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STEREOCONTROLLED SYNTHESES OF HYDROXYLATED TRICYCLIC SYSTEMS BY A NEW ANNULATION OF 2-CYCLOHEXEN-1-ONE

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Abstract. Tricyclic keto-diols have been synthesised by a three-step annulation procedure in which hydroxyenones, prepared by the coupling of 2-cyclohexen-1-one with aldehydes, are diastereoselectively epoxidised and the *syn*-epoxides cyclised with tin(IV) chloride. Kinetic resolution of the hydroxyenones was achieved by enantiomeric epoxidation.

The stereocontrolled construction of polycarbocyclic systems continues to attract interest,[1] chiefly because of the large number of classes of natural products[2] with differing arrangements of the carbon skeleton. Particularly challenging are polyhydroxylated natural products which contain a central seven-membered ring, such as gnididin **1**,[3] a diterpenoid orthoester possessing substantial anti-tumour activity, the irritant esters of ingenol **2** [3,4] and the cardiotoxic diterpenoid grayanotoxin **3** [5] (Figure 1).

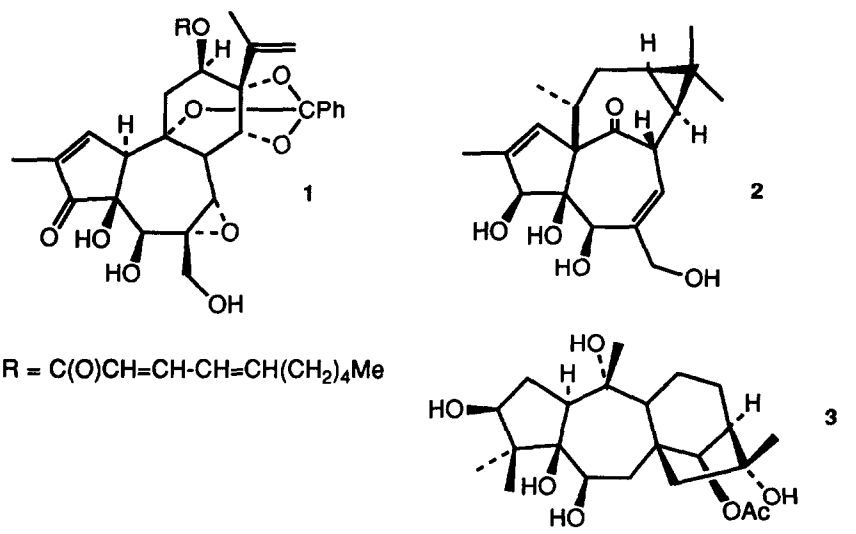
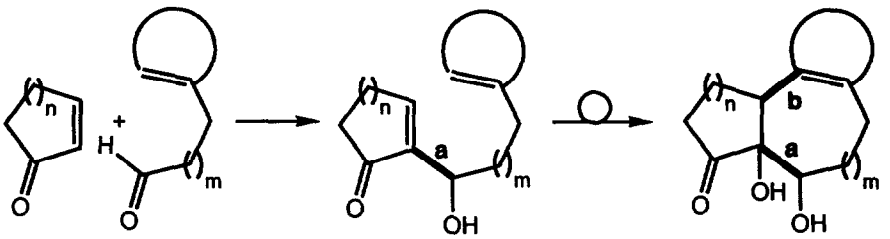


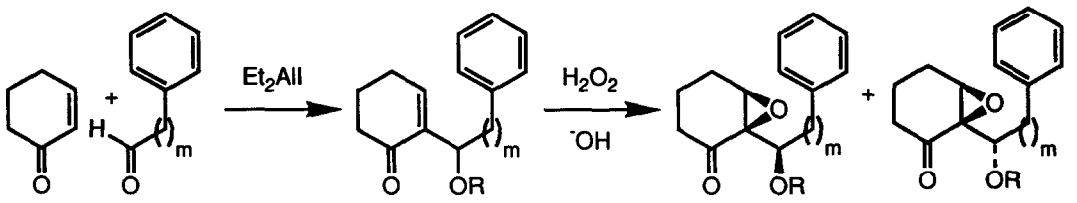
Figure 1

In a recent communication,[6] we reported a new and convergent route to hydroxylated tricyclic systems, based upon an annulation of 2-cyclohexen-1-one (Scheme 1).



Scheme 1

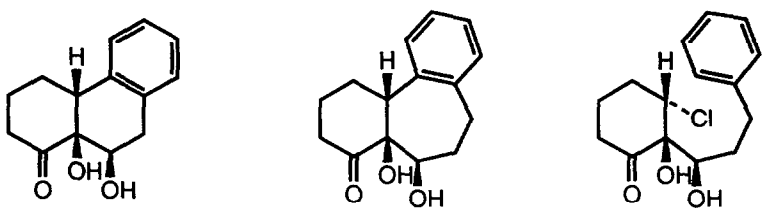
The three-step procedure is achieved under mild conditions and is notable for the stereoselective introduction of hydroxyl groups, often crucial to the conferment of biological activity.[7] The annulation is of an uncommon type[8] in which carbon-carbon bond formation at Cα of an α,β-unsaturated carbonyl compound occurs prior to carbon-carbon bond formation at the β-position.



	m	R
4a	1	H
4b	2	H
4c	1	$COCH_3$
4d	2	$COCF_3$
4e	1	$SiMe_2Bu^t$
4f	2	$SiMe_2Bu^t$

	m	R
5a	1	H
5b	2	H
5f	2	$SiMe_2Bu^t$

	m	R
6a	1	H
6b	2	H
6f	2	$SiMe_2Bu^t$



7 **8** **9**

Scheme 2

Synthesis of Tricyclic Keto-diols (7) and (8)

The perhydrophenanthrene ring-system, common to numerous terpenoids, was selected as an initial test of the annulation methodology. A variety of nucleophilic termini residing on the aldehydic fragment was envisaged; the modest π-nucleophile, an unactivated benzene ring, was initially selected in order to provide an effective test of the cyclisation step, and so that a comparison could be made with known epoxy-arene cyclisations.[9] Coupling of phenylacetaldehyde (1.5 equiv.) with 2-cyclohexen-1-one (1.0 equiv) was effected with Et_2AlI[10] (1.2 equiv.; 1M in toluene) at -80 °C to give hydroxyenone **4a** (58%) (Scheme 2). Treatment of **4a** with H_2O_2 (1.05 equiv.; 35%) in methanolic NaOH (1.5 equiv.; 0.2 M) at 0 °C afforded quantitatively a 5:2 mixture of *syn*:*anti* epoxides **5a** and **6a**, respectively, which were separated by chromatography giving the *syn*[11]-hydroxy-epoxy-ketone **5a** as an oil (69%) and the *anti*-diastereoisomer **6a** as a crystalline solid (27%). Treatment of epoxide **5a** with $SnCl_4$ (5 equiv., 20 °C, 24 h) afforded keto-diol (73%) **7**.

X-ray crystallographic analysis[12] of a single crystal of the keto-diol **7** showed that the fused cyclohexanone ring adopts a chair conformation and is *cis*-fused to the six-membered ring which adopts a twist-chair conformation. Molecules are linked in sheets *via* hydrogen bonds between the hydroxyl oxygen atoms and the carbonyl oxygen atoms of molecule related across crystallographic inversion centres. The relative configuration of epoxide **5a** is secured both by its cyclisation to ketone **7**, and is inferred from of the relative configuration of the diastereoisomer **6a**, established by an X-ray determination.

