A Fragmentation Approach to a Maytansine Synthon: Lithium Dimethylcuprate-opening of Substituted Cyclohexene Epoxides. *X*-Ray Structure Determination of Ethyl *t*-2,3-Epoxy-*c*-6-*p*-methoxybenzoyloxy-1-methylcyclohexane-*r*-1-carboxylate

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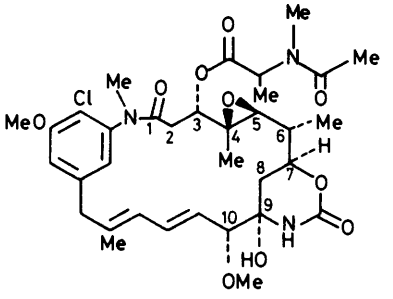
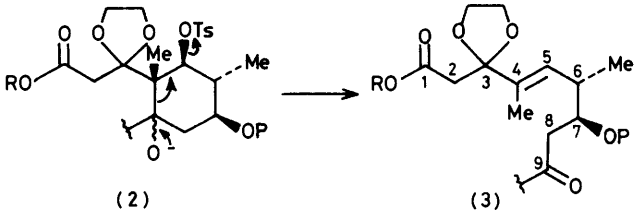
A scheme for the synthesis of maytansine synthons (3) is proposed. As background to this work, the stereoselective synthesis of several cyclohexene epoxides and their reactions with lithium dimethylcuprate are described. The sterically hindered cyclohexadiene monoepoxide (10) and the hydroxycyclohexene epoxide (13) were unreactive towards the cuprate reagent. However, epoxidation of the *c*-6-hydroxy-1-methylcyclohex-2-ene-*r*-1-carboxylate derivatives (18)—(23) gave, selectively, the *trans*-epoxides (24)—(29) which reacted regioselectively with lithium dimethylcuprate to give the alcohols (37)—(39). Epoxidations of the *c*-6-acyloxy-*t*-2-hydroxy-1-methylcyclohex-3-ene-*r*-1-carboxylates (44)—(46) were not stereoselective, whereas methyl *c*-6-benzyloxy-*c*-4-methoxy-1-methylcyclohex-2-ene-*r*-1-carboxylate (55) gave the *trans*-epoxide (56) which was converted into the alcohol (57) on treatment with lithium dimethylcuprate. Sodium borohydride reduction of the ketone (58) gave the *cis*-alcohol (59) which, on epoxidation and treatment with lithium dimethylcuprate, gave the lactone (61).

The structure of the major epoxide (28) obtained on epoxidation of ethyl *c*-6-*p*-methoxybenzoyloxy-1-methylcyclohex-2-ene-*r*-1-carboxylate (22) was confirmed by an *X*-ray structure determination.

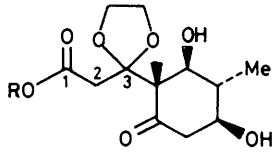
Recently several elegant approaches to the synthesis of maytansine (1), and maytansinoids, have been described.[1] We were interested in developing a maytansine synthesis in which the key step was a Wharton fragmentation [2] of a cyclohexyl toluene-*p*-sulphonate such as compound (2) to generate the synthon (3) which has several features of the 'western zone' of maytansine. In particular, the stereochemistry of the fragmentation precursor (2) should ensure that the C(4)–C(5) double-bond is formed with the correct geometry, and that the chiral centres at C(6) and C(7) have the desired configuration. Moreover the C(9) carbonyl group is introduced during the fragmentation step. As a development of this approach, the introduction of the chiral centres at C(3) and C(10) stereoselectively into the fragmentation precursor was envisaged. We here describe attempts to synthesize polysubstituted cyclohexane derivatives related to the fragmentation precursor (2).



(1)



(2) (3)



(4)

