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Lewis Acid Mediated Reactions of 2,3-Epoxyalcohols: an Efficient Stereocontrolled Route to Polycyclic Diols

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Abstract: *2,3-epoxyalcohols are shown to undergo stereoselective reactions in the presence of tin tetrachloride. The resulting diols when treated with acid are converted into polycyclic aromatic hydrocarbons or polycyclic ketones*

Background

The strategic placement of hydroxy groups on a carbon skeleton is known to enhance biological activity,[1,2] in certain cases by increasing the rate of addition of cysteine.[3] Natural products that incorporate a *cis*-1,2-diol moiety and exhibit pronounced pharmacological activity include the anti-leukaemic agent gnidimacrin[4], the highly poisonous terpenoid daphnetoxin[5] and the irritant ingenol[6,7] (*Figure 1*). Related compounds that possess 1,2-dioxygenated functionality and a hydroxy group at a ring junction include resiniferatoxin, which shows potent antinoceptive activity.[8]

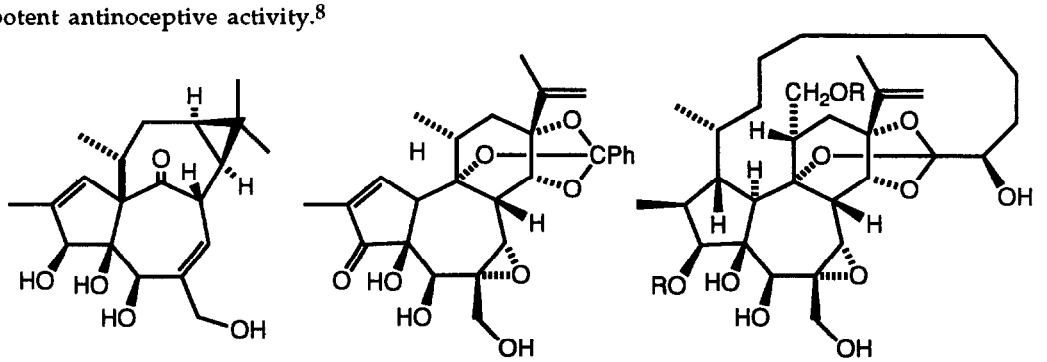
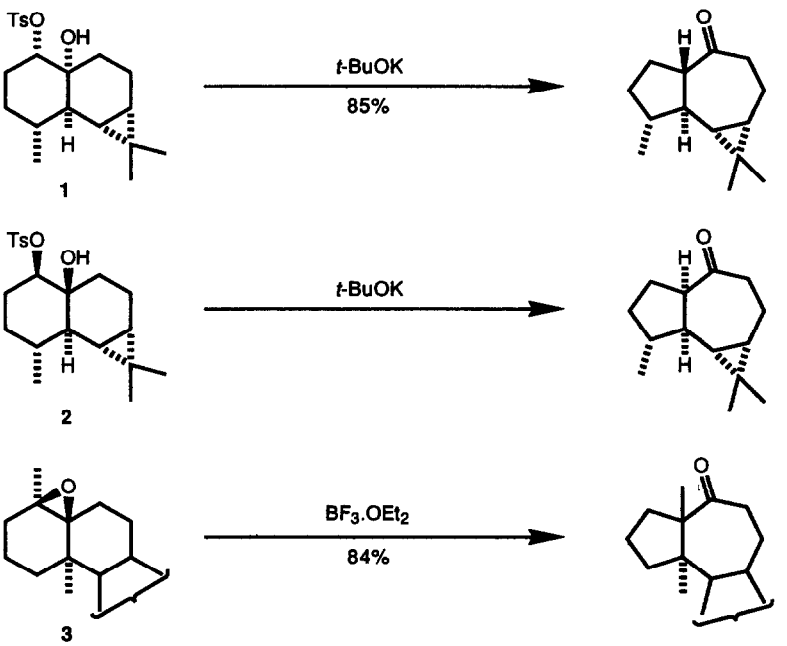


Figure 1: Some Biologically Active *Cis*-1,2-Diols

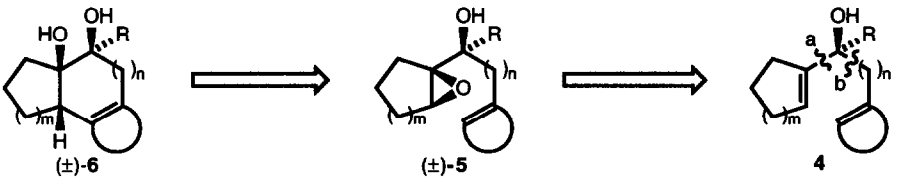
As part of an ongoing programme, we have developed new methods for the construction of polyhydroxylated polycyclic systems.[9,10] We herein report a procedure for obtaining 1,2-dihydroxylated polycyclic systems[11] generally containing one or more aromatic rings; such compounds, especially the related benzo-fused diol epoxides, are crucial in studies of carcinogenesis. Additionally, where one of the hydroxy groups is situated at a ring junction, rearrangements of the ring skeleton can be induced.[12] For example, monotosylates of *cis*-1,2-diols derived from the bicyclo[4.4.0]decane ring system are converted by *t*-butoxide into bicyclo[5.3.0]decanes, *e.g.* tosylates **1** and **2** (*Scheme 1*). A related skeletal rearrangement[12d] of the epoxide **3** has been induced by a Lewis acid.



Scheme 1: Skeletal Rearrangements of *Cis*-1,2-Dioxygenated Polycyclic Compounds

1,2-Diols, including those which undergo pinacol rearrangement on treatment with protic or Lewis acids, are frequently prepared by 1,2-dihydroxylation of an existing carbon framework. We sought a more general route to bicyclic and tricyclic diols that would be convergent and also employ readily available starting materials (*Scheme 2*). The approach adopted depends upon the epoxidation of allylic alcohols **4** followed by cyclisation of the resulting epoxides **5** to give the 1,2-diols **6**. Although this strategy was modelled upon a similar sequence involving 2-(1-hydroxyalkenyl)-2-cycloalken-1-ones,[9,10] the absence of a carbonyl group in the present study meant that the behaviour of the 1,2-diols **6** in the presence of protic or Lewis acids would be expected to be different (since in the former sequence a pinacol rearrangement involving an α-ketocarbocation could be excluded). Although completely diastereoselective epoxidation to give **5** could not be expected, this paper reports that the sequence shown (*Scheme 2*) is in practice a

general and efficient route to diols **6** which are generally obtained as pure diastereoisomers. We have also studied the action of protic and Lewis acids upon some of the diols **6** and report examples of dehydration to aromatic hydrocarbons as well as pinacol rearrangements to ketones. In addition, examination of the limitations of ring assembly (*Scheme 2*) revealed an unprecedented cyclisation induced by an epoxide: the first known cyclisation to afford a spirocycle (**6l**, *Table*)



