*-3a** in the same 1:0.7 diastereomeric ratio, presumably via **10**.

Scheme 3: Base Promoted Cyclization (Avoiding Epimerization).



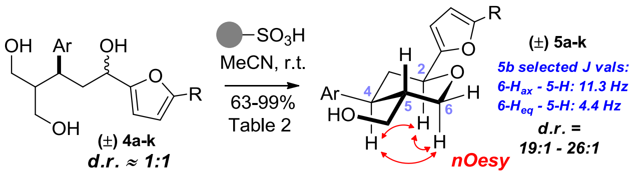
It is therefore unlikely that stereochemical equilibration at the furanyl center occurs under these basic conditions. ***Syn*-3a** and ***anti*-3a** could be separated (at length) by careful column chromatography. The 2,4-*anti* diastereomer had an identical ^{1}H NMR spectrum to the minor component from the acid catalyzed cyclization. The isolated ***anti*-3a**, when exposed to the polymer supported sulfonic acid resin in acetonitrile, was cleanly converted to ***syn*-3a**, consistent with the proposed mechanism. Having established that the C-4 substituent could exert control of the configuration at C-2, we next investigated simultaneous control over the 2 and 5 positions.

Figure 1. X-Ray Structure of ***syn*-3e** (Thermal Ellipsoids Drawn at 50%)



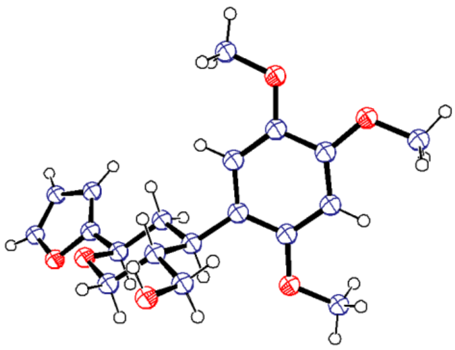
$LiAlH_4$ reduction of ketodiesters **8a-k** afforded triols **4a-k** (Scheme 2). Using the same acidic conditions established for the diol substrates, cyclization of triol **4a** (d.r.=1:0.8) proceeded smoothly and, after equilibration, the product **5a** was formed in high yield and with high diastereoselectivity. The two major diastereomers were formed in a ratio of 26:1. Similar results were also obtained for a number of other triol substrates, present as approximately 1:1 mixtures of diastereomers (Table 2). In each case, key NMR signals for major and minor diastereomers closely mirrored those of **5a**. ^{1}H NMR coupling constants, chemical shifts and NOESY correlations were consistent with the major products having 2,4,5-*syn,anti* stereochemistry with all substituents in equatorial positions, as predicted. This was confirmed by single crystal X-ray analysis of ***syn,anti*-5g** (Figure 2). The main observable minor diastereomer had a significantly higher chemical shift for the C-2 hydrogen, consistent with an equatorial orientation, indicating that this diastereomer was epimeric at the furanyl ether center. Although the reaction was clearly very diastereoselective, we sought clarity as to the nature and distribution of all minor diastereomers (several NMR peaks of which were dwarfed and obscured by those of the major product).

Table 2. Triol Cyclization Results.



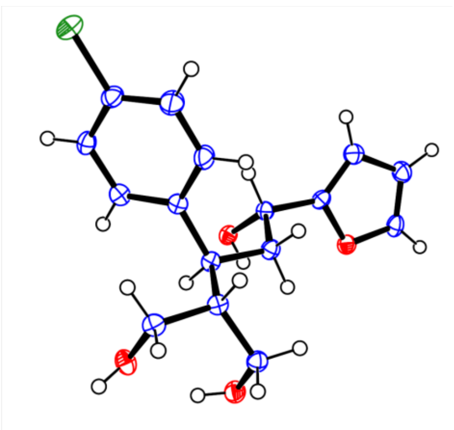
Entry	Ar	R	Triol (d.r.)	Yld	Prod (d.r.)
1	C_6H_5	H	**4a** (1:0.8)	99%	**5a** (26:1)
2	4-C_6H_4-Cl	H	**4b** (1:0.8)	95%	**5b** (21:1)
3	4-C_6H_4-Cl	H	***anti*-4b**	92%	**5b** (21:1)
4	4-C_6H_4-Cl	H	***syn*-4b**	94%	**5b** (21:1)
5	4-C_6H_4-OMe	H	**4c** (1:0.65)	87%	**5c** (20:1)
6	4-C_6H_3-Me	H	**4d** (1:0.75)	89%	**5d** (25:1)
7	3,4-C_6H_3-$(OMe)_2$	H	**4e** (1:1)	89%	**5e** (24:1)
8	4-C_6H_4-Br	H	**4f** (0.8:1)	86%	**5f** (20:1)
9	2,4,5-C_6H_2-$(OMe)_3$	H	**4g** (1:0.5)	96%	**5g** (20:1)
10	4-C_6H_4-Br	Me	**4h** (1:0.6)	63%	**5h** (19:1)
11	C_6H_5	Me	**4i** (1:0.5)	84%	**5i** (20:1)
12	4-C_6H_4-CH_3	Me	**4j** (1:0.6)	75%	**5j** (21:1)
13	4-C_6H_4-Cl	Me	**4k** (1:0.6)	87%	**5k** (20:1)

Figure 2. X-ray structure of **2,4,5-*syn,anti*-5g** (thermal ellipsoids shown at 50%)



Chromatographic isolation of minor diastereomers eluded our efforts. Fortuitously, we found that the *anti* diastereomer of the *para*-chloro triol compound, ***anti*-4b**, was crystalline whilst ***syn*-4b** was an oil. This discovery suggested a possible means of accessing all four possible cyclization products and, by comparison of spectra, of determining the product distribution obtained during the triol cyclization. At length, repeated cycles of recrystallization from ethyl acetate furnished useful quantities of the diastereomerically pure triols, ***anti*-4b** and ***syn*-4b**. In addition to facilitating this separation, the crystalline nature of ***anti*-4b** provided, through X-ray crystallography, unambiguous determination of its relative stereochemistry (and therefore the relative stereochemistry of ***syn*-4b** also), Figure 3.

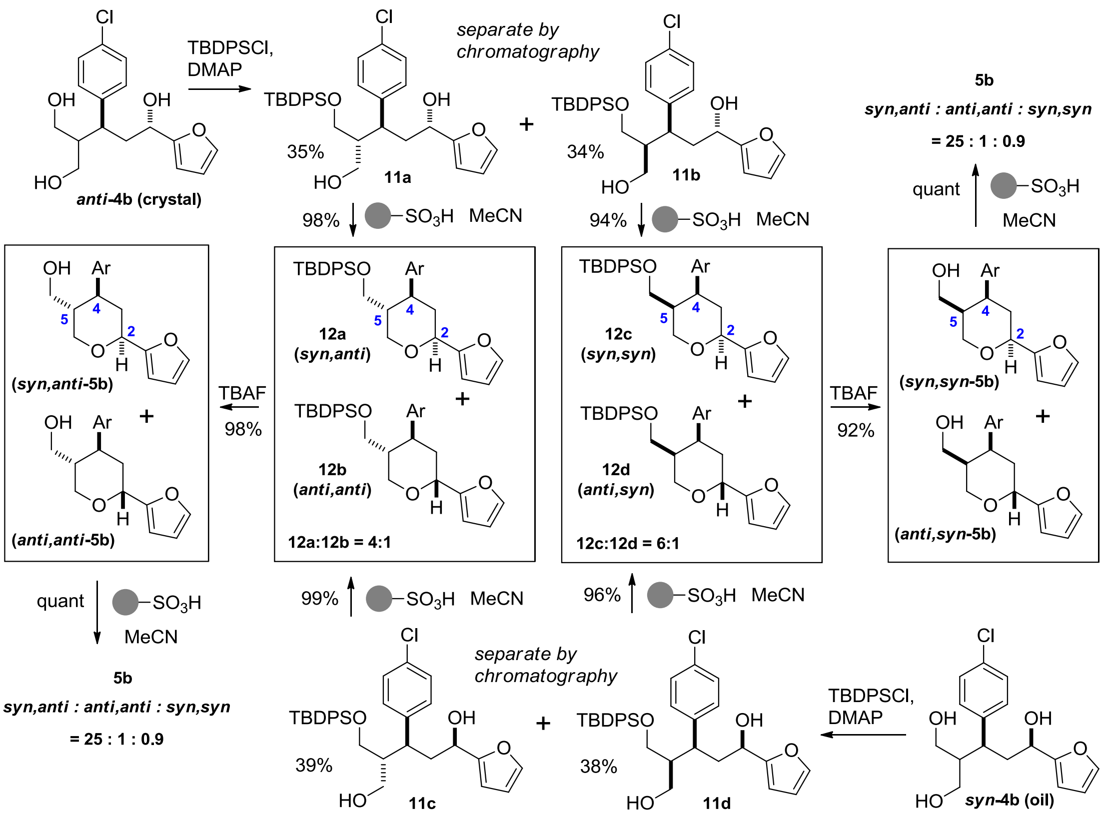
Figure 3. X-ray structure of ***Anti*-4b** (thermal ellipsoids at 50%)



Consistent with the proposed mechanism, either of these pure triol diastereomers, when exposed to the cyclization conditions, furnished the same 21:1 ratio of products as obtained from cyclization of the original 1:0.8 mixture of diastereomers (Table 2, entries 3 and 4). Triols ***anti*-4b** and ***syn*-4b** could be converted to the corresponding mixtures of mono-TBDPS ethers **11a,b** and **11c,d** where, in each case, the TPDPS ether was formed at one of the two primary alcohols (Scheme 4). The pair of mono-TBDPS ethers, **11a** and **11b**, were separated from each other by careful column chromatography on silica gel, as were **11c** and **11d**. Following their isolation, each of these diastereomerically pure diols was then independently cyclized under the established acidic conditions. With one hydroxymethyl group now tied up as a TBDPS ether, epimerization of the bis(hydroxymethyl) group was no longer possible, thus fixing the C-4/C-5 relative stereochemistry. Epimerization was limited to the furanyl center at C-2. As expected, the stereochemistry at the configurationally labile furanyl center in the starting material had no bearing on the stereochemical outcome of the reaction. Each diol **11a-d** produced only one of the two possible pairs of products (**12a,b** or **12c,d**), depending only on the C-4/C-5 relative stereochemistry. Thus, **11a** and **11c**, whose relative stereochemistries differ only at the C-2 furanyl alcohol, both afforded the same mixture of tetrahydropyrans **12a,b,** epimeric at C-2, in the same diastereomeric ratio. Likewise, when either **11b** or **11d** were cyclized, the same mixture of C-2 epimers **12c** and **12d** was formed. These cyclization reactions were left for only 3 hours in order to obtain observable NMR peaks for the minor products rather than attempt to achieve greater diastereoselectivity. In each pair, the ^{1}H NMR spectrum of the major component was consistent with having an axial hydrogen at C-2. Once the TBDPS groups of the **12a,b** and **12c,d** mixtures were removed, using TBAF, the NMR spectra of the resulting mixtures of alcohols ([***syn,anti*-5b** + ***anti,anti*-5b**] from **12a,b** and [***syn,syn*-5b** + ***anti,syn*-5b**] from **12c,d**) were compared with that obtained following the cyclization of triol **4b**. It was found that ***syn,anti*-5b**, ***anti,anti*-5b**, and

syn,syn*-5b** were present in the triol cyclization product, in a ratio of 25:1:0.9, whilst the remaining diastereomer, ***anti,syn*-5**, was not present at all. Interestingly, cyclization of either **11b** or **11d** to the mixture of products **12c,d** was also diastereoselective (d.r. = 6:1, unoptimized). Once the restraining TPDPS group was removed from each pair of tetrahydropyrans, acid catalyzed equilibration of either [syn,syn*-5b** + ***anti,syn*-5b**] or [***syn,anti*-5b** + ***anti,anti*-5b**] led cleanly to the same 25:1:0.9 mixture of diastereomers as obtained from cyclization of triol **4b** (Scheme 4).

Scheme 4. Stereochemical correlations



In conclusion, the formation of 2,4-disubstituted tetrahydropyrans occurs via a highly diastereoselective acid mediated cyclization-epimerization reaction which favors the 2,4-*syn* diastereomer capable of adopting the energetically favorable diequatorial chair conformation.

The reaction harnesses the propensity of the furanyl ether moiety to epimerize in the presence of a suitable acid catalyst, presumably via a furanyl cation intermediate. Extending the concept further, 2,4,5-trisubstituted tetrahydropyrans are also formed in a reaction which displays very high levels of double diastereoselectivity favoring the 2,4,5-*syn,anti* diastereomer.

Experimental Section

NMR spectra were recorded in $CDCl_3$, CD_3CN or CD_3OD solutions at room temperature with a 400 MHz spectrometer (400 MHz for ^1H, 100 MHz for ^{13}C) or a 300 MHz spectrometer (300 MHz for ^1H, 75 MHz for ^{13}C). $CDCl_3$ was stored over granular anhydrous potassium carbonate in a brown glass bottle. The ^1H and ^{13}C chemical shifts are reported relative to tetramethylsilane (0.0 ppm). Coupling constants (*J*-values) are reported in Hz. In a few instances, apodization was used to facilitate *J*-value determination. Protons coupling to two other non-identical protons but with identical coupling constants are generally referred to as doublets of doublets, rather than triplets (or apparent triplets). Assignment of peaks in the proton NMR spectra was carried out using chemical-shift values, coupling constants, COSY, TOCSY, HMBC and HSQC. Peak assignments given in the ^1H NMR data follow the numbering scheme used for THP rings in the manuscript (see diagrams in Supporting Information for details). Melting point temperatures are uncorrected. TLC analysis was carried out using silica gel impregnated with fluorescent indicator on aluminium backed plates. Plates were visualized either by UV fluorescence (254 nm) or by staining with acidic vanillin solution or alkaline potassium permanganate solution. Column chromatography was carried out using silica gel. Where anhydrous tetrahydrofuran was required, this was either purchased in anhydrous form or was obtained by passing reagent grade unstabilized solvent through alumina packed columns under nitrogen (Grubbs system). Where anhydrous diethyl ether was required, this was obtained by stirring reagent grade diethyl ether with calcium hydride under a nitrogen atmosphere. All other solvents were used as supplied without further purification. HRMS measurements were carried out on an LCMS mass spectrometer using electrospray ionization and a TOF analyzer. Infrared spectra were obtained using a thin film (evaporated from solution) on an ATR spectrometer. Single-crystal X-ray diffraction analyses of **3e, 3g,** *anti*-**4b** and **5g** were performed using an area detector mounted at the window of a rotating anode generator with a Mo anode (λ=0.71075Å) and equipped with a cryostream device. The crystals were mounted on loops and the data were collected at 100 K. Data were processed and empirical absorption corrections were carried out using CrystalClear SM-Expert.[7] The structures were solved by charge-flipping using SUPERFLIP[8] and refined on F_o^2 by full-matrix least squares refinement using SHELXL-2014.[9] All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were added at calculated positions to carbon atoms with isotropic displacement parameters based on the equivalent isotropic displacement parameter (Ueq) of the parent atom. The CIF files for the crystal structures have been deposited with the CCDC and been given the deposition numbers 1410355 (**3e**), 1410356 (**5g**), 1410357 (**3g**) and 1410358 (*anti*-**4b**).

General Procedure for Malonate Additions to form 8a-k

Sodium hydride (60% dispersion in mineral oil, 221 mg, 5.52 mmol, 2 equiv.) was suspended in anhydrous tetrahydrofuran (14 mL), under an atmosphere of dry nitrogen. The mixture was then cooled to −18 °C (ice/acetone bath). Dimethyl malonate (632 µL, 729 mg, 5.52 mmol, 2 equiv.) was then added dropwise (causing effervescence) and the reaction mixture was then stirred for 15 minutes at room temperature. The mixture was again cooled to −18 °C and the corresponding enone **7a-k** (2.76 mmol, 1 equiv.) was added dropwise as a solution in anhydrous tetrahydrofuran (5 mL). The reaction was stirred for approximately 4 hours at room temperature. Upon completion, the reaction mixture was partitioned between diethyl ether (20 mL) and saturated ammonium chloride (20 mL). The aqueous phase was extracted with diethyl ether (3 × 20 mL) and the combined organic phases were washed with water (50 mL) and brine (50 mL). The organic phase was then dried over magnesium sulfate and concentrated under reduced pressure. Material was then taken through to the next step without further purification. A small portion of each ketodiester product was purified by column chromatography for spectroscopic characterization, using silica gel and a solvent gradient starting at petroleum ether and reaching 1:1 petroleum ether-diethyl ether.

Dimethyl 2-(3-(furan-2-yl)-3-oxo-1-phenylpropyl)malonate 8a

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (1H, dd, *J* = 1.7, 0.7, 11-H), 7.30 - 7.16 (5H, m, Ar-H), 7.15 (1H, dd, *J* = 3.6, 0.7, 9-H), 6.48 (1H, dd, *J* = 3.6, 1.7, 10-H), 4.16 (1H, ddd, *J* = 9.6, 8.3, 5.8, 4-H), 3.86 (1H, d, *J* = 9.6, 5-H), 3.73 (3H, s, OMe), 3.51 (3H, s, OMe), 3.39 (1H, dd, *J* = 16.5, 8.3, 3-H), 3.32 (1H, dd, *J* = 16.5, 5.8, 3-H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 186.4, 168.5, 168.0, 152.4, 146.3, 146.3, 140.0, 128.4, 128.0, 127.2, 117.2, 112.2, 57.1, 52.6*, 52.4* (show very fine splitting, 3 Hz), 42.1, 40.5; IR (thin film) νmax 3125, 3097, 2957, 1724, 1664, 1563, 1473, 1455, 1430, 1403, 1352, 1332, 1294, 1268, 1236, 1218, 1195, 1152, 1095, 1071, 1044, 1018, 1002, 980, 950, 918, 881, 860, 771, 759, 699, 683, 618, 564, 531 cm^{-1}; HRMS MNa^+ ($C_{18}H_{18}O_6Na$) calcd 353.1001, found 353.1017.

Dimethyl 2-(1-(4-chlorophenyl)-3-(furan-2-yl)-3-oxopropyl)malonate 8b

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (1H, dd, *J* = 1.7, 0.7, 11-H), 7.21 (4H, s, Ar-H), 7.15 (1H, dd, *J* = 3.6, 0.7, 9-H), 6.49 (1H, dd, *J* = 3.6, 1.7, 10-H), 4.14 (1H, ddd, *J* = 9.5, 8.1, 6.0, 4-H), 3.82 (1H, d, *J* = 9.5, 5-H), 3.74 (3H, s, OMe), 3.53 (3H, s, OMe), 3.35 (1H, dd, *J* = 16.7, 8.1, 3-H) , 3.29 (1H, dd, *J* = 16.7, 6.0, 3-H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 186.2, 168.3, 167.8, 152.5, 146.4, 138.7, 133.0, 129.5, 128.6, 117.2, 112.3, 56.9, 52.7, 52.5, 41.9, 39.9; IR (thin film) ν_{max} 3131, 2956, 2853, 1743, 1726, 1662, 1562, 1491, 1467, 1433, 1417, 1399, 1307, 1274, 1251, 1199, 1157, 1113, 1090, 1069, 1039, 1022, 993, 945, 928, 910, 831 cm^{-1}; HRMS MNa^{+} ($C_{18}H_{17}O_6NaCl$) calcd 387.0611, found 387.0619.

Dimethyl 2-(3-(furan-2-yl)-1-(4-methoxyphenyl)-3-oxopropyl)malonate 8c

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (1H, dd, *J* = 1.7, 0.7, 11-H), 7.17 (2H, d, *J* = 8.7, Ar-H), 7.15 (1H, m, 9-H), 6.77 (2H, d, *J* = 8.7, Ar-H'), 6.48 (1H, dd, *J* = 3.6, 1.7, 10-H), 4.11 (1H, ddd, *J* = 9.6, 8.2, 6.1, 4-H), 3.81 (1H, d, *J* = 9.6, 5-H), 3.74 (3H, s, OMe), 3.73 (3H, s, OMe), 3.51 (3H, s, OMe), 3.40-3.38 (2H, m, 3-H,H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 186.6, 168.7, 168.1, 158.5, 152.5, 146.3, 131.9, 129.1, 117.2, 113.8, 112.2, 57.4, 55.1, 52.7, 42.3, 40.0; IR (thin film) ν_{max} 3126, 3098, 2956, 2838, 1727, 1665, 1612, 1583, 1515, 1474, 1431, 1421, 1402, 1289, 1270, 1252, 1233, 1192, 1179, 1159, 1115, 1089, 1078, 1045, 1032, 998, 981, 951, 919, 881, 827, 769, 734, 677, 598, 563, 533 cm^{-1}; HRMS MNa^{+} ($C_{19}H_{20}O_7Na$) calcd 383.1107, found 383.1094.