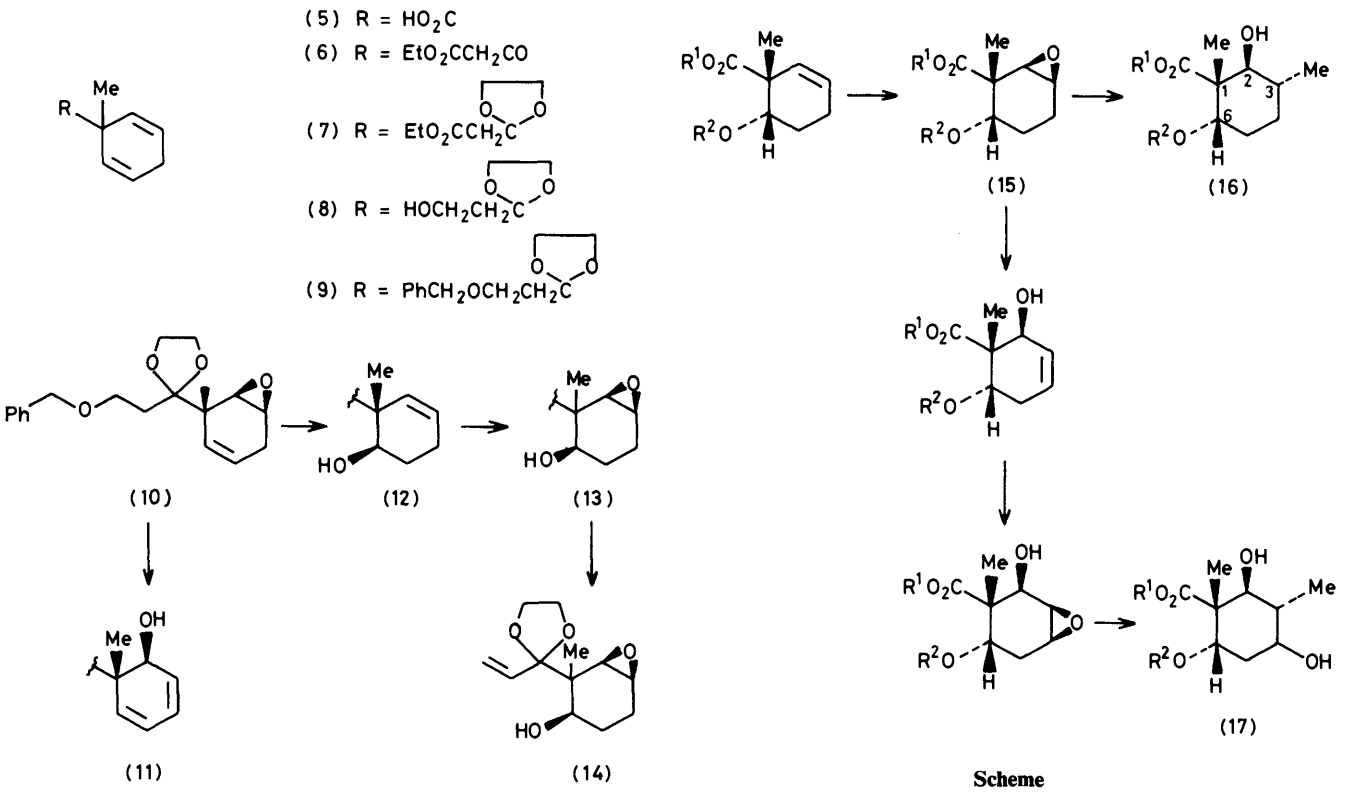
Results and Discussion

The ketone (4) was selected as the initial target. The first approach examined involved the introduction of the bulky C(1)–C(3) side-chain onto a cyclohexadiene ring which was then functionalized using the bulkiness of the side-chain to control the stereochemistry.

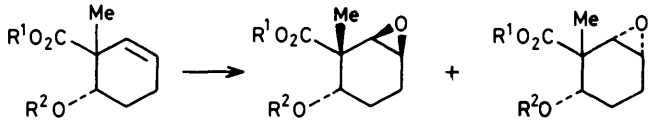
Preparation and Epoxidation of 3-*Benzyloxy*-1-(1-*methylcyclohexa*-2,5-*dien*-1-*yl*)*propan*-1-*one Ethylene Acetal* (9).—Condensation of ethyl acetate with the acid chloride derived from 1-methylcyclohexa-2,5-diene-1-carboxylic acid (5) [3] gave the keto-ester (6) (90%), protected (90%) as its acetal (7).[4] Epoxidation of ester acetal (7) was not very clean; however, reduction with lithium aluminium hydride and treatment with benzyl bromide gave the crystalline ether (9) which, with one equivalent of *m*-chloroperoxybenzoic acid (MCPBA) gave, after chromatography and crystallization, a single epoxide (64%) identified as the *trans*-isomer (10). A small amount of the *cis*-epoxide was detected in the crude epoxidation mixture, the epoxidation stereoselectivity being *ca.* 19 : 1. The stereochemistry shown was assigned on the basis of steric control of the epoxidation.[5]

The plan at this stage was to open the epoxide (10) with lithium dimethylcuprate.[6] However, mainly unchanged starting material (70%) was isolated when the epoxide (10) was treated with an excess of the cuprate reagent, methyl magnesium iodide–copper(I) iodide [7] gave a complex mixture of products, and methyl-lithium gave the diene alcohol (11).[8]

Reduction of the epoxide (10) with lithium aluminium hydride gave the alcohol (12) (97%), regioselectively, as confirmed by its ^{1}H n.m.r. spectrum. Epoxidation of this alcohol



Scheme



(18) R^1 = Me, R^2 = MeCO
(19) R^1 = Et, R^2 = MeCO
(20) R^1 = Me, R^2 = PhCO
(21) R^1 = Me, R^2 = *p*-$MeOC_6H_4CO$
(22) R^1 = Et, R^2 = *p*-$MeOC_6H_4CO$
(23) R^1 = Me, R^2 = $PhCH_2$

(24) R^1 = Me, R^2 = MeCO
(25) R^1 = Et, R^2 = MeCO
(26) R^1 = Me, R^2 = PhCO
(27) R^1 = Me, R^2 = *p*-$MeOC_6H_4CO$
(28) R^1 = Et, R^2 = *p*-$MeOC_6H_4CO$
(29) R^1 = Me, R^2 = $PhCH_2$

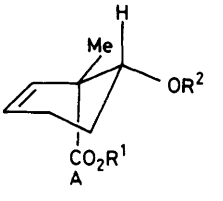
(30) R^1 = Me, R^2 = MeCO
(31) R^1 = Et, R^2 = MeCO
(32) R^1 = Me, R^2 = PhCO
(33) R^1 = Me, R^2 = *p*-$MeOC_6H_4CO$
(34) R^1 = Et, R^2 = *p*-$MeOC_6H_4CO$
(35) R^1 = Me, R^2 = $PhCH_2$

with MCPBA gave a single epoxide, 70% after recrystallization, assigned structure (13) on the assumption that epoxidation had occurred on the less hindered side, *cis* to the hydroxy-group. However, the epoxide (13) was also unreactive towards ring-opening. Thus, unchanged epoxide was obtained after treatment with lithium dimethylcuprate, and methyl magnesium iodide gave a complex mixture of products. Methyl-lithium gave an alkene, tentatively identified as the propene (14).

