Stereoselectivity of Epoxidation of Substituted Cyclohexa-1,4-dienes: Influence of an Allylic Methoxycarbonyl Group

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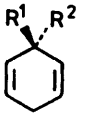
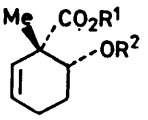
Epoxidations of methyl 1-methylcyclohexa-2,5-diene-1-carboxylate (1), methyl cyclohexa-2,5-diene-1-carboxylate (2), 3-hydroxymethyl-3-methylcyclohexa-1,4-diene (3), and the corresponding tetrahydropyranyl ether (4), have been studied. The observed stereoselectivities are explained in terms of steric hindrance to the approaching peracid, and do not require any *cis*-directing effect of the methoxycarbonyl group to be invoked. Epoxidation of methyl *cis*-6-acetoxy-1-methylcyclohex-2-ene-1-carboxylate (5) was highly stereoselective; the epoxides (15) and (16) were obtained in a 9 : 1 ratio, respectively.

THE stereoselectivity of epoxidation continues to be an area of considerable interest because of the importance of epoxides in organic synthesis.[1] Recently it was claimed that an allylic methoxycarbonyl group exerts a *cis*-directing effect in epoxidation reactions [2] reminiscent of that exhibited by an allylic hydroxy-group,[3] although the generality of this effect has since been questioned.[4] A short while ago we had cause to study the stereoselectivity of epoxidation of several cyclohexa-1,4-dienes. We now report our results which confirm that the methoxycarbonyl group does *not* exert a strong *cis*-directing effect in epoxidation reactions. In addition we have observed a strong directing effect of a homoallylic substituent which is explained in terms of a conformational effect.

RESULTS

The epoxidations, using *m*-chloroperoxybenzoic acid, of methyl 1-methylcyclohexa-2,5-diene-1-carboxylate (1) [5] and





(1) $R^1 = CO_2Me, R^2 = Me$
(2) $R^1 = CO_2Me, R^2 = H$
(3) $R^1 = CH_2OH, R^2 = Me$
(4) $R^1 = CH_2OTHP, R^2 = Me$

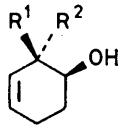
(5) $R^1 = Me, R^2 = Ac$
(6) $R^1 = R^2 = H$

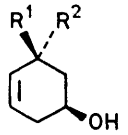
methyl cyclohexa-2,5-diene-1-carboxylate (2),[6] were studied, and the observed stereoselectivities are shown in the Table, together with preliminary results obtained for epoxidation of 3-hydroxymethyl-3-methylcyclohexa-1,4-diene (3) [7] and its tetrahydropyranyl ether (4). In addition the stereoselectivity of epoxidation of methyl *cis*-6-acetoxy-1-methylcyclohex-2-ene-1-carboxylate (5) is also shown in the Table.

Cyclohexa-1,4-dienes (1)—(3) are known compounds. The acetate (5) was prepared from *cis*-2-hydroxy-1-methylcyclohex-5-ene-1-carboxylic acid (6) [8] by esterification and acetylation (see Experimental section).

The epoxides (7) and (8) were separated and fully characterized. The isomer which had the smaller R_F on silica, and the larger retention time on g.l.c., was identified as the isomer with the epoxide ring *cis* to the methoxycarbonyl group since on reduction with lithium aluminium hydride it gave a mixture of *cis*-1,3-diol (17) and *cis*-1,4-diol (19).[8] This reduction was extremely regioselective, the ratio of the 1,3-diol (17) to the 1,4-diol being greater than 98 : 2, respectively. Reduction of the other epoxide (8) with lithium aluminium hydride was less regioselective; a mixture of two diols, ratio 7 : 3 was obtained. The major isomer was isolated by crystallization, and was identified as the *trans*-1,3-diol (18) on the basis of its ^1H n.m.r. spectrum. The minor isomer was not obtained pure, but was assumed to be the *trans*-1,4-diol (20). The *cis*-epoxide (7) was also prepared, free of the *trans*-isomer (8), by treatment of the bromohydrin (21) [8] with potassium carbonate in methanol.