Dimethyl 2-(3-(furan-2-yl)-3-oxo-1-(p-tolyl)propyl)malonate 8d

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (1H, d, *J* = 1.6, 11-H), 7.15 (1H, d, *J* = 3.6, 9-H), 7.13 (2H, d, *J* = 8.0, Ar-H), 7.04 (2H, d, *J* = 8.0, Ar-H'), 6.48 (1H, dd, *J* = 3.6, 1.6, 10-H), 4.12 (1H, ddd, *J* = 9.5, 8.1, 6.0, 4-H), 3.82 (1H, d, *J* = 9.5, 5-H), 3.73 (3H, s, OMe), 3.51 (3H, s, OMe), 3.21 (1H, dd, *J* = 16.6, 8.1, 3-H), 3.32 (1H, dd, *J* = 16.6, 6.0, 3-H'), 2.26 (3H, s, Ar-Me); ^{13}C NMR (75 MHz, $CDCl_3$) δ 186.6, 168.6, 168.1, 152.5, 146.3, 136.9, 136.8, 129.2, 127.8, 117.2, 112.2, 57.3, 52.7, 52.4, 42.2, 40.2, 21.0; IR (thin film) ν_{max} 3126, 3097, 2948, 1743, 1730, 1665, 1565, 1516, 1473, 1433, 1401, 1347, 1319, 1306, 1273, 1250, 1241, 1194, 1116, 1089, 1076, 1044, 1022, 992, 974, 951, 929, 912, 882, 854, 820, 778, 770, 735, 720, 596, 552 cm^{-1}; HRMS MNa$^+$ ($C_{19}H_{20}O_6Na$) calcd 367.1158, found 367.1174.

Dimethyl 2-(1-(3,4-dimethoxyphenyl)-3-(furan-2-yl)-3-oxopropyl)malonate 8e

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (1H, dd, *J* = 1.7, 0.7, 11-H), 7.14 (1H, dd, *J* = 3.6, 0.7, 9-H), 6.81 – 6.70 (3H, m, Ar-H), 6.48 (1H, dd, *J* = 3.6, 1.7, 10-H), 4.10 (1H, ddd, *J* = 9.3, 8.9, 5.3, 4-H), 3.83 (1H, d, *J* = 9.3, 5-H), 3.82 (3H, s, OMe), 3.80 (3H, s, OMe), 3.72 (3H, s, OMe), 3.52 (3H, s, OMe), 3.35 (1H, dd, *J* = 16.4, 8.9, 3-H) , 3.26 (1H, dd, *J* = 16.4, 5.3, 3-H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 186.6, 168.6, 168.1, 152.5, 148.5, 147.9, 146.3, 132.5, 119.8, 117.2, 112.2, 111.4, 110.9, 57.3, 55.8, 55.7, 52.7, 52.5, 42.1, 40.3; IR (thin film) ν_{max} 2953, 2838, 1732, 1671, 1592, 1568, 1518, 1465, 1435, 1394, 1257, 1236, 1195, 1142, 1025, 910, 883, 766, 728, 646, 595 cm^{-1}; HRMS MNa^+ ($C_{20}H_{22}O_8Na$) calcd 413.1212, found 413.1216.

Dimethyl 2-(1-(4-bromophenyl)-3-(furan-2-yl)-3-oxopropyl)malonate 8f

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (1H, dd, *J* = 1.6, 0.7, 11-H), 7.34 (2H, d, *J* = 8.5, Ar-H), 7.15 - 7.11 (3H, m, Ar-H', 9-H), 6.46 (1H, dd, *J* = 3.6, 1.6, 10-H), 4.12 (1H, ddd, *J* = 9.3, 8.5, 5.7, 4-H), 3.80 (1H, d, *J* = 9.3, 5-H), 3.70 (3H, s, OMe), 3.49 (3H, s, OMe), 3.34 (1H, dd, *J* = 16.7, 8.5, 3-H) , 3.27 (1H, dd, *J* = 16.7, 5.7, 3-H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 186.0, 168.2, 167.7, 152.2, 146.4, 139.1, 131.4, 129.8, 121.0, 117.2, 112.2, 56.7, 52.6, 52.4, 41.7, 39.8; IR (thin film) ν_{max} 3131, 2955, 2924, 2854, 1740, 1724, 1660, 1561, 1488, 1466, 1432, 1411, 1332, 1306, 1253, 1217, 1200, 1155, 1084, 1065, 1021, 1011, 991, 944, 927, 909, 875, 846, 827, 813, 793, 765, 554 cm^{-1}; HRMS MNa^+ ($C_{18}H_{17}O_6NaBr$) calcd 431.0106, found 431.0119.

Dimethyl 2-(3-(furan-2-yl)-3-oxo-1-(2,4,5-trimethoxyphenyl)propyl)malonate 8g

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (1H, dd, *J* = 1.7, 0.6, 11-H), 7.16 (1H, dd, *J* = 3.6, 0.6, 9-H), 6.71 (1H, s, Ar-H), 6.48 (1H, dd, J = 3.6, 1.7, 10-H), 6.43 (1H, s, Ar-H'), 4.23 – 4.13 (2H, m, 5-H,4-H), 3.83 (3H, s, OMe), 3.81 (3H, s, OMe'), 3.76 (3H, s, OMe''), 3.73 (3H, s, OMe'''), 3.54 – 3.44 (4H, m, OMe'''', 3-H), 3.22 (1H, dd, *J* = 15.9, 4.0, 3-H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.1, 169.0, 168.4, 152.6, 151.6, 148.6, 146.2, 142.3, 118.6, 117.1, 114.3, 112.1, 97.3, 56.4, 56.1, 55.9, 54.9, 52.5, 52.3, 40.5, 37.8; IR (thin film) ν_{max} 2953, 2837, 1733, 1672, 1611, 1568, 1511, 1466, 1436, 1205, 1154, 1128, 1030, 915, 883, 859, 832, 768, 733, 702 cm^{-1}

Dimethyl 2-(1-(4-bromophenyl)-3-(5-methylfuran-2-yl)-3-oxopropyl)malonate 8h

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (2H, d, *J* = 8.5, Ar-H), 7.14 (2H, d, *J* = 8.5, Ar-H'), 7.07 (1H, d, *J* = 3.4, 9-H), 6.10 (1H, dd, *J* = 3.4, 0.9, 10-H), 4.10 (1H, ddd, *J* = 9.6, 8.5, 5.7, 4-H), 3.82 (1H, d, *J* = 9.6, 5-H), 3.73 (3H, s, OMe), 3.52 (3H, s, OMe), 3.25 (1H, dd, *J* = 16.4, 8.5, 3-H), 3.23 (1H, dd, *J* = 16.4, 5.7, 3-H'), 2.34 (3H, s, 11-Me); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.3, 168.3, 167.9, 157.9, 151.1, 139.2, 131.5, 129.9, 121.1, 119.4, 109.0, 56.8, 52.8, 52.5, 41.5, 40.2, 14.0; IR (thin film) ν_{max} 2953, 2923, 2852, 1730, 1660, 1514, 1488, 1433, 1241, 1206, 1159, 1074, 1038, 992, 960, 909, 826, 795, 765, 718, 692, 556 cm^{-1}; HRMS MNa^+ ($C_{19}H_{19}O_6NaBr$) calcd 445.0263, found 445.0278.

Dimethyl 2-(3-(5-methylfuran-2-yl)-3-oxo-1-phenylpropyl)malonate 8i

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 – 7.23 (5H, m, Ar-H), 7.07 (1H, d, *J* = 3.4, 9-H), 6.09 (1H, d, *J* = 3.4, 10-H), 4.14 (1H, ddd, *J* = 9.6, 8.3, 5.7, 4-H), 3.86 (1H, d, *J* = 9.6, 5-H), 3.73 (3H, s, OMe), 3.49 (3H, s, OMe), 3.28 (1H, dd, *J* = 16.1, 8.3, 3-H), 3.26 (1H, dd, *J* = 16.1, 5.7, 3-H'), 2.35 (3H, s, 11-Me); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.7, 168.6, 168.1, 157.7, 151.3, 140.1, 128.4, 128.1, 127.2, 119.3, 108.9, 57.2, 52.7, 52.4, 41.8, 40.9, 14.0; IR (thin film) ν_{max} 2954, 2922, 1746, 1727, 1659, 1516, 1456, 1433, 1417, 1293, 1252, 1205, 1149, 1074, 1040, 1027, 977, 956, 925, 904, 788, 764, 702, 564, 530 cm^{-1}; HRMS MNa^+ ($C_{19}H_{20}O_6Na$) calcd 367.1158, found 367.1140.

Dimethyl 2-(3-(5-methylfuran-2-yl)-3-oxo-1-(p-tolyl)propyl)malonate 8j

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.13 (2H, d, *J* = 8.1, Ar-H), 7.08 (1H, d, *J* = 3.4, 9-H), 7.04 (2H, d, *J* = 8.1, Ar-H), 6.09 (1H, dd, *J* = 3.4, 0.8, 10-H), 4.09 (1H, ddd, *J* = 9.5, 7.9, 6.0, 4-H), 3.83 (1H, d, *J* = 9.5, 5-H), 3.73 (3H, s, OMe), 3.51 (3H, s, OMe), 3.26-3.10 (2H, m, 3-H,H'), 2.34 (3H, s, 11-Me), 2.25 (3H, s, Ar-Me); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.8, 168.7, 168.1, 157.7, 151.3, 137.0, 136.7, 129.1, 127.9, 119.3, 108.9, 57.3, 52.6, 52.4, 41.9, 40.5, 21.0, 14.0; IR (thin film) ν_{max} 2953, 2922, 2852, 1749, 1729, 1660, 1515, 1432, 1360, 1379, 1301, 1239, 1221, 1196, 1144, 1115, 1081, 1041, 983, 959, 906, 816, 794, 722, 560, 533 cm^{-1}; HRMS MNa^+ ($C_{20}H_{22}O_6Na$) calcd 381.1314, found 381.1311.

Dimethyl 2-(1-(4-chlorophenyl)-3-(5-methylfuran-2-yl)-3-oxopropyl)malonate 8k

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.13 (4H, s, Ar-H), 7.06 (1H, d, *J* = 3.5, 9-H), 6.08 (1H, d, *J* = 3.5, 10-H), 4.07 (1H, ddd, *J* = 9.7, 8.6, 5.6, 4-H), 3.79 (1H, d, *J* = 9.7, 5-H), 3.71 (3H, s, OMe), 3.49 (3H, s, OMe), 3.22 (1H, dd, *J* = 16.3, 8.6, 3-H), 3.20 (1H, dd, *J* = 16.3, 5.6, 3-H'), 2.30 (3H, s, 11-Me); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.5, 168.4, 167.9, 158.0, 151.0, 138.5, 132.9, 129.4, 128.5, 119.6, 109.0, 57.0, 52.7, 52.5, 41.5, 40.1, 13.9; IR (thin film) ν_{max} 2954, 1728, 1660, 1515, 1491, 1435, 1272, 1239, 1221, 1164, 1082, 1039, 1015, 960, 907, 828, 795, 728, 648, 559 cm^{-1}

General Procedure for Krapcho Decarboxylations of ketodiesters 8a-k to form ketoesters 9a-k

A portion of crude keto-diester **8a-k** (2.00 mmol, 1 equiv.) was dissolved in a 5:1 mixture of dimethyl sulfoxide and water (30 mL). To this was added lithium chloride (3.39 g, 80 mmol, 40 equiv.) and the mixture was heated at 110 °C for 36 hours. Upon completion the reaction mixture was partitioned between diethyl ether (50 mL) and water (50 mL). The aqueous phase was extracted with diethyl ether (3 × 30 mL). The combined organic phases were then washed with water (2 × 100 mL) and brine (100 mL) and dried over magnesium sulfate. The solution was then concentrated under reduced pressure and the crude product purified by column chromatography using silica gel and a solvent gradient from hexane to 1:1 hexane:diethyl ether, affording the product **9a-k**.

Methyl 5-(furan-2-yl)-5-oxo-3-phenylpentanoate 9a

245 mg from 396 mg **7a** (45%, 2 steps), m.p. 85.2-85.6 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (1H, m, 11-H), 7.28 – 7.14 (5H, m, Ar-H), 7.13 (1H, d, *J* = 3.6, 9-H), 6.47 (1H, m, 10-H), 3.83 (1H, dddd, *J* = 7.3, 7.3, 7.3, 7.3, 4-H), 3.55 (3H, s, OMe), 3.19 (2H, d, *J* = 7.3, 3-H, 3-H'), 2.78 (1H, dd, *J* = 15.5, 7.3, 5-H), 2.67 (1H, dd, *J* = 15.5, 7.3, 5-H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.2, 172.1, 152.6, 146.3, 142.9, 128.5, 127.2, 126.8, 117.1, 112.2, 51.5, 44.3, 40.4, 37.4; IR (thin film) ν_{max} 3128, 3100, 2950, 1726, 1660, 1565, 1466, 1430, 1396, 1354, 1288, 1245, 1219, 1197, 1064, 1086, 1064, 1043, 1007, 985, 952, 919, 882 cm^{-1}; HRMS MNa^+ ($C_{16}H_{16}O_4Na$) calcd 295.0946, found 295.0945.

Methyl 3-(4-chlorophenyl)-5-(furan-2-yl)-5-oxopentanoate 9b

64 mg from 442 mg **7b** (11%, 2 steps), m.p. 83.3-84.2 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (1H, m, 11-H), 7.25 (2H, d, J = 8.2, Ar-H), 7.19 (2H, d, *J* = 8.2, Ar-H'), 7.17 (1H, dd, *J* = 3.6, 0.4, 9-H), 6.51 (1H, dd, *J* = 3.6, 1.7, 10-H), 3.78 (1H, m, 4-H), 3.58 (3H, s, OMe), 3.18 (2H, d, *J* = 7.2, 3-H, 3-H'), 2.78 (1H, dd, *J* = 15.6, 6.8, 5-H), 2.66 (1H, dd, *J* = 15.6, 8.2, 5-H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 186.9, 171.9, 152.6, 146.4, 141.4, 132.5, 128.7 (2xC) , 117.3, 112.3, 51.7, 44.1, 40.3, 36.8; IR (thin film) ν_{max} 3124, 3098, 2952, 1721, 1661, 1563, 1494, 1473, 1430, 1398, 1362, 1327, 1306, 1290, 1267, 1216, 1195, 1155, 1106, 1089, 1066, 1042, 1014, 1000, 986, 950, 920, 906, 881, 873, 827, 770, 730, 709, 597, 536, 519 cm^{-1}; HRMS MNa^+ ($C_{16}H_{15}O_4NaCl$) calcd 329.0557, found 329.0566.

Methyl 5-(furan-2-yl)-3-(4-methoxyphenyl)-5-oxopentanoate 9c

108 mg from 479 mg **7c** (17%, 2 steps), viscous oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (1H, m, 11-H), 7.19 – 7.13 (3H, m, Ar-H, 9-H), 6.80 (2H, d, *J* = 8.57, Ar-H'), 6.49 (1H, dd, *J* = 3.5, 1.2, 10-H), 3.83 (1H, m, 4-H), 3.75 (3H, s, OMe), 3.57 (3H, s, OMe), 3.16 (2H, d, *J* = 7.2, 3-H, 3-H'), 2.76 (1H, dd, *J* = 15.4, 6.9, 5-H), 2.64 (1H, dd, *J* = 15.4, 8.1, 5-H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 186.9, 171.8, 157.9, 152.2, 146.1, 146.1, 134.6, 127.9, 116.9, 113.5, 111.9, 54.7, 54.6, 51.1, 51.0, 44.1, 40.2, 36.4; IR (thin film) ν_{max} 2952, 2837, 1731, 1669, 1611, 1583, 1567, 1512, 1466, 1435, 1394, 1364, 1300, 1278, 1245, 1177, 1152, 1112, 1085, 1029, 915, 882, 829, 763, 729, 594, 557 cm^{-1}; HRMS MNa^+ ($C_{17}H_{18}O_5Na$) calcd 325.1052, found 325.1059.

Methyl 5-(furan-2-yl)-5-oxo-3-(p-tolyl)pentanoate 9d

201 mg from 425 mg **7d** (35 %, 2 steps), viscous oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (1H, dd, *J* = 1.7, 0.7, 11-H), 7.17 – 7.06 (5H, m, Ar-H, 9-H), 6.50 (1H, dd, *J* = 3.6, 1.7, 10-H), 3.83 (1H, dddd, *J* = 7.6, 7.3, 7.3, 7.3, 4-H), 3.58 (3H, s, OMe), 3.18 (2H, d, *J* = 7.3, 3-H, 3-H'), 2.78 (1H, dd, *J* = 15.5, 7.3, 5-H), 2.66 (1H, dd, *J* = 15.5, 7.6, 5-H'), 2.28 (3H, s, Ar-Me); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.3, 172.2, 152.6, 146.3, 139.8, 136.3, 129.2, 127.0, 117.2, 112.2, 51.5, 44.4, 40.5, 37.0, 21.0; IR (thin film) ν_{max} 3131, 3022, 2951, 2921, 1732, 1670, 1592, 1568, 1515, 1467, 1449, 1435, 1394, 1362, 1314, 1276, 1211, 1193, 1154, 1085, 1019, 990, 914, 883, 816, 762, 722, 695 cm^{-1}

Methyl 3-(3,4-dimethoxyphenyl)-5-(furan-2-yl)-5-oxopentanoate 9e

117 mg from 480 mg **7e** (19%, 2 steps), m.p. 94.4-95.6 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (1H, dd, *J* = 1.7, 0.6, 11-H), 7.13 (1H, dd, *J* = 3.6, 0.6, 9-H), 6.75 (3H, s (br), Ar-H), 6.48 (1H, dd, *J* = 3.6, 1.7, 10-H), 3.83 (3H, s, OMe), 3.80 (3H, s, OMe), 3.78 (1H, m, 4-H), 3.56 (3H, s, OMe), 3.16 (2H, d, *J* = 7.4, 3-H, 3-H'), 2.75 (1H, dd, *J* = 15.4, 7.0, 5-H), 2.65 (1H, dd, *J* = 15.4, 8.0, 5-H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.3, 172.1, 152.6, 148.7, 147.6, 146.3, 135.5, 118.9, 117.1, 112.2, 111.1, 110.7, 55.7, 55.7, 51.5, 44.4, 40.6, 37.1; IR (thin film) ν_{max} 3130, 3100, 3008, 2957, 2836, 1735, 1658, 1589, 1562, 1519, 1465, 1438, 1425, 1397, 1329, 1293, 1281, 1254, 1230, 1187, 1160, 1142, 1087, 1039, 1019, 999, 974, 919, 895, 881, 859, 847, 805, 776, 763, 734, 642, 661, 596, 566, 538, 520 cm^{-1}; HRMS MNa^+ ($C_{18}H_{20}O_6Na$) calcd 355.1158, found 355.1166.

Methyl 3-(4-bromophenyl)-5-(furan-2-yl)-5-oxopentanoate 9f

190 mg from 571 mg **7f** (26 %, 2 steps), m.p. 83.9-95 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (1H, dd, *J* = 1.6, 0.7, 11-H), 7.40 (2H, d, *J* = 8.5, Ar-H), 7.17 – 7.12 (3H, m, Ar-H', 9-H), 6.51 (1H, dd, *J* = 3.6, 1.6, 10-H), 3.82 (1H, dddd, J = 7.9, 7.2, 7.2, 7.0, 4-H), 3.59 (3H, s, OMe), 3.18 (2H, d, *J* = 7.2, 3-H, 3-H'), 2.78 (1H, dd, *J* = 15.7, 7.0, 5-H), 2.65 (1H, dd, *J* = 15.7, 7.9, 5-H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 186.9, 171.9, 152.5, 146.4, 141.9, 131.6, 129.1, 120.6, 117.3, 112.3, 51.7, 44.0, 40.2, 36.8; IR (thin film) ν_{max} 3124, 3097, 2951, 1722, 1662, 1563, 1488, 1472, 1430, 1398, 1361, 1326, 1306, 1290, 1267, 1214, 1193, 1160, 1105, 1077, 1065, 1041, 1010, 1000, 986, 950, 920, 906, 881, 873, 824, 769, 724, 703, 610, 535, 518 cm^{-1}; HRMS MNa^+ ($C_{16}H_{15}O_4NaBr$) calcd 373.0051, found 373.0069.