Scheme 2: A General Route to Polycyclic Diols

Results and Discussion

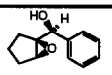
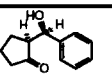
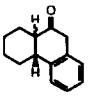
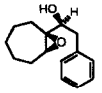
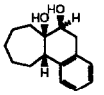
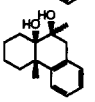
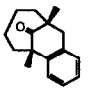
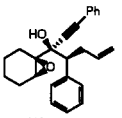
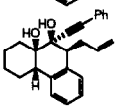
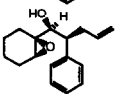
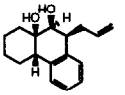
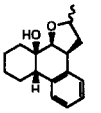
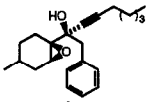
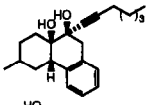
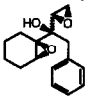
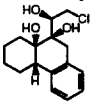
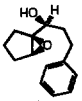
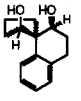
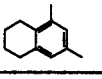
The preparation of many of the alcohols **4** by reaction of organometallic species with carbonyl compounds, in which either bond 'a' or bond 'b' is formed (*Scheme 2*), has been described in the preceding paper.[11] Therein also were presented preparations of epoxy alcohols **5**, and a rationalisation for the predominance of *syn*-epoxides in terms of torsional strain and non-bonding interactions.[10]

Formation of Cyclic Diols

Cyclisations of 2,3-epoxyalcohols **5** are given in the *Table*. Various Lewis acids were investigated, including $BF_3.OEt_2$, $TiCl_4$ and $SnBr_4$; however, $SnCl_4$ proved to be the superior catalyst, in all cases tested. Importantly, the ring opening of the epoxide by chloride was not found to be significant in any of the examples investigated except entry 11, and even in this case the nucleophilic attack was a complementary reaction that did not interfere with the formation of the fused tricyclic system.

The convenience of the procedure is illustrated by entries 2-4. Although in each case a mixture of diastereomeric epoxides was treated with the Lewis acid, the tricyclic diols isolated were all stereochemically pure. No products derived from the *anti*-epoxides were observed; some related *anti*-2-(1-hydroxyalkyl)-2-cycloalken-1-ones have been shown to fragment in the presence of tin tetrachloride.[10,13] The accomplishment of such cyclisations without significant dehydration to the aromatic hydrocarbon is notable. The aromatic π-nucleophile attacked the epoxide solely with inversion of configuration (*Figure 2*), as expected.[14] Cyclisation to give a central six-membered ring succeeds with five-, six- and seven-membered cycloalkene oxides (entries 2-4); the epoxide carbon atom undergoing attack may be quaternary (entry 7). A tertiary alcohol can cyclise to the corresponding diol (entries 7, 8 and 10), although the propensity for dehydration is enhanced (entry 5, for which no diol was isolated).

Table: Synthesis and Reactions of Cyclic Diols

Entry	Epoxide[15]		Reaction Cond[ns]	Diol[16]		Yield[17] (%)	Aromatised product[16]		Yield[17] (%)	Rearranged product[16]		Yield[17] (%)
1		5a	0°C, 12 0h								8a	34
2		5b	0°C, 2 0h		6b	67						
3		5c	0°C, 2 0h		6c	94		7c	71[18]		8c	63[18]
4		5d	0°C, 1 5h		6d	61						
5		5e	0°C, 2 0h					7e	52			
6		5f	-80°C 0 5h		6f	73						
7		5g	-80°C, 0 2h		6g	42					8g	23
8		5h	-80°C, 0 8h		6h	96						
9		5i	-80°C, 3.0h		6i	89					8i	41[18]
10.		5j	-80°C, 1 1h		6j	68						
11		5k	0°C, 1 0h		6k	88						
12		5l	0°C, 2.0h		6l	50						
13		5m	0°C, 2 0h		6m	21						
14		5n	0°C, 2 0h					7n	29		8n	20

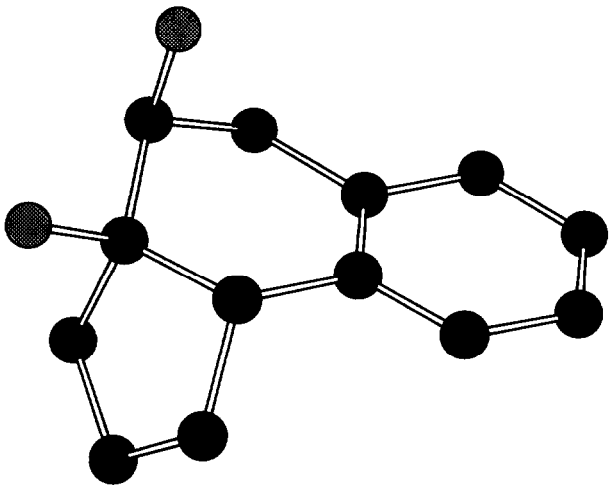


Figure 2: Structure of **6b** Determined by X-Ray Crystallography

The cyclisation conditions have been shown to tolerate functional groups (entries 8, 9 and 10), although the diepoxide **5k** was attacked by chloride at the less substituted epoxide moiety. In this competitive cyclisation, the more substituted, but more hindered epoxide participates in ring-closure. Since either epoxide can co-ordinate to a tin species bound to the tertiary alcohol oxygen atom, the observed chemoselectivity provides tentative evidence for the development of a carbocation, the secondary cation being the more stable. The relative configuration of the less substituted epoxide is predicted by a previous model[10] on the assumption that the vinyl group adopts an orientation away from the cyclohexane ring (being bulkier than the benzyl substituent), and is established by X-ray crystallography (*Figure 3*).

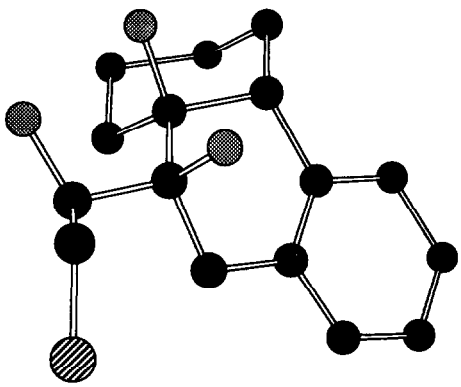


Figure 3: Structure of **6k** Determined by X-Ray Crystallography

The *Table* illustrates the scope and some limitations of the cyclisation of epoxides **5** to diols **6**. With a view to developing a succinct synthesis of bicyclic diols (from 1-cycloalkene-1-carboxaldehydes) epoxide **5m** was treated with $SnCl_4$ (2.0 mmol, -5° C, 16 h). The chlorodiol **6m** was isolated as an approximately equimolar mixture of four diastereoisomers, indicating chloride attack on the intermediate carbocation following cyclisation rather than chloride opening of any oxygen-bridged intermediate (where inversion of configuration would give only two diastereoisomers). Although an alkenic terminus is well known to participate as a π-nucleophile in epoxide cyclisations,[19,20] the failure of **6m** to aromatise provides a potentially useful extension of 2,3-epoxyalcohol cyclisations, to give bicyclic systems. However, entries 5 and 14 show that a tertiary alcohol may undergo aromatisation and/or pinacol rearrangement, that preclude the preparation of the 1,2-diol.