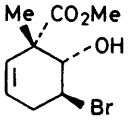
The epoxides (9) and (10) were fairly unstable. Extensive decomposition occurred during attempted g.l.c. analysis of the mixture, and during column chromatography partial isomerization to methyl 3-hydroxycyclohexa-1,5-diene-1-carboxylate (22) [9] was observed. Nevertheless, pure

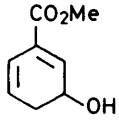


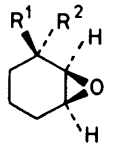


(17) $R^1 = CH_2OH, R^2 = Me$
(18) $R^1 = Me, R^2 = CH_2OH$

(19) $R^1 = CH_2OH, R^2 = Me$
(20) $R^1 = Me, R^2 = CH_2OH$







(21)

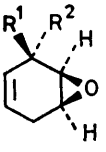
(22)

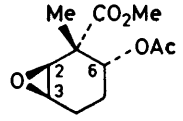
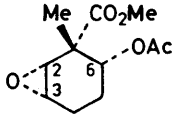
(23) $R^1 = CO_2Me, R^2 = H$
(24) $R^1 = H, R^2 = CO_2Me$

samples of both isomers were obtained for formal characterization. Attempted reduction of the epoxides (9) and (10), using lithium aluminium hydride, gave complex mixtures of products, presumably arising from non-regioselective epoxide ring-opening and over-reduction. Similarly attempted hydrogenation to prepare the known saturated epoxides (23) and (24) [4] using palladium on charcoal or Raney nickel catalysts, was unsuccessful; complicated mixtures of hydroxy-esters were obtained due to unselective hydrogenolysis of the epoxide rings. However it was found that hydrogenation of a solution of the epoxides (9) and (10) in benzene, using $[Rh(Ph_3P)_3Cl]$ as catalyst, proceeded without hydrogenolysis, and the saturated epoxides (23) and (24) were obtained quite

cleanly.[10] Hydrogenation of a crude mixture of the epoxides (9) and (10) under these conditions gave a mixture of the saturated epoxides (23) and (24) in the ratio (23) : (24) = 35 : 65, respectively. Hydrogenation of a sample of the major unsaturated epoxide gave exclusively the *trans*-saturated epoxide (24), so confirming that the major unsaturated epoxide was the *trans*-isomer (10), and that epimerization was not taking place during hydrogenation. The ^{1}H n.m.r. spectra of the epoxides (9) and (10) were also consistent with these assignments. In particular the H(1),H(2) coupling constant for the *trans*-isomer (10) was very small.[4]

Epoxides



Alkene		Ratio of epoxides
(1)	(7) $R^1 = CO_2Me$, $R^2 = Me$ (8) $R^1 = Me$, $R^2 = CO_2Me$	(7) : (8) = 55 : 45 [a]
(2)	(9) $R^1 = CO_2Me$, $R^2 = H$ (10) $R^1 = H$, $R^2 = CO_2Me$	(9) : (10) = 35 : 65
(3)	(11) $R^1 = CH_2OH$, $R^2 = Me$ (12) $R^1 = Me$, $R^2 = CH_2OH$	(11) : (12) = 65 : 35
(4)	(13) $R^1 = CH_2OTHP$,[b] $R^2 = Me$ (14) $R^1 = Me$, $R^2 = CH_2OTHP$	(13) : (14) = 40 : 60
(5)	  (15) (16)	(15) : (16) = 90 : 10

[a] Similar results were obtained using $Mo(CO)_6$–Bu^tO_2H. [b] Mixture of OTHP isomers.

The hydroxy-epoxides (11) and (12) were rather unstable. They were not separated, but were reduced together to give a mixture of the *cis*- and *trans*-1,3-diols (17) and (18) which was analysed by g.l.c. Similarly, the tetrahydropyranyl ether epoxides (13) and (14) were not separated.* On t.l.c. and g.l.c. they behaved as one compound, and in the ^{1}H n.m.r. spectrum of the crude epoxidation mixture only one methyl singlet was observed. However this singlet was split into three on addition of a shift reagent, so showing that at least three isomers were present. This crude epoxide mixture was reduced using lithium aluminium hydride, and the reduction product hydrolysed, to give a mixture of the *cis*- and *trans*-1,3-diols (17) and (18) which was analysed by g.l.c.

Epoxidation of the acetate (5) gave a crystalline mixture of mono-epoxides from which the major isomer was isolated by recrystallization. Chromatography of the mother-liquor gave the minor isomer. The major isomer was identified as isomer (15), the one with the epoxide ring *trans* to the acetoxy and methoxycarbonyl substituents, on the basis of conformational considerations (see Discussion section). Moreover this stereochemical assignment is consistent with the ^{1}H n.m.r. spectrum of these epoxides. In particular the double-doublet due to H(2) of the major isomer is deshielded by over 0.5 p.p.m. with respect to the doublet due to H(2) of the minor isomer. This is consistent with H(2) of the major isomer being *cis* with respect to an axial 6-acetoxy-substituent. The 6-acetoxy-substituent is believed to be axial because of the long range H(2),H(6) coupling, and the small half-height width of the H(6) multiplet, which suggest that H(6) is equatorial.