Methyl 5-(furan-2-yl)-5-oxo-3-(2,4,5-trimethoxyphenyl)pentanoate 9g

347 mg from 499 mg **7g** (55 %, 2 steps), gum; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (1H, dd, *J* = 1.6, 0.6, 11-H), 7.16 (1H, dd, *J* = 3.6, 0.6, 9-H), 6.73 (1H, s, Ar-H), 6.49 (1H, dd, *J* = 3.6, 1.6, 10-H), 6.47 (1H, s, Ar-H'), 4.00 (1H, m , 4-H), 3.84 (3H, s, OMe), 3.80 (3H, s, OMe), 3.79 (3H, s, OMe), 3.58 (3H, s, OMe), 3.26 (1H, dd, *J* = 14.7, 6.0, 3-H), 3.18 (1H, dd, *J* = 14.7, 6.2, 3-H'), 2.83 (1H, dd, *J* = 13.2, 4.9, 5-H), 2.76 (1H, dd, *J* = 13.2, 5.2, 5-H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.0, 172.7, 152.7, 151.3, 148.2, 146.3, 142.6, 121.8, 117.2, 112.8, 112.1, 97.6, 56.5, 56.2, 56.0, 51.5, 42.8, 38.6, 33.4; IR (thin film) ν_{max} 2950, 2835, 1733, 1671, 1611, 1568, 1511, 1467, 1438, 1397, 1314, 1276, 1206, 1163, 1122, 1031, 916, 883, 830, 767 cm^{-1}

Methyl 3-(4-bromophenyl)-5-(5-methylfuran-2-yl)-5-oxopentanoate 9h

262 mg from 585 mg **7h** (36 %, 2 steps), m.p. 77.6-79.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (2H, d, *J* = 8.4, Ar-H), 7.14 (2H, d, *J* = 8.4, Ar-H'), 7.06 (1H, d, *J* = 3.4, 9-H), 6.12 (1H, dd, *J* = 3.4, 0.8, 10-H), 3.76 (1H, m, 4-H), 3.58 (3H, s, OMe), 3.11 (2H, d, *J* = 7.3, 3-H, 3-H'), 2.78 (1H, dd, *J* = 15.7, 8.3, 5-H), 2.65 (1H, dd, *J* = 15.7, 8.3, 5-H'), 2.36 (3H, s, 11-Me); ^{13}C NMR (75 MHz, $CDCl_3$) δ 186.1, 171.9, 158.0, 151.3, 142.0, 131.6, 129.1, 120.6, 119.4, 109.1, 51.7, 43.8, 40.2, 37.1, 14.1; IR (thin film) ν_{max} 2952, 2916, 1735, 1654, 1590, 1516, 1489, 1448, 1437, 1421, 1407, 1386, 1366, 1306, 1291, 1220, 1209, 1195, 1178, 1165, 1104, 1087, 1070, 1036, 1025, 1010, 987, 959, 950, 933, 910, 873, 823, 792, 725, 706, 670, 526 cm^{-1}; HRMS MNa$^+$ ($C_{17}H_{17}O_4NaBr$) calcd 387.0208, found 387.0225.

Methyl 5-(5-methylfuran-2-yl)-5-oxo-3-phenylpentanoate 9i

154 mg from 374 mg **7i** (31%, 2 steps), m.p. 99.3-100.6°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 – 7.12 (5H, m, Ar-H), 7.06 (1H, d, *J* = 3.5, 9-H), 6.11 (1H, dd, *J* = 3.5, 0.8, 10-H), 3.83 (1H, m, 4-H), 3.57 (3H, s, OMe), 3.13 (2H, d, *J* = 7.2, 3-H, 3-H'), 2.80 (1H, dd, *J* = 15.5, 6.8, 5-H), 2.69 (1H, dd, *J* = 15.5, 8.1, 5-H'), 2.36 (3H, s, 11-Me); ^{13}C NMR (75 MHz, $CDCl_3$) δ 186.5, 172.2, 157.8, 151.5, 143.1, 128.6, 127.3, 126.8, 119.2, 109.0, 51.5, 44.1, 40.4, 37.8, 14.0; IR (thin film) ν_{max} 2952, 1730, 1659, 1515, 1495, 1436, 1456, 1372, 1360, 1284, 1248, 1226, 1211, 1161, 1090, 1074, 1034, 989, 978, 954, 931, 882, 796, 783, 761, 699, 559 cm^{-1}

Methyl 5-(5-methylfuran-2-yl)-5-oxo-3-(p-tolyl)pentanoate 9j

177 mg from 434 mg **7j** (31 %, 2 steps), m.p. 79.3-80.2 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.16 – 7.06 (5H, m, Ar-H, 9-H), 6.10 (1H, dd, *J* = 3.5, 0.8, 10-H), 3.79 (1H, dddd, *J* = 7.6, 7.3, 7.3, 7.0, 4-H), 3.56 (3H, s, OMe), 3.10 (2H, d, *J* = 7.3, 3-H, 3-H'), 2.77 (1H, dd, *J* = 15.5, 7.0, 5-H), 2.65 (1H, dd, *J* = 15.5, 7.6, 5-H'), 2.34 (3H, s, Me), 2.27 (3H, s, Me); ^{13}C NMR (75 MHz, $CDCl_3$) δ 186.5, 172.2, 157.7, 151.3, 138.9, 136.1, 129.1, 127.0, 119.2, 108.8, 51.4, 44.1, 40.3, 37.2, 20.9, 13.9; IR (thin film) ν_{max} 2951, 2920, 1729, 1659, 1515, 1448, 1435, 1422, 1385, 1368, 1334, 1312, 1296, 1270, 1223, 1211, 1180, 1162, 1113, 1085, 1072, 1037, 1026, 991, 958, 873, 816, 795, 755, 722, 666, 528 cm^{-1}; HRMS MNa^{+} ($C_{18}H_{20}O_4Na$) calcd 323.1259, found 323.1248.

Methyl 3-(4-chlorophenyl)-5-(5-methylfuran-2-yl)-5-oxopentanoate 9k

177 mg from 466 mg **7k** (29 %, 2 steps), m.p. 65.7-66.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 – 7.14 (4H, m, Ar-H), 7.04 (1H, d, *J* = 3.5, 9-H), 6.09 (1H, dd, *J* = 3.5, 0.8, 10-H), 3.79 (1H, dddd, *J* = 7.6, 7.2, 7.2, 7.0, 4-H), 3.54 (3H, s, OMe), 3.09 (2H, d, *J* = 7.2, 3-H, 3-H'), 2.76 (1H, dd, *J* = 15.6, 7.0, 5-H), 2.63 (1H, dd, *J* = 15.6, 7.9, 5-H'), 2.32 (3H, s, 11-Me); ^{13}C NMR (75 MHz, $CDCl_3$) δ 186.0, 171.8, 157.8, 151.2, 141.4, 132.3, 128.6, 128.5, 119.3, 108.9, 51.5, 43.7, 40.1, 36.9, 13.9; IR (thin film) ν_{max} 2998, 2953, 2920, 1735, 1654, 1591, 1514, 1492, 1448, 1438, 1423, 1411, 1385, 1369, 1329, 1306, 1291, 1271, 1220, 1209, 1196, 1178, 1164, 1105, 1088, 1071, 1036, 1026, 1014, 987, 959, 912, 887, 873, 825, 791, 729, 711, 672, 537, 526 cm^{-1}; HRMS MNa^{+} ($C_{17}H_{17}O_4NaCl$) calcd 343.0713, found 343.0706.

General Procedure for the reduction of ketoesters 9a-k to form diols 1a-k

Solid lithium aluminium hydride (304 mg, 8.00 mmol, 10 equiv.) was suspended in anhydrous tetrahydrofuran (4 mL) under dry nitrogen. The reaction mixture was cooled to −15 °C. Keto-ester **9a-k** (0.80 mmol, 1 equiv.) was added dropwise in anhydrous tetrahydrofuran (5 mL) at this temperature. The reaction mixture was then stirred at room temperature for a further 15 minutes after which TLC analysis indicated that reaction was complete. The reaction was quenched by adding diethyl ether (10 mL) followed by the slow dropwise addition of a 4:1 mixture of diethyl ether and acetone (15 mL). The reaction mixture was then diluted in ethyl acetate (40 mL) and washed with water (100 mL) and 2.0 M aqueous sodium hydroxide (150 mL). The combined aqueous phase was extracted with ethyl acetate (5 × 50 mL). The combined organic phases were then washed with water (2 × 100 mL) and brine (100 mL) before being dried over magnesium sulfate. The organic phase was then concentrated under reduced pressure to afford the product **1a-k** as a colorless oil which was used without any further purification (except in the case of **1b**, whose diastereomers were able to be partly separated by careful column chromatography, using a solvent gradient from petroleum ether to diethyl ether). In general, ^{1}H NMR data for each diastereomer in the mixtures are listed sequentially, although signals from each diastereomer were often significantly overlapped. For **1b**, the ^{1}H, ^{13}C, IR and MS data for each diastereomer is listed separately.

1-(Furan-2-yl)-3-phenylpentane-1,5-diol 1a

195 mg from 218 mg **9a**, 99 %, d.r. = 1:0.7; ^{1}H NMR (300 MHz, CD_3CN) δ major diastereomer: 7.44 (1H, dd, *J* = 1.8, 0.8, 11-H), 7.36 – 7.23 (5H, m, Ar-H), 6.37 (1H, dd, *J* =

3.2, 1.8, 10-H), 6.20 (1H, d, *J* = 3.2, 9-H), 4.33 (1H, dd, J = 7.3, 7.3, 2-H), 3.45 – 3.15 (3H, m, 6-H,H',OH), 2.69 – 2.54 (2H, m, 4-H,OH), 2.24 – 1.64 (4H, m, 3-H,H', 5-H,H); minor diastereomer: 7.36 (1H, dd, *J* = 1.8, 0.8, 11-H), 7.36 – 7.23 (5H, m, Ar-H), 6.31 (1H, dd, *J* = 3.2, 1.8, 10-H), 6.14 (1H, d, *J* = 3.2, 9-H), 4.18 (1H, dd, *J* = 10.0, 3.2, 2-H), 3.45 – 3.15 (3H, m, 6-H,H',OH), 3.03 (H, m, b-4-H), 2.69 – 2.54 (1H, m, OH), 2.24 – 1.64 (4H, m, 3-H',H', 5-H,H'); ^{13}C NMR (75 MHz, CD_3CN) δ 159.0, 157.9, 145.9, 145.5, 142.8, 142.5, 129.3, 128.8, 128.5, 127.1, 111.0, 110.9, 107.0, 105.9, 65.7, 65.2, 60.4, 60.2, 43.2, 43.1, 40.6, 39.9, 39.3, 39.0; IR (thin film) ν_{max} 3318 (br), 2921, 2850, 1494, 1453, 1260, 1145, 1043, 1009, 913, 884, 808, 762, 740, 701, 634, 598, 533 cm^{-1}; HRMS MNa$^+$($C_{15}H_{18}O_3Na$) calcd 269.1154, found 269.1145.

3-(4-Chlorophenyl)-1-(furan-2-yl)pentane-1,5-diol 1b

55 mg from 61 mg **9b**, 99 %, d.r. = 1:0.75, separable by column chromatography;
major diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (1H, dd, *J* = 1.8, 0.8, 11-H), 7.27 (2H, d, *J* = 8.4, Ar-H), 7.08 (2H, d, *J* = 8.4, Ar-H'), 6.33 (1H, dd, *J* = 3.2, 1.8, 10-H), 6.17 (1H, d, *J* = 3.2, 9-H), 4.49 (1H, dd, *J* = 6.2, 6.2, 2-H), 3 52 (1H, m, 6-H), 3.39 (1H, m, 6-H'), 2.71 (1H, m, 4-H), 2.30 – 1.70 ([4H, m, 3-H,H', 5-H,H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.7, 142.7, 142.2, 132.1, 128.9, 128.7, 110.2, 106.7, 65.6, 60.5, 42.1, 38.8, 38.0; IR (thin film) ν_{max} 3328 (br), 2938, 2885, 1489, 1467, 1450, 1412, 1146, 1091, 1042, 1012, 940, 908, 883, 824, 730, 597, 566 cm^{-1}

minor diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (1H, dd, *J* = 1.8, 0.8, 11-H), 7.28 (2H, d, *J* = 8.5, Ar-H), 7.17 (2H, d, *J* = 8.5, Ar-H'), 6.29 (1H, dd, *J* = 3.2, 1.8, 10-H), 6.14 (1H, ddd, *J* = 3.2, 0.8, 0.7, 9-H), 4.33 (1H, d, *J* = 10.4, 2-H), 3.65 – 3.40 (2H, m, 6-H,H'), 3.14 (1H, m, 4-H), 2.22 (1H, ddd, *J* = 14.2, 10.4, 4.2, 3-H), 2.05 – 1.80 (3H, m, 3-H', 5-

H,H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.7, 155.7, 142.7, 142.3, 141.93, 141.87, 132.1, 129.2, 128.9, 128.77, 128.75, 110.2, 110.1, 106.8, 105.6, 65.7, 65.0, 60.6, 60.5, 42.1, 41.8, 39.6, 38.9, 38.0, 37.7; IR (thin film) ν_{max} 3314 (br), 2932, 1489, 1434, 1412, 1320, 1146, 1090, 1043, 1012, 884, 824, 737, 634, 598, 534 cm^{-1}

1-(Furan-2-yl)-3-(4-methoxyphenyl)pentane-1,5-diol 1c

188 mg from 215 mg **9c**, 96 %, d.r. = 1:0.75; ^1H NMR (300 MHz, $CDCl_3$) δ major diastereomer: 7.39 (1H, d, *J* = 1.7, 11-H), 7.07 (2H, d, *J* = 8.3, Ar-H), 6.87 – 6.84 (2H, m, Ar-H'), 6.33 (1H, dd, *J* = 2.7, 1.7, 10-H), 6.19 (1H, d, *J* = 2.7, a-9-H), 4.51 (1H, dd, *J* = 11.2, 5.9, a-2-H), 3.80 (3H, s(br), Ar-OMe), 3.62 – 3.38 (2H, m, 6-H,H'), 2.68 – 2.59 (1H, m, a-4-H), 2.29 – 1.79 (4H, m, a-3-H,H', 5-H,H'); minor diastereomer: 7.32 (1H, m, 11-H), 7.15 (2H, d, *J* = 8.5, Ar-H), 6.87 – 6.84 (2H, m, Ar-H'), 6.29 (1H, dd, *J* = 3.0, 1.6, 10-H), 6.15 (1H, d, *J* = 3.0, 9-H), 4.37 (1H, dd, *J* = 8.8, 3.6, 2-H), 3.80 (3H, s(br), Ar-OMe), 3.62 – 3.38 (2H, m, 6-H,H'), 3.13 – 3.02 (1H, m, 4-H), 2.29 – 1.79 (4H, m, 3-H',H', 5-H,H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.3, 157.1, 156.0, 142.2, 141.8, 136.0, 135.6, 128.7, 128.5, 114.12, 114.10, 110.1, 106.7, 105.4, 66.1, 65.3, 61.1, 60.9, 55.3, 42.6, 42.3, 40.0, 39.4, 38.2, 37.7; IR (thin film) ν_{max} 3347(br), 2933, 1609, 1510, 1441, 1365, 1301, 1243, 1177, 1146, 1029, 1008, 830, 736, 598, 574 cm^{-1}; HRMS MNa^+ ($C_{16}H_{20}O_4Na$) calcd 299.1259, found 299.1273.

1-(furan-2-yl)-3-(p-tolyl)pentane-1,5-diol 1d

62 mg from 101 mg **9d**, 68 %, d.r. = 1:0.74; ^{1}H NMR (300 MHz, $CDCl_3$) δ major diastereomer: 7.38 (1H, dd, *J* = 1.8, 0.8, 11-H), 7.13 – 7.02 (4H, m, Ar-H), 6.33 (1H, dd, *J* = 3.2, 1.8, 10-H), 6.18 (1H, d, *J* = 3.2, 9-H), 4.52 (1H, dd, *J* = 7.2, 7.2, 2-H), 3.61 – 3.38 (2H, m, 6-H,H), 2.66 (1H, m, 4-H), 2.33 (3H, s(br), Ar-Me), 2.28 – 1.72 (4H, m, 3-H,H', 5-H,H'); minor diastereomer: 7.32 (1H, dd, *J* = 1.8, 0.8, 11-H), 7.13 – 7.02 (4H, m, Ar-H), 6.28 (1H, dd, *J* = 3.2, 1.8, 10-H), 6.14 (1H, d, *J* = 3.2, 9-H), 4.36 (1H, ddd, *J* = 10.2, 2.8, 2-H), 3.61 – 3.38 (2H, m, 6-H,H'), 3.08 (1H, m, 4-H), 2.33 (3H, s(br), Ar-Me), 2.28 – 1.72 (4H, m, 3-H',H', 5-H,H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.0, 155.9, 142.2, 141.8, 140.9, 140.6, 136.11, 136.08, 129.4, 127.6, 127.4, 110.11, 110.08, 106.7, 105.4, 66.0, 65.2, 61.1, 60.9, 42.4, 42.0, 39.8, 39.2, 38.5, 38.0, 21.0; IR (thin film) ν_{max} 3317 (br), 2924, 1512, 1145, 1042, 1008, 884, 814, 735, 598, 572, 491 cm^{-1}; HRMS MNa^+ ($C_{16}H_{20}O_3Na$) calcd 283.1310, found 283.1320.

3-(3,4-dimethoxyphenyl)-1-(furan-2-yl)pentane-1,5-diol 1e

92 mg from 105 mg **9e**, 95 %, d.r. = 1:0.8; ^{1}H NMR (300 MHz, $CDCl_3$) δ major diastereomer: 7.44 (1H, dd, *J* = 1.8, 0.8, 11-H), 6.84 (1H, d, *J* = 8.2, Ar-H), 6.70 (1H, d, *J* = 2.0, Ar-H'), 6.65 (1H, dd, *J* = 8.2, 2.0, Ar-H''), 6.37 (1H, dd, *J* = 3.2, 1.8, 10-H), 6.20 (1H, d, *J* = 3.2, 9-H), 4.33 (1H, ddd, *J* = 8.3, 6.0, 6.0, 2-H), 3.77 (6H, s, OMe,OMe'), 3.41 – 3.16 (3H, m, 6-H,H',OH), 2.60 – 2.44 (2H, 4-H,OH), 2.20 – 1.60 (4H, m, 3-H,H', 5-H,H'); minor diastereomer: 7.36 (1H, dd, *J* = 1.8, 0.8, 11-H), 6.86 (1H, d, *J* = 8.1, Ar-H), 6.79 (1H, d, *J* = 1.9, Ar-H'), 6.75 (1H, dd, *J* = 8.1, 1.9, Ar-H''), 6.31 (1H, dd, *J* = 3.2, 1.8, 10-H), 6.14 (1H, d, *J* = 3.2, 9-H), 4.20 (1H, m, 2-H), 3.774 (3H, s, OMe), 3.767 (3H, s, OMe'), 3.41 – 3.16 (3H,

m, 6-H,H',OH), 2.95 (1H, m, 4-H), 2.60 – 2.44 (1H, OH), 2.20 – 1.60 (4H, m, 3-H',H', 5-H,H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 158.1, 150.0, 148.4, 142.8, 142.5, 138.4, 138.0, 120.7, 120.4, 112.4, 112.2, 112.0, 111.0, 107.1, 105.9, 65.8, 65.2, 60.5, 60.4, 56.1, 43.4, 43.3, 40.6, 40.0, 39.0, 38.7; IR (thin film) ν_{max} 3344(br), 2935, 2835, 1591, 1513, 1463, 1420, 1256, 1232, 1139, 1024, 912, 884, 808, 763, 727, 649, 599 cm^{-1}; HRMS MNa^+($C_{17}H_{22}O_5Na$) calcd 329.1365, found 329.1358.

3-(4-bromophenyl)-1-(furan-2-yl)pentane-1,5-diol 1f

147 mg from 160 mg **9f**, 99 %, d.r. = 1:0.76; ^{1}H NMR (300 MHz, $CDCl_3$) δ major diastereomer: 7.46 – 7.40 (2H, m, Ar-H), 7.39 (1H, dd, *J* = 1.8, 0.8, 11-H), 7.03 (2H, d, *J* = 8.4, Ar-H'), 6.33 (1H, dd, *J* = 3.2, 1.8, 10-H), 6.18 (1H, d, *J* = 3.2, 9-H), 4.49 (1H, dd, *J* = 6.7, 8.0, 2-H), 3.62 (2H, m, 6-H,H), 2.69 (1H, m, 4-H), 2.30 – 1.70 (4H, m, 3-H,H', 5-H,H'); minor diastereomer: 7.46 – 7.40 (2H, m, Ar-H), 7.32 (1H, dd, *J* = 1.8, 0.8, 11-H), 7.12 (2H, d, *J* = 8.4, Ar-H'), 6.29 (1H, dd, *J* = 3.2, 1.8, 10-H), 6.14 (1H, d, *J* = 3.2, 9-H), 4.33 (1H, dd, *J* = 10.4, 3.2, 2-H), 3.62 (2H, m, 6-H,H'), 3.13 (1H, m, 4-H), 2.30 – 1.70 (4H, m, 3-H',H', 5-H,H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.7, 155.7, 143.2, 142.8, 142.3, 141.9, 131.74, 131.71, 129.6, 129.3, 120.2, 110.2, 110.1, 106.8, 105.6, 65.7, 65.1, 60.7, 60.5, 42.1, 41.9, 39.6, 38.9, 38.2, 37.9; IR (thin film) ν_{max} 3312(br), 2929, 1486, 1431, 1230, 1146, 1069, 1042, 1008, 883, 818, 737, 598, 565, 494 cm^{-1}; HRMS MNa^+($C_{15}H_{17}O_3NaBr$) calcd 347.0259, found 347.0245.

