Epoxide opening reactions of aryl substituted dihydropyran oxides: regio- and stereochemical studies directed towards deoxy-aryl-*C*-glycosides

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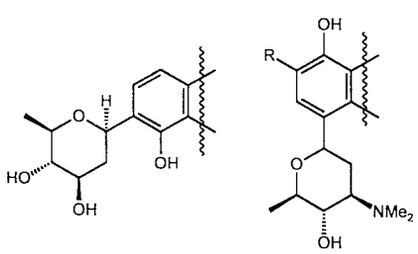
2-Aryl-substituted tetrahydropyrans with 3,4- or 4,5-*trans*-configured oxo substituents have been synthesized *via* ring-closing metathesis of allyl homoallyl ethers, epoxidation of the resulting dihydropyrans and opening of the epoxides with *O*-nucleophiles under different conditions. The substituent in the 2-position serves as an anchor group and adopts the equatorial configuration. Cleavage of the epoxide leads to the selective formation of *trans*-diaxial or *trans*-diequatorially substituted tetrahydropyrans, depending on the conditions and on the relative configuration of the starting epoxide. A mechanism for the formation of *trans*-diequatorial cleavage products *via* a sequential epoxide opening/anomerization is presented.

Introduction

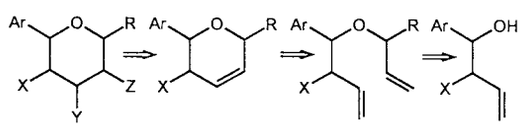
Functionalised tetrahydropyrans play an important role in many fields of synthetic organic and natural products chemistry.[1] Tetrahydropyrans with hydroxy substituents have found interest from several points of view, as they are structural elements in annonaceous acetogenins,[2] polyether antibiotics[3] and *C*-glycosides.[4,5] Members of the latter group are very often prepared starting from sugar electrophiles (derived from naturally occurring sugars) and *C*-nucleophiles. If the *C*-nucleophile is an electron rich aromatic system, an aryl-*C*-glycosides results,[6] which has a structural pattern which is found in many natural products derived from microorganisms[7] or plants.[8–11] In particular, compounds from microbial sources, such as aquayamycin, the vineomycins, hedamycin and the pluramycins, have attracted much attention because of their antibiotic and antitumor activity.[7] Compounds of this type have some structural features in common: one or two partially deoxygenated glycosidic moieties are linked directly to a comparatively large aromatic aglycon part, which has methoxy or hydroxy functionalities in the *ortho*- or *para*-position to the glycosidic substituent. Relative configuration of the hydroxy groups attached to the glycosidic core of the molecule is mostly *trans*.



aquayamycin
vineomycin

hedamycin
kidamycin

We are interested in *de novo* syntheses of the glycosidic part of aryl-*C*-glycosides based on ring closure by C–C-bond formation.[12] In Scheme 1 the synthetic concept is outlined: starting from homoallylic alcohols, allyl homoallyl ethers are prepared, ring-closing metathesis yields dihydropyrans which are subsequently elaborated towards aryl-*C*-glycosides *via* epoxidation and *trans*-selective cleavage of the dihydropyran oxides.



Ar = aryl; X, Y, Z = H, OR

Scheme 1

Dihydropyran oxide cleavage reactions have been thorougly investigated by Crotti *et al*. in the course of their studies towards regiochemical control of epoxide opening by chelating processes.[13] These investigations include unfunctionalised dihydropyran oxide,[14,15] 2-benzyloxydihydropyran oxide[16] and a 2-benzyloxy-6-methyldihydropyran oxide.[17] To the best of our knowledge, the cleavage of dihydropyran oxides with an aryl substituent in the 2-position has not been described so far. The following factors are likely to influence the course of the reaction: the acid catalyst and the nucleophile, the electronic nature of the aryl substituent, the relative configuration of the starting epoxide and the proximity of the oxirane ring to the aryl substituent. In this contribution we wish to describe our results for cleavage reactions of dihydropyran oxides under various conditions.

Results and discussion

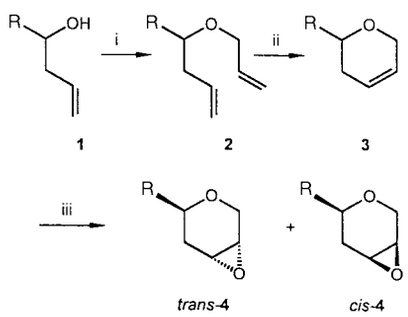
Preparation of the dihydropyran oxides and assignment of relative configuration

The dihydropyrans **3** required for this study were prepared by ring-closing metathesis[18] of allyl homoallyl ethers **2** which are easily accessible by allylation of homoallylic alcohols **1**. Five different substituents (four aryl substituents and one non-aromatic substituent with similar steric demand) were chosen for this investigation, which can all be expected to serve as a molecular anchor group (*i.e*. to adopt an equatorial configuration) but differ significantly in their electronic properties. Tetrahydropyran oxides **4** are easily accessible by epoxidation of dihydropyrans **3** with MCPBA. Both diastereomers are formed in equal amounts under these conditions and they can be easily separated by column chromatography on silica. In all cases the *trans*-isomer is less polar and is eluted first. Scheme 2 and Table 1 summarize the synthesis.

Synthesis of a dihydropyran oxide **10** with the aryl group in the neighbouring position is not straightforward, as alkylation

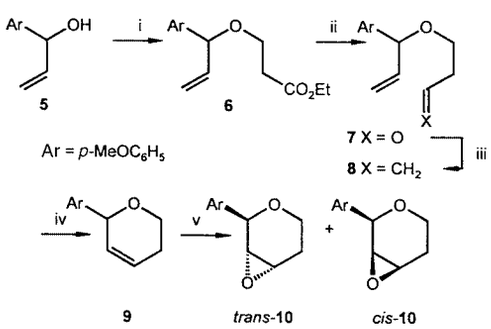
Table 1 Preparation of dihydropyran oxides **4**

R	No	Yield (%)	No	Yield (%)	No	Yield (%)
Cyclohexyl	**2a**	84	**3a**	90	**4a**	65
Phenyl	**2b**	85	**3b**	90	**4b**	72
2-Methoxyphenyl	**2c**	87	**3c**	93	**4c**	75
3-Methoxyphenyl	**2d**	92	**3d**	92	**4d**	70
4-Methoxyphenyl	**2e**	84	**3e**	92	**4e**	69



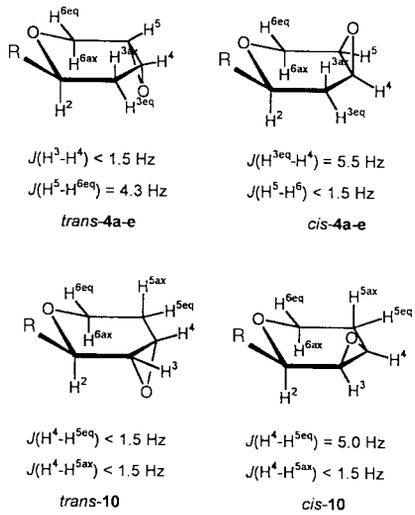
Scheme 2 *Reagents*: i, NaH, allyl bromide; ii, $Cl_2(PCy_3)_2Ru{=}CH{-}CH{=}CPh_2$ (2 mol%); iii, MCPBA, separate.

of the sodium salt of allyl alcohol **5** with commercially available 1-bromobut-3-ene does not produce the desired metathesis precursor **8**. Probably butadiene is formed *via* an elimination reaction, because the allylic alcohol **5** is recovered from the reaction. However, if **5** is alkylated with ethyl 3-bromopropionate, ester **6** is isolated in moderate yield. Ester **6** also results from the reaction of alcohol **5** with methyl acrylate in the presence of a catalytic amount of base. However, isolated yields are below 10%. Reduction of the ester functionality with DIBAL-H yields aldehyde **7** and subsequent Wittig-olefination gives the metathesis precursor **8**. At this step excess of base has to be carefully avoided as aldehyde **7** readily decomposes into the starting alcohol **5** and acrolein (acrylaldehyde). Ring-closing metathesis of **8** proceeds efficiently and leads to the dihydropyran **9** in good yield. Epoxidation of **9** with MCPBA is moderately stereoselective due to the proximity of the aryl substituent with the *trans*-diastereoisomer *trans*-**10** being the preferred product (dr = 4 : 1) (Scheme 3).



Scheme 3 *Reagents*: i, NaH, ethyl 3-bromopropionate; ii, DIBAL-H; iii, $[PMe(Ph)_3]Br$, BuLi; iv, $Cl_2(PCy_3)_2Ru{=}CH{-}CH{=}CPh_2$ (2 mol%); v, MCPBA.

Assignment of the relative configuration of the epoxides **4** is possible by comparison of the coupling constants ^3J(H-5/H-6) and ^3J(H-3/H-4) for the *cis*- and the *trans*-diastereomer. For ^3J(H-2/H-3_{ax}) in all cases a large coupling constant of approximately 11 Hz is observed, which indicates that the substituent in the 2-position adopts an equatorial configuration. For regioisomeric epoxides **10** the coupling constants ^3J(H-$5_{ax/eq}$/H-4) are most indicative for structural assignment. (Scheme 4).



Scheme 4

Epoxide cleavage reactions mediated by Brønsted-acids

From early investigations into the regiochemistry of the epoxide opening reactions of steroidal epoxides, Fürst and Plattner deduced the following rule:[19,20] conformationally rigid oxiranes annellated to six membered carbo- or heterocycles are cleaved by nucleophiles to give the *trans*-diaxial products (kinetic control). This effect is stereoelectronic in nature: *trans*-diaxial cleavage proceeds *via* an energetically favorable chair-like transition state, whereas *trans*-diequatorial epoxide opening (leading to the thermodynamically product) requires a boat-like transition state. Exceptions to this rule are to be expected if steric or electronic reasons dominate the stereoelectronic effect mentioned above, or if the six membered ring epoxide is conformationally mobile. From the work done by Crotti *et al*., it becomes clear, that for 2-benzyloxy substituted dihydropyran oxides (*i.e.* epoxides with an acetal functionality in the β-position), the *trans*-diaxial cleavage products are obtained preferentially under non-chelating conditions. However, *trans*-diequatorial byproducts are always observed in varying amounts between 3 and 37%, which can be explained by the fact that the dihydropyran oxides investigated in these studies are not conformationally rigid, which is attributed to the anomeric effect (*i.e*. the substituent in the 2-position, the benzyloxy group, may also adopt the axial orientation).[16] The dihydropyran oxides used in our study differ significantly from the ones used by Crotti *et al.* In order to gain insight into the conformational rigidity of the 2-aryl-substituted dihydropyran oxides and the resulting cleavage products, we investigated some opening reactions of *trans*- and *cis*-**4e** and its regioisomers *trans*- and *cis*-**10**.

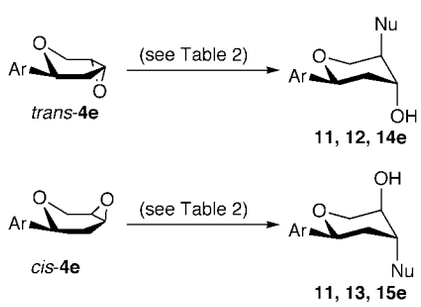
Cleavage of epoxides *trans*-**4e** and *cis*-**4e** with water in the presence of sulfuric acid (Table 2, entries 1 and 2), with water in the presence of ceric ammonium nitrate[21,22] (entries 3 and 4), with hydrochloric acid (entries 5 and 6) or with acetic acid (entries 7 and 8) gives *trans*-diaxial opening products in all cases with high selectivity, as no *trans*-diequatorial products are detectable from the H-NMR spectra of the crude reaction mixtures. Cleavage with hydrochloric acid results in the formation of a minor amount of diol **11**, and cleavage in refluxing acetic acid gives a 20% admixture of a diacetylated compound **16**, which is also a *trans*-diaxial cleavage product and is probably formed *via* an esterification of **14e** or **15e** under the reaction conditions. In all cleavage products the value for ^3J(H-3_{ax}–H-2) is approximately 11 Hz, indicating that the hydrogen H-2 adopts an axial position. From these results it may be concluded that the aryl substituent in the 2-position of the dihydropyran oxide or the tetrahydropyran serves as an

Table 2 Epoxide cleavage reactions of *trans*- and *cis*-**4e**

Entry	Epoxide	Reagents (T/°C)	Cleavage products (yield (%))
1	*trans*-**4e**	THF–H_2O–H_2SO_4 (65)	**11**, Nu = OH (88)
2	*cis*-**4e**	THF–H_2O–H_2SO_4 (65)	**11**, Nu = OH (89)
3	*trans*-**4e**	MeCN–H_2O–CAN (20)	**11**, Nu = OH (85)
4	*cis*-**4e**	MeCN–H_2O–CAN (20)	**11**, Nu = OH (84)
5	*trans*-**4e**	THF–HCl(aq.) (20)	**12**, Nu = Cl (70); **11** (30)
6	*cis*-**4e**	THF–HCl(aq.) (20)	**13**, Nu = Cl (78); **11** (22)
7	*trans*-**4e**	CH_3COOH (80)	**14e**, Nu = OAc (58); **16** (21)
8	*cis*-**4e**	CH_3COOH (80)	**15e**, Nu = OAc (58); **16** (21)

Table 3 Epoxide cleavage reactions mediated by boron trifluoride etherate

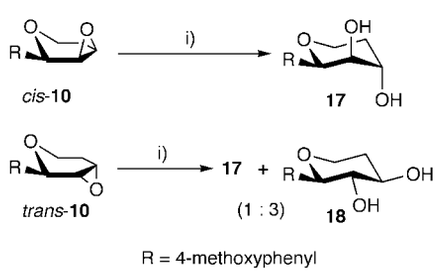
Entry	R	Epoxide (**No**)	Cleavage products (**No**) (ratio)	Total yield (%)
1	Cyclohexyl	*trans*-**4a**	Nu = OAc: **14a**	86
2	Cyclohexyl	*cis*-**4a**	Nu = OAc: **15a**	89
3	Phenyl	*trans*-**4b**	Nu = OAc: **14b**	91
4	Phenyl	*cis*-**4b**	Nu = OAc: **15b**	86
5	*o*-Methoxyphenyl	*trans*-**4c**	Nu = OAc: **14c**:**19c**:**23** (2:1:1)	82
6	*o*-Methoxyphenyl	*cis*-**4c**	Nu = OAc: **15c**	90
7	*m*-Methoxyphenyl	*trans*-**4d**	Nu = OAc: **14d**	88
8	*m*-Methoxyphenyl	*cis*-**4d**	Nu = OAc: **15d**	80
9	*p*-Methoxyphenyl	*trans*-**4e**	Nu = OAc: **14e**:**19e** (1:9)	98
10	*p*-Methoxyphenyl	*cis*-**4e**	Nu = OAc: **15e**	92
11	*p*-Methoxyphenyl	*trans*-**4e**	Nu = OBenzyl: **20e**:**21e** (2:1)	91
12	*p*-Methoxyphenyl	*cis*-**4e**	Nu = OBenzyl: **22e**	87



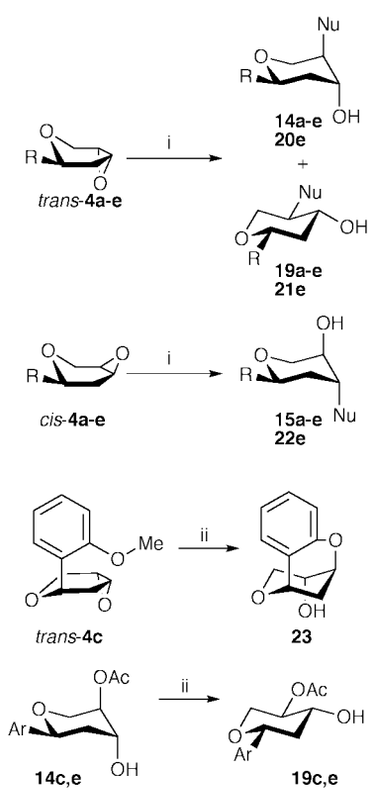
Scheme 5 *Reagents* (see Table 2).

anchor group. The results are summarized in Scheme 5 and Table 2.