* We carried out our epoxidations of tetrahydropyranyl ether (4) before the publication of ref. 11. We encountered no hazards in our experiments, but we have not repeated them since we became aware of the dangers.

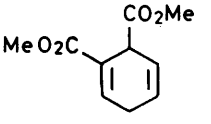
DISCUSSION

It has been claimed that the methoxycarbonyl group exerts a strong *cis*-directing effect in epoxidation reactions,[2] similar to that shown by an allylic hydroxy-group. Our results do not support this. The cyclohexa-1,4-diene ring is believed to be planar, or very nearly so.[12] Therefore epoxidation should take place preferentially on the side opposite to the largest allylic substituent, unless another effect is operating, indeed on this basis the stereoselectivities of epoxidation of alcohol (3) and ether (4) can be explained.

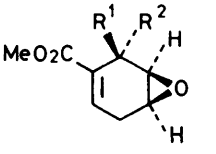
m-Chloroperoxybenzoic acid epoxidation of methyl 1-methylcyclohexa-2,5-diene-1-carboxylate (1) gave a 55 : 45 mixture of mono-epoxides (7) and (8), respectively. This slight preference for epoxidation to occur *cis* to the methoxycarbonyl group is consistent with the stereoselectivity one would expect on the basis of simple steric effects. The methoxycarbonyl group is slightly smaller than the methyl group,[13] and so one would expect slightly more epoxidation to take place *cis* to the methoxycarbonyl group, as is observed. However the small stereoselectivity observed is not consistent with any *strong cis*-directing influence of the methoxycarbonyl group.

Similarly the stereoselectivity of epoxidation of methyl cyclohexa-2,5-diene-1-carboxylate (2) is consistent with steric effects only being involved. The *trans*-epoxide (10) accounts for 65% of the mono-epoxide product, and is formed by epoxidation taking place on the other side of the cyclohexadiene ring to the methoxycarbonyl group.

The stereoselectivity of epoxidation of ester (2) is consistent with the reported epoxidation of methyl cyclohex-2-ene-1-carboxylate which gives the *trans*-epoxide (24) as the major product.[4] However it is not in agreement with the reported epoxidation of the cyclohexa-1,4-diene diester (25).[2] It has been claimed that



(25)

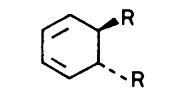


(26) $R^1 = CO_2Me$, $R^2 = H$
(27) $R^1 = H$, $R^2 = CO_2Me$

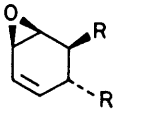
epoxidation of the diester (25) gives a mixture of mono-epoxides (26) and (27) in which the *cis*-epoxide (26), predominates. Configurations were assigned to epoxides (26) and (27) on the basis of their ^{1}H n.m.r. spectra, and

in view of the small chemical-shift differences involved, these data cannot be regarded as definitive. We suggest that the structures of the epoxides (26) and (27) may have been incorrectly assigned, and that the major epoxide may be the *trans*-isomer (27). Perhaps the structures of these epoxides should be studied further.

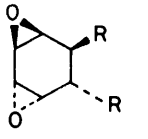
The stereoselectivities of epoxidation of the alcohol (3) and its tetrahydropyranyl ether (4) are consistent with this interpretation of cyclohexa-1,4-diene epoxidations. In the epoxidation of the alcohol (3), the weak *cis*-directing effect of the exocyclic homoallylic hydroxy group [1] outweighs any adverse steric effect, and the *cis*-epoxide (11) is the major product. However when this alcohol is converted into its tetrahydropyranyl ether (4), steric effects again become more important, and the *trans*-epoxide (14) is the major product.



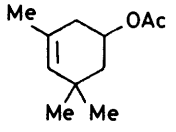
(28) R = CO_2Me
(29) R = OAc



(30) R = CO_2Me
(31) R = OAc



(32) R = CO_2Me



(33)

Therefore the methoxycarbonyl group does not, in general, exert a strong *cis*-directing effect in epoxidation reactions. The main piece of evidence in favour of such an effect is the epoxidation of dimethyl *trans*-1,2-dihydrophthalate (28) which is quite selective in giving the monoepoxide (30) and the diepoxide (32) as the major products.[2] However the analogous epoxide (31) is the major product of epoxidation of *trans*-5,6-diacetoxycyclohexa-1,3-diene (29),[14] and so it would seem that these selectivities are due to a special effect present in the *trans*-5,6-disubstituted cyclohexa-1,3-diene system. We suggest that the preferred conformation of the dihydrophthalate (28) is that shown in Figure 1, and

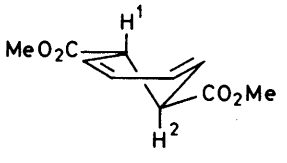


FIGURE 1

that the pseudoaxial allylic hydrogen atoms H^1 and H^2 direct the stereochemistry of epoxidation by providing more hindrance to the approaching peracid than the pseudoequatorial methoxycarbonyl substituents.