1-(furan-2-yl)-3-(2,4,5-trimethoxyphenyl)pentane-1,5-diol 1g

234 mg from 261 mg **9g**, 97 %, d.r. = 1:0.65; ^{1}H NMR (300 MHz, CD_3CN) δ major diastereomer: 7.42 (1H, dd, *J* = 1.8, 0.8, 11-H), 6.72 (1H, s, Ar-H), 6.60 (1H, s, Ar-H'), 6.35 (1H, dd, *J* = 3.2, 1.8, 10-H), 6.18 (1H, d, *J* = 3.2, 9-H), 4.37 (1H, m, 2-H), 3.80 ([3H, s, Ar-OMe), 3.73 (3H, s, Ar-OMe'), 3.69 (3H, s, Ar-OMe''), 3.40 – 3.15 (2H, m, 6-H,H), 3.02 (1H, dddd, *J* = 9.3, 9.3, 5.9, 5.9, 4-H), 2.19 – 1.98 (2H, m, 3-H,H'), 1.90 – 1.64 (2H, m, 5-H,H'); minor diastereomer: 7.36 (1H, dd, *J* = 1.8, 0.8, 11-H), 6.73 (1H, s, Ar-H), 6.64 (1H, s, Ar-H'), 6.30 (1H, dd, *J* = 3.2, 1.8, 10-H), 6.15 (1H, d, *J* = 3.2, 9-H), 4.24 (1H, m, 2-H), 3.80 (3H, s, Ar-OMe), 3.78 (3H, s, Ar-OMe'), 3.72 (3H, s, Ar-OMe''), 3.40 – 3.15 (3H, m, 4-H,6-H,H'), 2.19 – 1.98 (2H, m, 3-H,H'), 1.90 – 1.64 (2H, m, 5-H,H'); ^{13}C NMR (75 MHz, CD_3CN) δ 158.9, 158.4, 152.9, 152.6, 149.0, 148.9, 144.5, 144.2, 142.6, 142.5, 124.9, 124.5, 113.5, 111.0, 110.9, 106.8, 106.0, 99.8, 99.4, 65.9, 65.8, 60.8, 60.7, 57.5, 57.1, 57.0, 56.5, 42.3, 42.2, 39.6, 39.1, 31.9; IR (thin film) ν_{max} 3391 (br), 2929, 2853, 1509, 1464, 1440, 1398, 1315, 1273, 1203, 1180, 1147, 1121, 1031, 910, 860, 883, 813 cm^{-1}; HRMS MNa^+($C_{18}H_{24}O_6Na$) calcd 359.1471, found 359.1466.

3-(4-bromophenyl)-1-(5-methylfuran-2-yl)pentane-1,5-diol 1h

149 mg from 206 mg **9h**, 78 %, d.r. = 1:0.67; ^{1}H NMR (300 MHz, $CDCl_3$) δ major diastereomer: 7.42 (2H, d, *J* = 8.4, Ar-H), 7.03 (2H, d, *J* = 8.4, Ar-H'), 6.04 (1H, d, *J* = 3.1, 9-H), 5.89 (1H, dq, J = 3.1, 1.0, 10-H), 4.42 (1H, dd, *J* = 7.7, 6.8, 2-H), 3.62 – 3.35 (2H, m, 6-H,H), 2.71 (1H, m, 4-H), 2.28 (3H, d, *J* = 1.0, 11-Me), 2.26 – 1.70 (4H, m, 3-H,H', 5-H,H'); minor diastereomer: 7.43 (2H, d, *J* = 8.4, Ar-H), 7.12 (2H, d, *J* = 8.4, Ar-H'), 6.01 (1H, d, *J* = 3.1, 9-H), 5.85 (1H, dq, J = 3.1, 1.0, 10-H), 4.26 (1H, dd, *J* = 10.4, 3.3, 2-H), 3.62

– 3.35 (2H, m, 6-H,H'), 3.11 (1H, m, 4-H), 2.23 (3H, d, *J* = 1.0, 11-Me), 2.26 – 1.70 (4H, m, 3-H',H', 5-H,H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.8, 153.8, 152.0, 151.7, 143.3, 142.9, 131.7, 130.0, 129.4, 120.1, 107.7, 106.5, 106.0, 105.9, 65.7, 65.0, 60.7, 60.5, 41.9, 41.7, 39.6, 38.8, 38.1, 37.9, 13.6, 13.5; IR (thin film) ν_{max} 3309 (br), 2920, 1563, 1486, 1432, 1408, 1218, 1070, 1042, 1020, 1008, 889, 820, 784, 719, 565 cm^{-1}; HRMS MNa$^+$ ($C_{16}H_{19}O_3NaBr$) calcd 361.0415, found 361.0427

1-(5-methylfuran-2-yl)-3-phenylpentane-1,5-diol 1i

105 mg from 158 mg **9i**, 73 %, d.r. = 1:0.65; ^{1}H NMR (300 MHz, $CDCl_3$) δ major diastereomer: 7.35 – 7.14 (5H, m, Ar-H), 6.06 (1H, d, *J* = 3.2, 9-H), 5.90 (1H, m, 10-H), 4.44 (1H, dd, *J* = 7.2, 7.2, 2-H), 3.61 – 3.39 (2H, m, 6-H,H), 2.71 (1H, dddd, *J* = 9.7, 9.7, 5.6, 5.6, 4-H), 2.28 (3H, d, *J* = 0.7, 11-Me), 2.30 – 1.76 (4H, m, 3-H,H', 5-H,H'); minor diastereomer: 7.35 – 7.14 (5H, m, Ar-H), 6.01 (1H, d, *J* = 3.1, 9-H), 5.85 (1H, m, 10-H), 4.29 (1H, dd, *J* = 10.3, 3.3, 2-H), 3.61 – 3.39 (2H, m, 6-H,H'), 3.11 (1H, dddd, *J* = 10.1, 10.1, 5.5, 4.5, 4-H), 2.23 (3H, d, *J* = 0.7, 11-Me), 2.30 – 1.76 (4H, m, 3-H',H', 5-H,H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.0, 152.0, 144.2, 143.8, 128.6, 127.8, 127.6, 126.53, 126.50, 107.6, 106.4, 106.0, 105.9, 65.9, 60.9, 42.2, 41.9, 39.8, 39.1, 38.9, 38.5, 13.6, 13.5; IR (thin film) ν_{max} 3339 (br), 2922, 1562, 1494, 1452, 1364, 1219, 1044, 1020, 1001, 965, 937, 784, 762, 700, 596 cm^{-1}; HRMS MNa$^+$($C_{16}H_{20}O_3Na$) calcd 283.1310, found 283.1324.

1-(5-Methylfuran-2-yl)-3-(p-tolyl)pentane-1,5-diol 1j

126 mg from 145 mg **9j**, 95 %, d.r. = 1:0.7; ^{1}H NMR (300 MHz, $CDCl_3$) δ major diastereomer: 7.15 – 7.02 (4H, m, Ar-H), 6.05 (1H, d, *J* = 3.0, 9-H), 5.89 (1H, dq, *J* = 3.0, 0.9, 10-H), 4.45 (1H, dd, *J* = 7.4, 7.4, 2-H), 3.61 – 3.38 (2H, m, 6-H,H), 2.67 (1H, m, 4-H), 2.32 (3H, s, Ar-Me), 2.28 (3H, d, *J* = 0.9, 11-Me), 2.30 – 1.50 (4H, m, 3-H,H', 5-H,H'); minor diastereomer: 7.15 – 7.02 (4H, m, Ar-H), 6.01 (1H, d, *J* = 3.0, 9-H), 5.84 (1H, dq, J = 3.0, 1.0, 10-H), 4.30 (1H, dd, *J* = 10.4, 2.5, 2-H), 3.61 – 3.38 (2H, m, 6-H,H'), 3.11 (1H, m, 4-H), 2.32 (3H, s, Ar-Me), 2.23 (3H, d, *J* = 1.0, 11-Me), 2.30 – 1.50 (4H, m, 3-H',H', 5-H,H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 154.1, 151.9, 151.6, 141.1, 140.7, 136.03, 135.98, 129.3, 127.7, 127.4, 107.6, 106.3, 105.98, 105.97, 65.9, 65.1, 61.1, 60.9, 42.3, 41.9, 39.9, 39.1, 38.5, 38.1, 21.0, 13.6, 13.5; IR (thin film) ν_{max} 3314 (br), 2920, 2882, 1513, 1044, 1020, 784, 668, 631, 595, 533, 495 cm^{-1}; HRMS MNa^+($C_{17}H_{22}O_3Na$) calcd 297.1467, found 297.1477.

3-(4-chlorophenyl)-1-(5-methylfuran-2-yl)pentane-1,5-diol 1k

106 mg from 163 mg **9k**, 71 %, d.r. = 1:0.75; ^{1}H NMR (300 MHz, $CDCl_3$) δ major diastereomer: 7.30 – 7.24 (2H, m, Ar-H), 7.09 (2H, d, *J* = 8.4, Ar-H'), 6.05 (1H, d, *J* = 3.0, 9-H), 5.90 (1H, dq, *J* = 3.0, 1.0, 10-H), 4.42 (1H, m, 2-H), 3.60 – 3.35 (2H, m, 6-H,H'), 2.72 (1H, dddd, *J* = 9.6, 9.6, 5.5, 5.5, 4-H), 2.32 ([3H, s, Ar-Me), 2.28 (3H, d, *J* = 1.0, 11-Me), 2.28 – 1.70 (4H, m, 3-H,H', 5-H,H'); minor diastereomer: 7.30 – 7.24 (2H, m, Ar-H), 7.16 (2H, d, *J* = 8.4, Ar-H'), 6.01 (1H, d, *J* = 3.1, 9-H), 5.85 (1H, dq, *J* = 3.1, 1.0, 10-H), 4.26 (1H, m, 2-H), 3.60 – 3.35 (2H, m, 6-H,H'), 3.11 (1H, m, 4-H), 2.32 (3H, s, Ar-Me), 2.23 (3H, d, *J* = 1.0, 11-Me), 2.28 – 1.70 (4H, m, 3-H',H', 5-H,H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.9,

153.9, 151.9, 151.6, 142.9, 142.5, 131.9, 129.2, 128.9, 128.6, 107.5, 106.4, 106.0, 105.9, 65.4, 64.9, 60.33, 60.29, 42.0, 41.4, 39.6, 38.4, 37.8, 37.5, 13.54, 13.45; IR (thin film) ν_{max} 3323 (br), 2922, 1489, 1434, 1412, 1219, 1090, 1043, 1013, 965, 937, 891, 826, 784, 721, 702, 566, 500 cm^{-1}; HRMS MNa^+($C_{16}H_{19}O_3NaCl$) calcd 317.0920, found 317.0936.

General Procedure for the acid catalysed cyclisation of diols of 1a-k to form disubstituted tetrahydropyrans 3a-k

Diol **1a-k** (0.22 mmol) was dissolved in acetonitrile (2 mL). Quadrapure™ polymer supported sulfonic acid (20 mg, 5.0 mmol/g loading) was then added to the reaction mixture. The reaction mixture was stirred gently at room temperature for 10 hrs. Upon completion, the reaction mixture was filtered and the polymer beads washed three times with acetonitrile (5 mL). The solution was then concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (using a solvent gradient from petroleum ether to 1:1 petroleum ether - diethyl ether) to furnish the product **3a-k**. Only peaks corresponding to the major isomer are reported, except in the case of **3a**, whose *syn* and *ant*i diastereomers were separable by column chromatography (following the sodium hydride/tosyl chloride promoted cyclization, see below). Crystals of **3e** and **3g** for x-ray diffraction were obtained by slow evaporation of ethyl acetate solutions placed in glass vials plugged with cotton wool.

(±)-(2S,4R)-2-(furan-2-yl)-4-phenyltetrahydro-2H-pyran *syn*-3a

38 mg of *syn/anti*-**3a**, d.r. = 16:1, was afforded from 54 mg **1a**, 76 %. Data for *syn*-**3a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (1H, dd, *J* = 1.8, 0.8, 11-H), 7.38 – 7.20 (5H, m, Ar-H), 6.34 (1H, dd, *J* = 3.3, 1.8, 10-H), 6.29 (1H, ddd, *J* = 3.3, 0.8, 0.8, 9-H), 4.56 (1H, dd, *J* = 11.0, 2.6, 2-H), 4.24 (1H, ddd, *J* = 11.6, 4.3, 1.8, 6-eq), 3.77 (1H, ddd, *J* = 11.6, 11.6, 2.8, 6-ax), 2.92 (1H, dddd, 11.7, 11.7, 4.3, 4.3, 4-H), 2.16 – 1.78 (4H, m, 3-H,H', 5-H,H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.6, 145.2, 142.2, 128.6, 126.8, 126.5, 110.1, 106.3, 73.1, 68.6, 41.6, 37.1, 33.1; IR (thin film) ν_{max} 2938, 2917, 2844, 1495, 1452, 1374, 1352, 1252, 1227, 1194, 1169, 1145, 1123, 1079, 1044, 1030, 1012, 997, 958, 942, 927, 913, 884, 876, 840, 806, 736, 698, 629, 599, 547, 531 cm^{-1}; HRMS M^+($C_{15}H_{16}O_2$) calcd 228.1150, found 228.1142.

(±)-(2R,4R)-2-(Furan-2-yl)-4-phenyltetrahydro-2H-pyran *anti*-3a

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (1H, d, *J* = 1.7, 11-H), 7.39 – 7.21 (5H, m, Ar-H), 6.41 (1H, dd, *J* = 3.2, 1.7, 10-H), 6.37 (1H, ddd, *J* = 3.2, 0.8, 0.8, 9-H), 5.09 (1H, dd, *J* = 5.2, 2.7, 2-H), 3.87 (1H, ddd, *J* = 11.3, 4.2, 3.5, 6-H), 3.73 (1H, ddd, *J* = 11.3, 11.0, 2.8, 6-H'), 3.13 (1H, dddd, *J* = 11.1, 10.9, 4.3, 4.2, 4-H), 2.34 (1H, dddd, *J* = 13.7, 4.2, 2.7, 1.7, 3-H), 2.19 (1H, ddd, *J* = 13.7, 11.1, 5.2, 3-H'), 1.94 (1H, dddd, J = 13.4, 11.0, 10.9, 4.2, 5-H), 1.82 (1H, m, 5-H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.1, 145.2, 142.1, 128.6, 126.9, 126.4, 110.1, 108.0, 69.1, 62.7, 36.4, 34.1, 32.9; IR (thin film) ν_{max} 2959, 2948, 2926, 2897, 2873, 1498, 1452, 1439, 1431, 1377, 1351, 1341, 1310, 1269, 1241, 1229, 1181, 1174, 1158, 1146, 1119, 1110, 1093, 1080, 1060, 1027, 1013, 1005, 996, 952, 921, 898, 880, 829, 810, 799, 768, 739, 700, 669, 617, 599, 574, 534 cm^{-1}; HRMS M^+($C_{15}H_{16}O_2$) calcd 228.1150, found 228.1151.

(±)-(2S,4R)-4-(4-Chlorophenyl)-2-(furan-2-yl)tetrahydro-2H-pyran 3b

38 mg from 51 mg **1a**, 80%, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (1H, dd, *J* = 1.8, 0.8, 11-H), 7.30 (2H, d, *J* = 8.5, Ar-H), 7.19 (2H, d, *J* = 8.5, Ar-H'), 6.34 (1H, dd, *J* = 3.3, 1.8, 10-H), 6.29 (1H, d, *J* = 3.3, 8-H), 4.54 (1H, dd, *J* = 11.1, 2.5, 2-H), 4.23 (1H, ddd, *J* = 11.6, 4.1, 2.0, 6-H-eq), 3.68, (1H, ddd, *J* = 11.6, 11.4, 3.3, 6-H'-ax), 2.90 (1H, dddd, *J* = 11.4, 11.4, 4.4, 4.4, 4-H), 2.09 (1H, m, 3-H), 1.97 (1H, m, 3-H'), 1.94 – 1.75 (2H, m, 5-H,H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.4, 143.6, 142.2, 132.1, 128.7, 128.1, 110.1, 106.4, 73.0, 68.4, 41.0, 37.0, 33.0; IR (thin film) ν_{max} 2917, 2844, 1491, 1441, 1410, 1372, 1334, 1252, 1226, 1169, 1145, 1124, 1078, 1043, 1012, 998, 960, 943, 927, 884, 877, 843, 824, 803, 770, 736, 634, 599, 592 cm^{-1}; HRMS M^+($C_{15}H_{15}O_2Cl$) calcd 262.0761, found 262.0771.

(±)-(2S,4R)-2-(furan-2-yl)-4-(4-methoxyphenyl)tetrahydro-2H-pyran 3c

54 mg from 96 mg **1c**, 60 %, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (1H, dd, *J* = 1.8, 0.8, 11-H), 7.19 (2H, d, *J* = 8.6, Ar-H), 6.88 (2H, d, *J* = 8.7, Ar-H'), 6.34 (1H, dd, *J* = 3.2, 1.8, 10-H), 6.29 (1H, d, *J* = 3.2, 9-H), 4.55 (1H, dd, *J* = 11.1, 2.4, 2-H), 4.23 (1H, ddd, *J* = 11.5, 4.2, 1.9, 3-H), 3.80 (3H, s, Ar-OMe), 3.75 (1H, m, 6-H'), 2.87 (1H, m, 4-H), 2.13 – 1.75 (4H, m, 3-H,H', 5-H,H'); selected peaks for minor diastereomer: 7.45 (1H, d, *J* = 1.7, 11-H), 6.40 (1H, dd, *J* = 3.2, 1.7, 10-H), 6.36 (1H, m, 9-H), 5.07 (1H, dd, *J* = 5.0, 3.2, 2-H), 3.08 (1H, m, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.1, 154.6, 142.2, 137.4, 127.6, 113.9, 110.1, 106.3, 73.0, 68.6, 55.2, 40.7, 37.3, 33.3; IR (thin film) ν_{max} 2919, 2837, 1610, 1583, 1512, 1461, 1441,

1371, 1351, 1304, 1288, 1245, 1178, 1146, 1123, 1078, 1034, 1011, 998, 959, 943, 927, 848, 828, 806, 787, 753, 599, 547, 531, 504 cm^{-1}; HRMS $M^+(C_{16}H_{18}O_3)$ calcd 258.1256, found 258.1244.

(±)-(2S,4R)-2-(furan-2-yl)-4-(p-tolyl)tetrahydro-2H-pyran 3d

48 mg from 62 mg **1d**, 83 %, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (1H, m, 11-H), 7.26 (4H, m, Ar-H), 6.43 (1H, dd, *J* = 3.2, 1.7, 10-H), 6.39 (1H, d, *J* = 3.2, 9-H), 4.64 (1H, dd, *J* = 10.9, 2.5, 2-H), 4.33 (1H, ddd, *J* = 11.6, 4.3, 1.4, 6-H), 3.83 (1H, ddd, *J* = 11.6, 11.6, 2.6, 6-H'), 2.96 (1H, dddd, *J* = 11.7, 11.7, 4.2, 4.2, 4-H), 2.44 (3H, s, Ar-Me), 2.25 – 2.05 (2H, m, 3-H,H'), 2.04 – 1.83 (2H, m, 5-H,H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.3, 142.0, 141.9, 135.7, 129.0, 126.4, 109.8, 106.0, 72.8, 68.3, 40.8, 37.0, 33.0, 20.7; IR (thin film) ν_{max} 2916, 2847, 1514, 1440, 1373, 1349, 1251, 1226, 1193, 1169, 1142, 1121, 1108, 1078, 1039, 1011, 998, 959, 944, 924, 910, 875, 846, 804, 797, 734, 587, 600, 587, 600, 541, 505 cm^{-1}; HRMS $M^+(C_{16}H_{18}O_2)$ calcd 242.1307, found 242.1299.

(±)-(2S,4R)-4-(3,4-Dimethoxyphenyl)-2-(furan-2-yl)tetrahydro-2H-pyran 3e

75 mg from 84 mg **1e**, 95 %, m.p. = 87.5-88.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (1H, dd, *J* = 1.8, 0.8, 11-H), 6.86 – 6.77 (3H, m, Ar-H), 6.34 (1H, dd, *J* = 3.3, 1.8, 10-H), 6.29 (1H, d, *J* = 3.3, 9-H), 4.54 (1H, dd, *J* = 11.1, 2.4, 2-H), 4.23 (1H, ddd, *J* = 11.5, 4.2, 1.8, 6-H-eq), 3.89 (3H, s, Ar-OMe), 3.87 (3H, s, Ar-OMe'), 3.75 (1H, ddd, *J* = 11.5, 11.5, 3.3, 6-H'-

ax), 2.87 (1H, dddd, *J* = 11.6, 11.6, 4.3, 4.3, 4-H), 2.10 (1H, m, 3-H), 1.99 (1H, m, 3-H'), 1.95 – 1.75 (2H, m, 5-H,H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.6, 148.8, 147.5, 142.2, 137.9, 118.4, 111.2, 110.03, 109.96, 106.3, 73.0, 68.5, 55.8, 55.8, 41.2, 37.3, 33.3; IR (thin film) ν_{max} 2933, 2835, 1515, 1463, 1418, 1259, 1242, 1190, 1142, 1120, 1078, 1026, 1013, 951, 912, 882, 808, 762, 729, 638, 599, 541 cm^{-1}; HRMS M^+($C_{17}H_{20}O_4$) calcd 288.1362, found 288.1359.