The lack of reactivity of the epoxides (10) and (13) is probably due to the bulky acetal side-chain which, although cleanly directing epoxidation, screens the epoxides from nucleophilic attack. At this stage it was decided to look at alternative routes to the ketone (4) in which substitution of the cyclohexane ring is developed before introduction of the bulky C(1)–C(3) side-chain.

Preparation and Ring-opening of c-6-*Acyloxy*-t-2,3-*epoxy*-1-*methylcyclohexane*-r-1-*carboxylates*.—The Scheme shows the plan for the next stages of the work. Epoxidation of *c*-6-hydroxy-1-methylcyclohex-2-ene-*r*-1-carboxylic acid derivatives was expected to give selectively the *trans*-epoxides (15). Ring-opening of these epoxides with lithium dimethylcuprate. was envisaged as a route to the hydroxy-esters (16) which have the desired configuration at three chiral centres, C(1), C(2), and C(3), and an acyloxy-group at C(6). The epoxides (15) were also seen as precursors of the dihydroxy-ester (17), *via* isomerization, epoxidation, and (possibly regioselective) cuprate opening The dihydroxy-ester (17) was thought to be a useful precursor of the target ketone (4) since the cyclohexane ring is correctly substituted.

Thus a series of derivatives of *c*-6-hydroxy-1-methylcyclohex-2-ene-*r*-1-carboxylic acid was prepared and epoxidized.[9] In particular the methyl and ethyl ester acetates (18) and (19), the methyl ester benzoate (20), the methyl and ethyl ester *p*-methoxybenzoates (21) and (22), and the methyl ester benzyl ether (23), were prepared and epoxidized with MCPBA. In all cases good yields of epoxides were obtained. The stereo-



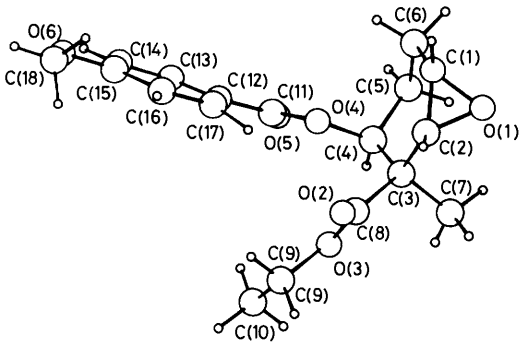


Figure 1. Molecular structure of the epoxide (28) showing the crystallographic numbering scheme used, SNOOPI (see E. K. Davies, ' SNOOPI User Guide,' Chemical Crystallography Laboratory, University of Oxford, Oxford)

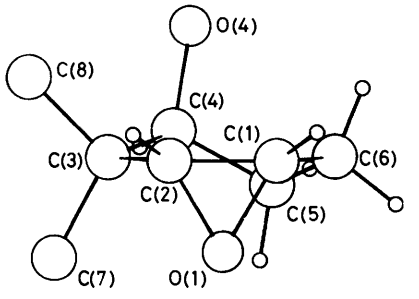
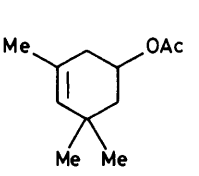


Figure 2. Conformation of the six-membered ring of the epoxide (28) (SNOOPI, see caption to Figure 1)

selectivity of epoxidation of the 6-acyloxy-derivatives (18)—(22) was *ca.* 9 : 1, whereas epoxidation of the benzyl ether (23) was slightly less stereoselective, being *ca.* 7 : 3. The major epoxide in each case was identified as the *trans*-epoxide, *i.e.* (24)—(29). This stereoselectivity was predicted assuming the conformation shown in structure A,* [10] the axial allylic alkoxycarbonyl substituent providing more steric hindrance to epoxidation than the equatorial allylic methyl substituent; [5] the epoxidation of 4-acetoxy-2,6,6-trimethylcyclohexene (36) provides an analogy. This predicted stereoselectivity was confirmed by an *X*-ray crystal structure determination for the major epoxide (28) derived from the ethyl ester *p*-methoxybenzoate. Figure 1 shows a computer-drawn projection of the molecule which clearly illustrates the fact that the epoxide is *cis* to the methyl substituent, and *trans* to the *p*-methoxybenzoyloxy and ethoxycarbonyl substituents. Figure 1 also shows the crystallographic numbering scheme used. Figure 2 shows a projection of the cyclohexane ring to illustrate its unsymmetrical half-chair conformation, with C(1), C(2), C(3), and C(6) in one plane from which C(4) and C(5) deviate in opposite directions by different amounts (0.297 and 0.433 Å). Rather unexpectedly the *p*-methoxybenzoyloxy-substituent is found to be in an axial position, probably because in an equatorial position there would be two gauche interactions. Configurations were assigned to the other epoxides by analogy, and were consistent with a detailed comparison of their ^{1}H n.m.r. spectra and other physical properties, *e.g.* all the major