Epoxidation of the acetate (5) was found to be highly stereoselective in contrast to the unselective epoxidations of the related cyclohexa-1,4-diene (1). The major epoxide obtained from (5) has been identified as the isomer with the epoxide ring *trans* to the acetoxy and methoxycarbonyl substituents by analogy with the reported stereoselective epoxidation of 4-acetoxy-2,6,6-trimethylcyclohexene (33).[15] The preferred conformation of the acetate (5), is probably that shown in Figure 2, with the acetoxy and methyl groups in equa-

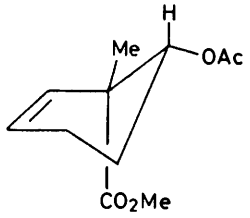


FIGURE 2

torial positions. In this conformation, the allylic methoxycarbonyl group is axial, and provides more hindrance to epoxidation than the equatorial allylic methyl group. Therefore epoxidation occurs preferentially away from the methoxycarbonyl group and the epoxide (15) is the major product.*

Finally, we briefly examined the stereoselectivity of epoxidation of the diene-ester (1) using t-butyl hydroperoxide and $Mo(CO)_6$ in refluxing benzene, but the stereoselectivity observed was very similar to that obtained on epoxidation using *m*-chloroperoxybenzoic acid.

EXPERIMENTAL

M.p.s were recorded on a Kofler hot-stage apparatus. I.r. spectra were recorded on a Perkin-Elmer 257 or on a Perkin-Elmer 297 spectrophotometer, and are for liquid films unless otherwise stated. ^1H N.m.r. spectra were measured on a Perkin-Elmer R12B (60 MHz), or on a Brucker HFX 90 (90 MHz) spectrometer. Mass spectra were determined on an A.E.I. MS 30 mass spectrometer.

Silica gel pre-coated plates (Merck 60F254) were used for analytical t.l.c. A Perkin-Elmer F11 (FID) gas chromatograph was used for analytical g.l.c. using a 15% Carbowax 20M on Chromosorb W 80—100 mesh column. Short-column chromatography was used for preparative purposes using Hopkin and Williams silica gel for t.l.c. (MFC without binder.) Throughout ether refers to diethyl ether.

Methyl cis-6-*Acetoxy*-1-*methylcyclohex*-2-*ene*-1-*carboxylate* (5).— *cis*-2-Hydroxy-1-methylcyclohex-5-ene-1-carboxylic acid (6) (24.6 g) in ether was esterified by addition of a solution of diazomethane in ether (not distilled) until a persistent yellow colour remained.[16] The ether was then evaporated to leave the crude methyl ester (23.9 g) as an oil, $\nu_{max.}$ 3 450, 3 020, 1 710, 1 275, 1 225, 1 117, and 1 060 cm^{-1}; $\delta(CDCl_3)$ 1.31 (3 H, s, CH_3), 1.5—2.5 (4 H, m, 2 × CH_2), 3.5br (1 H, s, exchanges with D_2O, OH), 3.68 (3 H, s, OCH_3), 3.6—3.9 (1 H, m, CHOH), and 5.65 (2 H, m, vinylic H).

The methyl ester was not purified, but was dissolved in

* Epoxidation stereoselectivity is frequently rationalized in terms of ground-state conformations. This is assumed not to breach the Curtin–Hammett Principle because the conformation of the transition state for epoxidation is believed to be similar to the conformation of the starting alkene.[1]

anhydrous pyridine (160 ml), acetic anhydride (26 ml) added, and the solution stirred overnight at room temperature and then at 70—75 °C for 3 h. The reaction mixture was poured onto ice, and extracted with ether. The ether extracts were washed with a cold 1 : 1 mixture of concentrated hydrochloric acid and water, dried ($MgSO_4$), and concentrated to give acetate (5) as an oil (24.4 g). A sample was recrystallized from ether–light petroleum to give *methyl* cis-6-*acetoxy*-1-*methylcyclohex*-2-*ene*-1-*carboxylate* (5), m.p. 41—42 °C, $\nu_{max.}$ 3 020, 1 735, 1 240, 1 116, and 1 040 cm^{-1}; $\delta(CDCl_3)$ 1.31 (3 H, s, CH_3), 2.01 (3 H, s, $OCOCH_3$), 1.5—2.5 (4 H, m, 2 × CH_2), 3.70 (3 H, s, OCH_3), 5.11 (1 H, m, CHOAc), and 5.77 (2 H, m, vinylic H) (Found: C, 62.45; H, 7.65. $C_{11}H_{16}O_4$ requires C, 62.25; H, 7.55%).