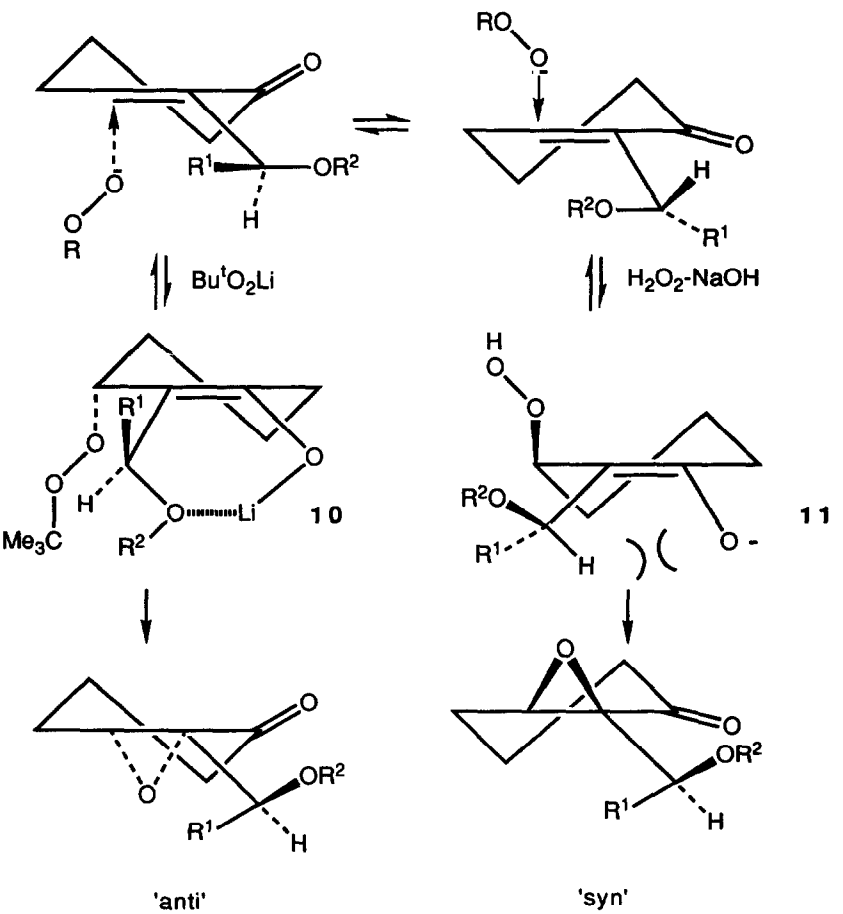
The importance and synthetic challenge of natural products incorporating a cycloheptane ring fused to a cyclohexane ring could be effectively met through a direct and efficient annulation. Accordingly, keto-diol **8** was selected as it provided a relatively stringent test of the annulation methodology, including a *7-Exo-Tet* ring closure with an unactivated benzene ring as the π-nucleophile. Coupling of dihydrocinnamaldehyde (1.9 equiv.) with 2-cyclohexen-1-one (1.0 equiv.) was effected with Et_2AlI[10] (1.25 equiv.; 1M in toluene) at -15 °C to give hydroxyenone **4b** as an oil (79%). Epoxidation of **4b** with H_2O_2 (1.05 equiv.; 35%) in methanolic NaOH (2.0 equiv.; 0.27 M) afforded in 97% yield an 11:2 mixture of epoxides **5b** and **6b** respectively, which were separated by chromatography to give **5b** (61%) and **6b** (10%). Treatment of **5b** with $SnCl_4$ (5.0 equiv.; 20 °C, 24 h) afforded, after chromatography, the keto-diol **8** (33%) and the chlorinated keto-diol **9** (46%). The relative configuration of the keto-diol **9** was established by converting it into the epoxide **5b** in 87% yield using aqueous NaOH, thus allowing an improved yield of **8** to be obtained by recycling of the undesired **9**.

An X-ray crystallographic analysis[12] of the keto-diol **8** showed that the fused cyclohexanone ring adopts a chair conformation and is *cis*-fused to the seven-membered ring which adopts a chair-like conformation. Molecules are linked in pairs across a crystallographic inversion centre *via* pairs of hydrogen bonds from the oxygen atom of the carbonyl group to the oxygen atom of the more remote hydroxyl group. The hydroxyl group at the ring junction does

not appear to engage in hydrogen bonding. The configurations of the hydroxy-epoxy-ketones **5b** and **6b** were deduced by comparison of their ^1H NMR data with that of the homologues **5a** and **6a**, respectively. The relative configuration of **5b** can also be inferred from its cyclisation to the keto-diol **8**.

Diastereoselectivity of the Epoxidation Step

The high *syn*-diastereoselection observed during the alkaline epoxidations of hydroxyenones **4a** and **4b** with H_2O_2 had not been previously reported.[6] The ratio of 11:2 *syn:anti* **5b:6b** was not significantly affected by altering the concentration of the base, or by changing from NaOH to LiOH or LiH. Although *syn*-stereoselective epoxidations of cycloalkenols have been reported with peracids,[13,14] hydrogen bonding involving the hydrogen atom of the alcohol was postulated.[13,15]



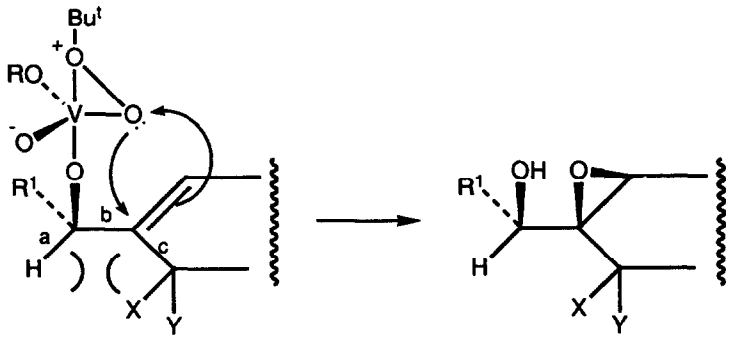
Scheme 3. Stereoselective epoxidation of hydroxyenones and their derivatives (only one enantiomer depicted).

Desiring to reverse the selectivity, thereby favouring the *anti*-epoxides, the *tert*-butyldimethylsilyl derivative **4f** was prepared. Epoxidation of **4f** with alkaline H_2O_2 afforded a 5:2 mixture of *syn*:*anti*-protected epoxides **5f** and **6f** (87% overall yield). Deprotection of this 5:2 diastereoisomeric mixture was effected with tetra-*n*-butylammonium fluoride in THF (5 d, 30 °C) gave a 5:2 mixture (98%) of the epoxides **5b** and **6b**. Evidently, in the epoxidation of hydroxyenones of the type **4** effected with alkaline H_2O_2, the diastereoselection is not principally due to hydrogen bonding of the hydrogen atom of the hydroxyl group of the hydroxyenone, and hence a transition-state model[13,15] proposed for the *syn*-epoxidation of cyclohexenes and unsaturated steroids bearing a free allylic hydroxyl group is not sufficient to account for the origin of the diastereofacial selectivity.