(±)-(2S,4R)-4-(4-Bromophenyl)-2-(furan-2-yl)tetrahydro-2H-pyran 3f

80 mg from 88 mg **1f**, 96 %, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (2H, d, *J* = 8.5, Ar-H), 7.40 (1H, dd, *J* = 1.8, 0.8, 11-H), 7.14 (2H, d, *J* = 8.5, Ar-H), 6.35 (1H, dd, *J* = 3.3, 1.8, 10-H), 6.30 (1H, d, *J* = 3.3, 9-H), 4.55 (1H, dd, *J* = 11.0, 2.4, 2-H), 4.24 (1H, ddd, *J* = 11.5, 4.1, 2.0, 6-H-eq), 3.75 (1H, ddd, *J* = 11.5, 11.4, 3.7, 6-H'-ax), 2.88 (1H, dddd, *J* = 11.4, 11.4, 4.3, 4.3, 4-H), 2.09 (1H, m, 3-H), 2.00 (1H, m, 3-H'), 1.93 – 1.75 (2H, m, 5-H,H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.3, 144.1, 142.2, 131.6, 128.5, 120.1, 110.1, 106.4, 72.9, 68.3, 41.0, 36.9, 32.9; IR (thin film) ν_{max} 2917, 2846, 1488, 1441, 1252, 1227, 1169, 1145, 1122, 1075, 1044, 1008, 959, 927, 911, 884, 842, 820, 768, 732, 673, 599, 555 cm^{-1}; HRMS M^+($C_{15}H_{15}O_2Br$) calcd 306.0255, found 306.0268.

(±)-(2S,4R)-2-(Furan-2-yl)-4-(2,4,5-trimethoxyphenyl)tetrahydro-2H-pyran 3g

107 mg from 122 mg **1g**, 93 %, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (1H, dd, *J* = 1.8, 0.7, 11-H), 6.79 (1H, s, Ar-H), 6.54 (1H, s, Ar-H'), 6.33 (1H, dd, *J* = 3.2, 1.8, 10-H), 6.28 (1H, d, *J* = 3.2, 9-H), 4.57 (1H, dd, *J* = 11.4, 2.2, 2-H), 4.22 (1H, ddd, *J* = 11.5, 4.3, 1.2, 6-H), 3.87 (3H,

s, OMe), 3.85 (3H, s, OMe), 3.82 (3H, s, OMe), 3.78 (1H, ddd, *J* = 12.0, 11.5, 2.2, 6-H’), 3.32 (1H, dddd, *J* = 12.1, 11.8, 3.8, 3.7, 4-H), 2.05 (1H, dddd, *J* = 12.3, 3.7, 2.2, 2.0, 3-H), 1.94 (1H, ddd, *J* = 12.3, 11.8, 11.4, 3-H’), 1.87 (1H, ddd, *J* = 12.3, 12.0, 4.3, 5-H), 1.74 (1H, m, 5-H’); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 150.8, 147.7, 142.9, 142.1, 124.8, 111.0, 110.0, 106.2, 97.5, 73.2, 68.7, 55.7, 58.3, 56.1, 36.1, 33.8, 31.9; IR (thin film) ν_{max} 2937, 2835, 1508, 1463, 1440, 1397, 1372, 1316, 1217, 1243, 1229, 1202, 1148, 1126, 1078, 1033, 1014, 982, 957, 943, 927, 883, 858, 814, 733 cm^{-1}; HRMS M$^+$ ($C_{18}H_{22}O_5$): calcd 318.1467, found 318.1458.

(±)-(2S,4R)-4-(4-bromophenyl)-2-(5-methylfuran-2-yl)tetrahydro-2H-pyran 3h

80 mg from 121 mg **1h**, 70 %, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (2H, d, *J* = 8.4, Ar-H), 7.14 (2H, d, *J* = 8.4, Ar-H), 6.16 (1H, d, *J* = 3.1, 9-H), 5.91 (1H, dq, *J* = 3.1, 0.9, 19-H), 4.47 (1H, dd, *J* = 10.7, 2.8, 2-H), 4.23 (1H, ddd, *J* = 11.6, 4.2, 2.0, 6-H-eq), 3.74 (1H, ddd, *J* = 11.6, 11.4, 3.5, 6-H’-ax), 2.87 (1H, dddd, *J* = 11.3, 11.3, 4.6, 4.6, 4-H), 2.29 (3H, d, *J* = 0.9, 11-Me), 2.09 – 1.93 (2H, m, 3-H,H’), 1.92 – 1.74 (2H, m, 5-H,H’); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.6, 152.1, 144.2, 131.6, 128.6, 120.1, 107.4, 106.0, 73.0, 68.4, 41.2, 36.8, 33.0, 13.6; IR (thin film) ν_{max} 2944, 2918, 2843, 1489, 1440, 1373, 1251, 1221, 1075, 1050, 1009, 964, 821, 786, 669, 535, 500 cm^{-1}; HRMS M$^+$($C_{16}H_{17}O_2Br$) calcd 320.0412, found 320.0403.

(±)-(2S,4R)-2-(5-methylfuran-2-yl)-4-phenyltetrahydro-2H-pyran 3i

65 mg from 79 mg **1i**, 88 %, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 – 7.18 (5H, m, Ar-H), 6.15 (1H, d, *J* = 3.1, 9-H), 5.89 (1H, dq, *J* = 3.1, 0.9, 10-H), 4.47 (1H, dd, *J* = 10.3, 3.2, 2-H), 4.22

(1H, ddd, *J* = 11.6, 4.4, 1.7 6-H-eq), 3.73 (1H, ddd, *J* = 11.6, 11.6, 2.7, 6-H'-ax), 2.88 (1H, dddd, *J* = 11.7, 11.7, 4.5, 4.5, 4-H), 2.27 (3H, d, *J* = 0.9, 11-Me), 2.10 – 1.94 (2H, m, 3-H,H'), 1.93 – 1.74 (2H, m, 5-H,H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.8, 152.0, 145.3, 128.6, 126.8, 126.5, 107.3, 106.0, 73.1, 68.5, 41.7, 36.9, 33.1, 13.6; IR (thin film) ν_{max} 2920, 2848, 1496, 1452, 1374, 1251, 1220, 1123, 1078, 1050, 1022, 1012, 964, 940, 907, 786, 757, 727, 698, 668, 647 cm^{-1}; HRMS M^+($C_{16}H_{18}O_2$) calcd 242.1307, found 242.1297.

(±)-(2S,4R)-2-(5-methylfuran-2-yl)-4-(p-tolyl)tetrahydro-2H-pyran 3j

63 mg from 78 mg **1j**, 86 %, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21 – 7.12 (4H, m, Ar-H), 6.17 (1H, d, *J* = 3.1, 9-H), 5.91 (1H, dq, *J* = 3.1, 0.9, 10-H), 4.49 (1H, dd, *J* = 10.5, 3.0, 2-H), 4.24 (1H, ddd, *J* = 11.6, 4.3, 1.7, 6-H-eq), 3.75 (1H, ddd, *J* = 11.6, 11.6, 2.8, 6-H'-ax), 2.88 (1H, dddd, *J* = 11.6, 11.6, 4.5, 4.5, 4-H), 2.35 (3H, s, Ar-Me), 2.30 (3H, d, *J* = 0.9, 11-Me), 2.12 – 1.76 (4H, m, 3-H,H', 5-H,H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.8, 152.0, 142.3, 136.0, 129.2, 126.6, 107.3, 105.9, 73.0, 68.5, 41.2, 37.0, 33.1, 21.0, 13.6; IR (thin film) ν_{max} 2919, 2847, 1566, 1515, 1441, 1372, 1250, 1221, 1164, 1122, 1108, 1077, 1049, 1020, 1011, 964, 940, 911, 846, 814, 781, 751, 732, 719, 643, 589, 568, 540, 515 cm^{-1}; HRMS M^+($C_{17}H_{20}O_2$) calcd 256.1463, found 256.1457.

(±)-(2S,4R)-4-(4-chlorophenyl)-2-(5-methylfuran-2-yl)tetrahydro-2H-pyran 3k

32 mg from 50 mg **1k**, 68 %, ^{1}H NMR (300 MHz, $CDCl_3$) δ7.30 (2H, d, *J* = 8.5, Ar-H), 7.19 (2H, d, *J* = 8.5, Ar-H'), 6.16 (1H, d, *J* = 3.2, 9-H), 5.91 (1H, dq, *J* = 3.2, 1.1, 10-H), 4.48 (1H,

dd, J = 10.6, 2.8, 2-H), 4.23 (1H, ddd, J = 11.5, 4.1, 1.9, 6-H-eq), 3.74 (1H, ddd, J = 11.5, 11.4, 3.0, 6-H'-ax), 2.88 (1H, dddd, J = 11.4, 11.4, 4.6, 4.6, 4-H), 2.29 (3H, d, J = 0.8, 11-Me), 2.10 – 1.74 (4H, m, 3-H,H', 5-H,H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.6, 152.0, 143.7, 132.1, 128.6, 128.1, 107.4, 106.0, 72.9, 68.3, 41.1, 36.8, 33.0, 13.6; IR (thin film) ν_{max} 2942, 2919, 2842, 1566, 1492, 1441, 1410, 1372, 1333, 1251, 1221, 1124, 1084, 1050, 1012, 965, 940, 912, 843, 826, 787, 635, 620, 565, 536 cm^{-1}; HRMS M^+($C_{16}H_{17}O_2Cl$) calcd 276.0917, found 276.0905.

Procedure for the sodium hydride and tosyl chloride mediated cyclization of diol of 1a to form 3a without equilibration

Diol **1a** (300 mg, 1.22 mmol, 1 equiv.) was dissolved in anhydrous tetrahydrofuran (10 mL) under nitrogen. To this was added sodium hydride (60% suspension in mineral oil, 487 mg, 12.2 mmol, 10 equiv.), which caused effervescence, and the mixture was stirred at room temperature for 30 minutes. *p*-Toluenesulfonyl chloride (465 mg, 2.44 mmol, 2 equiv.) was added in one portion. The mixture was stirred at room temperature overnight after which TLC analysis indicated that the reaction had gone to completion. The reaction was quenched by adding to 2.0 M aqueous sodium hydroxide solution (40 mL) with stirring. The mixture was extracted with ethyl acetate (3 x 30 mL) and the combined organic phases were washed with water (2 × 50 mL) and brine (50 mL). The organic phase was then dried over magnesium sulfate and concentrated under reduced pressure. The diastereomeric ratio of tetrahydropyrans in the crude material was 1:0.7 (by ^{1}H NMR analysis). The crude material was purified by careful column chromatography on silica gel (Merck 9385 grade) eluting with a gradient from petrol ether to 98:2 petrol ether : diethyl ether then to 95:5 petrol ether :

diethyl ether. Fractions containing mixtures of the two diastereomers were recombined and chromatography was repeated. Chromatography was carried out thrice in total to afford two diastereomerically pure fractions of ***syn*-3a** (27 mg, 10%) and ***anti*-3a** (46 mg, 17%) as well as a diastereomeric mixed fraction (103 mg, 37%).

General Procedure for the reduction of ketodiesters 8a-k to form triols 4a-k

Solid lithium aluminium hydride (380 mg, 10.0 mmol, 10 equiv.) was suspended in anhydrous tetrahydrofuran (15 mL) under dry nitrogen. This was cooled to −15 °C before crude keto-diester **8a-k** (1.00 mmol, 1 equiv.) in anhydrous tetrahydrofuran (10 mL) was added dropwise. The reaction was then stirred at room temperature for 20 minutes after which TLC analysis indicated the reaction had gone to completion. The reaction was then quenched by the addition of diethyl ether (20 mL) followed by the slow dropwise addition of a 4:1 mixture of diethyl ether and acetone (20 mL) at −15 °C. The reaction mixture was then diluted with ethyl acetate (60 mL) and washed with water (150 mL) and 2M sodium hydroxide solution (250 mL). The combined aqueous phase was extracted with ethyl acetate (6 × 60 mL). The combined organic phase was then washed with brine (3 × 100 mL) before being dried over magnesium sulfate. The solution was then concentrated under reduced pressure. The crude product was purified by column chromatography using silica gel and a solvent gradient from dichloromethane reaching 97:3 dichloromethane-methanol. Following removal of solvent under reduced pressure, the product **4a-k** was isolated as a mixture of diastereomers. ^{1}H NMR data for each diastereomer of a mixture are generally listed separately. In the case of **4e**, the 1:1 ratio prevented the assignment of peaks to each diastereomer and the peaks are provided as a single list. In the case of **4b**, the diastereomers of which were separated by recrystallization, the data for each are listed separately. Separation of ***syn*** and ***anti*-4b** was achieved through repeated recrystallisation from hot (ca. 50 °C) ethyl acetate solutions which were cooled in the refrigerator (ca. 3 °C).

1-(Furan-2-yl)-4-(hydroxymethyl)-3-phenylpentane-1,5-diol 4a

45 mg from 142 mg **7a**, 23 % 2 steps, d.r. = 1:0.8; ^{1}H NMR (300 MHz, $CDCl_3$) δ major diastereomer: 7.30 (2H, d, *J* = 8.5, Ar-H), 7.19 (2H, d, *J* = 8.5, Ar-H'), 6.16 (1H, d, *J* = 3.2, 9-H), 5.91 (1H, dq, *J* = 3.2, 1.1, 10-H), 4.48 (1H, dd, *J* = 10.6, 2.8, 2-H), 4.23 (1H, ddd, *J* = 11.5, 4.1, 1.9, 6-H-eq), 3.74 (1H, ddd, *J* = 11.5, 11.4, 3.0, 6-H'-ax), 2.88 (1H, dddd, *J* = 11.4, 11.4, 4.6, 4.6, 4-H), 2.29 (3H, d, *J* = 0.8, 11-Me), 2.10 – 1.74 (4H, m, 3-H,H', 5-H,H'); minor diastereomer: 7.33 – 7.16 (5H, m, Ar-H, 11-H), 7.10 – 7.02 (1H, m, Ar-H'), 6.23 (1H, dd, *J* = 3.2, 1.8, 10-H), 6.04 (1H, d, *J* = 3.2, 9-H), 4.18 (1H, dd, *J* = 10.8, 1.6, 2-H), 3.94 – 3.10 (7H, m, 4-H,6-H,H',7-H,H',OH,OH), 2.59 – 1.60 (4H, m, 3-H,H',5-H,OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.1, 155.4, 142.40, 142.36, 142.1, 141.6, 128.6, 128.5, 128.3, 128.1, 126.6, 110.1, 110.0, 107.1, 105.2, 65.9, 64.9, 63.7, 63.4, 62.3, 46.6, 40.1, 38.9, 38.6; IR (thin film) ν_{max} 3317(br), 2889, 1494, 1453, 1146, 1000, 963, 907, 812, 727, 701, 646, 598, 492, 456 cm^{-1}

(±)-(1S,3S)-3-(4-chlorophenyl)-1-(furan-2-yl)-4-(hydroxymethyl)pentane-1,5-diol *anti*-4b

3.92 g of *syn/anti*-**4b** were obtained from 3.80 g **7b** (77 %, 2 steps), d.r. = 1:0.8 (in favour of *syn*-**4b**) . The diastereoisomers of **4b** were separated by repeated recrystallization from ethyl acetate. Data for *anti*-**4b**: ^{1}H NMR (400 MHz, CD_3CN) δ 7.35 (1H, dd, *J* = 1.8, 0.8, 11-H), 7.32 (2H, d, J = 8.5, Ar-H), 7.22 (2H, d, J = 8.5, Ar-H'), 6.30 (1H, dd, J = 3.2, 1.8, 10-H), 6.13 (1H, ddd, J = 3.2, 0.8, 0.8, 9-H), 4.06 (1H, ddd, J = 10.7, 5.7, 2.6, 2-H), 3.78 – 3.65 (1H, m, 6-H,H'), 3.39 (1H, ddd, J = 10.6, 4.9, 4.1, 7-H), 3.26 (1H, m, 2-OH), 3.25 (1H, ddd, J = 10.6, 7.0, 5.4, 7-H'), 3.11 (1H, ddd, J = 12.6, 9.0, 3.6, 4-H), 2.92 (1H, dd, J = 5.2, 5.2, 6-OH), 2.74 (1H, dd, J = 5.4, 4.9, 7-OH), 2.25 (1H, ddd, J = 14.1, 10.7, 3.6, 3-H), 1.99 (1H, ddd, J = 14.1, 12.6, 2.6, 3-H') (obscured by residual MeCN in CD_3CN), 1.78 (1H, m, 5-H); ^{13}C NMR (100 MHz, CD_3CN) δ 159.0, 143.0, 142.5, 132.1, 131.2, 129.0, 111.0, 105.9, 65.1, 62.8, 62.1, 48.4, 40.0, 39.4; IR (thin film) ν_{max} 3363(br), 3212, 2932, 2897, 1488, 1453, 1412, 1360, 1331, 1226, 1147, 1119, 1082, 1068, 1048, 1013, 996, 966, 875, 847, 761, 739, 668, 638, 617, 598, 569, 543, 513 cm^{-1}; HRMS MNa^+($C_{16}H_{19}O_4ClNa$) calcd 333.0870, found 333.0860.

(±)-(1R,3S)-3-(4-chlorophenyl)-1-(furan-2-yl)-4-(hydroxymethyl)pentane-1,5-diol *syn*-4b

^1H NMR (400 MHz, CD_3CN) δ 7.45 (1H, dd, J = 1.8, 0.8, 11-H), 7.33 (2H, d, J = 8.5, Ar-H), 7.12 (2H, d, J = 8.5, Ar-H'), 6.38 (1H, dd, J = 3.2, 1.8, 10-H), 6.21 (1H, d, J = 3.2, 9-H), 4.18 (1H, ddd, J = 9.8, 5.2, 5.1, 2-H), 3.73 – 3.65 (1H, m, 6-H,H'), 3.36 (1H, ddd, J = 10.6, 4.6, 4.2, 7-H), 3.28 (1H, d, J = 5.2, 2-OH), 3.14 (1H, ddd, J = 10.7, 6.8, 5.1, 7-H'), 2.93 (1H, dd, J = 5.0, 5.0, 6-OH), 2.72 (1H, dd, J = 5.1, 4.6, 7-OH), 2.58 (1H, ddd, J = 11.1, 8.8, 4.1, 4-H), 2.43 (1H, ddd, J = 13.7, 9.8, 4.1, 3-H), 2.09 (1H, ddd, J = 13.4, 11.1, 5.1, 3-H'), 1.78 (1H, m, 5-H); ^{13}C NMR (100 MHz, CD_3CN) δ 157.4, 143.2, 142.9, 132.1, 130.9, 129.0, 110.9, 107.4, 66.1, 62.4, 62.1, 48.3, 40.5, 39.4 ; IR (thin film) ν_{max} 3348(br), 2891, 1490, 1411, 1331, 1235, 1146, 1090, 1047, 1012, 964, 946, 908, 884, 859, 814, 727, 645, 598, 510 cm^{-1}; HRMS MNa^+($C_{16}H_{19}O_4ClNa$) calcd 333.0870, found 333.0860.

1-(Furan-2-yl)-4-(hydroxymethyl)-3-(4-methoxyphenyl)pentane-1,5-diol 4c

101 mg from 231 mg **7c**, 33 % 2 steps, d.r. = 1:0.65; ^{1}H NMR (300 MHz, $CDCl_3$) δ major diastereomer: 7.33 (1H, dd, *J* = 1.9, 0.7, 11-H), 6.95 (2H, d, *J* = 8.6, Ar-H), 6.84 – 6.77 (2H, m, Ar-H'), 6.28 (1H, dd, *J* = 3.2, 1.9, 10-H), 6.13 (1H, d, *J* = 3.2, 9-H), 4.33 (1H, dd, *J* = 8.8, 5.3, 2-H), 3.92 – 3.71 (2H, m, 7-H,H'), 3.76 (3H, s, Ar-OMe), 3.58 – 3.01 (6H, m, 4-H,6-H,H', 3 x OH), 2.54 – 1.70 (3H, m, 3-H,H',5-H); minor diastereomer: 7.25 (1H, m, 11-H), 7.09 (2H, d, *J* = 8.6, Ar-H), 6.84 – 6.77 (2H, m, Ar-H'), 6.23 (1H, dd, *J* = 3.2, 1.8, 10-H), 6.06 (1H, d, *J* = 3.2, 9-H), 4.20 (1H, dd, *J* = 11.0, 1.6, 2-H), 3.92 – 3.71 (2H, m, 7-H,H'), 3.76 (3H, s, Ar-OMe), 3.58 – 3.01 (6H, m, 4-H,6-H,H', 3 x OH), 2.54 – 1.70 (3H, m, 3-H,H',5-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.1, 157.2, 155.4, 142.1, 141.6, 134.23, 134.19, 129.2, 128.9, 114.0, 113.9, 110.1, 110.0, 107.1, 105.2, 66.0, 64.9, 63.8, 63.7, 62.6, 55.2, 50.6, 46.7, 39.3, 38.7, 38.1; IR (thin film) ν_{max} 3311(br), 2944, 2887, 2834, 1609, 1509, 1440, 1301, 1244, 1177, 1146, 1008, 963, 910, 883, 828, 736, 668, 649, 618, 598, 556 cm^{-1}; HRMS MNa^+($C_{17}H_{22}O_5Na$) calcd 329.1365, found 329.1361.