Acid-mediated hydrolysis of regioisomeric dihydropyran oxides *trans*- and *cis*-**10** gives slightly different results: while for epoxide *cis*-**10** under the reaction conditions the *trans*-diaxial cleavage product **17** results exclusively (which is in accord with the Fürst–Plattner-rule), its diastereoisomer *trans*-**10** is preferably cleaved with different regiochemistry to give the all-equatorial isomer **18** (dr = 3:1). In the latter case attack of the nucleophile occurs at the remote 4-position because the 3-position is shielded by the aryl substituent. Obviously, in this case the stereoelectronic effect, which is the origin for the Fürst–Plattner selectivity, is dominated by a steric effect, whereas in the case of *cis*-**10**, the steric and stereoelectronic effects work in the same direction (Scheme 6).



Scheme 6 *Reagents*: i, H_2O–H_2SO_4.

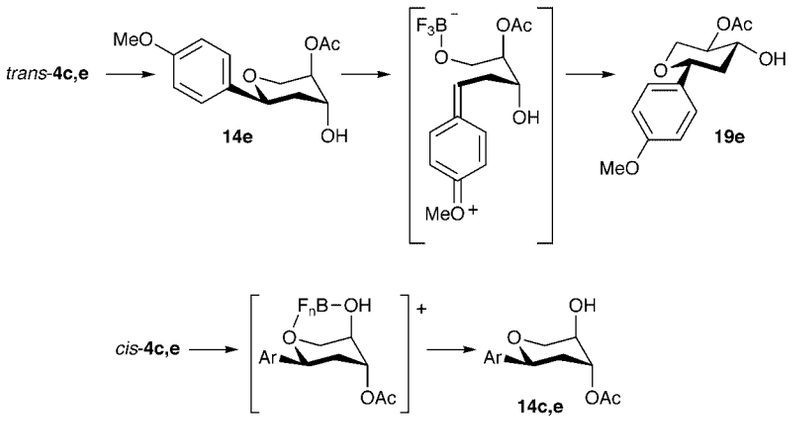


Scheme 7 *Reagents*: i, NuH, BF_3·OEt_2 (see Table 3); ii, BF_3·OEt_2.

Epoxide cleavage reactions mediated by boron trifluoride–diethyl ether

Boron trifluoride–diethyl ether is probably among the most commonly used Lewis acids in organic synthesis. We therefore investigated the cleavage of various dihydropyran oxides **4** in the presence of this Lewis acid. Acetic acid was chosen as the nucleophile, as acetates are easily hydrolysed or reduced to liberate the free hydroxy functionality. The results are summarized in Scheme 7 and Table 3.

If R = cyclohexyl, phenyl or 3-methoxyphenyl, the Fürst–



Scheme 8

Plattner products are obtained in very high selectivity, regardless of the relative configuration of the starting epoxide (entries 1–4 and 7, 8). Different results are obtained if R = 2- or 4-methoxyphenyl. Starting from dihydropyran oxide *trans*-**4e** (entry 9), the expected Fürst–Plattner product **14e** becomes the minor cleavage product. The major product (**14e**:**19e** = 1:9) under these conditions is a *trans*-diequatorial tetrahydropyran **19e**, which is a diastereoisomer, not a regioisomer, of **14e**. Reaction of *cis*-**4e** under the conditions exclusively yields the normal *trans*-diaxial opening product **15e** (entry 10). Qualitatively the same results were obtained if benzylic alcohol was used as a nucleophile: cleavage of the *trans*-epoxide **4e** gave a mixture of *trans*-diaxial and *trans*-diequatorial tetrahydropyrans, however the ratio was reversed (**20e**:**21e** = 2:1) (entry 11). Opening of *cis*-**4e** exclusively yields the expected product **22e** (entry 12). Similar results are obtained for the dihydropyran oxides with the 2-methoxyphenyl substituent, *trans*- and *cis*-**4c**. However, one significant difference is observed compared to **4e**: if *trans*-**4c** reacts with acetic acid under the conditions described above for *trans*-**4e**, three products are observed: the *trans*-diaxial tetrahydropyran **14c**, its *trans*-diequatorial diastereomer **19c** and an unexpected tricyclic product **23** (entry 5). Cleavage of *cis*-**4c** again yields the Fürst–Plattner product **15c** exclusively (entry 6). Because tetrahydropyrans **19c**,**e** are diastereomers and not regioisomers of **14c**,**e** it becomes likely that **19c**,**e** are consecutive products of **14c**,**e** formed *via* a Lewis acid mediated isomerization reaction. In order to check this hypothesis, **14c** and **14e** were isolated in pure form by column chromatography and treated with boron trifluoride–diethyl ether under the reaction conditions. In both cases an isomerization to the thermodynamically more stable *trans*-diequatorial product occurs. In the case of the 2-methoxyphenyl-substituted tetrahydropyran **14c** only the *trans*-diequatorial product **19c** and the starting material **14c** (**19c**:**14c** = 6:1 mixture of diastereomers) result. Because no tricyclic product **23** is observed under these conditions, it may be concluded that **23** results from an intramolecular cleavage of the starting epoxide. This assumption was checked by treating *trans*-**4c** with boron fluoride–diethyl ether under the reaction conditions in the absence of a nucleophile: **23** is formed as the only defined product, albeit in very low yield, along with a variety of unidentified oligomeric decomposition products. In an attempt to reduce the amount of byproduct **23**, the epoxide cleavage was carried out in neat acetic acid. However, under these conditions the formation of **23** is preferred even more (**14c**:**23** = 3:2), whereas the rearrangement of **14c** to **19c** is suppressed. Thus, for preparative purposes, **19c** is best prepared in a two-step procedure by cleavage of *trans*-**4c** in refluxing acetic acid and subsequent treatment of the resulting *trans*-diaxial product **14c** with boron trifluoride–diethyl ether, whereas the 4-methoxyphenyl derivative **19e** is best prepared *via* the sequential reaction of epoxide cleavage–rearrangement.

Isomerizations of axially to equatorially substituted dihydropyrans are not without precedence in the literature. Suzuki and co-workers have postulated a mechanism to explain related anomerizations which they observed in the course of their synthetic studies directed towards the construction of the aryl-*C*-glycosidic linkage *via* *O*→*C*-glycosidic rearrangement.[23–27] Taking the Suzuki mechanism into account, our experimental results can be explained in the following way (Scheme 8): dihydropyran oxides **4** are cleaved by acetic acid catalyzed by the Lewis acid to give the expected Fürst–Plattner products **14** and **15**. Products **14** (with the acetoxy group in the 5-position) subsequently undergo a cleavage of the C-2–O bond initiated by attack of the Lewis acid at the tetrahydropyran oxygen, followed by rotation around the C-2–C-3 bond. Ring closure gives tetrahydropyrans **19** in an all-axial conformation, which will undergo rapid inversion to the all-equatorial conformation. Alternatively, a conformational change in the acyclic intermediate and subsequent C–O-bond formation will also give the all-equatorial product **19**. All-equatorial products are only observed for the 2-methoxyphenyl and the 4-methoxyphenyl substituent, indicating that efficient stabilization of positive charge in the benzylic position is necessary to achieve C–O bond cleavage. Interestingly, for *trans*-diaxial cleavage products **15** with a hydroxy group in the 5-position rearrangement to the thermodynamically more stable *trans*-diequatorial products is inhibited. This can probably be explained if a five membered chelate complex is assumed in which the Lewis acidity of the boron (and hence its ability to cleave the C-2–O bond) would be lowered. Tetracoordinate chelate complexes of boron trifluoride and 1,3-dicarbonyl compounds have been described,[28] and pentacoordinate species have recently been postulated as intermediates in certain syntheses.[29]

Conclusions

2-Aryl-substituted tetrahydropyrans with oxo substituents are conveniently prepared by a sequence of ring-closing metathesis, epoxidation and acid mediated epoxide cleavage reactions. Cleavage of dihydropyran oxides results in the formation of *trans*-diaxial opening products in very high regio- and stereoselectivity, regardless of the relative configuration of the starting epoxides. If the aryl substituent in the 2-position provides enough electronic stabilisation of the benzylic position, and if boron fluoride–diethyl ether is used as a Lewis acid, anomerization to the thermodynamic *trans*-diequatorial products occurs. Thus, depending on the conditions, *trans*-diaxial and *trans*-diequatorial cleavage products become selectively accessible. Application of the epoxide cleavage–isomerization sequence described in this contribution to the synthesis of deoxy-*C*-aryl glycosides is currently under investigation.

Experimental

General remarks

All experiments were conducted in dry reaction vessels in an atmosphere of dry argon. Solvents were purified by standard procedures. ^{1}H NMR spectra were recorded at 400 MHz in $CDCl_3$ with $CHCl_3$ as internal standard ($\delta = 7.24$). ^{13}C NMR spectra were recorded at 100 MHz in $CDCl_3$ with $CDCl_3$ as internal standard ($\delta = 77.0$). In a few cases NMR spectra were recorded in CD_3OD (^{1}H NMR: CD_2HOD as internal standard, $\delta = 3.39$; ^{13}C NMR: CD_3OD as internal standard, $\delta = 52.2$) or in C_6D_6 (^{1}H NMR: C_6D_5H as internal standard, $\delta = 7.18$). *J* values are given in Hz. The number of coupled protons was analysed by DEPT experiments and is denoted by a number in parentheses following the δ_C value. IR: spectra were recorded as films on NaCl plates or in KBr. The peak intensities are defined as very strong (vs), strong (s), medium (m), and weak (w). Mass spectra were obtained at 70 eV. Melting points are not corrected. Alcohols **1a**,[30] **1b**–**e**[31] and **5**[32] were prepared according to literature procedures. The ruthenium catalyst $Cl_2(PCy_3)_2Ru$=CH–CH=CPh_2 was prepared following Grubbs' procedure.[33,34]

Preparation of dihydropyrans 3 and 9 and dihydropyran oxides 4 and 10

General procedure for the preparation of allyl ethers 2. NaH (1.14 g 80% dispersion in mineral oil, 38 mmol) is suspended in dry THF (40 mL). A solution of the corresponding homoallylic alcohol **1** (33 mmol) in THF (35 mL) is added dropwise with stirring at ambient temperature. After the addition is complete, the mixture is heated to reflux for 30 min and then cooled to ambient temperature. Allyl bromide (3.5 mL, 40 mmol) is added slowly causing an exothermic reaction and formation of a white precipitate. The mixture is stirred for one hour, after which time the starting material is consumed completely, as monitored by TLC. Water (20 mL) is carefully added with stirring and the mixture is diluted with methyl *tert*-butyl ether (MTBE) (50 mL). The organic layer is washed with saturated NH_4Cl solution and dried with $MgSO_4$. The solvent is evaporated and the residue distilled.

*(1-Allyloxybut-3-enyl)cyclohexane (**2a**).* Obtained from **1a** as a colourless liquid, bp 110 °C (0.3 mbar), yield: 6.1 g (84%). Anal.: Found: C, 79.8; H, 11.2. Calc. for $C_{13}H_{22}O$: C, 80.3; H, 11.4%. LRMS (EI): *m*/*z* 193 ($M^+ - 1$, 5%), 153 ($M^+ - 41$, 32), 111 (39), 83 (100), 41 (83). ^{1}H NMR: δ 5.87 (dddd, 1H, *J* = 17.3, 10.3, 5.5, 5.5, OCH_2CH=), 5.83 (dddd, 1H, *J* = 17.3, 10.3, 7.0, 7.0, $CHCH_2CH$=), 5.22 (ddd, 1H, *J* = 17.3, 3.3, 1.5, =CH_2), 5.09 (dm, 1H, *J* = 10.3, =CH_2), 5.04 (dm, 1H, *J* = 17.3, =CH_2), 5.00 (dm, 1H, *J* = 10.3, =CH_2), 4.01 (dddd, 1H, *J* = 12.8, 5.5, 1.5, 1.3, OCH_2), 3.92 (dddd, 1H, *J* = 12.8, 5.5, 1.5, 1.3, OCH_2), 3.06 (ddd, 1H, *J* = 6.0, 6.0, 6.0, (C_6H_{11})C*H*O-), 2.30–2.16 (2H, CHCH*H*CH=), 1.85–1.55 (5H, C_6H_{11}), 1.43 (m, 1H, C_6H_{11}), 1.25–0.85 (5H, C_6H_{11}). ^{13}C NMR: δ 135.6 (1), 135.5 (1), 116.3 (2), 116.2 (2), 83.2 (1), 71.0 (2), 41.1 (1), 35.4 (2), 29.0 (2), 28.5 (2), 26.6 (2), 26.3 (2), 26.2 (2). IR: ν(NaCl, neat)/cm^{-1} 3077 (m), 2925 (s), 2853 (s), 1641 (m), 1450 (m), 1134 (m), 1088 (m), 1076 (s), 914 (s).

*(1-Allyloxybut-3-enyl)benzene (**2b**).* Obtained from **1b** (6.5 g, 44 mmol) as a colourless liquid, bp 175 °C (8 mbar), yield: 7.0 g (85%). ^{1}H NMR: δ 7.30–7.15 (5H, Ph), 5.81 (dddd, 1H, *J* = 17.3, 10.3, 6.0, 5.0, OCH_2CH=), 5.69 (dddd, 1H, *J* = 17.3, 10.3, 7.0, 7.0, $CHCH_2CH$=), 5.15 (dm, 1H, *J* = 17.3, =CH_2), 5.06 (dm, 1H, *J* = 10.3, =CH_2), 4.96 (dm, 1H, *J* = 17.3, =CH_2), 4.92 (dm, 1H, *J* = 10.3, =CH_2), 4.25 (dd, 1H, *J* = 7.3, 6.0, ArC*H*O-), 3.83 (ddm, 1H, *J* = 12.8, 5.0, OCH_2), 3.68 (ddm, 1H, *J* = 12.8, 6.0, OCH_2), 2.52 (ddd, 1H, *J* = 14.3, 7.3, 7.0, $CHCH_2CH$=), 2.33 (ddd, 1H, *J* = 14.3, 7.0, 6.0, $CHCH_2CH$=). ^{13}C NMR: δ 141.9 (0), 134.9 (1), 134.8 (1), 128.3 (1), 127.5 (1), 126.7 (1), 116.8 (2), 116.7 (2), 81.1 (1), 69.4 (2), 42.6 (2).