In the search for a more profound effect on the diastereoselectivity of the epoxidation of hydroxyenones **4a** and **4b**, reactions under strongly alkaline, aprotic conditions were studied. Meth-Cohn and co-workers[16] employed *n*-butyllithium and *tert*-butyl hydroperoxide for the *anti*-selective epoxidation of α,β-unsaturated esters. Reaction of **4a** with Meth-Cohn's reagent in benzene at -80 °C gave predominantly the *anti*-epoxide **6a** (**6a**:**5a** = 5:2) in a moderate yield. An analogous epoxidation of **4b** in benzene with *n*-butyllithium and *tert*-butyl hydroperoxide failed, but when a solvent of benzene:THF (2:3 v/v) was used, a 3:2 mixture of **6b**:**5b** was obtained though in an overall yield of only 34%. Scheme 3 provides a possible rationalisation of the stereoselective epoxidation of hydroxyenones (R^2 = H) and their derivatives (e.g. R^2 = $SiMe_2Bu^t$). That both R^2 = H and $SiMe_2Bu^t$ afford the *syn*-product suggests an orientation of the R^2O group as in **11**; for other epoxidations stereoelectronic factors[17] have been cited, and this model also satisfies a small non-bonding interaction between C-H and C-O^-, as well as a favourable net dipole arising from the C-O bonds. In contrast, geometry as shown for **10** could be favoured for the reaction with LiO_2Bu^t which gives the *anti*-product. In enolate **10**, the peroxide moiety and R^1 reside on opposite faces of the ring, thereby minimising steric interactions. The extent to which this arrangement is enhanced by O-Li chelation is not known, although such has been involved for the reaction of LiO_2Bu^t with acyclic α,β-unsaturated esters.[16]

Failure to improve on the diastereoselectivity of the epoxidation with anionic peroxides led us to explore other reagents. Treatment of **4a** with TBHP and $VO(acac)_2$ in benzene at reflux afforded exclusively the *syn*-epoxide **5a** in 91%; similarly **4b** afforded **5b** in 56%. During these studies, a report on epoxidation of allylic hydroxyenones under Sharpless conditions appeared.[18] The requirement for a free allylic OH group in the TBHP-$VO(acac)_2$ epoxidations was confirmed by the failure of the acetate **4c** or the *tert*-butyldimethylsilyl derivative **4e** to afford detectable quantities of epoxides (1.1 equiv. TBHP, benzene, reflux). The exclusively *syn*-epoxides reported here obtained from $VO(acac)_2$-TBHP and $Ti(^iOPr)_4$-TBHP-DIPT epoxidations can be rationalised by assuming that the O atom bound to the vanadium species is delivered from a stereoelectronically preferred conformation[17,19] in which non-bonding interactions are minimised (Scheme 4). Thus, in complex **12**, epoxidation occurs at the β-face. Were it to occur

at the α-face, greater eclipsing interactions would be expected (between R^1 and bond *c* or between R^1 and X/Y, or both 1,2- and 1,3-eclipsing interactions).



Scheme 4

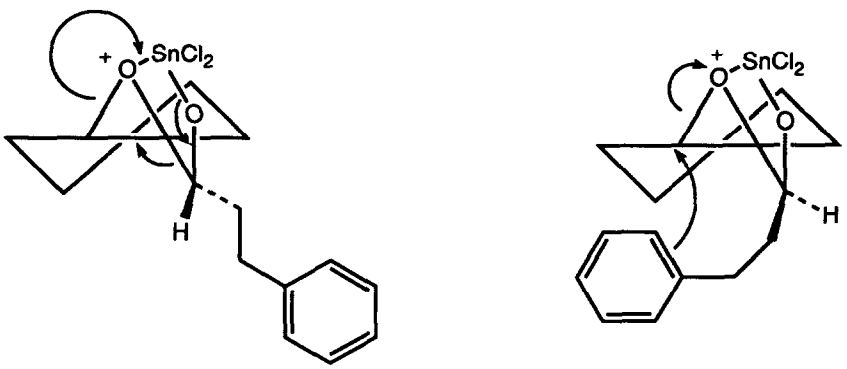
Such principles were first discussed by Sharpless and Verhoeven.[17] Thus, acyclic allylic alcohols have been shown to afford predominantly *syn*-epoxides;[20] ketones (X,Y = O) have been shown to give exclusively *syn*-epoxides in the present work, and elsewhere,[18] as have derivatives of cyclopentenylmethanol.[21]

Kinetic Resolution of (4a) by Enantioselective Epoxidation

Treatment of **4a** with anhydrous TBHP (3.4M in toluene)/titanium(IV) isopropoxide/(+)-di-isopropyl tartrate afforded **5a** (39%) as the only epoxide, in both diastereoisomerically pure and in > 75% enantiomeric excess. Column chromatography enabled optically active **4a** (35%) to be isolated (m.p. 58-61.5 °C). No other products were detected in appreciable quantity. Enantiomeric excesses were determined by ^{1}H NMR analysis using europium(III) tris[3-(heptafluoropropylhydroxymethylene)-d-camphorate], Eu(hfc)$_3$;[22] comparison experiments were made using racemic **5a** prepared from **4a** and alkaline H_2O_2. An analogous kinetic resolution of **4b** afforded **5b** (21%) as the only epoxide, in > 60% enantiomeric excess. The absolute configurations of **4a** and **5a** have not been established experimentally. However, since (1-cyclohexenyl)-1-ethanol and related allylic alcohols have been shown[20] to undergo kinetic resolution into the *(R)*-allylic alcohol and the *erythro*-epoxide derived from the *(S)*-enantiomer, the corresponding kinetic resolutions of **4a** and **4b** would be expected to afford the *(R)*-hydroxyenones and therefore the *syn*-epoxides **5a** and **5b** derived from the *(S)*-hydroxyenones. In any case, the kinetic resolution demonstrates that enantiomerically enriched tricyclic keto-diols can be obtained in three steps from two achiral carbonyl compounds in a convergent and flexible annulation.

Scope and Limitations of Cyclisation Reactions

Hydroxyenones **4a** and **4b** were unaffected by $SnCl_4$ at 20 °C for periods of up to 5 days. Hydroxyenone **4b** was completely consumed after 16 h on treatment with $AlCl_3$ in CH_2Cl_2 at 20 °C. However, no major product could be identified from the resulting mixture. Treatment of hydroxyenone **4b** with $BF_3.OEt_2$ at 20 °C also gave a mixture, 80% of **4b** being consumed after 6 h. The action of CF_3CO_2H (20 °C, 24 h) on **4b** afforded the trifluoroacetate **4d** (73%), but no cyclised product. Treatment of **9** with $SnCl_4$ did not afford any cyclised material. Solutions of the *anti*-epoxides **6a** and **6b** in CH_2Cl_2 when treated with $SnCl_4$ (5 equiv.) at 20 °C, afforded no cyclised products, but instead products consistent with fragmentation to aldehydes (from **6b**, 3-phenylpropionaldehyde was identified by ^1H NMR spectroscopy). A possible rationalisation is given in Figure 2.



fragmentation of *anti* - **6b** cyclisation of *syn* - **5b**

Figure 2

In the case of epoxide **5b** the side-chain bearing the phenyl group is appropriately positioned for cyclisation. In the case of epoxide **6b** the side-chain is directed away from the epoxide group which may allow other reactions, such as fragmentation, to occur. Competitive attack of **6b** by Cl^- may occur, as has been demonstrated for **5b**.