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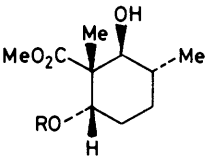
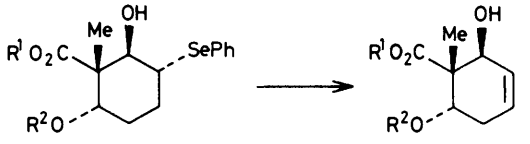


(37) R = $PhCH_2$
(38) R = PhCO
(39) R = *p*-$MeOC_6H_4CO$



(40) R^1 = Me, R^2 = MeCO
(41) R^1 = H, R^2 = MeCO
(42) R^1 = Et, R^2 = MeCO
(43) R^1 = Et, R^2 = *p*-$MeOC_6H_4CO$

(44) R^1 = Me, R^2 = MeCO
(45) R^1 = Et, R^2 = MeCO
(46) R^1 = Et, R^2 = *p*-$MeOC_6H_4CO$

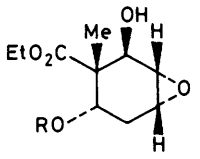
epoxides showed a long range coupling between the epoxide proton H(2) and the equatorial C*H*OR proton.

Next, reactions of the *trans*-epoxides with lithium dimethylcuprate were examined. It was found that, whereas treatment of the acetoxy epoxide (24) with an excess of lithium dimethylcuprate gave a complex mixture of products, the corresponding benzyl ether epoxide (29) reacted cleanly and gave the expected alcohol (37) in good yield (85%). The benzoyloxy epoxide (26) was intermediate in behaviour, the alcohol (38) being isolated in 44% yield, and the *p*-methoxybenzoyloxy epoxide (27) was slightly better giving 55% of chromatographed alcohol (39). The yields of alcohols (37)—(39) would appear to improve as the alcohol protecting group becomes more stable towards nucleophilic attack.

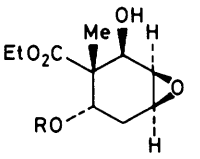
Structures (37)—(39) were assigned to the alcohol products on the basis of their spectroscopic data. Their ^{1}H n.m.r. spectra all showed a new methyl group as a doublet (*J* 6 Hz), together with a double doublet (*J* 3 and *ca.* 11 Hz) which collapsed to a doublet (*J ca.* 11 Hz) on D_2O exchange. This was assigned to the C*H*OH proton, confirming both the regioselectivity of epoxide opening and the *trans* diequatorial relationship of the hydroxy and the new methyl substituents. The C*H*OR (R = $PhCH_2$, PhCO, and *p*-$MeOC_6H_4CO$) proton was shown to be equatorial by its half-height width, consistent with the assigned stereochemistry.

Having prepared alcohols related to structure (16) (Scheme), the proposed route to the diols (17) was studied. Thus the *trans*-acetoxy epoxide (24) was treated with sodium phenylselenide in benzene under reflux to give the crystalline hydroxyselenide (40) (50%).[12,13] This epoxide opening was inefficient because of competing methyl ester cleavage, the free acid (41) being isolated from the aqueous phase after work-up. Use of the ethyl ester epoxide (25) avoided this problem, and the corresponding hydroxy-selenide (42) was isolated in 80% yield. The use of anhydrous conditions during the sodium phenylselenide step was necessary to avoid cleavage of the acetoxy-group during these reactions. The ethyl *p*-methoxybenzoyloxy epoxide (28) similarly gave the hydroxy-selenide (43) (80%). Oxidative elimination of the selenides (40), (42), and (43) gave the allylic alcohols (44)—(46) in yields of 60—65%. Fairly vigorous conditions were required for these selenoxide eliminations, which were carried out either in tetrahydrofuran (THF) under reflux, with an excess of hydro-

* Epoxidation stereoselectivity is frequently explained using ground-state conformations.[11] 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 that of the starting alkene.



(47) R = *p*-MeOC$_6$H$_4$CO

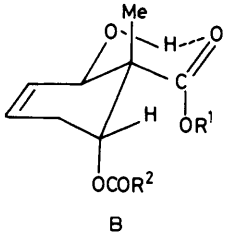


(48) R = *p*-MeOC$_6$H$_4$CO

gen peroxide added in portions,[14] or by using MCPBA at 0 °C followed by addition of the reaction mixture to carbon tetrachloride while heated under reflux.[15]

However, epoxidations of the allylic alcohols (44)—(46) were not stereoselective. It was found that treatment of the alcohols (44) and (45) with MCPBA gave 1 : 1 mixtures of two monoepoxides which could not be separated. Epoxidation of the *p*-methoxybenzoyloxy-alcohol (46) with MCPBA gave a 7 : 3 mixture of two epoxides which were partially separated, with difficulty, by chromatography; the major isomer was found to be that with the epoxide ring *trans* to the hydroxy-function, *i.e.* isomer (47). This assignment was made on the basis of zero coupling between the C*H*OH proton and the vicinal epoxide proton, 3-H, in its ^{1}H n.m.r. spectrum.[16] In contrast a 2.9 Hz coupling was observed between the corresponding protons in the ^{1}H n.m.r. spectrum of the minor isomer identified as the epoxide (48).