*1-(1-Allyloxybut-3-enyl)-2-methoxybenzene (**2c**).* Obtained from **1c** (4.0 g, 22 mmol) as a colourless liquid, bp 120 °C (0.2 mbar), yield: 4.3 g (87%). LRMS (EI): *m*/*z* 177 ($M^+ - C_3H_5$, 90%), 161 (100), 135 (20). ^{1}H NMR: δ 7.33 (dd, 1H, *J* = 7.5, 1.8, Ar), 7.16 (ddd, 1H, *J* = 8.3, 7.4, 1.8, Ar), 6.90 (ddd, 1H, *J* = 7.5, 7.4, 0.8, Ar), 6.78 (dd, 1H, *J* = 8.3, 0.8, Ar), 5.83 (dddd, 1H, *J* = 17.1, 10.3, 5.9, 5.0, OCH_2CH=), 5.80 (dddd, 1H, *J* = 17.1, 10.3, 7.0, 6.8, $CHCH_2CH$=), 5.18 (dddd, 1H, *J* = 17.1, 1.8, 1.8, 1.8, =CH_2), 5.06 (dddd, 1H, *J* = 10.3, 1.8, 1.3, 1.3, =CH_2), 4.97 (dddd, 1H, *J* = 17.1, 2.0, 1.5, 1.5, =CH_2), 4.93 (dm, 1H, *J* = 10.3, =CH_2), 4.77 (dd, 1H, *J* = 6.3, 6.3, ArC*H*O-), 3.87 (dddd, 1H, *J* = 12.8, 5.0, 1.5, 1.5, OCH_2), 3.74 (s, 3H, OMe), 3.72 (dddd, 1H, *J* = 12.8, 5.9, 1.5, 1.5, OCH_2), 2.42–2.37 (2, CHCH*H*CH=). ^{13}C NMR: δ 156.8 (0), 135.4 (1), 135.1 (1), 130.3 (0), 128.1 (1), 126.7 (1), 120.6 (1), 116.4 (2), 116.2 (2), 110.2 (1), 74.5 (1), 69.7 (2), 55.2 (3), 41.1 (2). IR: ν(NaCl, neat)/cm^{-1} 3076 (m), 2936 (m), 2837 (m), 1601 (m), 1490 (s), 1240 (s), 1083 (s), 916 (s), 755 (s).

*1-(1-Allyloxybut-3-enyl)-3-methoxybenzene (**2d**).* Obtained from **1d** (3.5 g, 20 mmol) as a colourless liquid, bp 125 °C (0.2 mbar), yield: 4.0 g (92%). LRMS (EI): *m*/*z* 177 ($M^+ - C_3H_5$, 100%), 161 (90). ^{1}H NMR: δ 7.18 (dd, 1H, *J* = 8.3, 8.0, Ar), 6.87–6.72 (3, Ar), 5.83 (dddd, 1H, *J* = 17.1, 10.3, 6.0, 5.0, OCH_2CH=), 5.71 (dddd, 1H, *J* = 17.1, 10.3, 7.0, 7.0, $CHCH_2CH$=), 5.17 (dddd, 1H, *J* = 17.1, 1.8, 1.5, 1.5, =CH_2), 5.08 (dddd, 1H, *J* = 10.3, 1.5, 1.3, 1.3, =CH_2), 4.98 (dddd, 1H, *J* = 17.1, 2.0, 1.5, 1.5, =CH_2), 4.94 (dm, 1H, *J* = 10.3, =CH_2), 4.24 (dd, 1H, *J* = 7.4, 5.8, ArC*H*O-), 3.87 (dddd, 1H, *J* = 12.8, 5.0, 1.8, 1.5, OCH_2), 3.74 (s, 3H, OMe), 3.71 (dddd, 1H, *J* = 12.8, 6.0, 1.5, 1.3, OCH_2), 2.52 (ddddd, 1H, *J* = 14.2, 7.4, 7.0, 1.3, 1.3, $CHCH_2CH$=), 2.34 (ddddd, 1H, *J* = 14.2, 7.0, 5.8, 1.3, 1.3, $CHCH_2CH$=). ^{13}C NMR: δ 159.7 (0), 143.6 (0), 134.8 (1), 134.8 (1), 129.3 (1), 119.2 (1), 116.8 (1), 113.0 (2), 112.0 (2), 81.0 (1), 69.5 (2), 55.1 (3), 42.5 (2). IR: ν(NaCl, neat)/cm^{-1} 3076 (w), 2937 (m), 2857 (m), 1600 (s), 1489 (s), 1265 (s), 1079 (s), 918 (m).

*1-(1-Allyloxybut-3-enyl)-4-methoxybenzene (**2e**).* Obtained from **1e** as a colourless liquid, bp 110 °C (0.3 mbar), yield: 6.1 g (84%). Anal.: Found: C, 77.0; H, 8.7. Calc. for $C_{14}H_{18}O_2$: C, 77.0; H, 8.3%. LRMS (EI): *m*/*z* 217 ($M^+ - 1$, 1%), 177 (100), 161 (90). ^{1}H NMR: δ 7.21 (d, 2H, *J* = 8.8, Ar), 6.87 (d, 2H, *J* = 8.8, Ar), 5.88 (dddd, 1H, *J* = 17.1, 10.8, 5.8, 5.5, OCH_2CH=), 5.75 (dddd, 1H, *J* = 17.1, 10.3, 7.0, 7.0, $CHCH_2CH$=), 5.22 (d, 1H, *J* = 17.1, =CH_2), 5.19 (d, 1H, *J* = 10.3, =CH_2), 5.03 (d, 1H, *J* = 17.1, =CH_2), 4.99 (d, 1H, *J* = 10.8, =CH_2), 4.27 (dd, 1H, *J* = 7.0, 7.0, ArC*H*O-), 3.89 (dd, 1H, *J* = 12.8, 5.5, OCH*H*), 3.79 (s, 3H, OMe), 3.74 (dd, 1H, *J* = 12.8, 5.9, OCH_2), 2.60 (ddd, 1H, *J* = 14.1, 7.0, 7.0, $CHCH_2CH$=), 2.39 (ddd, 1H, *J* = 14.1, 7.0, 7.0, CHCH*H*CH=). ^{13}C NMR: δ 159.0 (0), 134.9 (1), 134.9 (1), 133.8 (0), 127.9 (1), 116.7 (2), 116.6 (2), 113.7 (1), 80.6 (1), 69.1 (2), 55.1 (3), 42.5 (2). IR: ν(NaCl, neat)/cm^{-1} 3076 (w), 3001 (m), 1642 (w), 1611 (s), 1512 (s), 1302 (m), 1247 (s), 1173 (m).

General procedure for the preparation of dihydropyrans 3. Dienes **2** (5.0 mmol) are dissolved in DCM (40 mL). The ruthenium catalyst (95 mg, 2 mol%) is added and the mixture stirred until the starting material is fully consumed (monitored by TLC). The solvent is removed *in vacuo* and the residue purified by Kugelrohr distillation or flash chromatography.

*2-Cyclohexyl-3,6-dihydro-2H-pyran (**3a**).* Obtained from **2a** (3.30 g, 17.0 mmol) as a colourless liquid. Purification by column chromatography on silica using hexanes–MTBE (50 : 1) as eluent, yield: 2.55 g (90%). LRMS (EI): *m*/*z* 165 ($M^+ - 1$, 20%), 149 (80), 111 (60), 83 (100). ^{1}H NMR: δ 5.74 (dddd, 1H, *J* = 10.1, 5.4, 4.2, 2.0, H-4/H-5), 5.63 (dm, 1H, *J* = 10.1, H-4/H-5), 4.12 (dm, 1H, *J* = 16.5, H-6), 4.07 (dm, 1H, *J* = 16.5, H-6), 3.13 (ddd, 1H, *J* = 10.3, 7.0, 3.5, H-2), 1.99 (ddm, 1H, *J* = 17.0, 10.3, H-3_{ax}), 1.93–1.83 (2H, C_6H_{11} + H-3_{eq}), 1.72–1.55 (4H, C_6H_{11}), 1.32 (m, 1H, C_6H_{11}), 1.23–1.02 (3H, C_6H_{11}), 1.00–0.84 (2H, C_6H_{11}). ^{13}C NMR: δ 126.3 (1), 124.5 (1), 78.0 (1), 66.2

(2), 42.8 (1), 29.1 (2), 28.3 (2), 28.2 (2), 26.6 (2), 26.1 (2), 26.0 (2). IR: ν(NaCl, neat)/cm^{-1} 3033 (m), 2923 (s), 2851 (s), 1449 (s), 1387 (s), 1183 (s), 1091 (s), 1018 (s), 854 (m).

*2-Phenyl-3,6-dihydro-2H-pyran (**3b**).* Obtained from **2b** (1000 mg, 5.3 mmol) as a colourless liquid, yield: 770 mg (90%). Purified by flash chromatography (silica, hexanes–MTBE 10 : 1). ^{1}H NMR: δ 7.42–7.25 (5H, Ph), 5.92 (dm, 1H, J = 10.3, H-4/H-5), 5.81 (dm, 1H, J = 10.3, H-4/H-5), 4.56 (dd, 1H, J = 10.2, 3.5, H-2), 4.42–4.31 (2H, H-6), 2.37 (ddm, 1H, J = 17.3, 10.2, H-3$_{ax}$), 2.26 (dm, 1H, J = 17.3, H-3$_{eq}$). ^{13}C NMR: δ 142.5 (0), 128.3 (1), 127.4 (1), 126.4 (1), 125.8 (1), 124.4 (1), 75.6 (1), 66.5 (2), 32.8 (2).

*2-(2-Methoxyphenyl)-3,6-dihydro-2H-pyran (**3c**).* Obtained from **2c** (2650 mg, 12.1 mmol) as a colourless liquid, bp 150 °C (0.14 mbar), yield: 2140 mg (93%). LRMS (EI): *m*/*z* 190 (M$^+$, 65%), 173 (100). ^{1}H NMR: δ 7.44 (dd, 1H, J = 7.5, 1.7, Ar), 7.24 (ddd, 1H, J = 8.3, 7.4, 1.7, Ar), 7.00 (dd, 1H, J = 7.5, 7.4, Ar), 6.86 (d, 1H, J = 8.3, Ar), 5.93 (dm, 1H, J = 10.0, H-4/H-5), 5.79 (dm, 1H, J = 10.0, H-4/H-5), 4.93 (dd, 1H, J = 10.2, 3.3, H-2), 4.44–4.32 (2H, H-6), 3.82 (s, 3H, OMe), 2.35 (dm, 1H, J = 17.3, H-3$_{eq}$), 2.21 (ddm, 1H, J = 17.3, 10.2, H-3$_{ax}$). ^{13}C NMR: δ 155.7 (0), 131.1 (0), 128.1 (1), 126.1 (1), 126.1 (1), 125.0 (1), 120.8 (1), 110.1(1), 70.0 (1), 66.6 (2), 55.2 (3), 31.8 (2). IR: ν(NaCl, neat)/cm^{-1} 3034 (w), 2835 (m), 1603 (m), 1494 (s), 1243 (s), 1092 (s), 755 (s).

*2-(3-Methoxyphenyl)-3,6-dihydro-2H-pyran (**3d**).* Obtained from **2d** (1110 mg, 5.1 mmol) as a colourless liquid, bp 170 °C (0.2 mbar), yield: 880 mg (92%). LRMS (EI): *m*/*z* 190 (M$^+$, 100%), 173 (100), 162 (60), 147 (50). ^{1}H NMR: δ 7.20 (dd, 1H, J = 8.0, 7.6, Ar), 6.91–6.84 (2H, Ar), 6.77 (d, 1H, J = 7.6, Ar), 5.86 (dm, 1H, J = 10.0, H-4/H-5), 5.75 (dm, 1H, J = 10.0, H-4/H-5), 4.48 (dd, 1H, J = 10.1, 3.6, H-2), 4.32–4.29 (2, H-6), 3.75 (s, 3H, OMe), 2.30 (ddm, 1H, J = 17.3, 10.1, H-3$_{ax}$), 2.20 (dm, 1H, J = 17.3, H-3$_{eq}$). ^{13}C NMR: δ 159.7 (0), 144.2 (0), 129.3 (1), 126.3 (1), 124.4 (1), 118.1 (1), 113.2 (1), 111.1 (1), 75.5 (1), 66.5 (2), 55.2 (3), 32.9 (2). IR: ν(NaCl, neat)/cm^{-1} 3035 (w), 2834 (m), 1603 (s), 1490 (s), 1260 (s), 1091 (s), 785 (s).

*2-(4-Methoxyphenyl)-3,6-dihydro-2H-pyran (**3e**).* Obtained from **2e** (1090 mg, 5.0 mmol) as a colourless liquid, bp 170 °C (0.2 mbar), yield: 880 mg (92%). Anal.: Found: C, 76.2; H, 7.9. Calc. for $C_{12}H_{14}O_2$: C, 75.8; H, 7.4%. LRMS (EI): *m*/*z* 190 (M$^+$, 11%), 136 (100), 121 (20). ^{1}H NMR: δ 7.45 (d, 2H, J = 8.8, Ar), 7.03 (d, 2H, J = 8.8, Ar), 6.06 (dm, 1H, J = 10.3, H-4/H-5), 5.94 (dm, 1H, J = 10.3, H-4/H-5), 4.65 (dd, 1H, J = 10.3, 3.5, H-2), 4.52–4.46 (2H, H-6), 3.93 (s, 3H, OMe), 2.51 (ddm, 1H, J = 17.3, 10.3, H-3$_{ax}$), 2.36 (dm, 1H, 17.3, H-3$_{eq}$). ^{13}C NMR: δ 158.9 (0), 134.7 (0), 127.1 (1), 126.3 (1), 124.4 (1), 113.6 (1), 75.2 (1), 66.5 (2), 55.1 (3), 32.7 (2). IR: ν(NaCl, neat)/cm^{-1} 3034 (w), 2833 (w), 1613 (m), 1515 (s), 1248 (s), 1089 (m), 828 (m).