EXPERIMENTAL

General Details. - All melting points were determined with a Kofler hot-stage apparatus and are uncorrected. NMR spectra were run in $CDCl_3$ or C_6D_6; chemical shifts are quoted in ppm downfield from internal tetramethylsilane, and the line separations (*J*) are expressed in Hertz. The following abbreviations are used to describe NMR signals: s, singlet; d, doublet; dd double

doublet; t, triplet; q, quartet; m, multiplet; b, broad. ^1H NMR spectra were determined on a Perkin Elmer R-34 spectrometer operating at 220 MHz, and ^{13}C and ^1H NMR spectra on a Bruker AM-250 instrument operating at 68.8 and 250 MHz repectively, or on a Bruker WN 400 with an Aspect computer operating at 100.62 and 400.13 MHz repectively. Mass spectra were obtained on a Kratos MS-25 instrument. Microanalytical data were obtained on a Perkin Elmer 2400 CHN elemental analyser. Infra-red spectra were obtained on Perkin-Elmer 684 or 157G instruments as a thin film, KBr disc or in nujol. Yields are for material judged to be homogeneous by tlc and ^1H NMR. Thin-layer chromatography was performed on Merck 0.2 mm aluminium-backed silica plates and visualised using ultra-violet light or developed using ceric sulphate spray. Column chromatography was performed using Merck silica gel 60 (230-400 mesh) under gravity. Petroleum (40-60 fraction), ethyl acetate, benzene, toluene, acetyl chloride, dimethyl formamide, methanol and tetrahydrofuran were distilled prior to use. Evaporation refers to the removal of solvent under reduced pressure, unless otherwise stated.

2-(2-Phenyl-1-hydroxyethyl)cyclohex-2-en-1-one (4a). Phenylacetaldehyde (3.8ml, 32.5 mmol) in dichloromethane (21 ml) and diethylaluminium iodide (25 ml, 25.0 mmol, 1.0M solution in toluene) were added at the same rate over 40 min from separate dropping funnels to a stirred solution of 2-cyclohexen-1-one (2.0 ml, 20.6 mmol) in dichloromethane (20 ml) at -80 °C. On completion of the addition the mixture was stirred at -80 °C for 30 min. The solution was then diluted with diethyl ether (40 ml), followed by the careful addition of dilute hydrochloric acid (30 ml, 1M). The organic layer was then washed with dilute hydrochloric acid (20 ml, 1M), water (2x20 ml), brine (20 ml), dried (Na_2SO_4) and filtered. Evaporation of the solvent gave a brown oil which was subjected to column chromatography on silica gel, using light petroleum:diethyl ether (4:1) as eluent. This yielded **4a** (2.61 g, 58%) as a needles, R_f [chloroform] 0.11, m.p. 59-62 °C. Found: C, 77.6; H, 7.4%; $C_{14}H_{16}O_2$ requires: C, 77.8; H, 7.5%; IR (nujol) 3430 (br) and 1660 (s) cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 7.35-7.10 (5H, m), 6.75 (1H, t, J = 4 Hz), 4.55 (1H, dd, J = 5 and 7 Hz), 3.01 (1H, dd, J = 5 and 12 Hz), 2.83 (1H, dd, J = 7 and 12 Hz), 2.62 (1H, br s), 2.45 (2H, t, J = 7 Hz), 2.33 (2H, m) and 1.97 (2H, quintet, J = 7 Hz); δ_C ($CDCl_3$, 63 MHz) 200.0 (s), 146.3 (d), 139.8 (s), 138.4 (s), 129.4 (d), 128.3 (d), 126.3 (d), 72.2 (d), 43.3 (t), 38.6 (t), 25.6 (t) and 22.5 (t); MS m/e (%) 217 (13), 199 (100), 125 (63), 91 (47) and 65 (23).

2-(3-Phenyl-1-hydroxypropyl)-cyclohex-2-en-1-one (4b). Diethylaluminium iodide (12.5 ml, 12.5 mmol, 1.0M in toluene) was added, *via* a syringe, to a stirred solution of 2-cyclohexen-1-one (1.0 g, 10.4 mmol) and hydrocinnamaldehyde (2.51 g, 19 mmol) in dichloromethane (30 ml) at -15 °C under nitrogen. The mixture darkened and was stirred for 30 min at -15 °C. The solution was then diluted with diethyl ether (40 ml), followed by the careful addition of dilute hydrochloric acid (30 ml, 1M). The organic layer was then washed with dilute hydrochloric acid (20 ml, 1M), water (2x20 ml), brine (20 ml), dried (Na_2SO_4), filtered and solvent removed to yield a residue which was subjected to column chromatography on silica gel, initially using chloroform:ethyl acetate (10:1) as eluent. This yielded **4b** (1.89 g, 79%) as a pale yellow oil, R_f [chloroform:ethyl acetate (10:1)] 0.25, which charred on attempted distillation. IR (film) 3420, 3025, 2930 and 1670 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 7.33-7.12 (5H, m), 6.85 (1H, dt, J = 1 and 4 Hz), 4.31 (1H, t, J = 7 Hz),

3.01 (1H, br s), 2.80 (1H, m), 2.66 (1H, m), 2.37 (4H, m) and 1.98 (4H, m); δ_C ($CDCl_3$, 63 MHz) 200.5 (s), 145.8 (d), 141.8 (s), 140.8 (s), 128.4 (d), 128.3 (d), 125.7 (d), 71.0 (d), 38.6 (t), 37.6 (t), 32.2 (t), 25.6 (t) and 22.5 (t). 2,4-Dinitrophenylhydrazone as needles, m.p. 114 °C (decomp.). Found: C, 61.3; H, 5.4; N, 13.7%; $C_{21}H_{22}N_4O_5$ requires: C, 61.5; H, 5.4; N, 13.7%.

***syn*- and *anti*-2,3-Oxirano-2-(2-phenyl-1-hydroxyethyl)cyclohexan-1-one (5a) and (6a).** Sodium hydroxide (0.60 g, 15.0 mmol) in water (3 ml) was added to a solution of **4a** (2.12 g, 9.80 mmol) and hydrogen peroxide (1.15 ml, 10.1 mmol, 30% solution in water) in methanol (70 ml) at 0 °C. The mixture was stirred at 0 °C for 30 min then diluted with water (150 ml) and extracted with dichloromethane (3x50 ml). The combined organic extracts were washed with water (3x50 ml), brine (30 ml), dried (Na_2SO_4) and filtered. Evaporation of the solvent gave a mixture of *syn*- and *anti*-2,3-oxirano-2-(2-phenyl-1-hydroxyethyl)cyclohexan-1-one (2.18 g, 96%), in a ratio of 5:2 (^1H NMR). Column chromatography on silica gel using chloroform as eluent gave **5a** (1.56 g, 69%) as a colourless oil, R_f [chloroform] 0.20. IR (film) 3410 and 1695 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 7.35-7.10 (5H, m), 4.51 (1H, dd, J = 7 and 3.5 Hz), 3.40 (1H, br s, OH), 3.02 (1H, dd, J = 3.5 and 14.5 Hz), 2.85 (1H, dd, J = 7 and 14.5 Hz), 2.55 (1H, dt, J = 16.5 and 3.5 Hz) and 2.18-1.57 (6H, m); δ_C ($CDCl_3$, 63 MHz) 206.0 (s), 137.7 (s), 129.7 (d), 128.2 (d), 126.5 (d), 67.2 (d), 61.5 (s), 58.2 (d), 38.9 (t), 37.5 (t), 22.9 (t) and 17.4 (t); MS m/e (%) 250 (14), 215 (67), 197 (64) and 91 (100); and **6a** as needles, (0.62 g, 27%), R_f [chloroform] 0.17, m.p. 94-96 °C. Found: C, 72.4; H, 7.1%; $C_{14}H_{16}O_3$ requires: C, 72.4, H, 6.9%; IR (film) 3410 and 1695 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 7.36-7.14 (5H, m), 3.92 (1H, dd, J = 15 and 8 Hz), 3.18 (1H, t, J = 2 Hz), 2.99 (1H, dd, J = 6.5 and 13 Hz), 2.92 (1H, dd, J = 8 and 20.5 Hz), 2.57 (1H, dtd, J = 16, 4.5 and 1 Hz), 2.19-1.98 (2H, m), 1.93-1.73 (2H, m) and 1.74-1.49 (3H, m); δ_C ($CDCl_3$, 63 MHz) 208.0 (s), 137.7 (s), 129.2 (d), 128.6(d), 126.7(d), 73.3 (d), 61.7 (s), 60.0 (d), 40.0 (t), 37.4 (t), 22.8 (t) and 17.3 (t).