These non-selective epoxidations were disappointing, and were rationalized on the basis of the conformation of the allylic alcohol shown in structure B. The *syn*-directing in-



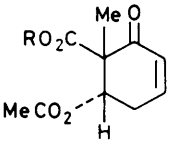
B

fluence of an allylic alcohol substituent in peracid epoxidation is known to be rather weak.[11] In the conformation shown it is possible that the axial methyl and acyloxy substituents dominate the epoxidation stereoselectivity, the allylic alcohol being hydrogen-bonded to the neighbouring ester. This conformation is consistent with the ^{1}H n.m.r. spectra of these allylic alcohols.

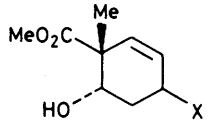
The epoxidation of the allylic alcohols (44) and (45) by t-butyl hydroperoxide in the presence of VO(acac)$_2$ and of Mo(CO)$_6$ was investigated, but in both cases the major products were the enones (49) and (50).[17] The oxidation of conformationally ' rigid ' equatorial allylic alcohols to enones is known to predominate over epoxidation under these conditions.[28]

At this point the synthesis of the diol (17) by the route outlined in the Scheme was discontinued because of the problems associated with the stereoselectivity of the second epoxidation step and because preliminary reactions between the minor epoxide (48) and lithium dimethylcuprate were not encouraging. Instead an alternative route was pursued involving allylic oxidation of *c*-6-hydroxy-1-methylcyclohex-2-ene-*r*-1-carboxylic acid derivatives.

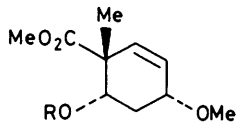
Allylic Oxidation of Methyl c-6-*Hydroxy*-1-*methylcyclohex*-2-*ene*-r-1-*carboxylate* (51).—Treatment of the parent methyl hydroxy-ester (51) with *N*-bromosuccinimide [19] gave the



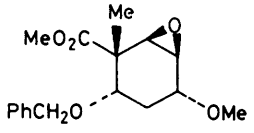
(49) R = Me
(50) R = Et



(51) X = H
(52) X = Br



(53) R = H
(54) R = *p*-MeOC$_6$H$_4$CO
(55) R = PhCH$_2$



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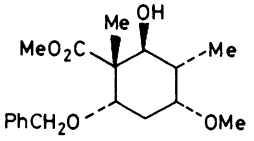
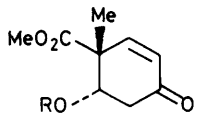


(57)

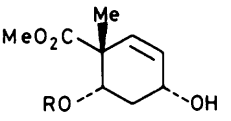
allylic bromides (52) which on methanolysis gave a single product identified as methyl *c*-6-hydroxy-*c*-4-methoxy-1-methylcyclohex-2-ene-*r*-1-carboxylate (53). The structure of the hydroxy-ether (53) was established by the ^{1}H n.m.r. spectrum of its *p*-methoxybenzoate (54). In particular, a multiplet (δ 3.97) which collapsed to a small triplet (*J* 1.5 Hz), on irradiation of the methylene protons, was assigned to C*H*OMe, this proton being axial with small vicinal and moderate allylic coupling. A double doublet at δ 5.02 was assigned to C*H*OCOAr (*J* 4.6 and 9.7 Hz) showing this proton to be axial.

Treatment of the benzyl ether (55) prepared from the alcohol (53) using benzyl bromide–sodium hydride with MCPBA gave two epoxides in the ratio 3 : 1. The major epoxide was identified as isomer (56), and was treated with lithium dimethylcuprate to give the alcohol (57). A comparison of this alcohol with the target ketone (4) shows that the alcohol has all the desired cyclohexyl substituents, and has the correct stereochemistry apart from the configuration of the C(4) methoxy-group. The stereochemistry assigned to the alcohol was consistent with its ^{1}H n.m.r. spectrum. A doublet (after shaking with D_2O) at δ 4.38 was assigned to C*H*OH; its splitting (*J* 11.8 Hz) showed that the hydroxy and newly introduced methyl groups were *trans* and diequatorial. A narrow multiplet at δ 3.84, with a half-height width of 6 Hz, characteristic of an equatorial proton, was assigned to C*H*OBz. A multiplet at δ 1.78 was assigned to C*H*Me. This, on irradiation of the methyl doublet, collapsed to a double doublet (*J* 4 and 11.8 Hz), the smaller coupling being an axial–equatorial coupling with C*H*OMe. These data support the stereochemical assignments made in structure (57).