1-(Furan-2-yl)-4-(hydroxymethyl)-3-(p-tolyl)pentane-1,5-diol 4d

103 mg from 250 mg **7d**, 30 % 2 steps, d.r. = 1:0.75; ^{1}H NMR (300 MHz, $CDCl_3$) δ major diastereomer: 7.31 (1H, dd, *J* = 1.7, 0.6, 11-H), 7.10 – 7.06 (2H, m, Ar-H), 6.92 (2H, d, *J* = 8.0, Ar-H'), 6.27 (1H, dd, *J* = 3.1, 1.7, 10-H), 6.14 (1H, d, *J* = 3.1, 9-H), 4.33 (1H, dd, *J* = 8.8, 5.4, 2-H), 3.90 – 3.00 (7H, m, 4-H,6-H,H',7-H,H',OH,OH), 2.54 – 1.70 (4H, m, 3-H,H',5-H,OH), 2.30 (3H, s, a-Ar-Me); minor diastereomer: 7.24 (1H, dd, *J* = 1.7, 0.7, 11-H), 7.10 – 7.06 (4H, m, Ar-H), 6.22 (1H, dd, *J* = 3.1, 1.7, 10-H), 6.06 (1H, d, *J* = 3.1, 9-H), 4.19 (1H, dd, *J* = 10.9, 1.5, 2-H), 3.90 – 3.00 (7H, m, 4-H,6-H,H',7-H,H',OH,OH), 2.54 – 1.70

(4H, m, 3-H,H',5-H,OH), 2.30 (3H, s, Ar-Me); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.2, 155.4, 142.1, 141.6, 139.2, 139.1, 136.00, 135.95, 129.3, 129.2, 128.1, 127.9, 110.04, 109.98, 107.0, 105.2, 65.9, 64.9, 63.62, 63.58, 63.4, 62.2, 46.7, 46.6, 39.8, 38.6, 38.5, 21.0; IR (thin film) ν_{max} 3315 (br), 2922, 2889, 1512, 1435, 1147, 1010, 964, 909, 884, 814, 730, 632, 599, 533 cm^{-1}; HRMS MNa^+($C_{17}H_{22}O_4Na$) calcd 313.1416, found 313.1407.

3-(3,4-Dimethoxyphenyl)-1-(furan-2-yl)-4-(hydroxymethyl)pentane-1,5-diol 4e

1.25 g from 1.13 g **7e**, 85 % 2 steps, d.r. = 1:1; ^{1}H NMR (400 MHz, CD_3CN) δ 1:1 mixture of diastereomers, peaks could not be assigned to individual diastereomers (a and b) 7.33 (1H, dd, *J* = 1.7, 0.6, a/b-11-H), 7.26 (1H, m, b/a-11-H), 6.80 – 6.70 (2H + 2H, a+b-Ar-H), 6.61 – 6.35 (1H + 1H, a+b-Ar-H'), 6.29 (1H, dd, *J* = 3.1, 1.7, a/b-10-H), 6.24 (1H, dd, *J* = 3.2, 1.7, b/a-10-H), 6.15 (1H, d, *J* = 3.1, a/b-9-H), 6.07 (1H, d, *J* = 3.2, b/a-9-H), 4.36 (1H, dd, *J* = 8.7, 5.3, a/b-2-H), 4.24 (1H, dd, *J* = 11.0, 1.5, b/a-2-H), 4.00 – 3.72 (8H + 8H, m, a+b-6-H,H',2 x OMe), 3.65 – 3.01 (6H + 6H, m, a+b-7-H,H',4-H,3 x OH), 2.60 – 1.70 (3H + 3H, m, a+b-3-H,H',5-H); ^{13}C NMR (100 MHz, CD_3CN) δ 157.1, 155.5, 148.9, 148.7, 147.5, 142.1, 141.6, 134.86, 134.85, 120.3, 119.9, 111.2, 111.09, 110.08, 110.04, 107.0, 105.2, 66.0, 65.0, 64.0, 63.9, 63.6, 62.6, 55.84, 55.78, 46.8, 39.7, 38.7, 38.6; IR (thin film) ν_{max} 3330(br), 2934, 2835, 1590, 1511, 1493, 1420, 1323, 1255, 1233, 1139, 1022, 914, 884, 861, 808, 764, 728, 646, 598 cm^{-1}; HRMS MNa^+($C_{18}H_{24}O_6Na$) calcd 359.1471, found 359.1455.

3-(4-Bromophenyl)-1-(furan-2-yl)-4-(hydroxymethyl)pentane-1,5-diol 4f

132 mg from 297 mg **7f**, 35 % 2 steps, d.r. = 0.8:1; ^{1}H NMR (400 MHz, CD_3OD) δ major diastereomer: 7.47 – 7.42 (2H, Ar-H), 7.36 (1H, s, 11-H), 7.19 (2H, d, *J* = 8.3, Ar-H'), 6.28 (1H, m, 10-H), 6.14 (1H, d, *J* = 3.0, 9-H), 4.13 (1H, dd, *J* = 10.6, 2.5, 2-H), 3.76 (2H, d, *J* = 4.9, 6/7-H,H'), 3.43 ([1H, m, 7/6-H), 3.35 – 3.23 (1H, m, 7/6-H') (obscured by solvent), 3.23 – 3.10 (1H, m, 4-H), 2.33 (1H, ddd, *J* = 14.0, 10.6, 3.4, 3-H), 2.07 (1H, m, 3-H'), 1.90 – 1.79 (1H, 5-H); minor diastereomer: 7.47 – 7.42 (3H, 11-H, Ar-H), 7.06 (2H, d, *J* = 8.3, Ar-H'), 6.35 (1H, m, 10-H), 6.20 (1H, d, *J* = 3.0, 9-H), 4.20 (1H, dd, *J* = 10.1, 4.7, 2-H), 3.70 (2H, d, *J* = 5.1, 6/7-H,H'), 3.43 (1H, m, 7/6-H), 3.23 – 3.10 (1H, m, 7/6-H'), 2.60 (1H, m, 3-H), 2.50 (1H, ddd, *J* = 13.8, 10.3, 3.9, 4-H), 2.18 (1H, ddd, *J* = 13.1, 12.9, 4.7, 3-H'), 1.90 – 1.79 (1H, 5-H); ^{13}C NMR (100 MHz, CD_3OD) δ 159.0, 157.2, 143.43, 143.40, 143.3, 142.8, 132.49, 132.46, 131.8, 131.6, 121.05, 121.03, 111.07, 111.04, 108.1, 106.2, 66.7, 65.9, 62.2, 61.9, 61.7, 61.6, 49.4 (obscured by CD_3 septet), 41.3, 40.9, 39.8, 39.7; IR (thin film) ν_{max} 3355 (br), 2933, 2895, 1485, 1449, 1407, 1331, 1225, 1147, 1119, 1046, 1007, 964, 924, 875, 860, 845, 808, 736, 669, 634, 597, 569, 541 cm^{-1}; HRMS MNa^+($C_{16}H_{19}O_4NaBr$) calcd 377.0364, found 377.0369.

1-(Furan-2-yl)-4-(hydroxymethyl)-3-(2,4,5-trimethoxyphenyl)pentane-1,5-diol 4g

881 mg from 781 mg **7g**, 89 % 2 steps, d.r. = 1:0.5; ^{1}H NMR (300 MHz, CD_3CN) δ major diastereomer: 7.40 (1H, dd, *J* = 1.8, 0.8, 11-H), 6.68 (1H, s(br), Ar-H), 6.59 (1H, s, Ar-H'), 6.35 (1H, dd, *J* = 3.2, 1.8, 10-H), 6.17 (1H, d, *J* = 3.2, 9-H), 4.23 – 4.10 (1H, m, 2-H), 3.807 (3H, s, Ar-OMe), 3.73 (3H, s, Ar-OMe'), 3.65 (3H, s, Ar-OMe''), 3.82 – 3.60 (2H, m, 6-H,H'), 3.45 – 3.13 (2H, m, 7-H,H'), 2.95 (1H, dd, *J* = 5.2, 5.2, 6-OH), 2.85 (1H, m, 4-H), 2.67 (1H, dd, *J* = 5.3, 5.3, 7-OH), 2.35 (1H, ddd, *J* = 13.8, 9.7, 4.3, 3-H), 2.24 – 2.00 (1H, m,

3-H’), 1.90 – 1.80 (1H, m, 5-H); minor diastereomer: 7.35 (1H, dd, *J* = 1.8, 0.8, 11-H), 6.72 (1H, s, Ar-H), 6.65 (1H, s, Ar-H’), 6.29 (1H, dd, *J* = 3.2, 1.8, 10-H), 6.13 (1H, d, *J* = 3.2, 9-H), 4.23 – 4.10 (1H, m, 2-H), 3.811 (3H, s, Ar-OMe), 3.78 (3H, s, Ar-OMe’), 3.71 (3H, s, Ar-OMe’’), 3.82 – 3.60 (2H, m, 6-H,H’), 3.45 – 3.13 (3H, m, 4-H,7-H,H’), 3.03 (1H, dd, *J* = 5.3, 5.3, 6-OH), 2.77 (1H, dd, *J* = 5.8, 5.3, 7-OH), 2.24 – 2.00 (2H, m, 3-H,H’), 1.90 – 1.80 (1H, m, 5-H); ^{13}C NMR (75 MHz, CD_3CN) δ 159.1, 157.9, 153.1, 152.8, 149.1, 149.0, 144.3, 144.1, 142.6, 123.12, 123.07, 110.9, 107.2, 105.8, 99.6, 99.1, 66.4, 65.8, 63.5, 63.1, 62.7, 57.4, 57.0, 56.4, 47.73, 47.66, 38.9, 38.8, 30.8, 30.3; IR (thin film) ν_{max} 3355 (br), 2933, 1510, 1464, 1440, 1398, 1316, 1271, 1203, 1180, 1147, 1126, 1028, 865, 819, 741 cm^{-1}; HRMS MNa^+($C_{19}H_{26}O_7Na$) calcd 389.1576, found 389.1566.

3-(4-bromophenyl)-4-(hydroxymethyl)-1-(5-methylfuran-2-yl)pentane-1,5-diol 4h

95 mg from 271 mg **7h**, 28 % 2 steps, d.r. = 1:0.6; ^{1}H NMR (300 MHz, $CDCl_3$) δ major diastereomer: 7.39 (2H, d, *J* = 7.7, Ar-H), 6.96 (2H, d, *J* = 7.7, Ar-H’), 6.04 (1H, d, *J* = 2.7, 9-H), 5.88 (1H, d, *J* = 2.7, 10-H), 4.30 (1H, dd, *J* = 8.1, 4.5, 2-H), 4.10 – 1.60 (11H, m, 6-H,H’,7-H,H’,4-H,5-H,3-H,H’, 3 x OH), 2.23 (3H, s, 11-Me); minor diastereomer: 7.46 (2H, d, *J* = 7.4, Ar-H), 7.09 (2H, d, *J* = 7.4, Ar-H’), 5.96 (1H, d, *J* = 2.8, 9-H), 5.83 (1H, d, *J* = 2.8, 10-H), 4.14 (1H, d, *J* = 10.1, 2-H), 4.10 – 1.60 (11H, m, 6-H,H’,7-H,H’,4-H,5-H,3-H,H’, 3 x OH), 2.20 (3H, s, 11-Me); ^{13}C NMR (100 MHz, CD_3CN) δ 154.9, 153.3, 152.0, 151.6, 141.7, 141.6, 131.7, 131.6, 130.1, 129.9, 120.3, 120.2, 108.1, 106.3, 106.1, 106.0, 66.0, 65.0, 64.1, 63.8, 46.5, 39.3, 38.5, 38.42, 38.36; IR (thin film) ν_{max} 3316(br), 2920, 1486, 1435, 1408, 1218, 1072, 1008, 962, 908, 819, 784, 727, 646, 554 cm^{-1}; HRMS MNa^+($C_{17}H_{21}O_4BrNa$) calcd 391.0521, found 391.0507.

4-(hydroxymethyl)-1-(5-methylfuran-2-yl)-3-phenylpentane-1,5-diol 4i

108 mg from 223 mg **7i**, 35 % 2 steps, d.r. = 1:0.5; ^{1}H NMR (300 MHz, $CDCl_3$) δ major diastereomer: 7.32 – 7.15 (3H, m, Ar-H), 7.10 – 7.04 (2H, m, Ar-H'), 6.04 (1H, d, *J* = 3.0, 9-H), 5.87 (1H, dq, *J* = 3.0, 0.9, 10-H), 4.30 (1H, dd, *J* = 9.0, 5.3, 2-H), 3.97 – 3.79 (2H, m, 6-H,H'), 3.57 – 3.28 (2H, m, 7-H,H'), 2.58 (1H, ddd, *J* = 10.5, 10.2, 4.1, 4-H), 2.43 (1H, ddd, *J* = 13.2, 9.0, 4.1, 3-H), 2.24 (3H, d, *J* = 0.9, 11-Me), 2.15 (1H, ddd, *J* = 13.2, 10.5, 5.3, 3-H'), 2.04 – 1.75 (1H, m, 5-H); minor diastereomer: 7.32 – 7.15 (5H, m, Ar-H), 5.95 (1H, d, *J* = 3.0, 9-H), 5.82 (1H, dq, *J* = 3.0, 0.9, 10-H), 4.16 (1H, dd, *J* = 10.8, 1.9, 2-H), 3.97 – 3.79 (2H, m, 6-H,H'), 3.57 – 3.28 (2H, m, 7-H,H'), 3.15 (1H, m, 4-H), 2.33 (1H, m, 3-H), 2.20 (3H, d, *J* = 0.9, 11-Me), 2.04 – 1.75 (2H, m, 3-H',5-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 153.5, 151.9, 151.4, 142.5, 128.6, 128.5, 128.3, 128.1, 126.6, 126.5, 108.0, 106.1, 106.0, 105.9, 66.1, 65.0, 64.1, 63.9, 62.9, 46.7, 46.6, 40.1, 39.1, 38.54, 38.48, 13.6, 13.5; IR (thin film) ν_{max} 3307(br), 2921, 1452, 1219, 1019, 961, 909, 783, 763, 729, 701, 646, 587 cm^{-1}; HRMS MNa^+($C_{17}H_{22}O_4Na$) calcd 313.1416, found 313.1411.

4-(hydroxymethyl)-1-(5-methylfuran-2-yl)-3-(p-tolyl)pentane-1,5-diol 4j

134 mg from 287 mg **7j**, 35 % 2 steps, d.r. = 1:0.6; ^{1}H NMR (300 MHz, $CDCl_3$) δ major diastereomer: 7.07 – 7.05 (2H, m, Ar-H), 6.95 (2H, d, *J* = 8.0, Ar-H'), 6.02 (1H, d, *J* = 3.0, 9-H), 5.86 (1H, dq, *J* = 3.0, 1.0, 10-H), 4.29 (1H, dd, *J* = 9.0, 5.4, 2-H), 3.95 – 3.73 (2H, m, 6-H,H'), 3.55 – 3.25 (2H, m, 7-H,H'), 2.52 (1H, ddd, *J* = 10.4, 10.4, 4.1, 4-H), 2.45 – 2.05 (2H, m, 3-H,H'), 2.31 (3H, s, Ar-Me), 2.23 (3H, s, 11-Me), 2.02 – 1.75 (1H, m, 5-H): minor

diastereomer: 7.07 – 7.05 (4H, m, Ar-H), 5.94 (1H, d, *J* = 3.1, b-9-H), 5.81 (1H, dq, *J* = 3.1, 1.0, 10-H), 4.16 (1H, dd, *J* = 10.7, 1.6, 2-H), 3.95 – 3.73 (2H, m, 6-H,H'), 3.55 – 3.25 (2H, m, 7-H,H'), 3.09 (1H, m, 4-H), 2.45 – 2.05 (1H, m, 3-H), 2.31 (3H, s, Ar-Me), 2.20 (3H, s, 11-Me), 2.02 – 1.75 (2H, m, 3-H',5-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.3, 153.6, 151.8, 151.3, 139.30, 139.28, 136.0, 135.9, 129.23, 129.17, 128.2, 127.9, 107.9, 106.03, 105.95, 105.8, 66.1, 64.9, 64.0, 63.8, 62.7, 46.74, 46.66, 39.8, 38.7, 38.6, 38.5, 21.0, 13.5, 13.4; IR (thin film) ν_{max} 3312(br), 2920, 1512, 1435, 1381, 1219, 1019, 962, 938, 909, 783, 727, 570 cm^{-1}; HRMS MNa^+($C_{18}H_{24}O_4Na$) calcd 327.1572, found 327.1561.

3-(4-chlorophenyl)-4-(hydroxymethyl)-1-(5-methylfuran-2-yl)pentane-1,5-diol 4k

70 mg from 180 mg **7k**, 30 % 2 steps, d.r. = 1:0.6; ^{1}H NMR (300 MHz, $CDCl_3$) δ major diastereomer: 7.23 (2H, d, *J* = 8.4, Ar-H), 7.00 (2H, d, *J* = 8.4, Ar-H), 6.03 (1H, d, *J* = 3.0, 9-H), 5.87 (1H, dq, *J* = 3.0, 0.9, 10-H), 4.29 (1H, dd, *J* = 9.0, 5.2, 2-H), 3.97 – 3.78 (2H, m, 6-H,H'), 3.60 – 2.80 (5H, m, 7-H,H',3 x OH), 2.61 (1H, ddd, *J* = 10.3, 9.9, 4.1, 4-H), 2.47 – 2.27 (1H, m, 3-H), 2.23 (3H, d, *J* = 0.9, 11-Me), 2.11 (1H, ddd, *J* = 13.5, 10.3, 5.2, 3-H'), 1.95 – 1.70 (1H, m, 5-H); minor diastereomer: 7.25 (2H, d, *J* = 8.4, Ar-H), 7.13 (2H, d, *J* = 8.4, Ar-H), 5.95 (1H, d, *J* = 3.0, 9-H), 5.82 (1H, dq, *J* = 3.0, 0.9, 10-H), 4.12 (1H, dd, *J* = 10.9, 1.9, 2-H), 3.97 – 3.78 (2H, m, 6-H,H'), 3.60 – 2.80 (6H, m , 4-H,7-H,H',3 x OH), 2.47 – 2.27 (1H, m, 3-H), 2.20 (3H, d, *J* = 0.9, 11-Me), 1.95 – 1.70 (2H, m, 3-H',5-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.0, 153.3, 152.0, 151.5, 141.2, 141.1, 132.1, 129.7, 129.4, 128.7, 128.6, 108.1, 106.3, 106.0, 105.9, 65.7, 64.9, 63.92, 63.86, 63.5, 62.7, 46.6, 46.5, 39.3, 38.5, 38.4, 13.52, 13.45; IR (thin film) ν_{max} 3316 (br), 2921, 1562, 1489, 1435, 1411, 1374, 1219, 1089, 1012, 962, 820, 784, 723, 703, 553 cm^{-1}; HRMS MNa^+($C_{17}H_{21}O_4ClNa$) calcd 347.1026, found 347.1019.

General Procedure for the cyclisation of triols 4a-k to form trisubstituted tetrahydropyrans 5a-k

Triol **4a-k** (0.18 mmol) was dissolved in acetonitrile (5 mL). Quadrapure™ polymer supported sulfonic acid (20 mg, 5.0 mmol/g loading) was then added to the reaction mixture. The reaction mixture was stirred gently at room temperature for 24 hrs. Upon completion, the reaction mixture was filtered and the polymer beads washed three times with acetonitrile (5 mL). The solution was then concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (using a solvent gradient from petroleum ether to 1:1 petroleum ether – diethyl ether) to furnish the product **5a-k**. Crystals of **5g** for x-ray diffraction were obtained by slow evaporation of an ethyl acetate solution from a glass vial plugged with cotton wool.

(±)-((3S,4S,6S)-6-(furan-2-yl)-4-phenyltetrahydro-2H-pyran-3-yl)methanol 5a

40 mg from 43 mg **4a**, 99 %, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 – 7.20 (6H, m, 11-H, Ar-H), 6.33 (1H, dd, *J* = 3.1, 1.8, 10-H), 6.28 (1H, d, *J* = 3.1, 9-H), 4.54 (1H, dd, *J* = 10.0, 3.7, 2-H), 4.36 (1H, dd, *J* = 11.4, 4.4, 6-H-eq), 3.63 (1H, dd, *J* = 11.4, 11.3, 6-H-ax), 3.47 (1H, dd, *J* = 11.0, 3.3, 7-H), 3.30 (1H, dd, *J* = 11.0, 6.8, 7-H'), 2.77 (1H, ddd, *J* = 11.0, 11.2, 6.1, 4-H), 2.20 – 2.00 (3H, m, 3-H,H', 5-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.2, 143.0, 142.2, 128.7, 127.4, 126.8, 110.0, 106.5, 73.0, 71.2, 62.0, 43.8, 43.2, 37.5; IR (thin film) ν_{max} 3407, 2920,

1720, 1601, 1494, 1452, 1378, 1336, 1278, 1228, 1174, 1147, 1128, 1042, 1011, 909, 884, 847, 813, 760, 729, 700 cm^{-1}; HRMS MNa^+($C_{16}H_{18}O_3Na$) calcd 281.1154, found 281.1143.