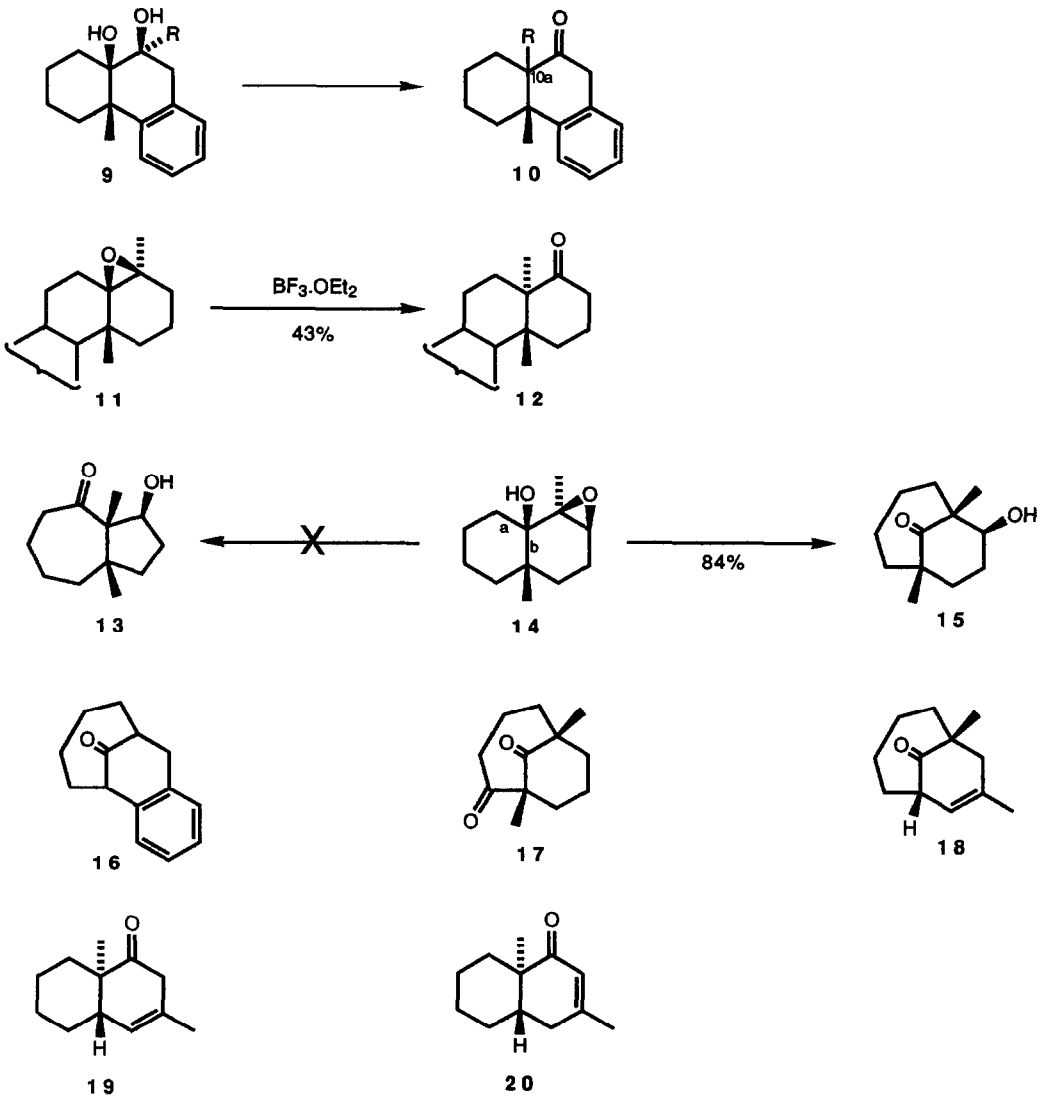
As expected, the formation of five- and seven membered rings is evidently much less favourable than the formation of six-membered rings. Thus, **5a** underwent conversion into the β-ketoalcohol **8a** (rather than forming a 5-5-6 fused tricyclic system). A 1,2-hydride shift was not firmly established in this case (although such 1,2-hydride shifts are known[14,21]), nor were mechanisms involving Payne rearrangements[22] excluded. However, the 88:12 mixture of *syn:anti*-epoxides **5a** afforded a separable mixture **8a** (34%) and the corresponding diastereoisomer (6%); these ratios support a stereospecific migration of hydride.

The ubiquity of 5-7-6 fused systems in biologically active diterpenoid compounds[6] prompted the reaction of **5l** with Lewis acids. However, on treatment with $SnCl_4$ (2.0 eq, CH_2Cl_2, 0 °C, 2 h) epoxyalcohol **5l** underwent an unprecedented cyclisation in an alternative mode whereby the quaternary centre of the epoxide (*alpha* to the hydroxy group) was attacked with inversion of configuration to give the spirocyclic 1,3-diol **6l** as the only isolated product. Co-ordination of tin to both oxygen atoms in a chair-like complex may be crucial to the formation of the diol **6l**, notable for the stereocontrolled placement of hydroxy groups in each of the spiro-fused rings. The formation of diol **6l** is unusual in that: i) the regioselectivity is contrary to the usual mode of attack[23] at C-3 of a 2,3-epoxyalcohol; ii) products derived from attack at C-2 are generally accompanied[24] by products derived from attack at C-3; iii) The uncommon instances[25] where a C-nucleophile attacks exclusively at C-2 have not hitherto resulted in a cyclisation; iv) A spirocyclic system is created.

Reaction of 1,2-Diols with Protic and Lewis Acids

The hydrocarbons **7e** and **7n** were the major products detected when the epoxides **5e** and **5n** were treated with $SnCl_4$ (2.0 eq) and it is presumed that the 1,2-dioxygenated intermediates undergo ready elimination to give the hydrocarbons. This was established for **6c**, which when treated with PPA (20 °C, 30 min) afforded tetrahydrophenanthrene **7c** in good yield. However, 1,2-migrations compete with aromatisation in this reaction, as in entries 7 and 14. Reaction of **6c** with P_2O_5 in benzene (20 °C, 4 h) afforded only a minor quantity of hydrocarbon **7c**, together with ketone **8c**, obtained as a 1:1 mixture of epimers. The infra-red spectrum of **8c** had υ_{max} at 1720 cm^{-1}, consistent with a six-membered ring ketone. Although seven-membered ring

ketones such as that derived from **3** (*Scheme 1*, υ_{max} 1694 cm^{-1}) can be formed by pinacol and related rearrangements, an initial *trans*-ring junction stereochemistry is usually required.[12d,26]



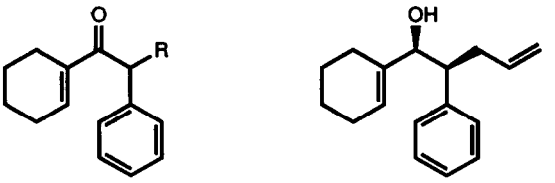
Scheme 3: Pinacol and Related Rearrangements of *Cis*-1,2-Dioxygenated Polycyclic Systems

Transformations related to conversion of **9** into **10** are known for R=CH_3, *e.g.* the formation of ketone **12** from epoxide **11**, a 1,2-migration of methyl with inversion at the quaternary centre. The formation of epimers of **8c** implies that even if a 1,2-migration of hydride operates, protonation of an enol intermediate (formed by deprotonation of the carbocation generated at C-10a) is the predominant (or exclusive) pathway. In the case of diol **6c**,

rearrangement to the bridged ketone **16** can be excluded. The related ketones **15** and **17** have carbonyl stretching vibrations at 1745 cm^{-1} and 1700 cm^{-1}, the former being the bridging carbonyl vibration.[27] Additionally, the two diastereoisomers of **8c** (υ_{max} 1720 cm^{-1}) could not be explained in terms of a structure **16** which would be precluded from being formed as a diastereomeric mixture both on grounds of mechanism and ring strain.