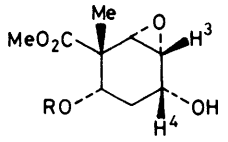
As a final attempt to establish the desired stereochemistry at C(4), methyl *c*-6-*p*-methoxybenzoyloxy-1-methylcyclohex-2-ene-*r*-1-carboxylate (21) was oxidized with 3,5-dimethylpyrazole–chromium trioxide [20] to give the crystalline enone (58). However, reduction of this enone with sodium borohydride gave a single alcohol (59). The C(4) configuration of this alcohol could not be unambiguously established by ^{1}H n.m.r., but formation of the *cis*-isomer shown involves ap-



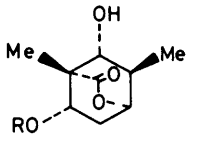
(58) R = *p*-$MeOC_6H_4CO$



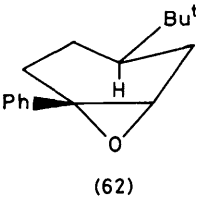
(59) R = *p*-$MeOC_6H_4CO$



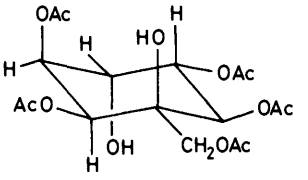
(60) R = *p*-$MeOC_6H_4CO$



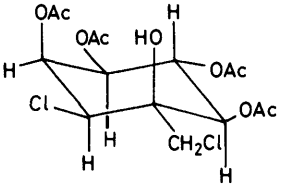
(61) R = *p*-$MeOC_6H_4CO$



(62)



(63)



(64)

proach of the hydride from the less hindered side of the carbonyl group. This stereochemistry was later confirmed (see below). Epoxidation of the alcohol (59) with MCPBA gave a single epoxide (60), shown to have the epoxide *cis* to the hydroxy-group by an H(3)–H(4) coupling in its proton spectrum. An excess of lithium dimethylcuprate reacted with the epoxide (60) at 0 °C to give a mixture of products; the major product was isolated by chromatography and identified as the bicyclic lactone (61). The formation of this lactone confirmed the stereochemistry assigned to the alcohol (59), and extensive spin-decoupling studies on the lactone were consistent with the other stereochemical assignments.

At this point, because of the success of other approaches to maytansine,[1] our work was discontinued. Improvements in acyclic stereochemical control since our project was first conceived have enabled shorter routes to maytansine synthons to be developed.[21] It would appear that the additional stereochemical complexities introduced in the preparation of polycyclic fragmentation precursors render fragmentation approaches to macrocyclic compounds inefficient except in special circumstances.[22] In our case, the synthesis could be continued from the hydroxy ether (57), an equilibration step later in the synthesis being used to correct the configuration at C(4), or an alternative procedure could be developed for the reduction of the ketone (58). However, it is likely that multiple protection and deprotection steps would be required in both of these routes, thus making them inefficient overall. Nevertheless, our work has established routes to several highly substituted cyclohexane derivatives, and has shown some limitations to the epoxidation–lithium dimethylcuprate procedure in these systems.

Discussion of the Crystal Structure of the Epoxide (28).—The crystal structure of the epoxide (28) is particularly interesting. The bond lengths and bond angles are given in Tables 1 and 2, respectively. The C(4)–C(5) bond (crystallographic numbering) is very short; no similar phenomenon was observed in the other three reasonable cyclohexene epoxide structures reported,[23,24] *e.g.* for the accurate structure of the epoxide (62), C(4)–C(5) = 1.549 (3) Å.[24] The atoms O(4) and H(51) are arranged in an almost antiperiplanar fashion about the C(4)–C(5) bond [torsion angle: O(4)–C(4)–C(5)–H(51) = 174.6°], and the structure may represent a position a short way along the reaction co-ordinate for the *trans*-elimination of *p*-methoxybenzoic acid, the bond shortening being due to the development of some double-bond character. However the O(4)–C(4) bond [1.440(3) Å] does not show any appreciable lengthening (*cf.* 1.445 Å from a survey of alkyl esters of aromatic acids [25]).

The two other accurate crystal structures [26,27] of cyclohexyl esters in which an oxycarbonyl group takes an axial position, (63) and (64), also show short equivalent carbon–carbon bonds and no lengthening of the oxygen–carbon bond [(63): C(2)–C(3) 1.506(5), C–O 1.433(5); (64): C(2)–C(3) 1.515, C(3)–C(4) 1.509, C–O 1.438 Å].

Table 1. Bond lengths (Å) for the epoxide (28) with e.s.d.s in parentheses

O(1)–C(1)	1.428(5)	C(3)–C(4)	1.532(4)
O(1)–C(2)	1.432(4)	C(3)–C(7)	1.524(4)
O(2)–C(8)	1.198(4)	C(3)–C(8)	1.506(5)
O(3)–C(8)	1.333(4)	C(4)–C(5)	1.505(5)
O(3)–C(9)	1.440(5)	C(5)–C(6)	1.530(5)
O(4)–C(4)	1.440(3)	C(9)–C(10)	1.458(7)
O(4)–C(11)	1.346(3)	C(11)–C(12)	1.460(4)
O(5)–C(11)	1.205(4)	C(12)–C(13)	1.388(4)
O(6)–C(15)	1.346(4)	C(12)–C(17)	1.390(4)
O(6)–C(18)	1.416(5)	C(13)–C(14)	1.363(5)
C(1)–C(2)	1.441(5)	C(14)–C(15)	1.397(5)
C(1)–C(6)	1.499(6)	C(15)–C(16)	1.377(4)
C(2)–C(3)	1.528(5)	C(16)–C(17)	1.368(4)

A further unusual feature of the epoxide (28) is the unsymmetrical values for the angles at C(4) between the O(4)–C(4) bond and the carbon–carbon bonds of the cyclohexane ring, O(4)–C(4)–C(3) = 104.2(2); O(4)–C(4)–C(5) = 109.9(3)°. The larger angle is close to what might be expected to be the preferred angle of departure of the aroyloxy-group in the elimination reaction.[28] However, the situation is further complicated by the close approach between O(4) and the carbonyl carbon C(8) (2.57 Å) where, although no covalent interaction is apparent,[29] there may be an electrical attraction.