Epoxidation of Methyl 1-*Methylcyclohexa*-2,5-*diene*-1-*carboxylate* (1).—*m*-Chloroperoxybenzoic acid (7.5 g) was added in small portions to a well stirred mixture of methyl 1-methylcyclohexa-2,5-diene-1-carboxylate (1) [5] (6 g) in dichloromethane (500 ml) and 0.5M-aqueous sodium hydrogencarbonate (150 ml), and the mixture stirred at 20 °C for 18 h.[17] The two layers were separated, and the organic layer washed with 1N-sodium hydroxide (150 ml) and water (150 ml), dried (Na_2SO_4), and concentrated to give a crude mixture of the epoxides (7) and (8). G.l.c. examination of this crude product (150 °C) showed two main components (I) and (II), relative retention times 10.7 and 17.5, respectively, in the ratio of (I) : (II) = 45 : 55. A portion of this mixture (3 g) was separated into the two components using column chromatography on silica (gradient elution using ether–hexane). The first fraction off the column corresponded to compound (I) on g.l.c., and was identified as the trans-*epoxide* (8), a colourless oil, homogeneous by g.l.c., $\nu_{max.}$ 3 040, 1 725, 1 650, 1 240, 1 115, 840, and 710 cm^{-1}; $\delta(CDCl_3)$ 1.4 (3 H, s, CH_3), 2.5 (2 H, m, CH_2), 3.35 (2 H, m, epoxide H), 3.67 (3 H, s, OCH_3), and 5.1—5.8 (2 H, m, vinylic H) (Found: C, 64.05; H, 7.2. $C_9H_{12}O_3$ requires C, 64.3; H, 7.15%). The second compound off the column corresponded to compound (II) on g.l.c., and was identified as the cis-*epoxide* (7), a low-melting solid, homogeneous by g.l.c., m.p. 35 °C, $\nu_{max.}$ (Nujol) 1 730, 1 260, 1 245, and 1 110 cm^{-1}; $\delta(CDCl_3)$ 1.34 (3 H, s, CH_3), 2.47 (2 H, m, CH_2), 3.32 (2 H, m, epoxide H), 3.72 (3 H, s, OCH_3), and 5.2—5.9 (2 H, m, vinylic H) (Found: C, 64.05; H, 7.25%).

Epoxidation of the diene ester (1) using t-butyl hydroperoxide and $Mo(CO)_6$ in benzene, following the procedure described in the literature,[18] gave an approximately 1 : 1 mixture of epoxides (7) and (8) (^1H n.m.r. and g.l.c.). Epoxidation using *m*-chloroperoxybenzoic acid in chloroform, in the presence of anhydrous sodium acetate, also gave a 1 : 1 mixture of the epoxides (7) and (8) (n.m.r.).

Separate solutions of the epoxides (7) and (8) (0.7 g) in ether (40 ml) were added to lithium aluminium hydride (0.5 g) in ether (30 ml) under dry nitrogen, and the mixtures heated under reflux for 3—4 h and then stirred for 18 h at 20 °C. Addition of water (0.5 g), 15% aqueous sodium hydroxide (0.5 g), and water (1.5 ml), gave granular precipitates which were filtered off, and the ethereal solutions were concentrated to give crude diol products. The *trans*-epoxide (8) gave a semisolid mixture (0.55 g) which g.l.c. (180 °C) showed to be a mixture of two components, (III) and (IV), with relative retention times of 10.25 and 12.4, respectively, in the ratio (III) : (IV) = 70 : 30. Selective crystallization from chloroform gave colourless crystals of the trans-1,3-*diol* (18), homogeneous by g.l.c., corresponding to compound (III), m.p. 95—97 °C, $\nu_{max.}$ (Nujol) 3 300, 3 010, 1 660, 1 085, 1 070, 1 050, and 720 cm^{-1}; $\delta(CDCl_3)$ 1.02 (3 H, s, CH_3), 1.5—1.9 and 2.0—2.3 (each 2 H, m, CH_2), 3.50 (2 H, s, CH_2OH), 2.8br and 3.0br (each 1 H, s, exchange with D_2O, OH), 3.90 (1 H, dd, *J* 5 and 10 Hz, CHOH), and 5.27 and 5.62 (each 1 H, m, vinylic H) (Found: C, 67.6; H, 9.85. $C_8H_{14}O_2$ requires C, 67.6; H, 9.85%). The *cis*-epoxide (7) gave an oil (0.6 g) which g.l.c. (180 °C) showed to contain one major component (>95% pure), retention time 8.8 relative to products (III) and (IV) above, and which was identical to an authentic sample of the *cis*-1,3-diol (17) (g.l.c. and n.m.r.).[8] A minor component (*ca.* 2%) of this crude reduction product corresponded on g.l.c. to the *cis*-1,4-diol (19),[8] retention time 12.8 relative to (III) and (IV) above, but was not characterized further.