In contrast to **6c**, the methyl substituted analogue **6g** undergoes pinacol rearrangement to the bridged ketone **8g** (υ_{max} 1730 cm^{-1}). This is consistent with the reported rearrangement of **14** into **15** catalysed by $BF_3.OEt_2$;[27] in both cases, the relevant relative stereochemistries are identical. The driving force for such rearrangements is presumably a combination of the ready development of an incipient cationic charge at the methyl-bearing carbon atom, and the adoption of a conformation in which bond 'a' (as in **14**) is aligned *trans*-coplanar to the departing C-O bond of the epoxide (or alcohol). By similar reasoning structure **8n** has been assigned to the ketone obtained from **5n** by rearrangement. The isomer **18** is considered less likely because no coupling is observed between the bridgehead and olefinic protons in the ^1H N.M.R. spectrum. The carbonyl stretching frequency at 1725 cm^{-1} is consistent with that of **8g** (1730 cm^{-1}) and of **15** and **17**, but inconsistent with that expected for the conjugated carbonyl group in **20**. Although cyclisation of **5n** followed by methyl migration could lead to either **19** or **20**, these structures can be excluded by I.R. and ^1H N.M.R. data; in particular, the methylene signal for **19** would be substantially more deshielded than the AB quartet at δ 2.15, and the chemical shift of the olefinic proton in **20** would be considerably higher than that which is observed (δ 5.32) for **8n**.

Entry 9 illustrates that the method can provide tricyclic diols incorporating four contiguous stereogenic centres. Allylation[11] of 1-(1-oxo-2-phenylethyl)cyclohexene **21** afforded the ketone **22** (*Figure 4*), which was reduced by $LiAlH_4$[11] in ether to give an oil from which **23** crystallised (93%). The formation of **23** as the predominant diastereoisomer is predicted by Cram's rule.[28] Epoxidation[11] of the single diasteroisomer **23** afforded predominantly the epoxide **5i** (66%, 9:1 diastereomeric ratio). This mixture was treated with $SnCl_4$ (2.0 eq, -80 °C) to give **6i** (89%) as the only product isolated. Reaction of **6i** with P_2O_5 afforded no products of skeletal rearrangement or dehydration; instead, a fused tetrahydrofuran **8i** was obtained. Although **8i** is a 1:1 mixture of epimers at the carbon bearing the methyl group, the relative configuration of the four contiguous stereogenic centres follows from Cram's rule and the stereoselectivity of epoxidation outlined here and in the preceding paper.[11] The participation of the tertiary hydroxy group in **6i**, to form a tetrahydropyran ring is excluded by ^1H N.M.R.



21 R=H
22 R=$CH_2CH=CH_2$

23

Figure 4

Conclusion

Cyclic 2,3-epoxyalcohols, conveniently prepared by oxidation of allylic alcohols, undergo cyclisation catalysed by $SnCl_4$ to give diols, as part of a bicyclic, tricyclic or even spirocyclic systems. The procedure is convenient and gives single diastereoisomers in almost every case. Substituted hydrocarbons and ketones can be obtained from the diols, or in certain cases directly from the epoxyalcohols. Where cyclisation of the epoxyalcohols to give a six-membered ring is not possible, synthetically valuable stereoselective 1,2-migrations are the norm, as described elsewhere.[29,30]

Experimental

All melting points were determined with a Kofler hot-stage apparatus and are uncorrected. Chemical shifts for NMR spectra 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. ^{13}C and ^{1}H NMR spectra were determined on a Bruker AM-250 NMR spectrometer operating at 68.8 and 250 MHz respectively. Mass spectra were obtained on a Kratos MS-25 instrument, operating in chemical ionisation (CI) or electron impact (EI) mode, as specified in the text. Microanalytical data were obtained on a Perkin-Elmer 2400 CHN elemental analyser. Infra-red spectra were obtained on Perkin-Elmer 684 or 157G instruments, state as specified. Yields are for material assessed as homogeneous by TLC and ^{1}H NMR. Thin-layer chromatography was performed on Merck 0.2 mm aluminum-backed silica plates and visualised using ultra-violet light or developed using cerium (IV) sulphate spray. Column chromatography was performed using Merck silica gel 60 (230-400 mesh) under gravity. Petroleum ether (40-60 fraction) and ethyl acetate were distilled prior to use. Evaporation refers to the removal of solvent under reduced pressure, unless otherwise stated. The 2,3-epoxyalcohols **5** were prepared as described in the preceding paper.

Reaction of 2,3-Epoxyalcohols with Lewis Acids: Typical Procedure:

(3a-α, 4-α, 9b-α)-(±)-2, 3, 3a, 4, 5, 9b-Hexahydro-3a, 4-dihydroxy-1*H*-cyclopenta[*a*] naphthalene (6b)

A solution of 1-(1,2-epoxycyclopentyl)-2-phenylethan-1-ol (0.15g, 0.74mmol) in dry dichloromethane (8ml) was treated dropwise at 0°C with tin (IV) chloride (0.17ml, 0.38g, 1.47mol). The mixture was stirred at 0°C for 2h (monitored by TLC) then poured onto ice (15g) and extracted with dichloromethane (3 x 10ml). The combined organic extracts were washed with dilute hydrochloric acid (30ml), water (2 x 80ml) and brine (30ml) then dried ($MgSO_4$), and concentrated *in vacuo* to give **6c** as a white solid (0.10g, 67%); mp 110-112°C (propan-2-ol);

found C, 76.27%, H, 7.92% ($C_{13}H_{16}O_2$ requires C, 76.44%, H, 7.90%); υ_{max} (KBr disc) 3400, 2960 and 1500 cm^{-1}; δ_H ($CDCl_3$) 7.20-7.05 (4H, m), 3.88 (1H, dd, *J*=7 and 5Hz), 3.17 (1H, t, *J*= 8Hz), 3.02 (1H, dd, *J*=7 and 15Hz), 2.93 (1H, dd, *J*=5 and 15Hz), 2.47-2.33 (1H, m), 2.31 (2H, bs), 2.00-1.80 (3H, m), 1.80-1.47 (2H, m); δ_C ($CDCl_3$) 138.9 (s), 132.6 (s), 128.8 (d), 128.3 (d), 126.5 (d), 125.8 (d), 81.4 (s), 71.0 (d), 50.5 (d), 37.7 (t), 34.7 (t), 34.5 (t), 22.9 (t); M/Z(%)+CI: 222 (20), 204 (23), 185 (72), 168 (100), 157 (25).