General procedure for the preparation of *cis*- and *trans*-dihydropyran oxides 4. Dihydropyrans **3** (5.1 mmol) are dissolved in DCM (40 mL). MCPBA (1600 mg of 70% w/w, 6.5 mmol) is added and the mixture is stirred for six hours. MTBE (50 mL) is added, the solution is washed with saturated Na_2SO_3 solution followed by saturated Na_2CO_3 solution, the organic layer is separated, dried with $MgSO_4$ and the solvent evaporated to give a waxy solid or a viscous oil (92–100% crude yield) consisting of 1:1 mixtures of *cis*- and *trans* diastereomers as indicated by NMR analysis. Separation of diastereomers is achieved by chromatography on silica using hexanes–MTBE mixtures of increasing polarity. In all cases the *trans*-isomer is less polar and is eluted first.

(1S,4S*,6R*)-4-Cyclohexyl-3,7-dioxabicyclo[4.1.0]heptane (trans-**4a**) and (1R*,4S*,6S*)-4-cyclohexyl-3,7-dioxabicyclo-[4.1.0]heptane (cis-**4a**).* Obtained from **3a** (2270 mg, 14 mmol) in 65% yield (*trans*-diastereomer (less polar) 850 mg; *cis*-diastereomer 800 mg). Anal.: Found: C, 72.0; H, 9.7. Calc. for $C_{11}H_{18}O_2$: C, 72.5; H, 9.9%. LRMS (EI): *m*/*z* 181 (M$^+$ − 1, 10%), 99 (M$^+$ − cyclohexyl, 100), 71 (90), 55 (90). *Diastereoisomer trans-**4a***: colourless liquid. ^{1}H NMR: δ 4.17 (dd, 1H, J = 13.6, 4.3, H-6$_{eq}$), 3.82 (dd, 1H, J = 13.6, 0.8, H-6$_{ax}$), 3.34 (dd, 1H, J = 4.3, 2.5, H-4), 3.21 (dd, 1H, J = 4.3, 4.3, H-5), 3.02 (ddd, 1H, J = 11.0, 6.8, 2.5, H-2), 2.01 (ddd, 1H, J = 14.3, 2.5, 2.5, H-3$_{eq}$), 1.80 (dm, 1H, J = 12.8, C$_6$H$_{11}$), 1.72–1.54 (5H, C$_6$H$_{11}$, H-3$_{ax}$), 1.29–1.02 (4H, C$_6$H$_{11}$), 0.99–0.80 (2H, C$_6$H$_{11}$). ^{13}C NMR: δ 74.2 (1), 66.1 (2), 51.5 (1), 51.3 (1), 42.4 (1), 29.0 (2), 28.3 (2), 28.2 (2), 26.5 (2), 26.1 (2), 25.9 (2). IR: ν(NaCl, neat)/cm^{-1} 2995 (m), 2925 (s), 2852 (s), 1450 (m), 1141 (m), 1111 (s), 1016 (m), 905 (m), 817 (m), 802 (m). *Diastereoisomer cis-**4a***: colourless solid, mp 42 °C. ^{1}H NMR: δ 4.14 (d, 1H, J = 13.2, H-6), 3.70 (dd, 1H, J = 13.2, 0.5, H-6), 3.29 (dd, 1H, J = 5.5, 4.3, H-4), 2.99 (d, 1H, J = 4.3, H-5), 2.81 (ddd, 1H, J = 11.3, 7.0, 4.3, H-2), 1.84 (ddd, 1H, J = 15.3, 5.5, 4.3, H-3$_{eq}$), 1.75 (dd, 1H, J = 15.3, 11.3, H-3$_{ax}$), 1.70–1.54 (5H, C$_6$H$_{11}$), 1.32–1.02 (4H, C$_6$H$_{11}$), 0.97–0.78 (2H, C$_6$H$_{11}$). ^{13}C NMR: δ 77.2 (1), 64.9 (2), 49.9 (1), 49.1 (1), 42.6 (1), 28.7 (2), 28.2 (2), 26.9 (2), 26.4 (2), 26.0 (2), 25.8 (2). IR: ν(NaCl, neat)/cm^{-1} 2992 (m), 2925 (s), 2852 (s), 1450 (m), 1123 (m), 1051 (w), 860 (m), 809 (m).

(1S,4S*,6R*)-4-Phenyl-3,7-dioxabicyclo[4.1.0]heptane (trans-**4b**) and (1R*,4S*,6S*)-4-phenyl-3,7-dioxabicyclo-[4.1.0]heptane (cis-**4b**).* Obtained from **3b** (950 mg, 5.9 mmol) in 72% yield (*trans*-diastereomer (less polar) 390 mg; *cis*-diastereomer 360 mg). *Diastereomer trans-**4b***: Colouress oil. LRMS (EI): *m*/*z* 175 (M$^+$ − 1, 30%), 159 (25), 133 (100), 105 (55). ^{1}H NMR: δ 7.37–7.25 (5H, Ph), 4.44 (dd, 1H, J = 11.0, 2.6, H-2), 4.37 (dd, 1H, J = 13.6, 4.3, H-6$_{eq}$), 4.11 (d, 1H, J = 13.6, H-6$_{ax}$), 3.48 (m, 1H, H-4), 3.34 (dd, 1H, J = 4.3, 4.3, H-5), 2.32 (ddd, 1H, J = 14.7, 2.6, 2.3, H-3$_{eq}$), 2.03 (ddd, 1H, J = 14.7, 11.0, 2.8, H-3$_{ax}$). ^{13}C NMR: δ 141.6 (0), 128.4 (1), 127.6 (1), 125.6 (1), 71.9 (1), 66.1 (2), 51.4 (1), 51.0 (1), 33.4 (2). IR: ν(NaCl, neat)/cm^{-1} 3005 (w), 2850 (m), 1452 (m), 1111 (s), 1017 (s), 811 (s), 699 (s). *Diastereomer cis-**4b***: colourless oil. LRMS (EI): *m*/*z* 175 (M$^+$ − 1, 15%), 105 (35), 54 (100). ^{1}H NMR: δ 7.35–7.25 (5H, Ph), 4.37 (d, 1H, J = 13.5, H-6), 4.22 (dd, 1H, J = 11.4, 4.4, H-2), 4.00 (d, 1H, J = 13.5, H-6), 3.45 (dd, 1H, J = 5.3, 4.5, H-4), 3.15 (d, 1H, J = 4.5, H-5), 2.20 (ddd, 1H, J = 15.5, 5.3, 4.4, H-3$_{eq}$), 2.09 (dd, 1H, J = 15.5, 11.4, H-3$_{ax}$). ^{13}C NMR: δ 141.5 (0), 128.3 (1), 127.6 (1), 125.7 (1), 75.1 (1), 65.2 (2), 49.8 (1), 48.8 (1), 31.8 (2). IR: ν(NaCl, neat)/cm^{-1} 3004 (w), 2844 (w), 1453 (m), 1374 (m), 1122 (s), 1026 (m), 806 (m), 701 (s).

(1S,4S*,6R*)-4-(2-Methoxyphenyl)-3,7-dioxabicyclo-[4.1.0]heptane (trans-**4c**) and (1R*,4S*,6S*)-4-(2-methoxy-phenyl)-3,7-dioxabicyclo[4.1.0]heptane (cis-**4c**).* Obtained from **3c** (2140 mg, 11.2 mmol) in 75% yield (*trans*-diastereomer (less polar) 720 mg; *cis*-diastereomer 1000 mg). *Diastereomer trans-**4c***: colouress oil. LRMS (EI): *m*/*z* 205 (M$^+$ − 1, 20%), 188 (40), 135 (100), 119 (70). ^{1}H NMR: δ 7.40 (dd, 1H, J = 7.7, 1.5, Ar), 7.24 (ddd, 1H, J = 8.1, 7.5, 1.5, Ar), 6.97 (dd, 1H, J = 7.7, 7.5, Ar), 6.85 (d, 1H, J = 8.1, Ar), 4.80 (dd, 1H, J = 11.2, 2.4, H-2), 4.38 (dd, 1H, J = 13.6, 4.3, H-6$_{eq}$), 4.11 (d, 1H, J = 13.6, H-6$_{ax}$), 3.82 (s, 3H, OMe), 3.47 (m, 1H, H-4), 3.34 (dd, 1H, J = 4.3, 4.3, H-5), 2.42 (ddd, 1H, J = 14.6, 2.4, 2.0, H-3$_{eq}$), 1.89 (ddd, 1H, J = 14.6, 11.2, 1.5, H-3$_{ax}$). ^{13}C NMR: δ 155.6 (0), 130.2 (0), 128.2 (1), 125.8 (1), 120.6 (1), 110.1 (1), 66.5 (1), 66.3 (2), 55.2 (3), 51.6 (1), 51.0 (1), 31.9 (2). IR: ν(NaCl, neat)/cm^{-1} 3002 (m), 2840 (m), 1603 (m), 1494 (s), 1243 (s), 1107 (s), 757 (s). *Diastereomer cis-**4c***: colourless oil. LRMS (EI): *m*/*z* 207 (M$^+$+1, 40%), 206 (M$^+$, 30), 189 (35), 160 (90), 135 (60), 119 (100). ^{1}H NMR: δ 7.44 (dd, 1H, J = 7.5, 1.5, Ar), 7.24 (ddd, 1H, J = 8.3, 7.8, 1.5, Ar), 6.97 (ddd, 1H, J = 7.8, 7.5, 1.8, Ar), 6.84 (d, 1H, J = 8.3, Ar), 4.58 (dd, 1H, J = 11.6, 4.0, H-2), 4.38 (d, 1H, J = 13.3, H-6), 4.00 (dd, 1H, J = 13.3, 0.5, H-6), 3.82 (s, 3H, OMe), 3.45 (dd, 1H, J = 5.8, 4.2, H-4), 3.14 (d, 1H, J = 4.2, H-5), 2.33 (ddd, 1H, J = 15.3, 5.8, 4.0, H-3$_{eq}$), 1.89 (dd, 1H, J = 15.3, 11.6, H-3$_{ax}$). ^{13}C NMR: δ 155.2 (0), 130.2 (0), 128.2 (1), 126.1 (1), 120.8 (1), 109.9 (1), 69.7 (1), 65.3 (2), 55.2 (3), 50.3 (1), 49.0 (1), 30.6 (2). IR: ν(NaCl, neat)/cm^{-1} 3001 (w),

2834 (m), 1602 (m), 1494 (s), 1246 (s), 1110 (s), 1026 (s), 807 (s), 757 (s).

(1S,4S*,6R*)-4-(3-Methoxyphenyl)-3,7-dioxabicyclo-[4.1.0]heptane (trans-**4d**) and (1R*,4S*,6S*)-4-(3-methoxyphenyl)-3,7-dioxabicyclo[4.1.0]heptane (cis-**4d**).* Obtained from **3d** (850 mg, 4.5 mmol) in 70% yield (*trans*-diastereomer (less polar) 340 mg; *cis*-diastereomer 310 mg). *Diastereomer trans-**4d***: colouress oil. LRMS (EI): *m*/*z* 206 (M^+, 50%), 135 (100). ^{1}H NMR: δ 7.25 (dd, 1H, J = 8.0, 8.0, Ar), 6.94–6.79 (3H, Ar), 4.42 (dd, 1H, J = 11.0, 2.6, H-2), 4.37 (dd, 1H, J = 13.8, 4.3, H-6_{eq}), 4.10 (d, 1H, J = 13.8, H-6_{ax}), 3.81 (s, 3H, OMe), 3.48 (m, 1H, H-4), 3.34 (dd, 1H, J = 4.3, 4.3, H-5), 2.31 (ddd, 1H, J = 14.7, 2.6, 2.3, H-3_{eq}), 2.02 (ddd, 1H, J = 14.7, 11.0, 1.8, H-3_{ax}). ^{13}C NMR: δ 159.6 (0), 143.3 (0), 129.4 (1), 117.8 (1), 113.1 (1), 111.0 (1), 71.8 (1), 66.1 (2), 55.1 (3), 51.4 (1), 51.0 (1), 33.3 (2). IR: ν(NaCl, neat)/cm^{-1} 3001 (w), 2838 (w), 1604 (s), 1589 (s), 1266 (s), 1112 (s), 1019 (s), 802 (s), 696 (s). *Diastereomer cis-**4d***: colourless oil. LRMS (EI): *m*/*z* 206 (M^+, 90%), 159 (60), 135 (100). ^{1}H NMR: δ 7.24 (dd, 1H, J = 8.2, 7.8, Ar), 6.93–6.85 (2H, Ar), 6.82 (dd, 1H, J = 8.2, 2.5, Ar), 4.38 (d, 1H, J = 13.3, H-6), 4.21 (dd, 1H, J = 11.4, 4.3, H-2), 4.00 (d, 1H, J = 13.3, H-6), 3.81 (s, 3H, OMe), 3.46 (dd, 1H, J = 5.4, 4.3, H-4), 3.16 (d, 1H, J = 4.3, H-5), 2.20 (ddd, 1H, J = 15.4, 5.4, 4.3, H-3_{eq}), 2.09 (dd, 1H, J = 15.4, 11.4, H-3_{ax}). ^{13}C NMR: δ 159.6 (0), 143.1 (0), 129.3 (1), 118.0 (1), 113.5 (1), 110.9 (1), 75.1 (1), 65.2 (2), 55.2 (3), 49.9 (1), 48.8 (1), 31.8 (2). IR: ν(NaCl, neat)/cm^{-1} 3001 (w), 2838 (w), 1602 (s), 1489 (s), 1267 (s), 1122 (s), 1044 (s), 810 (s), 700 (s).

(1S,4S*,6R*)-4-(4-Methoxyphenyl)-3,7-dioxabicyclo-[4.1.0]heptane (trans-**4e**) and (1R*,4S*,6S*)-4-(4-methoxyphenyl)-3,7-dioxabicyclo[4.1.0]heptane (cis-**4e**).* Obtained from **3e** (970 mg, 5.1 mmol) in 69% yield (*trans*-diastereomer (less polar) 385 mg; *cis*-diastereomer 330 mg). LRMS (EI): *m*/*z* 206 (M^+, 40%), 135 (100), 121 (39), 108 (33). *Diastereomer trans-**4e***: colouress oil. ^{1}H NMR: δ 7.21 (d, 2H, J = 8.8, Ar), 6.85 (d, 2H, J = 8.8, Ar), 4.36 (dd, 1H, J = 11.1, 2.6, H-2), 4.32 (dd, 1H, J = 13.7, 4.2, H-6_{eq}), 4.07 (d, 1H, J = 13.7, H-6_{ax}), 3.76 (s, 3H, OMe), 3.46 (m, 1H, H-4), 3.31 (dd, 1H, J = 4.3, 4.2, H-5), 2.25 (ddd, 1H, J = 14.6, 2.6, 2.3, H-3_{eq}), 2.01 (ddd, 1H, J = 14.6, 11.1, 1.5, H-3_{ax}). ^{13}C NMR: δ 159.0 (0), 133.5 (0), 127.0 (1), 113.7 (1), 71.6 (1), 66.2 (2), 55.2 (3), 51.5 (1), 51.0 (1), 33.1 (2). IR: ν(NaCl, neat)/cm^{-1} 3000 (w), 2838 (w), 1614 (m), 1515 (s), 1303 (m), 1247 (s), 1107 (s), 1034 (s), 811 (m). *Diastereomer cis-**4e***: colourless solid, mp 91 °C. Anal.: Found: C, 69.5; H, 6.8. Calc. for $C_{12}H_{14}O_3$: C, 69.9; H, 6.8%. ^{1}H NMR: δ 7.21 (d, 2H, J = 8.8, Ar), 6.84 (d, 2H, J = 8.8, Ar), 4.31 (d, 1H, J = 13.6, H-6), 4.13 (dd, 1H, J = 10.5, 5.2, H-2), 3.95 (d, 1H, J = 13.6, H-6), 3.75 (s, 3H, OMe), 3.42 (dd, 1H, J = 4.8, 4.3, H-4), 3.12 (d, 1H, J = 4.3, H-5), 2.12 (ddd, 1H, J = 15.6, 5.2, 4.8, H-3_{eq}), 2.06 (dd, 1H, J = 15.6, 10.5, H-3_{ax}). ^{13}C NMR: δ 159.1 (0), 133.7 (0), 127.1 (1), 113.8 (1), 74.8 (1), 65.3 (2), 55.2 (3), 50.0 (1), 48.9 (1), 31.8 (2). IR: ν(NaCl, neat)/cm^{-1} 3009 (w), 2921 (w), 1515 (s), 1302 (m), 1249 (s), 1177 (s), 1109 (m), 1029 (s), 834 (m).