Epoxidation of Methyl Cyclohexa-2,5-*diene*-1-*carboxylate* (2).—*m*-Chloroperoxybenzoic acid (14 g) in chloroform (200 ml) was added slowly to a solution of the diene-ester (2) [6] (10 g) in chloroform (50 ml) at 0 °C. The reaction mixture was allowed to warm to room temperature, and was stirred for a further 15 h, before the precipitate of *m*-chloroperoxybenzoic acid was filtered off. The filtrate was washed with 5% aqueous sodium sulphite, 5% aqueous sodium hydrogencarbonate (2 × 100 ml), water (100 ml), and brine (100 ml), and was then dried ($MgSO_4$). The ether was evaporated to leave a clear oil (10 g) which was shown to consist of a mixture of methyl benzoate (10%), unchanged starting material (2) (10%), mono-epoxides (9) and (10) (70%), and bis-epoxides derived from the diene-ester (2) (10%), by a combination of ^1H n.m.r. and t.l.c. The mono-epoxides were estimated to be in a 7 : 3 ratio by ^1H n.m.r. (relative intensities of the methyl ester peaks). The crude product was distilled to give a mixture of epoxides (9) and (10) (6 g), b.p. 61—70 °C at 0.25 mmHg; $\nu_{max.}$ 3 010, 1 730, and 1 660 cm^{-1}; $\delta(CDCl_3)$ 2.6 (2 H, m, CH_2), 3.2—3.9 (3 H, overlapping m, epoxide H and $CHCO_2CH_3$), 3.75 and 3.80 (3 H, s, OCH_3 of each isomer), and 5.6 (2 H, m, vinylic H) (Found: C, 61.95; H, 6.5. $C_8H_{10}O_3$ requires C, 62.35; H, 6.55%).

A crude sample of the mono-epoxides (9) and (10) (2 g), prepared as described above, was chromatographed on silica gel (150 g) (gradient elution using ether–light petroleum). Methyl benzoate (0.48 g) was eluted first, followed by the trans-*epoxide* (10) (0.59 g), a colourless oil, homogeneous by t.l.c., $\nu_{max.}$ 3 030, 1 730, 1 660, 1 280, 1 255, 1 195, 1 170, 1 015, 890, and 800 cm^{-1}; $\delta(CDCl_3)$ 2.57 (2 H, m, CH_2), 3.35 (1 H, m, H-3), 3.49 (1 H, d, slightly broadened by further splitting, *J* 4 Hz, H-2), 3.65 (1 H, m, H-1) 3.75 (3 H, s, OCH_3), and 5.59 (2 H, m, vinylic H) (Found: M^+, 154.062 9. $C_8H_{10}O_3$ requires *M*, 154.063 0). After a mixed fraction (0.1 g) the next product eluted off the column was the cis-*epoxide* (9) (0.15 g), a colourless oil, homogeneous t.l.c., $\nu_{max.}$ 3 030, 1 730, 1 660, 1 270, 1 195, 1 020, 863, 780, and 742 cm^{-1}; $\delta(CDCl_3)$ 2.54 (2 H, m, CH_2), 3.35 (1 H, m, H-3), 3.49 (1 H, m, H-2), 3.62 (1 H, m, H-1), 3.8 (3 H, s, OCH_3), and 5.65 (2 H, m, vinylic H) (Found: M^+, 154.063 0. $C_8H_{10}O_3$ requires *M*, 154.063 0). Finally methyl 3-hydroxycyclohexa-1,5-diene-1-carboxylate (22) (0.45 g), identical with an authentic sample (n.m.r., t.l.c.),[9] was eluted.

A crude sample of the mono-epoxides (9) and (10) (3 g), prepared as described above, was dissolved in anhydrous benzene (480 ml) containing $[Rh(PPh_3)_3Cl]$ (250 mg), and the solution stirred at room temperature under an atmosphere of hydrogen, for 21 h. The benzene was evaporated,

and the residue taken up in ether. The ether solution was washed several times with water, dried ($MgSO_4$), and concentrated, to give a red oil. G.l.c. showed the product to contain the saturated epoxides (23) and (24) in a 35 : 65 ratio, respectively, together with a little methyl benzoate. To confirm the structures of these products, a sample (1.7 g) of the crude hydrogenation mixture was chromatographed on silica (150 g) (ether–light petroleum, 1 : 2) to give *trans*-epoxide (24) (eluted first), and *cis*-epoxide (23) (eluted second) identical (^1H n.m.r., i.r., mass spec., t.l.c., and g.l.c.) with authentic samples prepared as described in the literature.[4]

A sample of chromatographed *trans*-epoxide (10) (380 mg) was hydrogenated as described above, and the product purified by column chromatography on silica. It was identified as the saturated *trans*-epoxide (24) by comparison (t.l.c., g.l.c., i.r., and n.m.r.) with an authentic sample. A trace (less than 1%) of the *cis*-epoxide (23) was detected in the product mixture by g.l.c.