***Erythro*and *threo*2-(Hydroxyphenylmethyl)cyclopentan-1-one (8a)**

Following the typical procedure (above), (1,2-epoxycyclopentyl)phenylmethanol (0.725g, 3.81mmol) afforded a residue which was purified by column chromatography on silica using 15% ethyl acetate: petroleum ether as eluent to give **8a** as two separate diastereoisomers, a white solid (DIASTEREOMER 'A', 0.245g, 34%); mp 122-123°C; found C, 75.54; H, 7.41% ($C_{12}H_{14}O_2$ requires C, 75.76; H, 7.42%); R_F=0.30 (20% ethyl acetate: petroleum ether); δ_H ($CDCl_3$) 7.40 (5H,m), 4.30 (1H, d, *J*=12Hz), 3.47 (1H, bs), 2.79-2.39 (3H, m) and 2.20-1.60 (4H, m); δ_C ($CDCl_3$) 210.1 (s), 141.7 (s), 128.5 (d), 127.2 (d), 126.9 (d), 78.8 (d), 53.9 (d), 39.2 (t), 32.1 (t) and 26.0 (t); M/Z(%)+EI: 190 (M, 52), 188 (28), 161 (87), 118 (70), 117 (100), 105 (30) and 91 (74); and a colourless oil (DIASTEREOMER 'B', 0.040g, 6%); R_F=0.22 (20% ethyl acetate: petroleum ether); δ_H ($CDCl_3$) 7.33 (3H, m), 7.16 (2H, m), 4.28 (1H, dd, *J*=15Hz, *J*=6Hz), 3.39 (1H, bs), 2.53 (1H, m), 2.26 (1H, m) and 2.04-1.51 (5H, m); δ_C ($CDCl_3$) 209.9 (s), 137.1 (s), 128.6 (d), 128.4 (d), 127.3 (d), 75.6 (d), 55.4 (d), 37.3 (t), 36.0 (t) and 22.9 (t).

(4a-α, 10-α, 10a-α)-(±)-1, 2, 3, 4, 4a, 9, 10, 10a-Octahydro-10, 10a-dihydroxyphenanthrene (6c)

Following the typical procedure (above), 1-(1,2-epoxycyclohexyl)-2-phenylethan-1-ol (1.00g, 4.72mmol) yielded a residue which was purified by recrystallisation (di-*iso*-propyl ether) to give **6c** as a white solid (0.94 g, 94%); mp 180-182°C; found C, 76.96%, H, 8.30% ($C_{14}H_{18}O_2$ requires C, 77.03%, H, 8.31%); υ_{max} (KBr disc) 3380, 3310, 2920, 1490 and1450 cm^{-1}; δ_H ($CDCl_3$) 7.22-7.01 (4H, m), 4.22 (1H, dd, *J*=6 and 9Hz), 3.20 (1H, dd, *J*=6 and 17Hz), 2.92 (1H, dd, *J*=9 and 17Hz), 2.82 (1H, m), 2.34 (1H, m), 2.05-1.20 (9H, m); δ_C ($CDCl_3$) 138.5 (s), 133.2 (s), 128.8 (d), 128.7 (d), 126.4 (d), 126.1 (d), 72.9 (s), 66.8 (d), 48.0 (d), 35.2 (t), 33.9 (t), 25.4 (t), 22.8 (t); M/Z(%)+CI: 236 (45), 218 (15), 200 (100), 185 (15), 171 (10), 157 (17), 141 (8).

(5a-α, 6-α, 11b-α)-(±)-2, 3, 4, 4a, 9, 10, 10a-Octahydro-5a, 6-dihydroxy-1*H*-cyclohepta[*a*] naphthalene (6d)

Following the typical procedure (above), 1-(1,2-epoxycyclopentyl)-2-phenylethan-1-ol (0.29g, 1.25mmol) yielded a residue which was purified by recrystallisation (ethyl acetate / di-*iso*-propyl ether) to give **6d** as a white solid (0.40g, 61%); mp 174-175°C; found C, 77.29%, H, 8.54% ($C_{15}H_{20}O_2$ requires C, 77.55%, H, 8.68%); υ_{max} (KBr disc) 3420, 3320, 2920 and 1500 cm^{-1}; δ_H (C_5D_5N) 7.28-7.07 (4H, m), 6.22 (1H, bs), 5.44 (1H, bs), 4.25 (1H, m), 3.51 (1H, dd, *J*=10 and 16Hz), 3.37 (1H ,d, *J*=7Hz), 3.22 (1H, dd, *J*=5.5 and 16Hz), 2.61 (1H, m), 2.08-1.58 (8H, m), 1.36-1.12 (1H, m). The broad signal at δ 4.25 ppm, being coupled the the vicinal OH proton at δ 6.22, was assigned as the CHOH. In a decoupling experiment irradiation of the OH peak at δ 6.22 ppm induced resolution of the signal at δ 4.25 to give a clear doublet of doublets (*J*= 5.5 and 10Hz) confirming the above assignment; δ_C (C_5D_5N) 142.2 (s), 130.0 (d), 128.8 (d), 126.4 (d), 125.6 (d), 78.0 (s), 71.4 (d), 51.9 (d), 39.0 (t), 36.0 (t), 35.5 (t), 30.5 (t), 21.6 (t) [note:- one aromatic quaternary centre is masked by the solvent peaks]; M/Z(%)+CI: 250 (7), 232 (27), 214 (100), 197 (70), 185 (18), 171 (30), 130 (37).

1, 2, 3, 4-Tetrahydro-10-methylphenanthrene (7e)

Following the typical procedure (above), 2-(1,2-epoxycyclohexyl)-3-phenylpropan-2-ol (1.5g, 6.46mmol) afforded a residue which was purified by column chromatography on silica using petroleum ether as eluent to give **7e** as a white solid (0.65g, 52%); mp 45.5-46°C (di-*iso*-propyl ether); found C, 91.75; H, 8.25% ($C_{15}H_{16}$ requires C, 91.78; H, 8.22%); υ_{max} (KBr disk) 3050, 2940, 2860, 1600, 1550 and 1505 cm^{-1}; δ_H 7.92 (1H, dd, *J*=8Hz, *J*=1Hz), 7.69 (1H, dd, *J*=8Hz, *J*=1Hz), 7.47 (1H, s), 7.39 (2H, m), 3.11 (2H, t, *J*=7Hz), 2.73 (2H, t, *J*=7Hz), 2.37 (3H, s) and 1.90 (4H, m); δ_C 135.4 (s), 134.3 (s), 132.1 (s), 131.7 (s), 131.4 (s), 127.8 (d), 125.9 (d), 125.1 (d), 124.9 (d), 122.8 (d), 27.7 (t), 26.4 (t), 23.2 (t), 23.0 (t) and 20.4 (q); M/Z(%)+EI: 197 (M+1, 20), 196 (M, 100), 181 (50), 168 (45), 165 (32), 155 (25) and 153 (25).

(4a-α, 10-α, 10a-α)-(±)-1, 2, 3, 4, 4a, 9, 10, 10a-Octahydro-10, 10a-dihydroxy-4a-methylphenanthrene (6f)

Following the typical procedure (above), 1-(1,2-epoxy-2-methylcyclopentyl)-2-phenylethan-1-ol (0.10g, 0.43mmol) yielded a residue which was purified by recrystallisation (ethyl acetate / petroleum ether) to give **6f** as a white solid (0.073g, 73%); mp 127-128°C (*iso*-propanol); found C, 77.37%, H, 8.76% ($C_{15}H_{20}O_2$ requires C, 77.55%, H, 8.68%); υ_{max} (KBr disc) 3365, 2942, 2865, 1490 and 1450 cm^{-1}; δ_H ($CDCl_3$) 7.07-7.30 (4H, m), 4.28 (1H, dd, *J*=9Hz, *J*=7Hz), 3.12 (1H, dd, *J*=16.5Hz, 7Hz), 3.03 (1H, dd, *J*=16.5Hz, 9Hz), 2.15 (2H, m), 1.55-1.90 (8H, m), 1.52 (3H, s); δ_C ($CDCl_3$) 144.6 (s), 132.1 (s), 128.8 (d), 126.8 (d), 126.6 (d), 125.8 (d), 74.9 (s), 66.8 (d), 43.3 (t), 41.5 (s), 35.1 (t), 30.2 (t), 22.6 (t), 21.0 (t), 21.4 (q); M/Z (%)+EI 214 (M-18, 100), 199 (93), 171 (34), 143 (55), 129 (86), 91 (79), 77 (35), 43 (75).