(±)-((3S,4S,6S)-4-(4-chlorophenyl)-6-(furan-2-yl)tetrahydro-2H-pyran-3-yl)methanol 5b

61 mg from 68 mg **4b**, 95 %, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (1H, dd, *J* = 1.7, 0.7, 11-H), 7.31 (2H, d, *J* = 8.5, Ar-H), 7.20 (2H, d, *J* = 8.5, Ar-H'), 6.33 (1H, dd, *J* = 3.2, 1.7, 10-H), 6.28 (1H, d, *J* = 3.2, 9-H), 4.53 (1H, m, 2-H), 4.35 (1H, dd, *J* = 11.4, 4.4, 6-H-eq), 3.64 (1H, dd, *J* = 11.4, 11.3, 6-H-ax), 3.47 (1H, dd, *J* = 11.0, 3.2, 7-H), 3.31 (1H, dd, *J* = 11.0, 6.7, 7-H'), 2.79 (1H, ddd, *J* = 11.1, 8.3, 5.8, 4-H), 2.15 – 2.01 (3H, m, 3-H,H', 5-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.0, 142.3, 141.6, 132.4, 128.9, 128.8, 110.1, 106.6, 73.0, 71.1, 61.8, 43.2, 43.1, 37.5; IR (thin film) ν_{max} 3398 (br), 2919, 2855, 1491, 1411, 1338, 1266, 1227, 1173, 1147, 1128, 1087, 1073, 1044, 1012, 924, 884, 826, 735, 702 cm^{-1}; HRMS MNa^+($C_{16}H_{17}O_3ClNa$) calcd 315.0764, found 315.0777.

(±)-((3S,4S,6S)-6-(furan-2-yl)-4-(4-methoxyphenyl)tetrahydro-2H-pyran-3-yl)methanol 5c

60 mg from 73 mg **4c**, 87 %,^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (1H, dd, *J* = 1.7, 0.7, 11-H), 7.19 (2H, d, *J* = 8.7, Ar-H), 6.88 (2H, d, *J* = 8.7, Ar-H'), 6.33 (1H, dd, *J* = 3.2, 1.7, 10-H), 6.28 (1H, d, *J* = 3.2, 9-H), 4.53 (1H, m, 2-H), 4.34 (1H, dd, *J* = 11.3, 4.4, 6-H-eq), 3.79 (3H, s, OMe), 3.62 (1H, dd, *J* = 11.3, 11.3, 6-H'-ax), 3.48 (1H, dd, *J* = 11.0, 3.3, 7-H), 3.32 (1H, dd, *J* = 11.0, 6.7, 7-H'), 2.72 (1H, ddd, *J* = 11.0, 8.3, 5.6, 4-H), 2.15 – 2.02 (3H, m, 3-H,H', 5-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.4, 154.3, 142.2, 135.2, 128.3, 114.2, 110.1, 106.4,

73.2, 71.2, 62.2, 55.3, 43.6, 43.2, 37.8; IR (thin film) ν_{max} 3390 (br), 2937, 2916, 2835, 1610, 1511, 1462, 1304, 1248, 1178, 1129, 1148, 1129,1108, 1073, 1036, 1011, 910, 830, 803, 732, 632, 600, 530, 515 cm^{-1}; HRMS MH^+($C_{17}H_{21}O_4$) calcd 289.1440, found 289.1433.

(±)-((3S,4S,6S)-6-(furan-2-yl)-4-(p-tolyl)tetrahydro-2H-pyran-3-yl)methanol 5d

72 mg from 86 mg, **4d**, 89 %, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (1H, dd, *J* = 1.8, 0.8, 11-H), 7.17 – 7.13 (4H, m, Ar-H), 6.33 (1H, dd, *J* = 3.2, 1.8, 10-H), 6.27 (1H, d, *J* = 3.2, 9-H), 4.54 (1H, dd, *J* = 9.4, 4.3, 2-H), 4.35 (1H, dd, *J* = 11.4, 4.4, 6-H-eq), 3.62 (1H, dd, *J* = 11.4, 11.3, 6-H-ax), 3.48 (1H, dd, *J* = 11.0, 3.4, 7-H), 3.32 (1H, dd, *J* = 11.0, 6.7, 7-H'), 2.73 (1H, m, 4-H), 2.34 (3H, s, Ar-Me), 2.17 – 2.00 (3H, m, 3-H,H', 5-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.3, 142.2, 140.1, 136.4, 129.5, 127.3, 110.1, 106.4, 73.1, 71.2, 62.3, 43.6, 43.4, 37.7, 21.0; IR (thin film) ν_{max} 3410 (br), 2918, 2859, 1514, 1458, 1435, 1377, 1353, 1337, 1227, 1172, 1147, 1128, 1110, 1072, 1040, 1009, 942, 922, 901, 883, 851, 815, 732, 668, 599, 586, 545, 507 cm^{-1}; HRMS MNa^+($C_{17}H_{20}O_3Na$) calcd 295.1310, found 295.1320.

(±)-((3S,4S,6S)-4-(3,4-dimethoxyphenyl)-6-(furan-2-yl)tetrahydro-2H-pyran-3-yl)methanol 5e

213 mg from 252 mg **4e**, 89 %, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (1H, dd, *J* = 1.7, 0.7, 11-H), 6.83 (3H, m, Ar-H), 6.34 (1H, dd, *J* = 3.2, 1.7, 10-H), 6.29 (1H, d, *J* = 3.2, 9-H), 4.53 (1H, m, 2-H), 4.35 (1H, dd, *J* = 11.4, 4.4, 6-H-eq), 3.89 (3H, s, OMe), 3.87 (3H, s, OMe), 3.63 (1H, dd, *J* = 11.4, 11.3, 6-H-ax), 3.51 (1H, ddd, *J* = 11.1, 3.9, 3.9, 7-H), 3.35 (1H, ddd, *J* = 11.1, 6.3, 6.3, 7-H'), 2.73 (1H, ddd, *J* = 11.0, 8.0, 6.3, 4-H), 2.16 – 2.01 (3H, m, 3-H,H', 5-

H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.3, 149.1, 147.8, 142.3, 135.7, 119.4, 111.3, 110.2, 110.1, 106.5, 73.2, 71.2, 62.3, 55.89, 55.86, 43.7, 43.6, 37.8; IR (thin film) ν_{max} 3445 (br), 2947, 2923, 2873, 2836, 1591, 1516, 1463, 1452, 1440, 1377, 1351, 1318, 1309, 1261, 1241, 1231, 1181, 1174, 1157, 1174, 1144, 1121, 1077, 1060, 1041, 1026, 1012, 952, 899, 881, 809, 767, 738, 701 cm^{-1}; HRMS $MH^+(C_{18}H_{23}O_5)$ calcd 319.1545, found 319.1530.

(±)-((3S,4S,6S)-4-(4-bromophenyl)-6-(furan-2-yl)tetrahydro-2H-pyran-3-yl)methanol 5f

75 mg from 92 mg **4f**, 86 %, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (2H, d, *J* = 8.4, Ar-H), 7.38 (1H, dd, *J* = 1.8, 0.7, 11-H), 7.14 (2H, dd, *J* = 8.4, Ar-H’), 6.33 (1H, dd, *J* = 3.3, 1.8, 10-H), 6.28 (1H, d, *J* = 3.3, 9-H), 4.53 (1H, m, 2-H), 4.35 (1H, dd, *J* = 11.4, 4.4, 6-H), 3.64 (1H, dd, *J* = 11.4, 11.3, 6-H’), 3.47 (1H, dd, *J* = 11.0, 3.1, 7-H), 3.31 (1H, dd, *J* = 11.0, 6.7, 7-H’), 2.79 (1H, ddd, *J* = 11.0, 8.2, 6.0, 4-H), 2.14 – 1.98 (3H, m, 3-H,H’, 5-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.9, 142.2, 142.1, 131.8, 129.1, 120.4, 110.1, 106.6, 72.9, 71.0, 61.6, 43.1, 43.0, 37.3; IR (thin film) ν_{max} 3391 (br), 2919, 1488, 1408, 1338, 1148, 1128, 1072, 1044, 1009, 908, 884, 822, 731, 702, 648, 632, 599, 536 cm^{-1}; HRMS $MNa^+(C_{16}H_{17}O_3BrNa)$ calcd 359.0259, found 359.0243.

(±)-((3S,4S,6S)-6-(furan-2-yl)-4-(2,4,5-trimethoxyphenyl)tetrahydro-2H-pyran-3-yl)methanol 5g

188 mg from 207 mg **4g**, 96 %, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 (1H, dd, *J* = 1.8, 0.8, 11-H), 6.79 (1H, s, Ar-H), 6.55 (1H, s, Ar-H), 6.35 (1H, dd, *J* = 3.2, 1.8, 10-H), 6.31 (1H, d, *J* = 3.2, 9-H), 4.57 (1H, dd, *J* = 11.2, 2.1, 2-H), 4.24 (1H, dd, *J* = 11.5, 4.3, 6-H-eq), 3.90 (3H, s, Ar-OMe), 3.86 (3H, s, Ar-OMe'), 3.85 (3H, s, Ar-OMe''), 3.83 (1H, m, 6-H-ax) (obscured. by OMe), 3.44 – 3.26 (3H, m, 7-H,H',4-H), 2.28 – 2.14 (2H, m, 3-H,5-H), 2.01 (1H, ddd, *J* = 13.1, 3.6, 2.1, 3-H'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.4, 150.7, 148.0, 143.8, 142.2, 122.3, 110.1, 106.4, 97.5, 73.2, 71.3, 61.7, 56.9, 56.5, 56.1, 44.5, 35.8, 30.3; IR (thin film) ν_{max} 3447 (br), 2924, 2851, 1509, 1463, 1440, 1399, 1318, 1266, 1204, 1178, 1075, 1034, 1012, 863, 816, 734, 701 cm^{-1}; HRMS MNa^+($C_{19}H_{24}O_6Na$) calcd 371.1471, found 371.1477.

(±)-((3S,4S,6S)-4-(4-bromophenyl)-6-(5-methylfuran-2-yl)tetrahydro-2H-pyran-3-yl)methanol 5h

48 mg from 80 mg **4h**, 63 %, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (2H, d, *J* = 8.4, Ar-H), 7.14 (2H, dd, *J* = 8.4, Ar-H'), 6.15 (1H, d, *J* = 3.1, 9-H), 5.90 (1H, dd, *J* = 3.1, 0.9, 10-H), 4.46 (1H, dd, J = 10.3, 3.3, 2-H), 4.34 (1H, dd, *J* = 11.4, 4.4, 6-H), 3.63 (1H, dd, *J* = 11.4, 11.3, 6-H'), 3.46 (1H, dd, *J* = 10.9, 3.1, 7-H), 3.29 (1H, dd, *J* = 10.9, 6.7, 7-H'), 2.76 (1H, ddd, *J* = 11.2, 11.2, 6.0, 4-H), 2.28 (3H, s, 11-Me), 2.13 – 1.98 (3H, m, 3-H,H', 5-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.0, 151.9, 142.1, 131.7, 129.1, 120.2, 107.5, 105.9, 72.8, 70.9, 61.4, 43.1, 42.9, 37.2, 13.4; IR (thin film) ν_{max} 3419 (br), 2945, 2919, 2862, 1565, 1488, 1408, 1378, 1337, 1223, 1131, 1103, 1072, 1050, 1009, 850, 822, 785, 718 cm^{-1}; HRMS MNa^+($C_{17}H_{19}O_3BrNa$) calcd 373.0410, found 373.0401.

(±)-((3S,4S,6S)-6-(5-methylfuran-2-yl)-4-phenyltetrahydro-2H-pyran-3-yl)methanol 5i

62 mg from 79 mg **4i**, 84 %, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 – 7.20 (5H, m, Ar-H), 6.15 (1H, d, *J* = 3.1, 9-H), 5.90 (1H, dq, *J* = 3.1, 0.9, 10-H), 4.48 (1H, dd, J = 10.8, 2.9, 2-H), 4.36 (1H, dd, *J* = 11.4, 4.3, 6-H-eq), 3.63 (1H, dd, *J* = 11.4, 11.3, 6-H-ax), 3.47 (1H, m, 7-H), 3.31 (1H, m, 7-H'), 2.76 (1H, ddd, *J* = 11.4, 11.4, 4.8, 4-H), 2.29 (3H, s, 11-Me), 2.22 – 2.00 (3H, m, 3-H,H', 5-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.4, 152.1, 143.2, 128.8, 127.4, 126.8, 107.5, 106.0, 73.1, 71.2, 62.2, 44.0, 43.3, 37.4, 13.6; IR (thin film) ν_{max} 3402 (br), 2942, 2918, 2853, 1565, 1494, 1452, 1435, 1378, 1335, 1221, 1129, 1067, 1048, 1018, 949, 923, 782, 760, 700, 636, 618, 569, 554, 533 cm^{-1}; HRMS MNa^{+}($C_{17}H_{20}O_3Na$) calcd 295.1310, found 295.1309.

(±)-((3S,4S,6S)-6-(5-methylfuran-2-yl)-4-(p-tolyl)tetrahydro-2H-pyran-3-yl)methanol 5j

68 mg from 96 mg **4j**, 75 %, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.17 – 7.09 (4H, m, Ar-H), 6.15 (1H, d, *J* = 3.1, 9-H), 5.90 (1H, dq, *J* = 3.1, 0.9, 10-H), 4.47 (1H, dd, *J* = 10.7, 2.9, 2-H), 4.34 (1H, dd, *J* = 11.4, 4.4, 6-H-eq), 3.60 (1H, dd, *J* = 11.4, 11.3, 6-H-ax), 3.46 (1H, dd, *J* = 11.1, 3.4, 7-H), 3.29 (1H, dd, *J* = 11.1, 6.8, 7-H'), 2.71 (1H, ddd, *J* = 11.4, 11.4, 4.8, 4-H), 2.34 (3H, s, Ar-Me), 2.28 (3H, d, *J* = 0.9, 11-Me), 2.20 – 1.97 (3H, m, 3-H,H', 5-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.4, 152.0, 140.1, 136.3, 129.4, 127.2, 107.4, 105.9, 73.1, 71.1, 62.2, 43.5, 43.3, 37.5, 21.0, 13.5; IR (thin film) ν_{max} 3402 (br), 2943, 2918, 2857, 1565, 1514,

1435, 1378, 1335, 1305, 1280, 1220, 1169, 1129, 1109, 1074, 1048, 1018, 942, 922, 898, 882, 852, 816, 782, 756, 722, 636, 587, 549, 508 cm^{-1}; HRMS MH^+ ($C_{18}H_{23}O_3$) calcd 287.1647, found 287.1637.

(±)-((3S,4S,6S)-4-(4-chlorophenyl)-6-(5-methylfuran-2-yl)tetrahydro-2H-pyran-3-yl)methanol 5k

52 mg from 63 mg **4k**, 87 %, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (2H, d, *J* = 8.5, Ar-H), 7.20 (2H, d, *J* = 8.5, Ar-H), 6.15 (1H, d, *J* = 3.1, 9-H), 5.90 (1H, dq, *J* = 3.1, 0.9, 10-H), 4.47 (1H, dd, *J* = 10.4, 3.2, 2-H), 4.35 (1H, dd, *J* = 11.4, 4.4, 6-H-eq), 3.63 (1H, dd, *J* = 11.4, 11.3, 6-H-ax), 3.47 (1H, dd, *J* = 11.0, 3.3, 7-H), 3.31 (1H, dd, *J* = 11.0, 6.7, 7-H'), 2.78 (1H, ddd, *J* = 11.3, 11.3, 5.4, 4-H), 2.28 (3H, d, *J* = 0.9, 11-Me), 2.15 – 2.00 (3H, m, 3-H,H', 5-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.2, 152.1, 141.7, 132.4, 128.9, 128.8, 107.6, 106.0, 73.0, 71.1, 61.9, 43.3, 43.2, 37.4, 13.6; IR (thin film) ν_{max} 3391 (br), 2945, 2919, 2855, 1564, 1491, 1453, 1435, 1411, 1378, 1336, 1297, 1221, 1129, 1085, 1073, 1048, 1013, 942, 850, 825, 784, 730, 692, 646, 634, 573, 543, 530 cm^{-1}; HRMS MH^+($C_{17}H_{20}ClO_3$) calcd 307.1101, found 307.1069.

Procedure for the silylation of the triol *anti*-4b to form mono TBDPS ethers 11a and 11b

***Anti*-4b** (100 mg, 0.32 mmol, 1 equiv) was dissolved in 2.5 mL anhydrous THF under dry nitrogen. DMAP (391 mg, 3.2 mmol, 10 equiv) was added at room temperature and the mixture was stirred until the DMAP dissolved. A few small grains of calcium hydride (from a freshly ground chunk) were added (causing effervescence). The mixture was stirred at room temperature under nitrogen for 1 hr, after which the effervescence had stopped. *tert*-Butyldiphenylsilyl chloride (83 μL, 88 mg, 0.32 mmol, 1 equiv.) was added dropwise. The reaction was stirred at room temperature for 10 minutes. TLC indicated that significant starting material was still present. Another quantity of the silyl chloride (25 μL) was added and stirring continued for another 10 minutes. TLC indicated that only a slight amount of starting material remained and that the mono-silylated products were the main components (a small amount of bis-silylated product may also have formed). After the reaction flask had been placed in an ice/water cold bath, the reaction was diluted by the addition of 5 mL of diethyl ether and was quenched by the slow dropwise addition of distilled water (3 mL) which was accompanied initially by effervescence. The mixture was diluted by the addition of a further 20 mL of diethyl ether and 20 mL of water, followed by vigorous shaking/separation in a separating funnel. The aqueous layer was extracted with diethyl ether (3 x 10 mL), washed with water (20 mL), brine (20 mL) and dried over magnesium sulfate. Following filtration, the solvent was removed under reduced pressure. The crude material was purified by column chromatography on silica gel (Merck 9385 grade) using a slow gradient from dichloromethane to 9:1 dichloromethane : diethyl ether. Following removal of solvent under reduced pressure, two clean monosilylated fractions were obtained: **11a** (62 mg, 35 %) and **11b** (59 mg, 34 %).

(±)-(1S,3S,4R)-4-(((tert-butyldiphenylsilyl)oxy)methyl)-3-(4-chlorophenyl)-1-(furan-2-yl)pentane-1,5-diol 11a

^{1}H NMR (300 MHz, CD_3CN) δ 7.52 – 7.02 (15H, m, 11-H, Ar-H, Si-Ar-H), 6.29 (1H, dd, *J* = 3.2, 1.9, 10-H), 6.12 (1H, ddd, *J* = 3.2, 0.7, 0.7, 9-H), 4.04 (1H, ddd, *J* = 10.7, 5.5, 2.8, 2-H), 3.90 – 3.74 (2H, m, 6-H,H'), 3.48 (1H, dd, *J* = 10.3, 4.3, 7-H), 3.42 (1H, dd, *J* = 10.3, 6.4, 7-H'), 3.24 (1H, d, *J* = 5.5, 2-OH), 3.12 (1H, m, 4-H), 2.78 (1H, dd, *J* = 5.2, 5.2, 6-OH), 2.35 – 2.25 (1H, m, 3-H), 1.97 – 1.85 (2H, m, 3-H', 5-H), 0.99 (9H, s, Si-^{t}Bu); ^{13}C NMR (75 MHz, CD_3CN) δ 159.0, 142.9, 142.5, 136.3, 136.2, 134.3, 134.2, 131.2, 130.64, 130.61, 129.8, 129.1, 128.62, 128.58, 111.0, 105.9, 65.1, 63.5, 60.9, 48.9, 40.1, 40.0, 27.1, 19.6; IR (thin film) ν_{max} 3345 (br), 2930, 2857, 1489, 1472, 1390, 1361, 1261, 1145, 1106, 1088, 1013, 970, 940, 858, 822, 738 cm^{-1}; HRMS MNa$^+$($C_{32}H_{37}O_4SiClNa$) calcd 571.2047, found 571.2019.