Hydrogenation of crude samples of the epoxides (9) and (10) under standard conditions using 5% palladium–charcoal and Raney nickel catalysts gave complex product mixtures (g.l.c.) which contained alcohol products (i.r.).

Preliminary Investigation of Epoxidation of 3-*Hydroxymethyl*-3-*methylcyclohexa*-1,4-*diene* (3).—A solution of *m*-chloroperoxybenzoic acid (5.71 g) in anhydrous dichloromethane was added dropwise to a solution of 3-hydroxymethyl-3-methylcyclohexa-1,4-diene (3) (3 g) in dichloromethane at 0 °C. The mixture was allowed to warm to 20 °C and was stirred for 18 h before the precipitate of *m*-chlorobenzoic acid was filtered off, and the filtrate stirred for 1 h over anhydrous potassium carbonate. Evaporation of the dichloromethane left the crude hydroxy-epoxides (11) and (12) (2.95 g) as a colourless oil, $\nu_{max.}$ 3 410, 1 640, 1 050, 910, 835, and 720 cm^{-1}; $\delta(CDCl_3)$ 1.15 and 1.16 (3 H, s, CH_3 of each isomer), 2.47 (2 H, m, CH_2), 2.9br (1 H, s, exchanges with D_2O, OH), 3.1 and 3.3 (each 1 H, m, epoxide H), 3.54 (2 H, s, CH_2OH), and 5.35 (2 H, m, vinylic H), together with minor impurity peaks. G.l.c. analysis of this crude mixture (110 °C) showed two major components (I) and (II), relative retention times 17.5 and 21 5, ratio 65 : 35, respectively.

A sample (1 g) of this crude hydroxy-epoxide mixture was reduced with lithium aluminium hydride (0.7 g) in ether using the procedure described above, to give a mixture of *cis*- and *trans*-1,3-diols (17) and (18) (1.1 g) identified by comparison (g.l.c. and n.m.r.) with authentic materials.

Preliminary Investigation of the Epoxidation of 3-*Methyl*-3-*tetrahydropyranyloxymethylcyclohexa*-1,4-*diene* (4).—3-Hydroxymethyl-3-methylcyclohexa-1,4-diene (6 g) and dihydropyran (8.74 ml) were dissolved in anhydrous ether containing toluene-*p*-sulphonic acid (100 mg) and the solution stirred for 18 h at 20 °C. The reaction mixture was then washed with aqueous potassium carbonate and dried (K_2CO_3). The ether was evaporated, and the product distilled, to give the tetrahydropyranyl ether (4) (8.5 g), a colourless oil, b.p. 72 °C at 2 mmHg, $\delta(CDCl_3)$ 1.05 (3 H, s, CH_3), 1.6 (6 H, m, 3 × CH_2 of the tetrahydropyran ring), 2.6 (2 H, m, CH_2 of the cyclohexadiene ring), 3.06 and 3.47 (each 1 H, d, *J* 9 Hz, CH_2O), 3.4—4.1 (2 H, m, CH_2CH_2O), 4.5 (1 H, m, OCHO), and 5.56 (4 H, m, vinylic H).

Solid *m*-chloroperoxybenzoic acid (2.58 g) was added in small portions to a mixture of the tetrahydropyranyl ether (4) (3 g) in dichloromethane (250 ml) and 0.5M-aqueous sodium hydrogen carbonate (75 ml). The mixture was stirred for 18 h at 20 °C before the two phases were separated. The organic layer was washed with 1N-aqueous sodium hydroxide and water and then dried (Na_2SO_4). Evaporation of the dichloromethane gave the crude product (3.2 g) which was distilled to give the *tetrahydropyranyl ether epoxides* (13) and (14) as a colourless oil, homogeneous by g.l.c. (160 °C), b.p. 80—120 °C at 0.5 mmHg, $\nu_{max.}$ 3 030, 1 660, 1 120, 1 080, 1 060, 1 040, 980, and 910 cm^{-1}; $\delta(CDCl_3)$ 1.1 (3 H, s, CH_3), 1.6 (6 H, m, 3 × CH_2 of the tetrahydropyran ring), 2.2 (2 H, m, CH_2 of the cyclohexene ring), 2.8—4.0 (6 H, complex m, epoxide H and 2 × CH_2O), 4.5 (1 H, m, OCHO), and 5.21 (2 H, m, vinylic H) (Found: C, 69.5; H, 9.2. $C_{13}H_{20}O_3$ requires C, 69.6; H, 8.9%). The singlet at δ 1.1 in the ^1H n.m.r. spectrum was split into three peaks on the addition of $Eu(fod)_3$.