(4a-α, 10-α, 10a-α)-(±)-1, 2, 3, 4, 4a, 9, 10, 10a-Octahydro-10, 10a-dihydroxy-4a, 10-dimethylphenanthrene (6g)

Following the typical procedure (above), 2-(1,2-epoxy-2-methylcyclohexyl)-1-phenylpropan-2-ol (0.33g, 1.34mmol) afforded a residue which was recrystallised (ethyl acetate: petroleum ether) to give **6g** as a white solid (0.14g, 42%); mp 107.5-110°C; found C, 77.80; H, 8.91% ($C_{16}H_{22}O_2$ requires C, 78.01; H, 9.00%); υ_{max} (KBr disc) 3450, 2980, 2940, 2860, 1600, 1575 and 1490 cm^{-1}; δ_H ($CDCl_3$)7.40-7.00 (4H, m), 3.10 (2H, s), 2.17-1.09 (10H, m), 1.37 (3H, s) and 1.34 (3H, s); δ_C ($CDCl_3$) 143.2 (s), 132.8 (s), 129.2 (d), 126.3 (d), 125.6 (d), 125.6 (d), 75.7 (s), 75.4 (s), 43.2 (s), 42.9 (t), 35.6 (t), 31.9 (t), 31.0 (q), 25.9 (q), 22.2 (t) and 22.0 (t); M/Z(%)+EI: 246 (M, 10), 228 (M-18, 75), 213 (23), 210 (7), 195 (16), 185 (52), 171 (34), 169 (17), 159 (100), 157 (52) and 155 (14).

(4a-α, 10-α, 10a-α)-(±)-1, 2, 3, 4, 4a, 9, 10, 10a-Octahydro-10, 10a-dihydroxy-10-(phenylethynyl)-9-(2-propenyl)phenanthrene (6h)

Following the typical procedure (above), 1-(1,2-epoxyclohexyl)-1-(1-phenylacetylenyl)-2-phenyl-4-penten-1-ol (1.0g, 2.79mmol) yielded a residue which was recrystallised from a mixture of light petroleum and ethyl acetate to give **6h** as a white solid (0.89g, 89%) as a single diastereoisomer; found C, 83.59 ; H, 7.26% ($C_{25}H_{26}O_2$ requires C, 83.76; H, 7.31%); υ_{max} (KBr disc) 3520, 3400, 2950, 2860, 2220, 1640, 1600, 1575 and 1490 cm^{-1}; δ_H ($CDCl_3$) 7.05-7.45 (9H, m), 6.13 (1H, m), 5.18 (1H, ddt, *J*=17Hz, 3Hz, 1.5Hz), 5.02 (1H, m, *J*=10Hz, 3Hz, 2Hz), 3.05-3.22 (3H, m), 2.98 (,1H, d, *J*=1.6Hz), 2.82 (1H, m), 1.00-2.30 (9H, m); δ_C ($CDCl_3$) 139.7 (d), 136.9 (s), 136.6 (s), 131.7 (d), 128.5 (d), 128.3 (d), 128.3 (d), 127.9 (d), 126.4 (d), 125.9 (d), 122.3 (s), 115.4 (t), 90.1 (s), 86.4 (s), 76.5 (s), 75.0 45.6 (d), 38.0 (d), 36.2 t 29.8 (t), 23.7 (t), 21.4 (t), 20.5 (t); M/Z (%)+EI: 358 (M, 48), 300 (25), 187 (28), 169 (40), 129 (100), 102 (61).

(4a-α, 10-α, 10a-α)-(±)-1, 2, 3, 4, 4a, 9, 10, 10a-Octahydro-10, 10a-dihydroxy-9-(20propenyl)phenanthrene (6i)

Following the typical procedure (above), 1-(1,2-epoxycyclohexyl)-2-phenyl-4-penten-1-ol (1.50g, 5.52mmol) yielded a residue which was recrystallised from a mixture of light petroleum and ethyl acetate to give **6i** as a white solid (1.44g, 100%); found C, 78.91; H, 8.61% ($C_{17}H_{22}O_2$ requires C, 79.03; H, 8.58%); υ_{max} (KBr disc) 3400, 1645, 1600, 1490, and 750 cm^{-1}; δ_H ($CDCl_3$) 7.35 (2H, m), 7.19 (2H, m), 6.13 (1H, m), 5.25 (1H, m, *J*=17Hz, 3Hz), 5.15 (1H, m, *J*=10Hz, 3Hz), 3.81 (1H, d, *J*=3.5Hz), 3.11 (2H, m), 2.87 (1H, m), 2.63 (1H, m), 1.20-2.30 (10H, m); δ_C ($CDCl_3$) 137.7 (s), 137.5 (d), 136.5 (s), 127.6 (d), 126.5 (d), 126.4 (d), 126.1 (d), 116.8 (t), 74.0 (t), 72.7 (s), 40.7 (d), 39.7 (d), 35.5 (t), 30.6 (t), 24.6 t 21.4 (t), 21.4 (t); M/Z (%)+EI: 258 (M, 13), 199 (100), 171 (75), 129 (87).

(4a-α, 10-α, 10a-α)-(±)-1, 2, 3, 4, 4a, 9, 10, 10a-Octahydro-10, 10a-dihydroxy-10-(1-heptynyl)-3-methylphenanthrene (6j)

Following the typical procedure (above), 1-(4-methyl-1,2-epoxycyclohexyl)-1-(1-heptynyl)-2-phenylethanol (1.0g, 3.07mmol) afforded a residue which was purified by column chromatography on silica gel using 10% ethyl acetate in petroleum ether as eluent to give **6j** as a colourless oil (0.68g, 68%); found C, 80.91; H, 9.17% ($C_{22}H_{30}O_2$ requires C, 80.93; H, 9.26%); M^+ 326.2253 ($C_{22}H_{30}O_2$ requires 326.2246); υ_{max} (liquid film) 3545, 3470, 2230, 1600, 1580, 1490, and 750 cm^{-1}; δ_H ($CDCl_3$) 7.40 (1H, d, *J*=7Hz), 7.15 (3H, m), 3.22 (2H, s), 3.15 (1H, bs), 2.50 (1H, bs), 2.22 (3H, t, *J*=7Hz), 1.82 (1H, m), 1.64-1.22 (12H, m), 0.92 (3H, t, *J*=7Hz) and 0.91 (3H, d, *J*=7Hz); δ_C ($CDCl_3$) 137.0 (s), 132.4 (s), 128.9 (d), 126.3 (d), 125.9 (d), 125.7 (d), 86.4 (s), 81.0 (s), 74.2 (s), 73.3 (s), 41.2 (t), 38.5 (d), 32.4 (t), 31.1 (t), 30.4 (t), 29.9 (t), 28.3 (t), 26.8 (d), 22.1 (q), 22.1 (t), 18.6 (t), 13.9 (q); M/Z (%)+EI: 326 (M, 10), 309 (100), 291 (44), 252 (38).