Ethyl 3-[1-(4-Methoxyphenyl)allyloxy]propionate (6). Allyl alcohol **5** (4.1 g, 25 mmol) is dissolved in THF (20 mL) and added under an argon atmosphere to a suspension of NaH (60% dispersion in mineral oil, 1.8 g, 45 mmol) in THF (20 mL). After the addition is complete, the mixture is heated to reflux until the evolution of hydrogen gas is finished. The reaction is cooled to 0 °C and a solution of ethyl 3-bromopropionate (6.5 mL, 45 mmol) in THF (10 mL) is slowly added. The reaction mixture is kept at this temperature for 2 hours and is then hydrolyzed by addition of water (30 mL). The solution is diluted with MTBE (50 mL), the organic layer is separated and the aqueous layer extracted with MTBE. The combined organic extracts are washed with saturated NH_4Cl solution, dried with $MgSO_4$ and the solvent is removed *in vacuo*. The residue is purified by chromatography on silica using hexanes–MTBE (5 : 1). Analytically pure samples are obtained by additional Kugelrohr distillation (135 °C/0.04 mbar). Yield: 2.4 g (36%). Anal.: Found: C, 68.2; H, 7.7. Calc. for $C_{15}H_{20}O_4$: C, 68.2; H, 7.6%. Colourless liquid. LRMS (EI): *m*/*z* 264 (M^+, 38%), 163 (70), 147 (100), 135 (80). ^{1}H NMR: δ 7.21 (d, 2H, J = 8.8, Ar), 6.84 (d, 2H, J = 8.8, Ar), 5.88 (ddd, 1H, J = 17.1, 10.3, 6.5, -C*H*=CH_2), 5.21 (d, 1H, J = 17.1, -CH=C*H*$_2$), 5.13 (d, 1H, J = 10.3, -CH=C*H*$_2$), 4.68 (d, 1H, J = 6.5, ArC*H*O), 4.11 (q, 1H, J = 7.0, OEt), 3.75 (s, 3H, OMe), 3.69 (ddd, 1H, J = 9.3, 6.5, 6.5, OCH*H*CH_2), 3.60 (ddd, 1H, J = 9.3, 6.5, 6.5, OCH*H*CH_2), 2.60–2.50 (2H, OCH_2CH*H*), 1.22 (t, 3H, J = 7.0, OEt). ^{13}C NMR: δ 171.5 (0), 159.0 (0), 138.9 (1), 132.8 (0), 128.0 (1), 115.9 (2), 113.7 (1), 82.0 (1), 63.8 (2), 60.3 (2), 55.1 (3), 35.2 (2), 14.1 (3). IR: ν(NaCl, neat)/cm^{-1} 2981 (s), 2908 (s), 1736 (vs), 1732 (vs), 1610 (s), 1465 (s), 1444 (s), 1248 (vs), 1185 (vs), 1035 (s), 830 (s).

3-[1-(4-Methoxyphenyl)allyloxy]propionaldehyde (7). Ester **6** (2.33 g, 8.8 mmol) is dissolved in ether (80 mL) under an atmosphere of dry argon. The solution is cooled to −90 °C and DIBAL-H (2.4 mL, 13.2 mmol) is added dropwise *via* a syringe. The solution is stirred at −90 °C until the starting material is completely consumed (TLC). Then methanol (20 mL) is added and the mixture is slowly warmed to −50 °C and stirred at this temperature for one hour. After warming the mixture to 0 °C, water (20 mL) and aqueous HCl (10%, 5 mL) is added. The organic layer is separated, the aqueous layer is extracted with ether and the combined organic layers are washed with saturated Na_2CO_3 solution and then dried with $MgSO_4$. Removal of the solvent and Kugelrohr distillation (190 °C/0.08 mbar) yields 1.74 g (90%). Colourless liquid. LRMS (EI): *m*/*z* 220 (M^+, 27%), 163 (47), 147 (100), 135 (58). ^{1}H NMR: δ 9.75 (dd, 1H, J = 1.8, 1.8, HC=O), 7.21 (d, 2H, J = 8.5, Ar), 6.91 (d, 2H, J = 8.5, Ar), 5.89 (ddd, 1H, J = 17.2, 10.3, 6.5, -C*H*=CH_2), 5.22 (dm, 1H, J = 17.2, =C*H*$_2$), 5.16 (dm, 1H, J = 10.3, =C*H*$_2$), 4.69 (d, 1H, J = 6.5, ArC*H*O), 3.77 (s, 3H, OMe), 3.77 (ddd, 1H, J = 9.5, 6.0, 6.0, OCH*H*CH_2), 3.66 (ddd, 1H, J = 9.5, 6.0, 6.0, OCH*H*CH_2), 2.64 (ddd, 2H, J = 6.0, 6.0, 1.8, OCH_2CH_2). ^{13}C NMR: δ 201.4 (1), 159.2 (0), 138.6 (1), 132.6 (0), 128.0 (1), 116.1 (2), 113.8 (1), 82.9 (1), 62.0 (2), 55.2 (3), 43.8 (2). IR: ν(NaCl, neat)/cm^{-1} 2958 (s), 2934 (s), 2869 (s), 1732 (s), 1728 (s), 1610 (s), 1515 (s), 1303 (s), 1245 (s), 1173 (s), 1089 (s), 1033 (s), 831 (s).

1-(1-But-3-enyloxyallyl)-4-methoxy benzene (8). Methyltriphenylphosphonium bromide (2.53 g, 7.1 mmol) is suspended in dry THF (50 mL) under an argon atmosphere and a solution of BuLi (1.39 M, 5.1 mL, 7.1 mmol) is added dropwise at room temperature. The yellow solution is stirred for 15 min and then cooled to −78 °C. A solution of aldehyde **7** (1.20 g, 5.4 mmol) in THF (20 mL) is added dropwise. After the addition is completed, the mixture is stirred at −78 °C for 20 min and then at room temperature for three hours. The reaction is quenched by addition of water (25 mL). The solution is extracted with MTBE, the organic layer is washed with saturated NH_4Cl solution, dried with $MgSO_4$ and the solvent is removed *in vacuo*. Chromatography on silica using hexanes–MTBE (10 : 1) mixtures as eluent yields 1.02 g (86%) of the title compound. Anal.: Found: C, 76.6; H, 8.5. Calc. for $C_{14}H_{18}O_2$: C, 77.0; H, 8.3%. Colourless liquid. LRMS (EI): *m*/*z* 218 (M^+, 15%), 147 (100), 135 (37), 91 (24), 55 (35). ^{1}H NMR: δ 7.25 (d, 2H, J = 8.8, Ar), 6.92 (d, 2H, J = 8.8, Ar), 5.93 (ddd, 1H, J = 17.1, 10.3, 6.5, CH–C*H*=CH_2), 5.81 (dddd, 1H, J = 17.1, 10.3, 6.8, 6.8, OCH_2–C*H*=CH_2), 5.23 (d, 1H, J = 17.1, =C*H*$_2$), 5.16 (d, 1H, J = 10.3, =C*H*$_2$), 5.07 (d, 1H, J = 17.1, =C*H*$_2$), 5.01 (d, 1H, J = 10.3, =C*H*$_2$), 4.69 (d, 1H, J = 6.5, ArC*H*O), 3.79 (s, 3H, OMe), 3.48 (ddd, 1H, J = 9.0, 6.8, 6.8, OCH*H*CH_2), 3.40 (ddd, 1H, J = 9.0, 6.8, 6.8, OCH*H*CH_2), 2.36 (ddd, 2H, J = 6.8, 6.8, 6.8, OCH_2CH_2). ^{13}C NMR: δ 159.0 (0), 139.2 (1), 135.3 (1), 133.3 (0), 128.0 (1), 116.2 (2), 115.8 (2), 113.8 (1), 82.5 (1), 67.8 (2),

55.2 (3), 34.3 (2). IR: ν(NaCl, neat)/cm^{-1} 3077 (m), 2978 (m), 2954 (s), 2933 (s), 2836 (s), 1641 (m), 1611 (s), 1511 (s), 1303 (s), 1173 (s), 1037 (s), 921 (s), 829 (m).

6-(4-Methoxyphenyl)-3,6-dihydro-2*H*-pyran (9). Diene **8** (1.02 g, 4.7 mmol) is dissolved in DCM (30 mL). Ruthenium catalyst (150 mg, 3.5 mol%) is added and the solution is stirred at room temperature for 3 hours, after which time the starting material is consumed (TLC). The solvent is evaporated and the residue is purified by Kugelrohr distillation (150 °C/0.02 mbar). Yield: 0.82 g (92%). Colourless liquid. LRMS (EI): *m*/*z* 190 (M^+, 67%), 135 (91), 112 (55), 70 (58), 57 (100). ^{1}H NMR: δ 7.29 (d, 2H, J = 8.8, Ar), 6.88 (d, 2H, J = 8.8, Ar), 5.99 (dddd, 1H, J = 10.3, 4.8, 2.5, 2.5, H-3), 5.79 (ddd, 1H, J = 10.3, 4.0, 2.0, H-4), 5.09 (ddd, 1H, J = 4.8, 2.3, 2.3, H-2), 3.97 (ddd, 1H, J = 11.3, 5.3, 4.0, H-6), 3.78 (s, 3H, OMe), 3.77 (ddd, 1H, J = 11.3, 8.5, 4.0, H-6), 2.33 (dm, 1H, J = 17.3, H-5), 2.05 (dm, 1H, J = 17.3, H-5). ^{13}C NMR: δ 159.2 (0), 133.4 (0), 129.5 (1), 128.8 (1), 125.1 (1), 113.9 (1), 75.5 (1), 62.8 (2), 55.2 (3), 25.1 (2). IR: ν(NaCl, neat)/cm^{-1} 2958 (m), 1611 (m), 1512 (s), 1246 (s), 1174 (s), 1080 (m), 1036 (m).

(1*S,2*R**,6*S**)-2-(4-Methoxyphenyl)-3,7-dioxabicyclo[4.1.0]-heptane (*trans*-10) and (1*R**,2*R**,6*R**)-2-(4-methoxyphenyl)-3,7-dioxabicyclo[4.1.0]heptane (*cis*-10).** Following the general procedure for the preparation of epoxides **4**, the title compounds are prepared from dihydropyran **19** (0.82 g, 4.3 mmol) and MCPBA (70%, 1.60 g, 6.5 mmol). The diastereomeric ratio has been determined by NMR spectroscopy of the crude mixture to be 4:1 (*trans*:*cis*). The diastereoisomers are separated by column chromatography on silica using hexanes–MTBE mixtures of increasing polarity. Diastereomer *trans*-**10** (less polar): 470 mg; diastereomer *cis*-**10**: 130 mg. Combined yield: 600 mg (68%). Anal.: Found: C, 69.5; H, 6.8. Calc. for $C_{12}H_{14}O_3$: C, 69.9; H, 6.8%. *Diastereoisomer trans-**10***: colourless liquid. LRMS (EI): *m*/*z* 206 (M^+, 20%), 189 (100), 121 (80). ^{1}H NMR: δ 7.31 (d, 2H, J = 8.8, Ar), 6.88 (d, 2H, J = 8.8, Ar), 4.76 (br s, 1H, H-2), 3.78 (s, 3H, OMe), 3.68 (ddd, 1H, J = 11.5, 6.1, 1.0, H-6$_{eq}$), 3.57 (ddd, 1H, J = 11.5, 11.5, 3.3, H-6$_{ax}$), 3.39 (m, 1H, H-4), 3.15 (d, 1H, J = 4.0, H-3), 2.15 (dddd, 1H, J = 14.6, 11.5, 6.1, 1.8, H-5$_{ax}$), 2.02 (dm, 1H, J = 14.6, H-5$_{eq}$). ^{13}C NMR: δ 159.3 (0), 132.0 (0), 127.9 (1), 113.9 (1), 76.5 (1), 59.4 (2), 55.6 (1), 55.2 (3), 50.3 (1), 25.3 (2). IR: ν(NaCl, neat)/cm^{-1} 2963 (s), 1614 (w), 1514 (m), 1413 (m), 1259 (s), 1078 (s), 1032 (s), 808 (s). *Diastereoisomer cis-**10***: colourless liquid. ^{1}H NMR: δ 7.46 (d, 2H, J = 8.5, Ar), 6.92 (d, 2H, J = 8.5, Ar), 4.75 (br s, 1H, H-2), 3.91 (ddd, 1H, J = 11.0, 6.5, 2.8, H-6$_{eq}$), 3.82 (s, 3H, OMe), 3.51 (ddd, 1H, J = 11.0, 10.5, 4.7, H-6$_{ax}$), 3.47 (dd, 1H, J = 4.9, 4.0, H-4), 3.28 (dd, 1H, J = 4.0, 0.8, H-3), 2.17 (ddd, 1H, J = 15.3, 10.5, 6.5, H-5$_{ax}$), 1.94 (dddd, 1H, J = 15.3, 4.9, 4.7, 2.8, H-5$_{eq}$). ^{13}C NMR: δ 159.4 (0), 131.3 (0), 128.6 (1), 113.8 (1), 75.0 (1), 62.9 (2), 55.2 (3), 52.4 (1), 50.8 (1), 23.6 (2). IR: ν(NaCl, neat)/cm^{-1} 2972 (m), 2917 (m), 1614 (s), 1515 (s), 1379 (m), 1303 (m), 1248 (s), 1165 (s), 1033 (s), 908 (m), 827 (s).