The mean C–O bond length in the epoxide ring of compound (28) is similar to that in unfused epoxides (1.436 Å),* though shorter than that for the similar fused epoxide (62) (1.457 Å). The plane of the epoxide ring makes an angle of 102.5° with the best plane through C(1), C(2), C(3), and C(6). In the aroyloxy-residue, the best plane through the benzene ring makes an angle of 21.4° with the carboxy-group.

Experimental

I.r. spectra were measured on Perkin-Elmer 257 and 297 spectrophotometers, and ^1H n.m.r. spectra on Perkin-Elmer

* Figure from the Cambridge Crystallographic Database excluding those structures with e.s.d.s >0.01 Å for C–C single bonds.

Table 2. Bond angles (°) for the epoxide (28) with e.s.d.s in parentheses

C(1)–O(1)–C(2)	60.5(2)	C(4)–C(5)–C(6)	111.6(3)
C(8)–O(3)–C(9)	118.4(3)	C(1)–C(6)–C(5)	111.9(3)
C(4)–O(4)–C(11)	118.5(2)	O(2)–C(8)–O(3)	123.2(3)
C(15)–O(6)–C(18)	118.5(3)	O(2)–C(8)–C(3)	126.8(3)
O(1)–C(1)–C(2)	59.9(2)	O(3)–C(8)–C(3)	110.0(3)
O(1)–C(1)–C(6)	115.4(3)	O(3)–C(9)–C(10)	107.1(4)
C(2)–C(1)–C(6)	121.6(3)	O(4)–C(11)–O(5)	122.4(3)
O(1)–C(2)–C(1)	59.6(2)	O(4)–C(11)–C(12)	112.0(3)
O(1)–C(2)–C(3)	114.9(3)	O(5)–C(11)–C(12)	125.6(3)
C(1)–C(2)–C(3)	122.3(3)	C(11)–C(12)–C(13)	119.0(3)
C(2)–C(3)–C(4)	111.4(3)	C(11)–C(12)–C(17)	122.5(3)
C(2)–C(3)–C(7)	109.9(3)	C(13)–C(12)–C(17)	118.5(3)
C(2)–C(3)–C(8)	108.6(3)	C(12)–C(13)–C(14)	120.7(3)
C(4)–C(3)–C(7)	110.9(3)	C(13)–C(14)–C(15)	120.3(3)
C(4)–C(3)–C(8)	108.0(3)	O(6)–C(15)–C(14)	116.1(3)
C(7)–C(3)–C(8)	108.0(3)	O(6)–C(15)–C(16)	124.5(3)
O(4)–C(4)–C(3)	104.2(2)	C(14)–C(15)–C(16)	119.4(3)
O(4)–C(4)–C(5)	109.9(3)	C(15)–C(16)–C(17)	120.0(3)
C(3)–C(4)–C(5)	112.7(3)	C(12)–C(17)–C(16)	122.0(3)

R 12 B and R 24, and on Bruker HFX-90 and WH-300 spectrometers. M.p.s were determined using a Kofler hot-stage apparatus. Mass spectra were measured on AEI MS 30 and VG-micromass ZAB-IF spectrometers [sometimes using chemical ionization which gave (M + 1) peaks].

T.l.c. was carried out on Merck $60F_{254}$ silica gel precoated plates, and short-column chromatography was used for preparative purposes using Hopkin and Williams silica gel for t.l.c. (MFC without binder), with ether–light petroleum as eluant unless stated otherwise. Light petroleum refers to the fraction with boiling range 20—30 °C and ether to diethyl ether throughout. All solvents were dried and distilled before use.

Ethyl 3-(1-*Methylcyclohexa*-2,5-*dien*-1-*yl*)-3-*oxopropanoate Ethylene Acetal* (7).—Ethyl acetate (4.4 g) was added to lithium isopropylcyclohexylamide (from 14.12 g isopropylcyclohexylamine) in ether–hexane at −78 °C followed, after 15 min, by 1-methylcyclohexa-2,5-dienoyl chloride (7.83 g). The reaction mixture was stirred for 20 min at −78 °C and allowed to warm to 0 °C. After addition of dilute hydrochloric acid (30 ml), and separation of the layers, ether extraction gave an oil (9.3 g), a sample of which was distilled and chromatographed to give *ethyl* 3-(1-*methylcyclohexa*-2,5-*dien*-1-*yl*)-3-*oxopropanoate* (6), b.p. 72—74 °C at 0.15 mmHg; $\nu_{max.}$ (film) 3 030, 1 740, 1 710, 1 315, 1 025, and 720 cm^{-1}; δ ($CDCl_3$) 1.26 (3 H, s, Me), 1.26 (3 H, t, J 7 Hz, CH_2CH_3), 2.79 (2 H, m, CH_2), 3.57 (2 H, s, $COCH_2CO$), 4.16 (2 H, q, J 7 Hz, OCH_2CH_3), and 5.5—5.95 (4 H, m, vinylic H); *m/e* 208 (M^+) and 93 (base peak).