(4a-α, 10-α, 10a-α,)-(±)-10-(2-Chloro-1-hydroxyethyl)-1, 2, 3, 4, 4a, 9, 10, 10a-octahydro-10, 10a-dihydroxyphenanthrene (6k)

Following the typical procedure (above), 1-(1,2-epoxycyclohexyl)-1-(epoxyethyl)-2-phenylethan-1-ol (0.45g, 1.73mmol) yielded a residue which was recrystallised from damp ethyl acetate to give **6k** as a white powdery solid (0.45g, 88%), as a single diastereoisomer; mp 137.5-139°C; found C, 55.00; H, 6.09% ($C_{16}H_{21}ClO_3.3H_2O$ requires C, 54.78; H, 6.03%); M^+ 296.1191 ($C_{16}H_{21}ClO_3$ requires 296.1179); R_F=0.2 (ethyl acetate); υ_{max} (KBr disk) 3380, 2960, 2860, 1585 and 1500 cm^{-1}; δ_H ($CDCl_3$) 7.30-6.93 (4H, m), 4.06 (1H, dd, *J*=12Hz, *J*=3Hz), 3.80 (2H, m), 3.55 (3H, bs), 3.12 (1H, s), 2.79 (2H, q_{AB}, *J*=18Hz), 2.23 (1H, d, *J*=15Hz), 2.01 (1H, tt, *J*=15Hz, *J*=2Hz), 1.85-1.47 (2H, m) and 1.48-0.99 (4H, m); δ_C ($CDCl_3$) 136.3 (s), 131.9 (s), 129.2 (d), 126.5 (d), 126.0 (d), 125.9 (d), 76.5 (s), 76.0 (d), 74.3 (s), 47.1 (t), 39.2 (d), 37.1 (t), 29.1 (t), 22.9 (t), 21.4 (t) and 20.2 (t); M/Z(%)+EI: 296 (M, 4), 279 (M-17, 15), 260 (30), 242 (40), 226 (55), 224 (70), 217 (75), 209 (50), 200 (90) and 199 (100).

2'-α, 6-β-(±)-2,3-Benza-6, 2'-dihydroxyspirocyclo[5.4]decane (6l)

Following the typical procedure (above), 1-(1,2-epoxycyclopentyl)-3-phenylpropan-1-ol (0.50g, 2.29mmol) afforded a residue which was purified by column chromatography on silica eluted with 20% ethyl acetate in petroleum ether to give **6l** as a colourless oil (0.25 g, 50%); found C, 76.78%, H, 8.27%, ($C_{14}H_{18}O_2$ requires C, 77.03%, H, 8.27%); υ_{max} (KBr disc) 3400, 3300, 2950 and 1500 cm^{-1}; δ_H ($CDCl_3$) 7.18-7.05 (4H, m), 4.60 (1H, t, *J*=6Hz), 4.22 (1H, dd, *J*=5 and 3Hz), 4.00-3.30 (2H, bs), 3.11 (1H, ddd, *J*=17, 9 and 7Hz), 2.76 (1H, ddd, *J*=17, 7 and 5Hz), 2.32-1.57 (8H, m); δ_C

($CDCl_3$) 141.1 (s), 136.1 (s), 128.8 (d), 126.4 (d), 126.0 (d), 125.7 (d), 81.5 (d), 71.4 (d), 52.0 (s), 38.1 (t), 33.8 (t), 27.0 (t), 25.2 (t), 21.3 (t); M/Z(%)+EI: 202 (20), 168 (38), 141 (50), 128 (100), 115 (55).

1-α, 3-α/β, 4a-α, 7a-α-(±)-3-Chlorobicyclo[4.3.0]nonane-1,7a-diol (6m)

Following the typical procedure (above), 1-(1, 2-epoxycyclopentyl)-3-buten-1-ol (0.60g, 3.84mmol) afforded a residue which was purified by column chromatography on silica using 20% ethyl acetate: petroleum ether as eluent to give **6m** as a colourless solid (0.115g, 21%); m.p. 56-58°C; M^+ 192.0728 ($C_9H_{15}Cl^{37}O_2$ requires 192.0731); R_F=0.14 (20% ethyl acetate: petroleum ether); υ_{max} (solution) 3400 and 3000 cm^{-1}; δ_H ($CDCl_3$) 4.29-3.51 (3H, m) and 2.46-1.19 (12H, m); δ_C ($CDCl_3$) 83.3 (s), 82.3 (s), 81.0 (s), 79.1 (s), 77.7 (d), 71.0 (d), 69.5 (d), 68.9 (d), 61.3 (d), 59.4 (d), 54.0 (d), 53.8 (d), 53.1 (d), 48.0 (d), 44.1 (d), 43.5 (d), 40.2 (t), 40.1 (t), 39.8 (t), 34.9 (t), 34.7 (t), 34.1 (t), 33.5 (t), 30.1 (t), 29.9 (t), 29.7 (t), 29.2 (t), 29.0 (t), 28.1 (t), 27.3 (t), 27.2 (t), 26.7 (t), 21.3 (t), 20.8 (t), 19.9 (t) and 19.4 (t); M/Z(%)+EI: 192 (M, 4), 190 (M, 12), 174 (M-18, 4), 172 (M-18, 12), 155 (70) and 137 (100).

1, 2, 3, 4-Tetrahydro-6, 8-dimethylnaphthalene (7n) and 1, 8-Dimethylbicyclo[4.3.1]-5-decen-8-one (8n)

Following the typical procedure (above), 2-(1,2-epoxycyclohexyl)-4-methyl-4-penten-2-ol (0.90g, 4.585mmol) afforded a residue which was purified by column chromatography on silica using 4% ethyl acetate: petroleum ether as eluent to give **7n** as a colourless oil (0.225g, 29%); M^+ 160.1250 ($C_{12}H_{16}$ requires 160.1252); R_F=0.94 (10% ethyl acetate: petroleum ether); δ_H ($CDCl_3$) 6.82 (s), 6.74 (s), 2.76 (2H, t, *J*=7Hz), 2.57 (2H, t, *J*=7Hz), 2.28 (3H, s), 2.18 (3H, s) and 1.82 (4H, m); δ_C ($CDCl_3$) 137.0 (s), 136.5 (s), 134.5 (s), 132.5 (s), 128.0 (d), 127.5 (d), 30.1 (t), 26.4 (t), 23.6 (t), 23.1 (t), 20.8 (q) and 19.4 (q); M/Z(%)+CI: 175 (22), 161 (M+1, 40), 160 (M, 39), 145 (M-15, 100), 132 (40), 115 (32), 105 (20), 91 (32), 77 (20), 63 (18), 51 (18) and 41 (16); plus **8n** as a colourless oil (0.160g, 20%); M^+ 178.1363 ($C_{12}H_{18}O$ requires 178.1358); R_F=0.69 (10% ethyl acetate: petroleum ether); υ_{max} (liquid film) 3000, 2940, 1725 and 1630 cm^{-1}; δ_H ($CDCl_3$) 5.32 (1H, bs), 2.92 (1H, m), 2.17 (2H, qAB, J=17Hz), 1.72 (3H, m), 1.70-1.40 (6H, m), 1.08 (3H, s) and 1.08-0.82 (2H, m); δ_C ($CDCl_3$) 216.7 (s), 134.1 (s), 123.9 (d), 49.7 (d), 46.8 (t), 40.1 (t), 32.2 (s), 31.8 (t), 27.5 (t), 25.0 (t), 24.1 (q) and 23.7 (q); M/Z(%)+EI: 178 (M, 48), 149 (50), 135 (52), 121 (31), 107 (60), 93 (52), 79 (56), 67 (48), 55 (62), 43 (72) and 41 (100).