(±)-(1S,3S,4S)-4-(((tert-butyldiphenylsilyl)oxy)methyl)-3-(4-chlorophenyl)-1-(furan-2-yl)pentane-1,5-diol 11b

^{1}H NMR (300 MHz, CD_3CN) δ 7.75 - 7.67 (4H, m, Si-Ar-H), 7.50 – 7.20 (11H, m, Si-Ar-H', Ar-H, 11-H), 6.30 (1H, dd, *J* = 3.2, 1.9, 10-H), 6.09 (1H, ddd, *J* = 3.2, 0.6, 0.6, 9-H), 4.08 (1H, ddd, *J* = 10.5, 5.3, 3.0, 2-H), 3.81 (1H, dd, *J* = 10.1, 4.9, 7-H), 3.76 (1H, dd, *J* = 10.1, 4.8, 7-H'), 3.45 (1H, m, 6-H), 3.35 – 3.21 (2H, m, 4-H, 6-H'), 3.20 (1H, d, *J* = 5.3, 2-OH), 2.55 (1H, dd, *J* = 5.5, 4.8, 6-OH), 2.28 – 2.19 (1H, m, 3-H), 2.02 – 1.85 (1H, m, 3-H', 5-H), 1.05 (9H, s, Si-^{t}Bu); ^{13}C NMR (75 MHz, CD_3CN) δ 159.0, 142.8, 142.5, 136.5, 136.4, 134.44, 134.40, 131.3, 130.71, 130.70, 129.8, 129.1, 128.71, 128.68, 111.0, 105.9, 65.1, 63.1, 61.3, 49.2, 40.2, 39.3, 27.2, 19.7; IR (thin film) ν_{max} 3365 (br), 2930, 2857, 1490, 1472, 1390, 1361, 1262, 1144, 1106, 1088, 1013, 940, 884, 822, 738 cm^{-1}; HRMS MNa$^+$($C_{32}H_{37}O_4SiClNa$) calcd 571.2047, found 571.2026.

Procedure for the silylation of *syn*-4b to form 11c and 11d

***Syn*-4b** (100 mg, 0.32 mmol, 1 equiv) was dissolved in 5 mL dichloromethane (which had previously been dried by stirring over calcium hydride under nitrogen, then allowed to settle) under dry nitrogen. DMAP (195 mg, 1.60 mmol, 5 equiv) was added at room temperature and the mixture was stirred until the DMAP dissolved. A few small grains of calcium hydride (from a freshly ground chunk) were added (causing effervescence). The mixture was stirred at room temperature under nitrogen for 1 hr, after which the effervescence had stopped. *tert*-Butyldiphenylsilyl chloride (83 µL, 88 mg, 0.32 mmol, 1 equiv.) was added dropwise. The reaction was stirred at room temperature for 10 minutes. TLC indicated that only a slight amount of starting material remained and that the mono-silylated products were the main components (a small amount of bis-silylated product may also have formed). After the reaction flask was placed in an ice/water bath, the reaction was diluted by the addition of 5 mL of diethyl ether and was quenched by the slow dropwise addition of distilled water (3 mL) which was accompanied initially by effervescence. The mixture was diluted by the addition of a further 20 mL of diethyl ether and 20 mL of water, followed by vigorous shaking/separation in a separating funnel. The aqueous layer was extracted with diethyl ether (3 x 10 mL), washed with water (20 mL), brine (20 mL) and dried over magnesium sulfate. Following filtration, the solvent was removed under reduced pressure. The crude material was purified by column chromatography on silica gel (Merck 9385 grade) using a slow gradient from dichloromethane to 9:1 dichloromethane : diethyl ether. Following removal of solvent under reduced pressure, two clean monosilylated fractions were obtained: **11c** (68 mg, 39 %) and **11d** (67 mg, 38 %).

(±)-(1R,3S,4R)-4-(((tert-butyldiphenylsilyl)oxy)methyl)-3-(4-chlorophenyl)-1-(furan-2-yl)pentane-1,5-diol 11c

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.28 (11H, m, Si-Ar-H, 11-H), 7.14 (2H, d, *J* = 8.0, Ar-H), 6.87 (2H, d, *J* = 8.0, Ar-H'), 6.34 (1H, s (br), 10-H), 6.22 (1H, s (br), 9-H), 4.30 (1H, m, 2-H), 3.99 (1H, m, 6-H), 3.91 (1H, m, 6-H'), 3.51 (1H, d, *J* = 10.0, 7-H), 3.34 (1H, dd, *J* = 10.0, 5.7, 7-H'), 2.66 (1H, dd, *J* = 10.1, 10.1, 4-H), 2.58 (1H, dd, *J* = 5.3, 5.3, 6-OH), 2.48 (1H, m, 3-H), 2.19 – 2.04 (2H, m, 2-OH, 3-H'), 1.86 (1H, m, 5-H), 0.99 (9H, s, Si-^{t}Bu); ^{13}C NMR (100 MHz, CD_3CN) δ 155.5, 142.2, 141.2, 135.4, 132.7, 132.6, 132.1, 129.83, 129.77, 129.4, 128.5, 127.74, 127.66, 110.1, 107.1, 66.2, 64.9, 63.5, 47.0, 39.4, 38.8, 26.8, 19.0; IR (thin film) ν_{max} 3364 (br), 2930, 1490, 1472, 1428, 1393, 1261, 1148, 1111, 1066, 1013, 823, 738 cm^{-1}; HRMS MNa^+($C_{32}H_{37}O_4SiClNa$) calcd 571.2047, found 571.2059.

(±)-(1R,3S,4S)-4-(((tert-butyldiphenylsilyl)oxy)methyl)-3-(4-chlorophenyl)-1-(furan-2-yl)pentane-1,5-diol 11d

^{1}H NMR (300 MHz, CD_3CN) δ 7.73 – 7.65 (4H, m, Si-Ar-H), 7.49 – 7.34 (7H, m, Si-Ar-H', 11-H), 7.27 (2H, d, *J* = 8.5, Ar-H), 7.09 (2H, d, *J* = 8.5, Ar-H'), 6.31 (1H, dd, *J* = 3.2, 1.9, 10-H), 6.10 (1H, d, *J* = 3.2, 9-H), 4.18 (1H, dd, *J* = 9.7, 5.0, 2-H), 3.79 (1H, dd, *J* = 10.3, 5.0, 7-H), 3.64 (1H, dd, *J* = 10.3, 5.6, 7-H'), 3.40 (1H, dd, *J* = 10.5, 4.2, 6-H), 3.27 (1H, s (br), 2-OH), 3.16 (1H, dd, *J* = 10.5, 7.9, 6-H'), 2.75 (1H, ddd, *J* = 11.5, 7.5, 4.2, 4-H), 2.50 (1H, s (br), 6-OH), 2.37 (1H, ddd, *J* = 13.5, 9.7, 4.2, 3-H), 2.15 (1H, ddd, *J* = 13.5, 11.5, 5.0, 3-H'), 1.84 (1H, m, 5-H), 1.04 (9H, s, Si-^{t}Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 142.9, 142.5, 136.4, 134.43, 134.40, 132.2, 131.1, 130.72, 130.69, 129.0, 128.70, 128.67, 110.9, 107.5, 66.3, 63.1, 60.9, 49.3, 40.5, 39.6, 27.3, 19.8; IR (thin film) ν_{max} 3365 (br), 2930, 2857, 1490, 1472, 1427, 1390, 1361, 1148, 1111, 1090, 1012, 941, 909, 884, 823, 778, 736 cm^{-1}; HRMS MNa$^+$($C_{32}H_{37}O_4SiClNa$) calcd 571.2047, found 571.2036.

General Procedure for the cyclization of silyl tetrahydopyrans 11a-d to form silyl tetrahydropyrans 12a-d.

These cyclisations were performed following the procedure outlined above for the cyclisation of triols **4a-k**. The reaction time was limited to 3 hours. **11a** (43 mg) provided 41 mg of **12a/b** (98 %). **11b** (53 mg) provided 48 mg of **12c/d** (94%). **11c** (47 mg) provided 45 mg of **12a/b** (99%). **11d** (59 mg) provided 55 mg of **12c/d** (96%).

(±)-tert-butyl(((3R,4S,6S)-4-(4-chlorophenyl)-6-(furan-2-yl)tetrahydro-2H-pyran-3-yl)methoxy)diphenylsilane 12a

^{1}H NMR (400 MHz, CD_3CN) δ 7.54 – 7.02 (11H, m, 11-H, Ar-H, Si-Ar-H), 6.32 (1H, dd, *J* = 3.1, 1.7, 10-H), 6.27 (1H, d, *J* = 3.1, 9-H), 4.54 (1H, dd, *J* = 10.3, 3.2, 2-H), 4.37 (1H, dd, *J* = 11.4, 4.3, 6-H), 3.73 (1H, dd, *J* = 11.4, 11.2, 6-H'), 3.40 (1H, dd, *J* = 10.7, 2.7, 7-H), 3.34 (1H, dd, *J* = 10.7, 6.5, 7-H'), 2.86 (1H, ddd, *J* = 11.3, 11.2, 5.1, 4-H), 2.13 – 1.94 (3H, m, 3-H,H', 5-H), 1.02 (9H, s, Si-^{t}Bu) (selected peaks for 12b: 6.42 (1H, dd, *J* = 3.2, 1.7, 10-H), 6.38 (1H, d, J = 3.2, 9-H), 5.08 (1H, d, J = 4.8, 2-H); ^{13}C NMR (100 MHz, CD_3CN) δ 155.8, 143.4, 143.1, 136.3, 136.2, 134.1, 134.0, 132.4, 130.74, 130.69, 130.2, 129.4, 128.7, 128.6, 111.1, 107.3, 73.6, 71.8, 63.5, 44.0, 43.5, 38.4, 27.1, 19.6; IR (thin film) ν_{max} 2929, 2856, 1589, 1491, 1471, 1427, 1389, 1149, 1110, 1076, 1046, 1013, 926, 823, 850, 738, 700 cm^{-1}; HRMS MNa$^+$($C_{32}H_{35}O_3ClSiNa$) calcd 553.1942, found 553.1937.

(±)-tert-butyl(((3S,4S,6S)-4-(4-chlorophenyl)-6-(furan-2-yl)tetrahydro-2H-pyran-3-yl)methoxy)diphenylsilane 12c

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 – 6.78 (15H, Ar-H, Si-Ar-H, 11-H), 6.36 (1H, dd, J = 3.2, 1.9, 10-H), 6.31 (1H, d, J = 3.2, 9-H), 4.60 (1H, m, 2-H), 4.55 (1H, dd, J = 11.4, 2.3, 6-H), 3.95 (1H, dd, J = 10.2, 10.2, 7-H), 3.93 (1H, m, 6-H'), 3.30 – 3.13 (2H, m, 4-H, 7-H'), 2.22 – 1.84 (3H, m, 3-H,H', 5-H), 0.94 (9H, s, Si-^{t}Bu); selected peak for 12d: 5.11, (H, dd, J = 4.9, 4.9, 2-H); ^{13}C NMR (100 MHz, CD_3CN) δ 156.2, 143.1, 142.6, 136.2, 136.1, 134.5, 134.3, 132.3, 130.62, 130.60, 129.5, 129.1, 128.9, 128.6, 111.2, 107.3, 73.8, 69.2, 60.3, 43.3, 41.8, 29.9, 27.0, 19.5; IR (thin film) ν_{max} 3070, 2929, 2889, 2856, 1589, 1492, 1472, 1428, 1390, 1362, 1253, 1152, 1111, 1091, 1013, 997, 924, 885, 860, 822, 797, 769, 739, 702 cm^{-1}; HRMS MNa$^+$($C_{32}H_{35}O_3SiClNa$) calcd 553.1942, found 553.1952.

General Procedure for the desilylation of silyl tetrahydopyrans 12a-d to form tetrahydropyrans 5b

Silyl-tetrahydropyrans **12a,b** (30 mg, 0.056 mmol, 1 equiv) were dissolved in tetrahydrofuran (5 mL). Tetrabutylammonium fluoride trihydrate (177 mg, 0.56 mmol, 10 equiv) was added and the mixture was stirred at room temperature under dry nitrogen for 36 hr, after which time TLC analysis indicated that the reaction had gone to completion. The mixture was partitioned between water (20 mL) and diethyl ether (20 mL). The aqueous layer was washed with diethyl ether (3 x 10 mL). The combined organic layers were washed with water (10 mL), brine (10 mL) and dried over magnesium sulfate. Following the removal of solvent under reduced pressure, NMR spectra of the crude material were obtained. The crude material was then purified by column chromatography on silica gel to afford a mixture of ***syn,anti*-5b** and ***anti,anti*-5b** (16 mg, 98 %). NMR analysis indicated that no significant change in d.r. had occurred during the deprotection step, or during the chromatographic purification. Similarly, 37 mg of **12c,d** provided 19 mg (92 %) of ***syn,syn*-5b** and ***anti,syn*-5b**.

(±)-((3R,4S,6S)-4-(4-chlorophenyl)-6-(furan-2-yl)tetrahydro-2H-pyran-3-yl)methanol *syn,syn*-5b

^{1}H NMR (400 MHz, CD_3CN) δ 7.47 (1H, s, 11-H), 7.36 (2H, d, *J* = 8.5, Ar-H), 7.27 (2H, d, *J* = 8.5, Ar-H'), 6.40 (2H, m, 10-H, 9-H), 4.53 (1H, dd, *J* = 11.5, 2.2, 2-H), 4.25 (1H, d, *J* = 11.3, 6-H), 3.75 (1H, d, *J* = 11.3, 6-H'), 3.65 (1H, ddd, *J* = 10.4, 10.4, 6.3, 7-H), 3.30 (1H, ddd, *J* = 13.1, 4.0, 4.0, 4-H), 3.06 (1H, m, 7-H'), 2.48 (1H, dd, *J* = 6.3, 4.5, 7-OH), 2.23 (1H, m, 3-H), 1.93 – 1.85 (2H, m, 3-H', 5-H); selected peaks for ***anti,syn*-5b**: 5.09 (1H, dd, *J* = 4.4, 4.4, 2-H), 3.87 (1H, dd, *J* = 11.7, 3.7, 6/7-H), 3.42 (1H, ddd, *J* = 9.2, 4.4, 4.4, 4-H); ^{13}C NMR (100 MHz, CD_3CN) δ 156.2, 143.1, 132.4, 129.8, 129.2, 111.2, 107.4, 73.8, 69.3, 58.1, 43.2, 42.3, 30.1; IR (thin film) ν_{max} 3397 (br), 2956, 1492, 1449, 1408, 1368, 1344, 1253, 1228, 1173, 1150, 1068, 1093, 1045, 1013, 990, 971, 885, 857, 825, 740, 701 cm^{-1}; HRMS MNa^+($C_{16}H_{17}O_3ClNa$) calcd 315.0764, found 315.0772.

Supporting Information

Supporting information: [^{1}H, ^{13}C, DEPT-135 NMR spectra of compounds **8a-k**, **9a-k**, **1a-k**, **3a-k**, **4a-k**, **5a-k**, **11a-k**, **12a,b**, **12c,d**, ***syn,syn*-5b**. TOCSY, NOESY, COSY, HMBC NMR spectra of selected compounds. X-ray crystallographic data for ***syn*-3e**, ***syn*-3g**, ***anti*-4b**, ***syn,anti*-5g**].

References:

1. (a) Brooks, H. A.; Gardner, D.; Poyser, J. P.; King, T. J., *J. Antibiot.* **1984,** 37, (11), 1501-1504; (b) Jansen, R.; Wray, V.; Irschik, H.; Reichenbach, H.; Höfle, G., *Tetrahedron Lett.* **1985,** 26, (49), 6031-6034; (c) Yotsu-Yamashita, M.; Haddock, R. L.; Yasumoto, T., *J. Am. Chem. Soc.* **1993,** 115, (3), 1147-1148; (d) Ruan, B. F.; Zhu, H. L., *Current Med. Chem.* **2012,** 19, (16), 2652-2664; (e) Smith, J. B.; Smith, L.; Pettit, G. R., *Biochem. Biophys. Res. Commun.* **1985,** 132, (3), 939-945; (f) Kinashi, H.; Ōtake, N.; Yonehara, H.; Sato, S.; Saito, Y., *Tetrahedron Lett.* **1973**, (49), 4955-4958; (g) Kusunoki, S.; Kato, K.; Tabu, K.; Inagaki, T.; Okabe, H.; Kaneda, H.; Suga, S.; Terao, Y.; Taga, T.; Takeda, S., *Gynecol. Oncol.* **2013,** 129, (3), 598-605; (h) Aicher, T. D.; Buszek, K. R.; Fang, F. G.; Forsyth, C. J.; Jung, S. H.; Kishi, Y.; Matelich, M. C.; Scola, P. M.; Spero, D. M.; Yoon, S. K., *J. Am. Chem. Soc.* **1992,** 114, (8), 3162-3164; (i) Towle, M. J.; Salvato, K. A.; Budrow, J.; Wels, B. F.; Kuznetsov, G.; Aalfs, K. K.; Welsh, S.; Zheng, W.; Seletsky, B. M.; Palme, M. H.; Habgood, G. J.; Singer, L. A.; DiPietro, L. V.; Wang, Y.; Chen, J. J.; Quincy, D. A.; Davis, A.; Yoshimatsu, K.; Kishi, Y.; Yu, M. J.; Littlefield, B. A., *Cancer Res.* **2001,** 61, (3), 1013-1021; (j) Kitagawa, I.; Kobayashi, M.; Katori, T.; Yamashita, M.; Tanaka, J.; Doi, M.; Ishida, T., *J. Am. Chem. Soc.* **1990,** 112, (9), 3710-3712; (k) Voigt, T.; Gerding-Reimers, C.; Ngoc Tran, T. T.; Bergmann, S.; Lachance, H.; Schölermann, B.; Brockmeyer, A.; Janning, P.; Ziegler, S.; Waldmann, H., *Angew. Chem. Int. Ed.* **2013,** 52, (1), 410-414.
2. (a) Nasir, N. M.; Ermanis, K.; Clarke, P. A., *Org. Biomol. Chem.* **2014,** 12, (21), 3323-3335; (b) Olier, C.; Kaafarani, M.; Gastaldi, S.; Bertrand, M. P., *Tetrahedron* **2010,** 66, (2), 413-445; (c) Clarke, P. A.; Nasir, N. M.; Sellars, P. B.; Peter, A. M.; Lawson, C. A.; Burroughs, J. L., *Org. Biomol. Chem.* **2016,** 14, (28), 6840-6852; (d) Watanabe, K.;

Li, J. M.; Veerasamy, N.; Ghosh, A.; Carter, R. G., *Org. Lett.* **2016,** 18, (8), 1744-1747; (e) Millan, A.; Smith, J. R.; Chen, J. L. Y.; Aggarwal, V. K., *Angew. Chem. Int. Ed.* **2016,** 55, (7), 2498-2502; (f) Elsworth, J. D.; Willis, C. L., *Chem. Commun.* **2008**, (13), 1587-1589; (g) Morris, W. J.; Custar, D. W.; Scheidt, K. A., *Org. Lett.* **2005,** 7, (6), 1113-1116; (h) Huang, H. B.; Panek, J. S., *J. Amer. Chem. Soc.* **2000,** 122, (40), 9836-9837; (i) Tadpetch, K.; Rychnovsky, S. D., *Org. Lett.* **2008,** 10, (21), 4839-4842; (j) Liu, F.; Loh, T.-P., *Org. Lett.* **2007,** 9, (11), 2063-2066; (k) Bai, Y.; Davis, D. C.; Dai, M., *Angew. Chem. Int. Ed.* **2014,** 53, (25), 6519-6522; (l) Liu, L.; Floreancig, P. E., *Angew. Chem. Int. Ed.* **2010,** 49, (17), 3069-3072.

3. (a) O'Brien, M.; Leach, A.; Armstrong, R. J.; Chong, K.; Sheridan, R., *Org. Biomol. Chem.* **2012,** 10, (12), 2392-2394; (b) O'Brien, M.; Cahill, S.; Evans, L. A., *Chem. Commun.* **2008**, (43), 5559-5561; (c) Cahill, S.; Evans, L. A.; O'Brien, M., *Tetrahedron Lett.* **2007,** 48, (32), 5683-5686; (d) Cahill, S.; O'Brien, M., *Tetrahedron Lett.* **2006,** 47, (22), 3665-3668.
4. (a) Danishefsky, S. J.; DeNinno, S.; Lartey, P., *J. Am. Chem. Soc.* **1987,** 109, (7), 2082-2089; (b) Maeba, I.; Iwata, K.; Usami, F.; Furukawa, H., *J. Org. Chem.* **1983,** 48, (18), 2998-3002.
5. Schreiber, S. L.; Wang, Z., *J. Am. Chem. Soc.* **1985,** 107, (18), 5303-5305.
6. (a) Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B., *J. Org. Chem.* **1981,** 46, (19), 3936-3938. (b) Achmatowicz Jr, O.; Bukowski, P.; Szechner, B.; Zwierzchowska, Z.; Zamojski, A., *Tetrahedron* **1971,** 27, (10), 1973-1996; (c) Wysocki, J.; Ortega, N.; Glorius, F., *Angew. Chem. Int. Ed.* **2014,** 53, (33), 8751-8755; (d) Oliver Kappe, C.; Shaun Murphree, S.; Padwa, A., *Tetrahedron* **1997,** 53, (42), 14179-14233; (e) Rigby*, J. H.; Pigge, F. C., [4 + 3] Cycloaddition Reactions. In *Organic Reactions*, John Wiley & Sons, Inc.: 2004.
7. CrystalClear 3.1, R. C., The Woodlands, Texas, U.S.A., 2013.
8. Palatinus, L.; Chapuis, G., *J. Appl. Cryst.* **2007,** 40, (4), 786-790.
9. (a) Sheldrick, G., *Acta Crystallographica Section C* **2015,** 71, (1), 3-8; (b) Hubschle, C. B.; Sheldrick, G. M.; Dittrich, B., *J. Appl. Cryst.* **2011,** 44, (6), 1281-1284.