Epoxide cleavage reactions mediated by Brønsted-acids

(2*R,4*R**,5*S**)-2-(4-Methoxyphenyl)-tetrahydropyran-4,5-diol (11).** Epoxide *trans*-**4e** or *cis*-**4e** (or mixtures of both isomers) (290 mg, 1.4 mmol) is dissolved in THF (5 mL) and water (1 mL). H_2SO_4 (3 drops) is added and the mixture is heated to 65 °C for 3 hours, after which time the starting material is completely consumed as monitored by TLC. The THF is removed *in vacuo*, and to the residue is added saturated aqueous Na_2CO_3 solution (10 mL) and ether (20 mL). The organic layer is separated, and the aqueous layer is extracted with ether. The combined organic layers are dried with $MgSO_4$. The solvent is evaporated, and the residue is dissolved in $CHCl_3$ (1 mL) and cooled to −30 °C for 12 hours. A white precipitate is formed which is dried *in vacuo*. Mp 108 °C; yield 280 mg (88%). *Alternative procedure*: epoxide *trans*-**4e** or *cis*-**4e** (230 mg, 1.1 mmol) is dissolved in acetonitrile (15 mL) and water (5 mL) and CAN (274 mg, 0.5 mmol) is added. The mixture is stirred at room temperature for 10 hours, after which time the colour of the solution changed from yellow to blue. The solution is diluted with water (20 mL) and MTBE (20 mL), the organic layer is dried with $MgSO_4$ and the solvent evaporated. Yield: 210 mg (85%). It turned out to be difficult to obtain colourless samples of **11**. LRMS (EI): *m*/*z* 224 (M^+, 50%), 135 (100). ^{1}H NMR (CD_3OD): δ 7.39 (d, 2H, J = 8.8, Ar), 6.95 (d, 2H, J = 8.8, Ar), 4.76 (dd, 1H, J = 11.5, 2.0, H-2), 4.13 (dd, 1H, J = 12.3, 1.5, H-6), 4.01 (m, 1H, H-4), 3.89 (d, 1H, J = 12.3, H-6), 3.84 (s, 3H, OMe), 3.57 (m, 1H, H-5), 2.28 (ddd, 1H, J = 14.2, 11.5, 2.8, H-3$_{ax}$), 1.77 (dm, 1H, J = 14.2, H-3$_{eq}$). ^{13}C NMR (CD_3OD): δ 161.7 (0, *C*OMe), 137.1 (0, *ipso*-C), 129.8 (1, Ar, C-3), 115.8 (1, Ar, C-2), 76.1 (1, C-1), 70.2 (1, C-4), 70.1 (2, C-5), 69.7 (1, C-3), 56.8 (3, OMe), 38.0 (2, C-2). IR: ν(KBr, disk)/cm^{-1} 3420 (s), 3347 (s), 2926 (m), 1614 (m), 1519 (m), 1253 (s), 1196 (m), 1032 (s), 824 (s).

(2*S,4*R**,5*R**)-5-Chloro-2-(4-methoxyphenyl)tetrahydropyran-4-ol (12).** Epoxide *trans*-**4e** (195 mg, 0.95 mmol) is dissolved in THF (5 mL) and water (1 mL). Aqueous HCl (10% w/w) (1 mL) is added and the solution stirred for 20 hours. The THF is removed *in vacuo* and the residue extracted with saturated Na_2CO_3 solution (15 mL) and ether (15 mL). The organic layer is dried with $MgSO_4$ and the solvent evaporated *in vacuo*. The residue consists of **12** (70%) and diol **11** (30%). Chloro compound **12** is isolated by column chromatography on silica with hexanes–MTBE (4:1) mixture as eluent. Colourless oil, yield 150 mg (65%). ^{1}H NMR: δ 7.30 (d, 2H, J = 8.8, Ar), 6.87 (d, 2H, J = 8.8, Ar), 4.78 (dd, 1H, J = 10.0, 3.3, H-2), 4.24 (dd, 1H, J = 12.7, 2.3, H-6), 4.10 (ddd, 1H, J = 4.0, 4.0, 3.8, H-4), 3.85 (dd, 1H, J = 12.7, 3.3, H-6), 3.81 (m, 1H, H-5), 3.79 (s, 3H, OMe), 2.42 (ddd, 1H, J = 14.3, 10.0, 3.3, H-3$_{ax}$), 2.40 (br s, 1H, OH), 1.77 (ddd, 1H, J = 14.3, 3.8, 3.3, H-3$_{eq}$). ^{13}C NMR: δ 159.1 (0, *C*OMe), 133.2 (0, *ipso*-C), 127.5 (1, Ar, C-3), 113.8 (1, Ar, C-2), 73.6 (1, C-1), 68.5 (1, C-3), 66.7 (2, C-5), 57.7 (1, C-4), 55.3 (3, OMe), 34.7 (2, C-2). IR: ν(NaCl, neat)/cm^{-1} 3417 (m), 2962 (w), 1613 (m), 1514 (m), 1251 (s), 1062 (s), 1028 (s).

(2*S,4*R**,5*R**)-4-Chloro-2-(4-methoxyphenyl)tetrahydropyran-5-ol (13).** Compound **13** is obtained analogously from epoxide *cis*-**4e** (195 mg, 0.95 mmol). White solid, mp 60 °C, yield: 180 mg (78%). Anal.: Found: C, 59.4; H, 6.2. Calc. for $C_{12}H_{15}ClO_3$: C, 59.3; H, 6.2%. LRMS (EI): *m*/*z* 242 (M^+, 26%), 207 (76), 137 (100). ^{1}H NMR: δ 7.26 (d, 2H, J = 8.8, Ar), 6.77 (d, 2H, J = 8.8, Ar), 4.75 (dd, 1H, J = 11.0, 1.8, H-2), 4.28 (m, 1H, H-4), 4.25 (d, 1H, J = 12.8, H-6), 3.87 (d, 1H, J = 12.8, H-6), 3.78 (s, 3H, OMe), 3.73 (br d, 1H, J = 5.8, H-5), 2.85 (m br, 1H, OH), 2.43 (ddd, 1H, J = 14.8, 11.0, 3.5, H-3$_{ax}$), 2.00 (d, 1H, J = 14.8, H-3$_{eq}$). ^{13}C NMR: δ 159.2 (0, *C*OMe), 132.9 (0, *ipso*-C), 127.2 (1, Ar, C-3), 113.8 (1, Ar, C-2), 73.5 (1, C-1), 67.9 (1, C-4), 67.3 (2, C-5), 56.6 (1, C-3), 55.3 (3, OMe), 35.5 (2, C-2). IR: ν(NaCl, neat)/cm^{-1} 3375 (m), 2962 (m), 1614 (m), 1515 (s), 1304 (s), 1244 (s), 1069 (s), 1043 (s), 965 (s), 825 (s).

Epoxide opening in refluxing acetic acid. Epoxides *trans*-**4e** or *cis*-**4e** (400 mg, 1.9 mmol) are dissolved in acetic acid (12 mL) and the mixture is heated to reflux for 7 hours. After cooling to room temperature, the mixture is diluted with ether (30 mL) and washed with saturated Na_2CO_3 solution until the acetic acid is completely removed. The organic layer is dried with $MgSO_4$ and the solvent is removed *in vacuo* to give **14** (from *trans*-**4e**) or **15** (from *cis*-**4e**) (300 mg, 58%) along with the diacetoxy compound **16** (120 mg, 21%). Analytical data for **15** and **16** are given below. Analytical data for the diacetoxy compound *(2S*,4R*,5R*)-4,5-diacetoxy-2-(4-methoxyphenyl)-tetrahydropyran (**16**)* colourless liquid. LRMS (EI): *m*/*z* 249 ($M^+ - CH_3CO$, 10%), 189 ($M^+ - 2\ CH_3CO$, 100). ^{1}H NMR:

δ 7.26 (d, 2H, J = 8.8, Ar), 6.85 (d, 2H, J = 8.8, Ar), 5.05 (m, 1H, H-4/H-5), 4.68 (m, 1H, H-4/H-5), 4.59 (dd, 1H, J = 11.4, 1.8, H-2), 4.02 (d, 1H, J = 13.1, H-6), 3.96 (dd, 1H, J = 13.1, 1.5, H-6), 3.75 (s, 3H, OMe), 2.16 (ddd, 1H, J = 14.6, 11.4, 3.0, H-3_{ax}), 2.11 (s, 3H, OAc), 2.09 (s, 3H, OAc), 1.90 (dm, 1H, J = 14.6, H-3_{eq}). ^{13}C NMR: δ 169.8 (0), 169.4 (0), 159.1 (0), 133.2 (0), 127.2 (1), 113.8 (1), 73.4 (1), 67.2 (1), 66.7 (1), 65.9 (2), 55.1 (3), 33.0 (2), 21.0 (3), 20.9 (3). IR: ν(NaCl, neat)/cm^{-1} 2963 (w), 1742 (s), 1614 (w), 1516 (m), 1372 (w), 1246 (s), 1230 (s), 1043 (m), 734 (m).

(2*R,3*R**,4*S**)-2-(4-Methoxyphenyl)tetrahydropyran-3,4-diol (17).** Starting from epoxide *cis*-**10** (50 mg, 0.24 mmol) the title compound is prepared following the procedure for **18**. NMR spectroscopy of the crude mixture indicates the formation of one diastereoisomer. The compound is purified by recrystallization from chloroform. Yield: 50 mg (93%). Colourless crystals, mp 115 °C. LRMS (EI): *m*/*z* 224 (M$^+$, 25%), 137 (100), 121 (44), 60 (16). ^{1}H NMR (CD_3OD): δ 7.22 (d, 2H, J = 8.8, Ar), 6.83 (d, 2H, J = 8.8, Ar), 4.77 (s, 1H, H-2), 4.06 (m, 1H, H-4), 3.91 (ddd, 1H, J = 12.6, 11.4, 2.6, H-6_{ax}), 3.86 (dd, 1H, J = 11.4, 6.0, H-6_{eq}), 3.72 (s, 3H, OMe), 3.54 (s br, 1H, H-3), 2.14 (dddd, 1H, J = 14.6, 12.6, 6.0, 2.6, H-5_{ax}), 1.45 (d, 1H, J = 14.6, H-5_{eq}). ^{13}C NMR (CD_3OD): δ_C 159.9 (0, *C*-OMe), 130.9 (0, ipso-C), 127.0 (1, Ar, C-3), 113.9 (1, Ar, C-2), 75.4 (1, C-1), 71.4 (1, C-2), 67.0 (1, C-3), 63.0 (2, C-5), 55.2 (3, OMe), 27.8 (2, C-4). IR: ν(KBr)/cm^{-1} 3474 (m), 3404 (m), 3309 (m), 2894 (w), 1614 (m), 1516 (s), 1249 (s), 1075 (s), 1056 (s), 1034 (s), 801 (s).

(2*R,3*S**,4*R**)-2-(4-Methoxyphenyl)tetrahydropyran-3,4-diol (18).** Sulfuric acid (three drops) is added to a solution of epoxide *trans*-**10** (260 mg, 1.3 mmol) in THF (5 mL) and water (1 mL). The solution is heated to reflux for six hours. The THF is evaporated and the residue is diluted with ether (20 mL). The sulfuric acid is neutralized with saturated Na_2CO_3 solution. The organic layer is dried with $MgSO_4$ and the solvent is evaporated. Two diastereomers are formed in a 5:1 ratio as determined by NMR spectroscopy of the crude mixture. Chromatography on silica (eluent hexanes–ethanol 9:1) yields 240 mg (85%) of diols **18** and **17** (3:1) as an inseparable mixture of diastereoisomers. Colourless oil. ^{1}H NMR (CD_3OD): δ 7.27 (d, 2H, J = 8.8, Ar), 6.87 (d, 2H, J = 8.8, Ar), 3.98 (ddd, 1H, J = 11.8, 5.2, 1.8, H-6_{eq}), 3.86 (d, 1H, J = 9.3, H-2), 3.56 (m, 1H, H-4), 3.77 (s, 3H, OMe), 3.50 (ddd, 1H, J = 12.7, 11.8, 1.8, H-6_{ax}), 3.26 (dd, 1H, J = 9.3, 9.0, H-3), 1.89 (dd, 1H, J = 12.8, 5.2, H-5_{eq}), 1.79 (dddd, 1H, J = 12.8, 12.8, 12.7, 5.0, H-5_{ax}). ^{13}C NMR (CD_3OD): δ 159.4 (0, *C*-OMe), 130.8 (0, *ipso*-C), 128.7 (1, Ar, C-3), 113.7 (1, Ar, C-2), 82.2 (1, C-1), 76.8 (1, C-2), 72.5 (1, C-3), 65.9 (2, C-5), 55.1 (3, OMe), 33.3 (2, C-4). IR: ν(NaCl, neat)/cm^{-1} 3406 (s br), 2955 (s), 2862 (s), 1613 (m), 1515 (s), 1250 (s), 1077 (s), 830 (m), 735 (m).

Epoxide cleavage reactions mediated by boron trifluoride etherate

General procedure for the boron fluoride catalysed epoxide cleavage with acetic acid. Epoxides **4** (1.0 mmol) and acetic acid (0.57 mL, 10 mmol) are dissolved in DCM (10 mL) and cooled to 0 °C. $BF_3{\cdot}OEt_2$ (three drops) is added and the mixture stirred at 0 °C for two hours and then for 12 hours at room temperature. Saturated Na_2CO_3 solution (30 mL) is added and the mixture is diluted with MTBE (20 mL). The organic layer is separated, dried with $MgSO_4$ and the solvent is evaporated. The products were purified by HPLC on silica using hexanes–ethyl acetate (2:1) mixtures as eluent. Diastereomeric ratios were determined from the ^{1}H NMR spectra of the crude mixtures.

(2S,4R*,5R*)-5-Acetoxy-2-cyclohexyltetrahydropyran-4-ol (**14a**).* A *trans*-diaxial cleavage product obtained from *trans*-**4a** (150 mg, 0.82 mmol) in 86% yield after column chromatography (silica; hexanes–MTBE 4:1). Colourless liquid. LRMS (EI): *m*/*z* 243 (M$^+$+1, 5%), 165 (30), 99 (100). ^{1}H NMR: δ 4.49 (d, 1H, J = 1.8, H-5), 3.92 (d, 1H, J = 2.5, H-4), 3.88 (dd, 1H, J = 13.1, 1.8, H-6), 3.77 (d, 1H, J = 13.1, H-6), 3.35 (ddd, 1H, J = 10.5, 7.3, 2.8, H-2), 2.90 (br s, 1H, OH), 2.04 (s, 3H, OAc), 1.89 (br d, 1H, J = 12.8, C_6H_{11}), 1.72–1.55 (5H, H-3 + C_6H_{11}), 1.30 (m, 1H, C_6H_{11}), 1.23–1.01 (4H, C_6H_{11}), 0.98–0.84 (2H, C_6H_{11}). ^{13}C NMR: δ 170.8 (0, OAc), 75.6 (1, C-1), 70.5 (1, C-4), 65.2 (2, C-5), 64.7 (1, C-3), 42.3 (1, C_6H_{11}), 31.5 (2, C-2), 28.9, 28.4, 26.4, 26.0, 25.9 (2, C_6H_{11}), 21.1 (3, OAc). IR: ν(NaCl, neat)/cm^{-1} 3436 (br s), 2925 (s), 2853 (s), 1741 (s), 1449 (m), 1372 (m), 1241 (s), 1076 (s), 1036 (m), 733 (w).