***Syn*- and *anti*-2,3-oxirano-2-(2-phenyl-1-hydroxyethyl)cyclohexan-1-one (5a) and (6a).** *Tert*-butyl hydroperoxide (0.11 g, 70%, 0.83 mmol) was refluxed in benzene (50 ml) with azeotropic removal of water for 2 h. The solution was cooled, the apparatus flushed with nitrogen, and then further cooled to -80 °C. *n*-Butyllithium (0.5 ml, 1.24M, 0.61 mmol) was then added, followed by **4a** (0.12 g, 0.61 mmol) in THF (10 ml). The mixture was allowed to warm to room temperature over 2 h and then water (100 ml) was added. The aqueous solution was extracted with diethyl ether (3x40 ml) and the combined organic extracts washed with water (2x40 ml), dried (Na_2SO_4) and filtered. Evaporation of the solvent gave an oil (0.1 g), which contained four components by tlc. R_f [ethyl acetate:light petroleum] 0.49 (minor), 0.35, 0.21 (major) and 0.09. Examination of the crude reaction product by ^1H NMR spectroscopy showed signals at δ_H ($CDCl_3$, 220 MHz) 4.51 (m), 3.97 (m), 3.35 (s) and 3.2 (s), consistent with the presence of *syn*- and *anti*-2,3-oxirano-2-(2-phenyl-1-hydroxyethyl)cyclohexan-1-one in a ratio of 2:5 respectively.

Epoxidation of 2-(3-phenyl-1-hydroxypropyl)-cyclohex-2-en-1-one (4b):

(a) Using methanolic H_2O_2-NaOH (2 equiv.). Sodium hydroxide (0.35g, 8.7 mmol) in water (2 ml) was added to a solution of **4b** (1.0 g, 4.3 mmol) and hydrogen peroxide (0.43 g, 4.5 mmol, 35%

solution in water) in methanol (30 ml) at 0 °C. The mixture was stirred at 0 °C for 30 min then diluted with water (100 ml) and extracted with dichloromethane (3x30 ml). The combined organic extracts were washed with water (3x30 ml), brine (20 ml), dried (Na_2SO_4) and filtered. Evaporation of the solvent gave a mixture of **5b** and **6b** (1.04 g, 97%), in a ratio of 11:2, by ^1H NMR. Column chromatography on silica gel using dichloromethane as eluent gave **5b** (0.65 g, 61%) as needles, R_f [dichloromethane] 0.21, recrystallised from light petroleum, m.p. 42-50 °C. Found: C, 73.0; H, 7.3%; $C_{15}H_{18}O_3$ requires: C, 73.2, H, 7.4%; IR (KBr disc) 3350 (br), 3020, 2940. 2920, and 1710 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 7.34-7.14 (5H, m), 4.17 (1H, dt, J = 9 and 3.5 Hz), 3.64 (1H, d, J = 2 Hz), 2.99-2.82 (1H, m), 2.79-2.63 (1H, m), 2.62-2.50 (1H, m), 2.31-2.20 (1H, m), 2.17 (1H, dd, J = 4 and 1 Hz) and 2.10-1.60 (6H, m); δ_C ($CDCl_3$, 63 MHz) 206.5 (s), 141.7 (s), 128.4 (d), 128.3 (d), 125.8 (d), 66.5 (d), 61.9 (s), 58.3 (d), 37.6 (t), 34.2 (t), 31.7 (t), 23.0 (t) and 17.4 (t); MS m/e (%) 264 (35), 229 (100), 104 (85) and 91 (98); and **6b** as a colourless oil (0.11 g, 10%), R_f [dichloromethane] 0.14. Found: C, 72.4: H, 7.5%: $C_{15}H_{18}O_3$ requires: C, 73.2; H, 7.4%; δ_H ($CDCl_3$, 250 MHz) 7.33-7.12 (5H, m), 3.86 (1H, dt, J = 12 and 4 Hz), 3.50 (1H, t, J = 2Hz), 2.90 (1H, ddd, J = 5.5, 9.5 and 14.5 Hz), 2.74-2.50 (3H, m), 2.30-2.17 (1H, m) and 2.13-1.56 (6H, m); δ_C ($CDCl_3$, 63 MHz) 208.2 (s), 141.5 (s), 128.4 (d, 2 equivalent signals), 125.9 (d), 70.3 (d), 62.4 (s), 59.3 (d), 37.4 (t), 34.0 (t), 32.0 (t), 23.0 (t) and 17.7 (t).

(b) Using methanolic H_2O_2-LiOH. Hydrated lithium hydroxide (0.18 g, 4.35 mmol) in water (0.5 ml) was added to a solution of **4b** (0.2 g, 0.87 mmol) and hydrogen peroxide (0.085 g, 0.88 mmol, 35% solution in water) in methanol (15 ml) at -10 °C. The mixture was stirred at -10 °C for 30 min, then diluted with water (50 ml) and extracted with dichloromethane (3x30 ml). The combined organic extracts were washed with water (3x30 ml), brine (20 ml), dried (Na_2SO_4) and filtered. Evaporation of the solvent gave a mixture of **5b** and **6b**, (0.21 g, 98%), in a ratio of 11:2, as determined by ^1H NMR.

(c) Using methanolic H_2O_2-LiH. Lithium hydride (0.14 g, 17.4 mmol) was added to a solution of **4b** (0.2 g, 0.87 mmol) and hydrogen peroxide (0.085 g, 0.88 mmol, 35% solution in water) in methanol (15 ml) at -10 °C. The mixture was stirred at -10 °C for 30 min, then diluted with water (50 ml) and extracted with dichloromethane (3x30 ml). The combined organic extracts were washed with water (3x30 ml), brine (20 ml), dried (Na_2SO_4) and filtered. Evaporation of the solvent gave a mixture of **5b** and **6b**, (0.20 g, 93%), in a ratio of 4:1, as determined by ^1H NMR.