1, 2, 3, 4 -Tetrahydrophenanthrene (7c)

(4a-α, 10-α, 10a-α)-(±)-1, 2, 3, 4, 4a, 9, 10, 10a-Octahydro-10, 10a-dihydroxyphenanthrene **(6c)** (0.150g, 0.69mmol) was treated with polyphosphoric acid (PPA) (3.0g), and the mixture was stirred with a glass rod for 5 min. The mixture was stirred mechanically for a further 30 min, ice was added and the mixture was stirred with a glass rod until the PPA was hydrolysed. The resulting solution was extracted with dichloromethane (2 x 50ml). The combined organic extracts were washed with saturated sodium hydrogen carbonate solution (50ml) and brine (50ml), dried ($MgSO_4$), and concentrated *in vacuo* to give a residue which was purified by column chromatography on silica using light petroleum as eluent to give **7c** as a white solid (0.090g (71%); mp 33.5-34.5°C (literature[31] mp 33-34°C); δ_H ($CDCl_3$) 8.05 (1H, dd, *J*=9Hz, *J*=1Hz), 7.82 (1H, dd, *J*=8Hz, *J*=1Hz), 7.60 (1H, d, *J*=9Hz), 7.55-7.40 (2H, m), 7.25 (1H, d, *J*=8Hz), 3.15 (2H, t, *J*=7Hz), 2.91 (2H, t, *J*=7Hz) and 1.95 (4H, m); δ_C ($CDCl_3$) 134.4 (s), 132.6 (s), 132.2 (s), 131.6 (s), 128.5 (d), 128.4 (d), 125.8 (d), 125.7 (d), 124.8 (d), 122.7 (d), 30.5 (t), 25.8 (t), 23.3 (t) and 23.1 9t).

1, 2, 3, 4, 4a, 10a-Hexahydro-10(9*H*)-phenanthrone (8c)

A stirred solution of (4a-α, 10-α, 10a-α)-(±)-1, 2, 3, 4, 4a, 9, 10, 10a-Octahydro-10, 10a-dihydroxyphenanthrene **(6c)** (0.40g, 1.83mmol) in benzene (30ml) was treated with P_2O_5 (0.22g, 1.55mmol) and the mixture was stirred under reflux for 4 hours. Water was added and the organic layer extracted with benzene (2 x 50ml). The combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo* to give a residue which was purified by column chromatography on silica using 10% ethyl acetate: petroleum ether as eluent to give **8c** as a mixture of isomers (*cis* and *trans* ring junction), as a yellow oil (0.23g, 63%); M^+ 200.1194 ($C_{14}H_{16}O$ requires 200.1201); υ_{max} (liquid film) 3060, 3005, 2920, 2845, 1720, 1600, 1490 and 1450 cm^{-1}; δ_H ($CDCl_3$) 7.25-7.00 (4H, m), 3.55 (2H, d, *J*=2Hz), 3.11-2.98 (1H, m), 2.70-2.40 (2H, m), 2.36-2.20 (1H, m) and 2.01-1.12 (6H, m); δ_C ($CDCl_3$) 211.6 (s), 211.5 (s), 140.9 (s), 140.5 (s), 133.0 (s), 132.5 (s), 128.5 (d), 127.9 (d), 127.7 (d), 126.8 (d), 126.7 (d), 123.9 (d), 50.9 (d), 48.0 (d), 44.9 (t), 43.4 (t), 43.2 (d), 40.2 (d), 31.9 (t), 29.4 (t), 26.8 (t), 25.7 (t), 25.6 (t), 25.4 (t), 24.9 (t) and 22.2 (t); M/Z(%)+EI: 200 (M, 100), 185 (35), 172 (30), 145 (35), 129 (90), 115 (43), 91 (34), 71 (22) and 43 (38).

7, 8-Benzo-1, 6-dimethyl-11-0xobicyclo[4.3.1]decane (8g)

Following the typical procedure above, (0°C, 1.5h), 2-(1,2-epoxy-2-methylcyclohexyl)-1-phenylpropan-2-ol (0.41g, 1.66mmol) yielded a residue which was purified by column chromatography on silica eluted with 3% ethyl acetate in petroleum ether to give **8g** as a colourless oil (0.093 g, 23%); M+ 228.1523 ($C_{16}H_{20}O$ requires 228.1514); υ_{max} (liquid film) 2980, 2940, 2860, 1730, 1500 and 1520 cm^{-1}; δ_H ($CDCl_3$) 7.30-7.10 (4H, m), 2.80 (2H, q_{AB}, *J*=17Hz), 1.70-1.00 (8H, m), 1.35 (3H, s), 1.25 (3H, s); δ_C ($CDCl_3$) 142.6 (s), 134.9 (s), 129.2 (d), 126.8 (d), 126.3 (d), 126.2 (d), 51.7 (s), 47.2 (s), 43.8 (t), 42.3 (t), 36.0 (t), 28.0 (q), 27.2 (t), 24.8 (t), 24.6 (q); M/Z(%)+EI: 228 (M, 100), 213 (30), 185 (50), 173 (55), 157 (35), 143 (55), 129 (67), 115 (40), 91 (35), 55 (37), 41 (53).

Tetrahydrofuran (8i)

A stirred solution of (4a-α, 10-α, 10a-α)-(±)-1, 2, 3, 4, 4a, 9, 10, 10a-Octahydro-10, 10a-dihydroxy-9-(2-propenyl)phenanthrene **(6i)** (0.10g, 0.39mmol) in benzene (30ml) was treated with P_2O_5 (0.10g) and the mixture was stirred under reflux for 4 hours. Water was added and the organic layer extracted with benzene (2 x 50ml). The combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo* to give a residue which was purified by column chromatography on silica using 10% ethyl acetate: petroleum ether as eluent to give **8i** as a yellow oil (0.41g, 41%); M-18 240.1511 ($C_{17}H_{22}O_2$-H_2O requires 240.1514); δ_H ($CDCl_3$) 7.17-7.05 (4H, m), 4.52 (1H, d, *J*=8Hz), 4.15 (1H, q, *J*=6Hz), 3.64 (1H, q, *J*=8Hz), 2.80 (1H, dd, *J*=8Hz, *J*=4Hz), 2.25 (1H, bs), 2.11 (1H, d, *J*=6Hz), 2.10 (1H, *J*=6Hz, *J*=1Hz), 1.92 (1H, m), 1.68 (4H, m), 1.39 (4H, m) and 1,18 (3H, d, *J*=6Hz); δ_C ($CDCl_3$) 138.4 (s), 137.3 (s), 128.3 (d), 127.7 (d), 126.3 (d), 126.2 (d), 75.8 (d), 74.8 (d), 71.4 (s), 43.0 (t), 41.6 (d), 40.6 (d), 33.3 (t), 23.4 (t), 22.5 (t) and 21.3 (q); M/Z(%)+EI: 258 (M, 25), 239 (41), 222 (17), 197 (19), 181 (100), 141 (41), 129 (41), 91 (29), 77 (17) and 55 (29).

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