(2S,4R*,5R*)-4-Acetoxy-2-cyclohexyltetrahydropyran-5-ol (**15a**).* A *trans*-diaxial cleavage product obtained from *cis*-**4a** (180 mg, 0.99 mmol) in 89% yield after column chromatography (silica; hexanes–MTBE 4:1). Colourless liquid. LRMS (EI): *m*/*z* 243 (M$^+$+1, 20%), 99 (10), 81 (100). ^{1}H NMR: δ 4.90 (br d, 1H, J = 3.3, H-4), 3.77 (d, 1H, J = 13.3, H-6), 3.73 (d, 1H, J = 13.3, H-6), 3.48 (br s, 1H, H-5), 3.24 (ddd, 1H, J = 11.3, 6.8, 1.8, H-2), 2.75 (br s, 1H, OH), 2.02 (s, 3H, OAc), 1.85 (d, 1H, J = 11.6, C_6H_{11}), 1.81 (ddd, 1H, J = 14.8, 11.3, 3.3, H-3_{ax}), 1.71–1.55 (5H, C_6H_{11} + H-3_{eq}), 1.30 (m, 1H, C_6H_{11}), 1.24–1.03 (3H, C_6H_{11}), 1.00–0.75 (2H, C_6H_{11}). ^{13}C NMR: δ 170.0 (0, OAc), 76.9 (1, C-1), 69.6 (1, C-3), 68.1 (2, C-5), 65.5 (1, C-4), 42.2 (1, C_6H_{11}), 28.7, 28.4, 28.3, 26.4, 26.0, 25.9 (2, C_6H_{11} + C-2), 21.1 (3, OAc). IR: ν(NaCl, neat)/cm^{-1} 3436 (br s), 2925 (s), 2852 (s), 1737 (s), 1721 (s), 1449 (m), 1373 (m), 1241 (s), 1097 (s), 1076 (m), 1033 (m).

(2S,4R*,5R*)-5-Acetoxy-2-phenyltetrahydropyran-4-ol (**14b**).* A *trans*-diaxial cleavage product obtained from *trans*-**4b** (100 mg, 0.57 mmol) in 91% yield. Colourless oil. LRMS (EI): *m*/*z* 237 (M$^+$+1, 15%), 177 (100), 159 (60), 129 (40). ^{1}H NMR: δ 7.42–7.25 (5H, Ph), 4.80 (dd, 1H, J = 11.6, 2.3, H-2), 4.65 (m, 1H, H-5), 4.15 (dd, 1H, J = 12.8, 1.5, H-6), 4.05 (m, 1H, H-4), 3.97 (d, 1H, J = 12.8, H-6), 2.90 (br s, 1H, OH), 2.16 (s, 3H, COMe), 2.11 (ddd, 1H, J = 14.1, 11.6, 3.0, H-3_{ax}), 1.88 (dm, 1H, J = 14.1, H-3_{eq}). ^{13}C NMR: δ 170.8 (0), 141.8 (0), 128.3 (1), 127.6 (1), 126.0 (1), 73.2 (1), 69.9 (1), 65.3 (2), 64.9 (1), 35.9 (2), 21.2 (3). IR: ν(NaCl, neat)/cm^{-1} 3447 (br s), 2963 (m), 1739 (s), 1258 (s), 1069 (s), 1042 (s), 800 (s), 700 (s).

(2S,4R*,5R*)-4-Acetoxy-2-phenyltetrahydropyran-5-ol (**15b**).* A *trans*-diaxial cleavage product obtained from *cis*-**4b** (100 mg, 0.57 mmol) in 86% yield. Colourless oil. LRMS (EI): *m*/*z* 235 (M$^+$ − 1, 20%), 159 (100), 105 (60). ^{1}H NMR: δ 7.41–7.24 (5H, Ph), 5.05 (m, 1H, H-4), 4.67 (dd, 1H, J = 11.4, 2.4, H-2), 4.02 (dd, 1H, J = 12.6, 1.5, H-6), 3.96 (d, 1H, J = 12.6, H-6), 3.64 (m, 1H, H-5), 2.85 (br s, 1H, OH), 2.25 (ddd, 1H, J = 14.8, 11.4, 3.0, H-3_{ax}), 2.15 (s, 3H, COMe), 1.92 (ddd, 1H, J = 14.8, 3.0, 2.4, H-3_{eq}). ^{13}C NMR: δ 170.0 (0), 141.1 (0), 128.4 (1), 127.7 (1), 125.8 (1), 74.5 (1), 69.6 (1), 68.4 (2), 65.1 (1), 32.7 (2), 21.2 (3). IR: ν(NaCl, neat)/cm^{-1} 3436 (br s), 2961 (m), 1741 (s), 1372 (m), 1239 (s), 1039 (s), 758 (m), 736 (m), 699 (m).

(2S,4R*,5R*)-5-Acetoxy-2-(2-methoxyphenyl)tetrahydropyran-4-ol (**14c**).* A *trans*-diaxial cleavage product obtained from *trans*-**4c** (200 mg, 0.97 mmol) in 46% yield along with the *trans*-diequatorial (**20c**) and the tricyclic product **25**. Colourless oil. Anal.: Found: C, 63.1; H, 6.9. Calc. for $C_{14}H_{18}O_5$: C, 63.1; H, 6.8%. LRMS (EI): *m*/*z* 267 (M$^+$ + 1, 5%), 249 (45), 206 (95), 189 (100), 159 (40). ^{1}H NMR: δ 7.51 (dd, 1H, J = 7.5, 1.8, Ar), 7.26 (ddd, 1H, J = 7.5, 7.5, 1.8, Ar), 7.00 (ddd, 1H, J = 7.5, 7.5, 0.8, Ar), 6.87 (d, 1H, J = 7.5, Ar), 5.19 (dd, 1H, J = 10.3, 3.3, H-2), 4.67 (m, 1H, H-5), 4.20 (dd, 1H, J = 13.1, 1.5, H-6), 4.09 (m, 1H, H-4), 4.03 (d, 1H, J = 13.1, H-6), 3.83 (s, 3H, OMe), 2.17 (s, 3H, OAc), 2.04–1.92 (2H, H-3). ^{13}C NMR: δ 170.7 (0), 155.7 (0), 130.5 (0), 128.3 (1), 126.3 (1), 120.7 (1), 110.2 (1), 69.9 (1), 67.6 (1), 65.7 (2), 65.3 (1), 55.3 (3), 35.1 (2), 21.2 (3). IR: ν(NaCl, neat)/cm^{-1} 3450 (br s), 2929 (m), 1739 (s), 1603 (m), 1494 (s), 1242 (s), 1069 (s), 1042 (s), 790 (s), 756 (s).

(2S,4S*,5S*)-5-Acetoxy-2-(2-methoxyphenyl)tetrahydropyran-4-ol (**19c**).* A *trans*-diequatorial cleavage product

obtained from *trans*-**4c** (200 mg, 0.97 mmol) in 10% yield along with the *trans*-diaxial and the tricyclic product. Colourless oil. Anal.: Found: C, 63.0; H, 6.9. Calc. for $C_{14}H_{18}O_5$: C, 63.1; H, 6.8%. LRMS (EI): *m*/*z* 265 ($M^+ - 1$, 5%), 249 ($M^+ - OH$, 10), 189 (100). ^{1}H NMR (C_6D_6): δ 7.73 (dd, 1H, J = 7.5, 1.3, Ar), 7.11 (ddd, 1H, J = 8.0, 7.7, 1.5, Ar), 6.97 (dd, 1H, J = 7.7, 7.5, Ar), 6.51 (d, 1H, J = 8.0, Ar), 4.93 (ddd, 1H, J = 10.5, 9.3, 5.2, H-5), 4.83 (dd, 1H, J = 11.1, 1.8, H-2), 4.21 (dd, 1H, J = 10.8, 5.3, H-6_{eq}), 3.75 (ddd, 1H, J = 11.3, 9.3, 5.3, H-4), 3.27 (s, 3H, OMe), 3.16 (dd, 1H, J = 10.8, 10.5, H-6_{ax}), 2.49 (ddd, 1H, J = 13.1, 5.2, 1.8, H-3_{eq}), 2.10 (br s, 1H, OH), 1.62 (s, 3H, OAc), 1.54 (ddd, 1H, J = 13.1, 11.3, 11.1, H-3_{ax}). ^{13}C NMR ($CDCl_3$): δ 171.4 (0), 155.5 (0), 130.3 (0), 128.5 (1), 126.0 (1), 120.8 (1), 110.2 (1), 74.5 (1), 72.7 (1), 71.2 (1), 67.2 (2), 55.3 (3), 39.9 (2), 21.1 (3). IR: ν(NaCl, neat)/cm^{-1} 3436 (br s), 2959 (m), 2840 (m), 1740 (s), 1604 (m), 1590 (m), 1495 (s), 1242 (s), 1093 (s), 787 (s), 758 (s). *Selective preparation of* ***19c*** *from* ***14c***: Tetrahydropyran **14c** (220 mg, 0.83 mmol) is dissolved in DCM (10 mL) and cooled to 0 °C. $BF_3{\cdot}OEt_2$ (0.11 mL, 0.9 mmol) is added and the mixture is stirred at 0 °C for 2 hours and then at room temperature for 12 hours. The reaction is quenched with Na_2CO_3 solution, the organic layer separated, dried with $MgSO_4$ and evaporated. Ratio of diastereomers (**19c**:**14c**) is 6:1 as determined by ^{1}H NMR spectroscopy of the crude mixture. Purification is achieved by HPLC to give 160 mg (72%) of **19c** and 30 mg (14%) of **14c**.

8,12-Dioxatricyclo[7.3.1.0^{2,7}]trideca-2,4,6-trien-10-ol (***23***). Obtained from *trans*-**4c** (200 mg, 0.97 mmol) in 26% yield along with the *trans*-diequatorial and the *trans*-diaxial isomer. Colourless oil. LRMS (EI): *m*/*z* 192 (M^+, 100%), 133 (86), 131 (67). HRMS (EI): *m*/*z* 192.0785 ($C_{11}H_{12}O_3$ requires *M* 192.0786). ^{1}H NMR: δ 7.26 (ddd, 1H, J = 8.3, 7.4, 1.8, Ar), 7.17 (dd, 1H, J = 7.5, 1.8, Ar), 6.91 (ddd, 1H, J = 7.5, 7.4, 1.1, Ar), 6.85 (dm, 1H, J = 8.3, Ar), 4.75 (dd, 1H, J = 3.5, 1.1, H-2), 4.57 (m, 1H, H-4), 3.76 (m, 1H, H-5), 3.61 (dd, 1H, J = 13.5, 1.0, H-6), 3.50 (dd, 1H, J = 13.5, 2.1, H-6), 2.58 (ddd, 1H, J = 13.9, 3.5, 1.8, H-3), 2.39 (br s, 1H, OH), 1.77 (dddd, 1H, J = 13.9, 4.1, 1.1, 1.1, H-3). ^{13}C NMR: δ 155.0 (0), 130.6 (1), 130.3 (1), 120.5 (1), 119.7 (0), 115.6 (1), 70.3 (1), 67.2 (1), 66.9 (1), 63.7 (2), 24.2 (2). IR: ν(NaCl, neat)/cm^{-1} 3417 (br s), 2954 (m), 1608 (m), 1584 (m), 1483 (s), 1053 (s), 788 (s), 755 (s). *Control experiment*: Epoxide *trans*-**4c** (270 mg, 1.3 mmol) was dissolved in DCM (10 mL) and cooled to 0 °C. $BF_3{\cdot}OEt_2$ (0.164 mL, 1.3 mmol) was added and the mixture stirred for 3 hours. The reaction was quenched with Na_2CO_3 solution, the organic layer was dried, evaporated and the title compound was isolated by HPLC. Yield; 50 mg (20%). No other defined products were present in the mixture as judged by NMR spectroscopy of the crude reaction mixture.

(2S,4R*,5R*)-4-Acetoxy-2-(2-methoxyphenyl)tetrahydropyran-5-ol* (***15c***). A *trans*-diaxial cleavage product obtained from *cis*-**4c** (150 mg, 0.73 mmol) in 90% yield. Colourless oil. LRMS (EI): *m*/*z* 266 (M^+, 5%), 189 (100). ^{1}H NMR: δ 7.46 (d, 1H, J = 7.5, Ar), 7.27 (ddd, 1H, J = 8.0, 7.5, 1.5, Ar), 6.99 (dd, 1H, J = 7.5, 7.5, Ar), 6.88 (d, 1H, J = 8.0, Ar), 5.07 (m, 1H, H-4), 5.01 (dd, 1H, J = 11.6, 2.3, H-2), 4.08 (d, 1H, J = 12.3, H-6), 4.01 (d, 1H, J = 12.3, H-6), 3.85 (s, 3H, OMe), 3.71 (m, 1H, H-5), 2.68 (br s, 1H, OH), 2.18 (s, 3H, OAc), 2.12 (ddd, 1H, J = 14.8, 11.6, 3.0, H-3_{ax}), 2.01 (d, 1H, J = 14.8, H-3_{eq}). ^{13}C NMR: δ 169.9 (0), 155.4 (0), 129.7 (0), 128.2 (1), 126.2 (1), 120.5 (1), 110.0 (1), 69.6 (1), 69.1 (1), 68.5 (2), 64.9 (1), 55.1 (3), 31.4 (2), 21.0 (3). IR: ν(NaCl, neat)/cm^{-1} 3436 (br s), 2960 (m), 1732 (s), 1494 (m), 1246 (s), 1039 (s), 757 (m), 734 (m).

(2S,4R*,5R*)-5-Acetoxy-2-(3-methoxyphenyl)tetrahydropyran-4-ol* (***14d***). A *trans*-diaxial cleavage product obtained from *trans*-**4d** (180 mg, 0.87 mmol) in 88% yield. Colourless oil. LRMS (EI): *m*/*z* 266 (M^+, 30%), 206 (100), 189 (30), 159 (30). ^{1}H NMR: δ 7.26 (dd, 1H, J = 8.0, 8.0, Ar), 6.97 (d, 1H, J = 8.0, Ar), 6.95 (s, 1H, Ar), 6.82 (d, 1H, J = 8.0, Ar), 4.78 (dd, 1H, J = 11.1, 1.3, H-2), 4.65 (m, 1H, H-5), 4.15 (d, 1H, J = 13.1, H-6), 4.05 (m, 1H, H-4), 3.98 (d, 1H, J = 13.1, H-6), 3.81 (s, 3H, OMe), 3.00 (br s, 1H, OH), 2.15 (s, 3H, OAc), 2.10 (ddd, 1H, J = 14.1, 11.1, 2.5, H-3_{ax}), 1.88 (dm, 1H, J = 14.1, H-3_{eq}). ^{13}C NMR: δ 170.8 (0), 159.6 (0), 143.5 (0), 129.4 (1), 118.2 (1), 113.0 (1), 111.6 (1), 73.1 (1), 69.9 (1), 65.3 (2), 64.9 (1), 55.2 (3), 36.0 (2), 21.2 (3). IR: ν(NaCl, neat)/cm^{-1} 3460 (br s), 2959 (s), 2860 (m), 1732 (s), 1716 (s), 1603 (s), 1586 (s), 1236 (s), 1070 (s), 1041 (s), 910 (s), 804 (s), 728 (s).