2-(3-Phenyl-1-hydroxypropyl)cyclohex-2-en-1-one (4b), *anti*-2,3-oxirano-2-(3-phenyl-1-hydroxypropyl)cyclohexan-1-one (6b), *syn*-2,3-oxirano-2-(3-phenyl-1-hydroxypropyl)-cyclohexan-1-one (5b) and 1-butyl-2-(3-phenyl-1-hydroxypropyl)cyclohexan-1-ol. *Tert*-butyl hydroperoxide (0.11 g, 0.83 mmol, 70% solution in water) was refluxed in benzene (50 ml) with azeotropic removal of water for 2 h. Then about 30 ml of benzene was removed by distillation and dry THF (30 ml) was added. The solution was cooled, the apparatus flushed with nitrogen, and then further cooled to -80 °C. 4b (0.33 g, 1.41 mmol) in THF (10 ml) was then added, followed by *n*-butyllithium (1.7 ml, 12.12 mmol, 1.24M solution in hexanes). The mixture was allowed to

warm to room temperature over 2 h and then water (100 ml) was added. The aqueous solution was extracted with diethyl ether (3x40 ml) and the combined organic extracts washed with water (2x40 ml), dried (Na_2SO_4) and filtered. Evaporation of the solvent gave an oil (0.39 g), which was subjected to column chromatography on silica gel, using light petroleum:ethyl acetate (5:1) as eluent. This gave **4b**, (0.053 g, 16% recovery), R_f [light petroleum:ethyl acetate 5:1] 0.13; **6b**, (0.07 g, 20%) R_f [light petroleum:ethyl acetate (5:1)] 0.15; **5b**, (0.05 g, 14%), R_f [light petroleum:ethyl acetate (5:1)] 0.18; and 12, (0.098 g, 24%) R_f [light petroleum:ethyl acetate (5:1)] 0.3, δ_H ($CDCl_3$, 220 MHz) 7.35-7.05 (5H, m) 5.85 (1H, t), 4.31 (1H, t), 2.9-2.51 (2H, m), 2.15-1.50 (10H, m), 1.40-1.10 (4H, m) and 0.85 (1H, t).

***syn*-2,3-Oxirano-2-(2-phenyl-1-hydroxyethyl)cyclohexan-1-one (5a).** To a solution of **4a** (181 mg, 0.84 mmol) and vanadyl acetylacetonate (3 mg) in refluxing benzene (40 ml) in a Dean-Stark apparatus was added *tert*-butyl hydroperoxide (0.12 ml, 0.93 mmol, 70% in water) over 5 min. The initially colourless solution turned bright green on the addition of the vanadyl acetylacetonate, the colour fading as the reflux temperature was approached. On addition of the *tert*-butyl hydroperoxide the mixture became dark green, being lime-green at the end of the reflux after 5 h. The solution was allowed to cool and then washed with saturated sodium hydrogen sulphate solution (2x50 ml), brine (50 ml), dried ($MgSO_4$), filtered and solvent removed to afford a residue that was subjected to column chromatography on silica gel using chloroform as eluent. This gave **5a** (176 mg, 91 %) as a colourless oil, R_f [chloroform] 0.20. δ_H ($CDCl_3$, 250 MHz) 7.35-7.10 (5H, m), 4.51 (1H, dd, J = 7 and 3.5 Hz), 3.40 (1H, br s, OH), 3.02 (1H, dd, J = 3.5 and 14.5 Hz), 2.85 (1H, dd, J = 7 and 14.5 Hz), 2.55 (1H, dt, J = 16.5 and 3.5 Hz) and 2.18-1.57 (6H, m).

***syn*-2,3-Oxirano-2-(3-phenyl-1-hydroxypropyl)cyclohexan-1-one (5b).** To a solution of **4b** (550 mg, 2.39 mmol) and vanadyl acetylacetonate (9 mg) in refluxing benzene (60 ml) in a Dean-Stark apparatus was added *tert*-butyl hydroperoxide (0.34 ml, 2.63 mmol, 70% in water) over 5 min. The initially colourless solution turned pale green on the addition of the vanadyl acetylacetonate, the colour fading slightly as the reflux temperature was approached. On addition of the *tert*-butyl hydroperoxide the mixture became deep red in colour, turning yellow during the 5 h reflux. The solution was allowed to cool and then washed with saturated sodium hydrogen sulphate solution (2x50 ml), brine (50 ml), dried ($MgSO_4$), filtered and solvent removed to afford a residue that was subjected to column chromatography on silica gel using light petroleum:diethyl ether (1:1) as eluent. This gave **5b** (332 mg, 56%) as needles, R_f [light petroleum:diethyl ether (1:1)] 0.44, m.p. 43-50°C. δ_H ($CDCl_3$, 220 MHz) 7.34-7.14 (5H, m), 4.17 (1H, dt, J = 9 and 3.5 Hz), 3.64 (1H, t, J = 2 Hz), 2.99-2.82 (1H, m), 2.79-2.63 (1H, m), 2.62-2.50 (1H, m), 2.31-2.20 (1H, m), 2.17 (1H, dd, J = 4 and 1 Hz) and 2.10-1.60 (6H, m).

2-(3-Phenyl-1-(*tert*-butyldimethylsiloxy)propyl)cyclohex-2-en-1-one (4f). **4b** (1.0 g, 4.3 mmol) was stirred in *N*,*N*-dimethylformamide (10 ml) at 0 °C. Imidazole (0.89 g, 13.0 mmol) was added, followed by *tert*-butyldimethylchlorosilane (0.98 g, 6.5 mmol) and the mixture stirred for 18 h at 25 °C. The mixture was then diluted with diethyl ether (100 ml), washed with water (2x50 ml),

dried (Na_2SO_4), filtered and solvent removed to afford a residue that was subjected to chromatography on silica gel, using dichloromethane:light petroleum (1:1) as eluent, to yield **4f** as a colourless oil, (0.41 g, 88%) R_f [dichloromethane:light petroleum 1:1] 0.60. Found: C, 72.6; H, 9.5%; $C_{21}H_{32}O_2Si$ requires: C, 72.6; H, 9.4%; δ_H ($CDCl_3$, 220 MHz) 7.35-7.15 (5H, m), 7.10 (1H, t, *J* = 4 Hz), 4.83 (1H, t, *J* = 2 Hz), 2.8-2.55 (2H, m), 2.41 (2H, t, *J* = 7 Hz), 2.36 (2H, t, *J* = 7 Hz), 2.10-1.69 (4H, m), 0.95 (9H, s), -0.10 (3H, s) and -0.19 (3H,s).

***Syn*- and *anti*-2-(3-phenyl-1-(*tert*-butyldimethylsiloxy)propyl)-2,3-oxiranocyclohexan-1-one (5f) and (6f).** Sodium hydroxide (0.174 g, 4.35 mmol) in water (5 ml) was added to a solution of **4f** (1.0 g, 2.90 mmol) and hydrogen peroxide (0.26 ml, 3.0 mmol, 35% solution in water) in methanol (20 ml) at 0 °C. The mixture was stirred at 0 °C for 30 min then diluted with water (100 ml) and extracted with diethyl ether (3x50 ml). The combined organic extracts were washed with water (3x30 ml), brine (20 ml), dried (Na_2SO_4) and filtered. Evaporation of the solvent and column chromatography on silica gel, using dichloromethane:light petroleum 1:2 as eluent, gave a mixture of **5f** and **6f** (0.91 g, 87%) as a colourless oil, in a ratio of 5:2 by ^1H NMR. These compounds could not be separated by column chromatography. However, MPLC using the same eluent, gave a pure sample of *syn*-2-(3-phenyl-1-(*tert*-butyldimethylsiloxy)propyl)-2,3-oxiranocyclohexan-1-one. Found: C, 70.2; H, 9.3%; $C_{21}H_{32}O_2Si$ requires C, 70.0; H, 9.0%; δ_H ($CDCl_3$, 220 MHz) 7.30-7.05 (5H, m), 4.5 (1H, t), 3.55 (1H, s), 2.85-2.6 (2H, m), 2.55-2.40 (1H, m), 2.30-2.15 (1H, m), 2.00-1.5 (6H, m), 0.9 (9H, s), -0.15 (3H, s) and -0.24 (3H, s).