In a separate experiment a crude mixture of the epoxides (13) and (14) (4 g) was reduced as described above using lithium aluminium hydride (1.5 g) to give a colourless oil (3.6 g) containing three main components (g.l.c.). A sample (1.5 g) of this oil was dissolved in methanol (30 ml) containing toluene-*p*-sulphonic acid (200 mg), and the solution stirred at 20 °C for 4 h followed by the addition of solid potassium carbonate (0.6 g). The mixture was stirred for 20 min, and the methanol evaporated. Ether was added, the insoluble potassium carbonate filtered off, and the ether evaporated to give a semisolid oil (0.9 g), which was shown to be a mixture of *cis*- and *trans*-1,3-diols (17) and (18) by g.l.c., ratio (17) : (18) = 43 : 57, respectively. Crystallization of the crude diol mixture gave a sample of the *trans*-1,3-diol (18) shown to be identical with an authentic sample (m.p., n.m.r., and g.l.c.).

Epoxidation of Methyl 6-*Acetoxy*-1-*methylcyclohex*-2-*ene*-1-*carboxylate* (5).—*m*-Chloroperoxybenzoic acid (1.62 g) was added to a solution of the acetate (5) (1 g) in anhydrous dichloromethane (20 ml) at 0 °C, and the mixture allowed to warm to room temperature, and stirred for 18 h. The mixture was then diluted with dichloromethane, washed with dilute aqueous sodium sulphite, aqueous sodium hydrogen carbonate, and water, and then dried (Na_2SO_4), and concentrated, to give the epoxides as a colourless solid (1.1 g). Recrystallization from chloroform–hexane gave *methyl* cis-6-*acetoxy*-1-*methylcyclohex*-2-*ene*-1-*carboxylate* trans-*epoxide* (15) (0.7 g) as colourless crystals, m.p. 72—73 °C, $\nu_{max.}(CHCl_3)$ 1 730, 1 240, 1 120, 1 040, and 990 cm^{-1}; δ 1.37 (3 H, s, CH_3), 1.54—1.80 (2 H, m, CH_2), 1.87—2.1 (2 H, m, CH_2), 2.0 (3 H, s, $COCH_3$), 3.37 (1 H, m, H-3), 3.61 (1 H, dd, *J* 1 Hz and 4 Hz, H-2), 3.72 (3 H, s, OCH_3) and 4.87 (1 H, m, $CHOAc$) (Found: C, 57.8; H, 7.0. $C_{11}H_{16}O_5$ requires C, 57.9; H, 7.1%). The mother-liquor from the recrystallization was then chromatographed (eluted with ether–hexane, 1 : 2) to give more *trans*-epoxide (15) (0.13 g) followed by *methyl* cis-6-*acetoxy*-1-*methylcyclohex*-2-*ene*-1-*carboxylate* cis-*epoxide* (16) (0.1 g), a low-melting solid, m.p. 37—38 °C, $\nu_{max.}(CHCl_3)$ 1 730, 1 245, 1 150, and 1 046 cm^{-1}; $\delta(CDCl_3)$ 1.38 (3 H, s, CH_3), 1.2—2.3 (4 H, overlapping m, 2 × CH_2), 2.03 (3 H, s, $COCH_3$), 3.10 (1 H, d, *J* 3.5 Hz, H-2), 3.25 (1 H, m, H-3), 3.77 (3 H, s, OCH_3), and 4.74 (1 H, m, CHOAc) (Found: C, 57.75; H, 7.1%).

Preparation of the Epoxide (7) *from the Bromohydrin* (21).—A solution of the bromohydrin (21) [8] (2 g) and potassium carbonate (1.08 g) in anhydrous methanol (12 ml) was stirred under a dry atmosphere for 2 h at 20 °C. The reaction mixture was then taken up in ether, water was added, and the two layers separated. The ether layer was

washed with water, dried ($MgSO_4$), and evaporated, to give the crude epoxide (7) (1.15 g) which was purified by column chromatography (ether–hexane, 2 : 1), and identified by comparison (g.l.c. and n.m.r.) with an authentic sample prepared by epoxidation of methyl 1-methylcyclohexa-2,5-diene-1-carboxylate, and separation of the isomers.

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