(2S,4R*,5R*)-4-Acetoxy-2-(3-methoxyphenyl)tetrahydropyran-5-ol* (***15d***). A *trans*-diaxial cleavage product obtained from *cis*-**4d** (160 mg, 0.78 mmol) in 80% yield. Colourless oil. LRMS (EI): *m*/*z* 266 (M^+, 80%), 189 (100), 159 (40). ^{1}H NMR: δ 7.27 (dd, 1H, J = 8.3, 8.0, Ar), 6.97–6.93 (2H, Ar), 6.83 (d, 1H, J = 8.0, Ar), 5.05 (m, 1H, H-4), 4.66 (dd, 1H, J = 11.5, 1.8, H-2), 4.02 (dd, 1H, J = 12.6, 1.3, H-6), 3.96 (d, 1H, J = 12.6, H-6), 3.81 (s, 3H, OMe), 3.65 (m, 1H, H-5), 2.90 (br s, 1H, OH), 2.25 (ddd, 1H, J = 14.8, 11.5, 3.0, H-3_{ax}), 2.15 (s, 3H, OAc), 1.92 (dm, 1H, J = 14.8, H-3_{eq}). ^{13}C NMR: δ 170.1 (0), 159.7 (0), 142.8 (0), 129.4 (1), 118.1 (0), 113.3 (1), 111.3 (1), 74.4 (1), 69.6 (1), 68.4 (2), 65.2 (1), 55.2 (3), 32.8 (2), 21.2 (3). IR: ν(NaCl, neat)/cm^{-1} 3435 (br s), 2962 (m), 1728 (s), 1586 (s), 1255 (s), 1039 (s), 786 (m), 731 (m).

(2S,4R*,5R*)-5-Acetoxy-2-(4-methoxyphenyl)tetrahydropyran-4-ol* (***14e***). A *trans*-diaxial cleavage product obtained from *trans*-**4e** (150 mg, 0.82 mmol) in 13% yield along with the *trans*-diequatorial isomer. Colourless solid, mp 90 °C. Anal.: Found: C, 62.8; H, 6.7. Calc. for $C_{14}H_{18}O_5$: C, 63.1; H, 6.8%. LRMS (EI): *m*/*z* 266 (M^+, 39%), 135 (100), 43 (58). ^{1}H NMR: δ 7.28 (d, 2H, J = 8.8, Ar), 6.85 (d, 2H, J = 8.8, Ar), 4.71 (dd, 1H, J = 11.5, 1.5, H-2), 4.61 (m, 1H, H-5), 4.12 (dd, 1H, J = 13.1, 1.5, H-6), 4.03 (m, 1H, H-4), 3.92 (d, 1H, J = 13.1, H-6), 3.77 (s, 3H, OMe), 2.80 (br s, 1H, OH), 2.12 (s, 3H, OAc), 2.10 (ddd, 1H, J = 14.1, 11.5, 2.8, H-3_{ax}), 1.82 (d, 1H, J = 14.1, H-3_{eq}). ^{13}C NMR: δ 170.8 (0, OAc), 159.0 (0, *C*OMe), 133.9 (0, *ipso*-C), 127.4 (1, Ar, C-3), 113.7 (1, Ar, C-2), 72.9 (1, C-1), 70.0 (1, C-4), 65.4 (2, C-5), 65.0 (1, C-3), 55.2 (3, OMe), 35.8 (2, C-2), 21.2 (3, OAc). IR: ν(KBr, disk)/cm^{-1} 3373 (s), 2961 (m), 1728 (s), 1614 (m), 1521 (m), 1444 (m), 1266 (s), 1244 (s), 1181 (s), 1972 (s), 1063 (s), 1037 (s), 836 (m), 815 (m).

(2S,4S*,5S*)-5-Acetoxy-2-(4-methoxyphenyl)tetrahydropyran-4-ol* (***19e***). A *trans*-diequatorial isomer obtained from *trans*-**4e** (150 mg, 0.82 mmol) in 85% yield along with the *trans*-diaxial isomer. Colourless solid, mp 87 °C. Anal.: Found: C, 62.8; H, 6.8. Calc. for $C_{14}H_{18}O_5$: C, 63.1; H, 6.8%. ^{1}H NMR: δ 7.27 (d, 2H, J = 8.8, Ar), 6.89 (d, 2H, J = 8.8, Ar), 4.79 (ddd, 1H, J = 10.3, 9.5, 5.5, H-5), 4.36 (dd, 1H, J = 11.5, 1.9, H-2), 4.19 (dd, 1H, J = 10.9, 5.5, H-6_{eq}), 3.91 (ddd, 1H, J = 11.5, 9.5, 5.0, H-4), 3.81 (s, 3H, OMe), 3.34 (dd, 1H, J = 10.9, 10.3, H-6_{ax}), 2.61 (br s, 1H, OH), 2.29 (ddd, 1H, J = 13.1, 5.0, 1.9, H-3_{eq}), 2.14 (s, 3H, OAc), 1.79 (ddd, 1H, J = 13.1, 11.5, 11.5, H-3_{ax}). ^{13}C NMR: δ 171.4 (0, OAc), 159.2 (0, *C*OMe), 132.8 (0, *ipso*-C), 127.2 (1, Ar, C-3), 113.8 (1, Ar, C-2), 78.0 (1, C-1), 74.2 (1, C-4), 71.1 (1, C-3), 67.1 (2, C-5), 55.2 (3, OMe), 40.9 (2, C-2), 21.0 (3, OAc). IR: ν(KBr, disk)/cm^{-1} 3449 (s), 2960 (s), 2934 (m), 1740 (vs), 1613 (m), 1515 (s), 1372 (m), 1305 (m), 1240 (vs), 1175 (m), 1091 (s), 1079 (m), 1064 (m), 1035 (m), 832 (m).

(2S,4R*,5R*)-4-Acetoxy-2-(4-methoxyphenyl)tetrahydropyran-5-ol* (***15e***). A *trans*-diaxial cleavage product obtained from *cis*-**4e** (202 mg, 0.98 mmol) in 92% yield. Colourless oil. ^{1}H NMR: δ 7.28 (d, 2H, J = 8.7, Ar), 6.86 (d, 2H, J = 8.7, Ar), 5.03 (m, 1H, H-4), 4.60 (dd, 1H, J = 11.4, 2.2, H-2), 3.99 (dd, 1H, J = 12.4, 1.5, H-6), 3.91 (d, 1H, J = 12.4, H-6), 3.78 (s, 3H, OMe), 3.61 (m, 1H, H-5), 2.80 (d, 1H, J = 7.3, OH), 2.23 (ddd, 1H, J = 14.7, 11.4, 3.1, H-3_{ax}), 2.13 (s, 3H, OAc), 1.87 (dm, 1H, J = 14.7, H-3_{eq}). ^{13}C NMR: δ 170.0 (0, OAc), 159.1 (0, *C*OMe), 133.3 (0, *ipso*-C), 127.2 (1, Ar, C-3), 113.8 (1, Ar, C-2), 74.2 (1, C-1), 69.7 (1, C-3), 68.4 (2, C-5), 65.2 (1, C-4), 55.2 (3, OMe), 32.5 (2, C-2), 21.2 (3, OAc). IR: ν(KBr, neat)/cm^{-1} 3436 (s), 2960 (s), 1732 (s), 1613 (s), 1516 (s), 1373 (s), 1303 (m), 1244 (s), 1178 (m), 1039 (s), 828 (m).

(2S,4R*,5R*)-5-Benzyloxy-2-(4-methoxyphenyl)tetrahydropyran-4-ol* (***20e***) *and (2S*,4S*,5S*)-5-benzyloxy-2-(4-methoxyphenyl)tetrahydropyran-4-ol* (***21e***). Epoxide *trans*-**4e** (260 mg, 1.26 mmol) and benzylic alcohol (1.30 mL, 12.6 mmol) are dissolved in DCM (10 mL) and cooled to 0 °C. $BF_3{\cdot}OEt_2$ (3 drops) is added and the mixture stirred for 2 hours at 0 °C and for 12 hours at room temperature. The reaction mixture is washed with saturated Na_2CO_3 solution, dried with $MgSO_4$ and the solvent removed *in vacuo*. The benzylic alcohol is removed by Kugelrohr distillation (0.2 mbar/50 °C). The diastereomeric ratio is 2:1 (**20e**:**21e**) as determined by NMR analysis of the crude mixture. Separation of the diastereomers is achieved by column chromatography on silica using hexanes–MTBE mixtures (2:1) as eluent. Diastereomer **20e**: colourless oil, 240 mg. Diastereomer **21e** (less polar): white solid, mp 75 °C, yield: 120 mg. Combined yield: 360 mg (91%). *Diastereomer 20e* (diaxial product): ^{1}H NMR: δ 7.40–7.32 (5H, Ph), 7.31 (d, 2H, J = 8.8, Ar), 6.87 (d, 2H, J = 8.8, Ar), 4.73 (dd, 1H, J = 10.8, 2.7, H-2), 4.67 (d, 1H, J = 12.3, OCH_2Ph), 4.53 (d, 1H, J = 12.3, OCH_2Ph), 4.02 (m, 1H, H-4), 3.96 (dd, 1H, J = 12.7, 2.3, H-6), 3.92 (dd, 1H, J = 12.7. 2.0, H-6), 3.86 (s, 3H, OMe), 3.22 (m, 1H, H-5), 2.66 (br s, 1H, OH), 2.26 (ddd, 1H, J = 14.1, 10.8, 3.0, H-3_{ax}), 1.73 (ddd, 1H, J = 14.1, 3.0, 2.7, H-3_{eq}). ^{13}C NMR: δ 158.8 (0, *C*OMe), 138.2 (0, *ipso*-C(Ph)), 134.0 (0, *ipso* C), 128.3, 127.6, 127.5, 127.4 (1, Ph, Ar-C-3), 113.6 (1, Ar, C-2), 74.9 (1, C-4), 73.0 (1, C-1), 70.7 (2, OCH_2Ph), 65.8 (1, C-3), 64.5 (2, C-5), 55.1 (3, OMe), 35.8 (2, C-2). IR: ν(KBr, film)/cm^{-1} 3441 (s), 3417 (s), 2955 (s), 2905 (s), 1613 (s), 1514 (s), 1463 (s), 1359 (s), 1303 (s), 1257 (s), 1177 (s), 1031 (s), 827 (s), 749 (s), 739 (s). *Diastereomer 21e* (diequatorial product) : ^{1}H NMR: δ 7.31–7.20 (5H, Ph), 7.17 (d, 2H, J = 8.5, Ar), 6.79 (d, 2H, J = 8.5, Ar), 4.61 (d, 1H, J = 11.6, OCH_2Ph), 4.54 (d, 1H, J = 11.6, OCH_2Ph), 4.26 (dd, 1H, J = 11.6, 2.0, H-2), 4.12 (dd, 1H, J = 11.2, 5.0, H-6_{eq}), 3.73 (m, 1H, H-4), 3.71 (s, 3H, OMe), 3.37 (ddd, 1H, J = 10.4, 8.8, 5.0, H-5), 3.22 (dd, 1H, J = 11.2, 10.4, H-6_{ax}), 2.56 (br s, 1H, OH), 2.12 (ddd, 1H, J = 13.1, 5.0, 2.0, H-3), 1.65 (ddd, 1H, J = 13.1, 11.6, 11.5, H-3). ^{13}C NMR: δ 159.2 (0, *C*OMe), 138.1 (0, *ipso*-C(Ph)), 133.2 (0, *ipso*-C), 128.6 (1, Ph), 128.0 (1, Ph), 127.9 (1, Ph), 127.2 (1, Ar, C-3), 113.8 (1, Ar, C-2), 79.8 (1, C-4), 78.0 (1, C-1), 72.6 (2, OCH_2Ph), 72.1 (1, C-3), 67.9 (2, C-5), 55.2 (3, OMe), 39.9 (2, C-2). IR: ν(KBr, disk)/cm^{-1} 3435 (s), 2919 (m), 1613 (m), 1515 (s), 1249 (s), 1177 (m), 1097 (s), 1080 (s), 1034 (s), 825 (m), 702 (m).

(2S,4R*,5R*)-4-Benzyloxy-2-(4-methoxyphenyl)tetrahydropyran-5-ol* (***22e***). Compound **22** is obtained analogously from epoxide *cis*-**4e** (175 mg, 0.84 mmol). Colourless solid, mp 71 °C, yield: 230 mg (87%). Anal.: Found: C, 72.3; H, 7.3. Calc. for $C_{19}H_{22}O_4$: C, 72.6; H, 7.1%. LRMS (EI): *m*/*z* 314 (M^+, 49%), 223 (100), 135 (51), 91 (58). ^{1}H NMR: δ 7.37–7.27 (5H, Ph), 7.26 (d, 2H, J = 8.8, Ar), 6.86 (d, 2H, J = 8.8, Ar), 4.69 (dd, 1H, J = 11.6, 2.7, H-2), 4.65 (d, 1H, J = 12.0, OCH_2Ph), 4.59 (d, 1H, J = 12.0, OCH_2Ph), 4.14 (dd, 1H, J = 12.3, 1.3, H-6), 3.87 (d, 1H, J = 12.3, H-6), 3.78 (s, 3H, OMe), 3.75 (m, 1H, H-4), 3.69 (br d, 1H, J = 8.0, H-5), 2.37 (d, 1H, J = 8.0, OH), 2.07 (ddd, 1H, J = 14.5, 11.6, 3.0, H-3), 1.94 (ddd, 1H, J = 14.5, 2.8, 2.7, H-3). ^{13}C NMR: δ 159.1 (0, *C*OMe), 138.4 (0, *ipso*-C(Ph)), 134.0 (0, *ipso*-C), 128.5, 127.7, 127.4 (1, Ph), 127.2 (1, Ar, C-3), 113.8 (1, Ar, C-2), 74.5 (1, C-3), 74.2 (1, C-1), 71.2 (2, OCH_2Ph), 68.6 (2, C-5), 66.0 (1, C-4), 55.3 (3, OMe), 32.9 (2, C-2). IR: ν(KBr, disk)/cm^{-1} 3410 (m), 2853 (m), 1611 (s), 1515 (s), 1454 (m), 1341 (m), 1246 (s), 1091 (s), 1074 (s), 1035 (s), 828 (m), 735 (s).

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