Deprotection of silylated enones (5f) and (6f). Tetra-*n*-butylammonium fluoride (0.67 ml, 0.66 mmol, 1M in THF) was added to a mixture of **5f** and **6f** (0.12 g, 0.33 mmol, 5:2) in THF (10 ml), and the resulting solution was stirred at 30 °C. The progress of the reaction was monitored by tlc, and was complete after 5 days. The mixture was diluted with water (100 ml) and extracted with diethyl ether (3x30 ml). The combined organic layers were washed with water (2x50 ml), brine (50 ml), dried (Na_2SO_4), filtered and solvent removed to afford a yellow oil (0.08 g, 98%), which was a 5:2 mixture of **5b** and **6b** as determined by ^1H NMR.

2-(2-Phenyl-1-(*tert*-butyldimethylsiloxy)ethyl)cyclohex-2-en-1-one (4e). **4a** (0.3 g, 1.4 mmol) was stirred in *N*,*N*-dimethylformamide (10 ml) at 0 °C. Imidazole (0.28 g, 4.2 mmol) was added, followed by *tert*-butyldimethylchlorosilane (0.314 g, 2.1 mmol) and the mixture stirred for 18 h at 25 °C. The mixture was then diluted with diethyl ether (100 ml), washed with water (3x30 ml), dried (Na_2SO_4), filtered and solvent removed to afford a residue that was subjected to chromatography on silica gel, using chloroform as eluent. This gave **4e** (0.41 g, 88 %) as a colourless oil, R_f [chloroform] 0.52. Found: C, 72.9; H, 9.3%; $C_{20}H_{30}O_2Si$: requires C, 72.7; H, 9.15%; δ_H ($CDCl_3$, 250 MHz) 7.28-7.10 (5H, m), 6.92 (1H, dt, *J* = 4 and 1 Hz), 4.74 (1H, m), 2.91 (1H, dd, *J* = 14 and 3 Hz), 2.49 (1H, dd, *J* = 14 and 8 Hz), 2.44-2.38 (2H, m) 2.37-2.28 (2H, m), 1.95 (2H, quintet, *J* = 6.5 Hz) 0.79 (9H, s), -0.26 (3H, s) and -0.35 (3H, s); δ_C ($CDCl_3$, 63 MHz) 198.3 (s), 145.5 (d), 142.1 (s), 139.0 (s), 130.2 (d), 127.7 (d), 126.0 (d), 69.6 (d), 44.6 (t), 38.6 (t), 25.8 (q), 22.9 (t), 18.1 (s) -5.2 (q) and -5.6 (q).

2-(2-Phenyl-1-acetoxyethyl)cyclohex-2-en-1-one (4c). A solution of **4a** (1.0 g, 4.62 mmol), acetyl chloride (6.6 ml, 99 mmol) and *N,N*-dimethylaniline (11.7 ml, 92 mmol) were refluxed in chloroform (100 ml) for 16 h, giving a purple solution. The solution was allowed to cool, and then diluted with chloroform (100 ml). The mixture was then washed with dilute hydrochloric acid (50 ml, 1M), aqueous sodium hydroxide (50 ml, 1M), dried (Na_2SO_4), filtered and solvent removed to afford a light brown oil that was subjected to column chromatography on silica gel using dichloromethane as eluent to give **4c** (0.75 g, 63%) as pale green oil, R_f [dichloromethane] 0.12. δ_H ($CDCl_3$, 250 MHz) 7.35-7.15 (5H, m), 6.75 (1H, t, J = 4 Hz), 5.9 (1H, m), 3.1 (1H, dd, J = 5 and 12 Hz), 2.85 (1H, dd, J = 7 and 12 Hz), 2.45 (2H, t, J = 7 Hz), 2.38-2.25 (2H, m), 2.00 (3H, s) and 2.12-1.85 (2H, m); δ_C ($CDCl_3$, 100 MHz) 197.3 (s), 169.5 (s), 145.6 (d), 137.7 (s), 137.3 (s), 129.5 (d), 128.0 (d), 126.3 (d), 71.4 (d), 40.3 (t), 38.3 (t), 25.6 (t), 22.4 (t) and 21.0 (q).

(4aβ,10β,10aβ)-3,4,4a,9,10,10a-Hexahydro-10,10a-dihydroxy-1(2*H*)-phenanthrenone (7). Tin (IV) chloride (1.86 ml, 16 mmol) was added to a solution of **5a** (0.74 g, 3 mmol) in dichloromethane (50 ml) at 0 °C. The mixture was stirred for 24 h at 20 °C and then poured onto ice and extracted with dichloromethane (3x40 ml). The combined organic extracts were washed with dilute hydrochloric acid (30 ml, 1M), water (2x30 ml), brine (20 ml), dried (Na_2SO_4), filtered and solvent removed to afford a pale green solid. Purification by column chromatography using chloroform as eluent gave **7** (0.54 g, 73%) as needles, R_f [chloroform] 0.16, recrystallised from diisopropyl ether, m.p. 160-162 °C. Found: C, 72.1; H, 7.0%; $C_{14}H_{16}O_3$ requires: C, 72.4, H, 6.9%; IR (KBr disc) 3410 (br), 2940, 1725 and 1495 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 7.20-7.05 (4H, m), 4.56 (1H, m), 4.38 (1H, s), 3.20 (1H, dd, H-9β, J = 16 and 6.5 Hz), 3.04 (1H, dd, H-10α, J = 12.5 and 5 Hz), 2.99 (1H, dd, H-9α, J = 16 and 11 Hz), 2.84-2.60 (2H, m), 2.27-2.01 (2H, m) and 1.93-1.75 (2H, m); δ_C ($CDCl_3$, 63 MHz) 211.9 (s), 136.9 (s), 132.9 (s), 129.1 (d), 128.7 (d), 126.6 (d), 80.7 (s), 67.8 (d), 53.0 (d), 37.5 (t), 35.3 (t), 34.7 (t) and 26.4 (t); MS m/e (%) 250 (62), 233 (100), 214 (90), 157 (41) and 115 (32).

(4aβ,5β,11bβ)-5*H*-4-Oxo-1,2,3,4,4a,6,7,11bβ-Octahydro-4a,5-dihydroxydibenzo[a,c]cycloheptene (8) and *rel* -(2*R*,3*R*)-2-Hydroxy-3-chloro-2-(3-phenyl-1(*S*)-hydroxypropyl)cyclohexan-1-one (9). Tin (IV) chloride (0.71 ml, 6.1 mmol) was added to a solution of 5b (0.33 g, 1.2 mmol) in dichloromethane (20 ml) at 0 °C. The mixture was stirred for 24 h at 20 °C and then poured onto ice and extracted with dichloromethane (2x30 ml). The combined organic extracts were washed with dilute hydrochloric acid (30 ml, 1M), water (2x30 ml), brine (20 ml), dried (Na_2SO_4) and filtered. The solvent was removed under reduced pressure and the residue subjected to column chromatography on silica gel, using dichloromethane initially, and then dichloromethane:ethyl acetate (10:1) as eluent. Keto-diol **8** was obtained (0.1 g, 33%), as needles, m.p. 183-184 °C. Found: C, 73.1; H, 7.4%; $C_{15}H_{18}O_3$ requires: C, 73.2; H, 7.4%; δ_H ($CDCl_3$, 250 MHz) 7.3-7.0 (4H, m), 4.51 (1H, dd, J = 11 and 3.5 Hz), 4.10 (1H, s), 3.05 (1H, ddd, J = 13.5, 12.5 and 1.5 Hz), 2.04 (1H, dd, J = 13.5 and 6.5 Hz), 2.88-2.75 (2H, m), 2.66 (1H, ddt, J = 13.5, 4.5 and 1.5 Hz), 2.52 (4H, m) and 1.95-1.70 (3H, m); δ_C ($CDCl_3$, 63 MHz) 211.6 (s), 139.9 (s), 138.9 (s), 131.7 (d), 130.3 (d), 127.5 (d), 127.0 (d), 82.3 (s), 74.0 (d), 58.3 (d), 36.9 (t), 32.1 (t), 31.8 (t), 28.1 (t) and 26.7 (t); and chloro-diol **9** (0.16 g, 46%), as needles m.p. 103-105 °C, R_f [dichloromethane:ethyl acetate (10:1)]

0.28. Found: C, 63.5; H, 6.7; Cl, 12.6%; $C_{15}H_{19}O_3Cl$ requires C, 63.7, H, 6.8, Cl, 12.5%; δ_H ($CDCl_3$, 250 MHz) 7.33-7.14 (5H, m), 4.36 (1H, dt, *J* = 6, 3.5 and 1 Hz), 3.93 (1H, s), 3.00-2.79 (2H, m), 2.74-2.58 (2H, m), 2.54-2.38 (2H, m), 2.24-2.02 (2H, m), 1.95-1.75 (2H, m) and 1.72-1.54 (1H, m); δ_C ($CDCl_3$, 63 MHz) 211.2 (s), 141.7 (s), 128.45 (d), 128.4 (d), 125.9 (d), 79.6 (s), 70.7 (d), 64.3 (d), 37.6 (t), 31.9 (t), 30.1 (t), 30.0 (t) and 21.5 (t).

Kinetic resolution of (4a) by enantiomeric epoxidation. To a solution of **4a** (300 mg, 1.39 mmol) and (+)-diisopropyl tartrate (49 mg, 0.21 mmol) in dichloromethane (15 ml) at 20 °C under nitrogen was added activated 3Å molecular sieves (90 mg). The stirred mixture, maintained under an inert atmosphere, was cooled to -20 °C, treated with titanium(IV) isopropoxide (39 mg, 0.14 mmol) and allowed to stir for 30 min at -20 °C. The reaction was then treated with a solution of anhydrous *tert*-butyl hydroperoxide[23] (0.28 ml, 0.96 mmol, 3.4M in toluene) added *via* a syringe. The reaction was stirred at -20 °C for 9 h. A freshly prepared solution of ferrous sulphate heptahydrate (16.5 g, 59.3 mmol) and citric acid monohydrate (5.5 g, 26.2 mmol) in a total volume of 50 ml of water was cooled to 0 °C. The epoxidation mixture was allowed to warm to 0 °C and then slowly poured into a beaker containing the pre-cooled stirring ferrous sulphate solution without external cooling. The two-phase mixture was stirred for 10 min and then transferred to separating funnel. The phases were separated and the aqueous phase extracted with diethyl ether (2x30 ml). The combined organic layers were treated with a pre-cooled (0 °C) solution of sodium hydroxide (30% w/v) in brine (10 ml). The two-phase mixture was stirred vigorously for 1 h at 0 °C. Following transfer to a separating funnel and dilution with water (50 ml), the phases were separated and the aqueous layer extracted with diethyl ether (2x40 ml). The combined organic layers were dried (Na_2SO_4), filtered and solvent removed to afford a residue that was subjected column chromatography using chloroform as eluent. This gave **5a** (126 mg, 39%) as a colourless oil, R_f [chloroform] 0.20. δ_H (C_6D_6, 400 MHz) 7.35-7.10 (5H, m), 4.45 (1H, dd, *J* = 7 and 3.5 Hz), 2.88 (1H, dd, *J* = 3.5 and 14.5 Hz), 2.76 (1H, dd, *J* = 7 and 14.5 Hz), 2.07 (1H, dt, *J* = 16.5 and 3.5 Hz),1.62 (1H, br s, OH), 1.49-1.21 (4H,m) and 0.82 (2H, m); and **4a** (117 mg, 35%) as needles, R_f [chloroform] 0.11, m.p. 58-61.5 °C. δ_H (C_6D_6, 400 MHz) 7.35-7.10 (5H, m), 6.23 (1H, t, *J* = 4 Hz), 4.54 (1H, m), 2.96 (1H, dd, *J* = 5 and 12 Hz), 2.72 (1H, dd, *J* = 7 and 12 Hz), 2.36 (1H, br s), 1.95 (2H, m), 1.47 (2H, m) and 1.19 (2H, quintet, *J* = 7 Hz).

Kinetic resolution of (4b) by enantiomeric epoxidation. To a solution of **4b** (480 mg, 2.08 mmol) and (+)-diisopropyl tartrate (73 mg, 0.31mmol) in dichloromethane (20 ml) at 20 °C under nitrogen was added activated 3Å molecular sieves (140 mg). The stirred mixture, maintained under an inert atmosphere, was cooled to -20 °C, treated with titanium(IV) isopropoxide (59 mg, 0.21 mmol) and allowed to stir for 30 min at -20 °C. The reaction was then treated with a solution of anhydrous *tert*-butyl hydroperoxide[23] (0.43 ml, 1.47 mmol, 3.4M in toluene) added *via* a syringe. The reaction was stirred at -20 °C for 9 h. A freshly prepared solution of ferrous sulphate heptahydrate (24.75 g, 89.0 mmol) and citric acid monohydrate (8.26 g, 39.3 mmol) in a total volume of 50 ml of water was cooled to 0 °C. The epoxidation mixture was allowed to warm to 0 °C and then worked up as described for the kinetic resolution of **4a**. Column chromatography using light petroleum:diethyl ether (1:1) as eluent gave **5b** (110 mg, 21%) as

needles, R_f [light petroleum:diethyl ether (1:1)] 0.44, recrystallised from light petroleum m.p. 44-47 °C. δ_H (C_6D_6, 250 MHz) 7.35-7.12 (5H, m), 4.28 (1H, dt, J = 9 and 3.5 Hz), 3.22 (1H, m), 3.04 (1H, m), 2.83 (1H, m), 2.26 (1H, m) and 2.06-0.93 (8H, m); and **4b** (151 mg, 31%) as a pale yellow oil, R_f [light petroleum:diethyl ether (1:1)] 0.24. δ_H ($CDCl_3$, 220 MHz) 7.30-7.13 (5H, m), 6.85 (1H, dt, J = 1 and 4 Hz), 4.35 (1H, t, J = 7 Hz), 3.21 (1H, br s), 2.69 (2H, m), 2.31 (4H, m) and 1.89 (4H, m).

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