The crude keto-ester (6) (3 g), toluene-*p*-sulphonic acid (0.2 g), and ethylene glycol (5.3 g) were heated in benzene under reflux using a Dean–Stark trap for 24 h. Conventional work-up and column chromatography gave *ethyl* 3-(1-*methylcyclohexa*-2,5-*dien*-1-*yl*)-3-*oxopropanoate ethylene acetal* (7) (2.35 g) as a colourless oil, $\nu_{max.}$ (film) 3 040, 1 730, 1 630, 1 195, 1 100, 1 040, and 720 cm^{-1}; δ ($CDCl_3$) 1.04 (3 H, s, Me), 1.25 (3 H, t, J 7 Hz, CH_2CH_3), 2.63 (2 H, m, CH_2), 2.75 (2 H, s, CH_2CO), 4.0—4.2 (6 H, m, OCH_2CH_2O and OCH_2CH_3), and 5.75 (4 H, m, vinylic H); *m/e* 253 (M^+ + 1) and 159 (base peak).

3-*Benzyloxy*-1-(1-*methylcyclohexa*-2,5-*dien*-1-*yl*)*propan*-1-*one Ethylene Acetal* (9).—The acetal ester (7) (22 g) in ether (50 ml) was added slowly to a suspension of lithium aluminium hydride (6.6 g) in ether (150 ml), and the mixture was heated under reflux for 3 h. Work-up with methanol and saturated aqueous ammonium chloride gave a granular precipitate; this was filtered off and the solvent was evaporated to give an oil, which after chromatography gave 3-*hydroxy*-1-(1-*methylcyclohexa*-2,5-*dien*-1-*yl*)*propan*-1-*one ethylene acetal* (8) (11.6 g) as a colourless oil, homogeneous by t.l.c.; $\nu_{max.}$ (film) 3 400, 3 030, 1 635, 1 100, 760, and 720 cm^{-1}; δ ($CDCl_3$) 1.05 (3 H, s, Me), 2.02 (2 H, t, J 5.7 Hz, OCH_2CH_2), 2.4 (1 H, br s, exch. D_2O, OH), 2.64 (2 H, m, CH_2), 3.70 (2 H, t, J 5.7 Hz, OCH_2CH_2), 4.09 (4 H, s, OCH_2CH_2O), and 5.71 (4 H, m, vinylic H); *m/e* 211 (M^+ + 1) and 117 (base peak).

The acetal alcohol (8) (3.6 g) and benzyl bromide (2.91 g) in anhydrous toluene (10 ml) were added to a suspension of sodium hydride (1.65 g; 50% dispersion in oil, washed with ether) in toluene (30 ml), and the mixture heated under reflux for 3 h. After cooling and catious quenching with water, ether extraction gave a crude product (5.1 g) which was crystallized from light petroleum to give 3-*benzyloxy*-1-(1-*methylcyclohexa*-2,5-*dien*-1-*yl*)*propan*-1-*one ethylene acetal* (9) (4.0 g), m.p. 52 °C; $\nu_{max.}$ ($CHCl_3$) 3 090, 3 070, 3 010, 1 635, 1 100, 950, and 700 cm^{-1}; δ ($CDCl_3$) 1.03 (3 H, s, Me), 2.12 (2 H, t, J 7 Hz, OCH_2CH_2), 2.60 (2 H, m, CH_2), 3.54 (2 H, t, J 7 Hz, OCH_2CH_2), 3.96 (4 H, m, OCH_2CH_2O), 4.47 (2 H, s, CH_2Ph), 5.71 (4 H, m, vinylic H), and 7.31 (5 H, s, aromatic H); *m/e* 301 (M^+ + 1) and 209 (base peak) (Found: C, 76.1; H, 8.1. $C_{19}H_{24}O_3$ requires C, 75.97; H, 8.05%).

r-1-(3-*Benzyloxy*-1-*oxopropyl*)-t-5,6-*epoxy*-1-*methylcyclohex*-2-*ene Ethylene Acetal* (10).—MCPBA (3.5 g) in chloroform (30 ml) was added to a solution of the diene (9) (5.7 g) in chloroform (20 ml) at 20 °C, and the mixture was stirred for 20 h. Anhydrous potassium carbonate was added and the solution filtered and concentrated under reduced pressure to give the crude epoxide (5.6 g) which was chromatographed on silica, and crystallized from ether–light petroleum to give the trans-*epoxide* (10) (3.6 g), m.p. 64 °C; $\nu_{max.}$ ($CHCl_3$) 3 050, 1 455, 1 370, 1 100, 1 043, and 855 cm^{-1}; δ ($CDCl_3$) 1.13 (3 H, s, Me), 2.08 (2 H, m, OCH_2CH_2), 2.45 (2 H, m, CH_2), 3.25 (2 H, m, epoxide H), 3.55 (2 H, t, J 7 Hz, OCH_2CH_2), 4.00 (4 H, m, OCH_2CH_2O), 4.48 (2 H, s, OCH_2Ph), 5.38 (2 H, m, vinylic H), and 7.32 (5 H, s, aromatic H); *m/e* 317 (M^+) (Found: C, 72.15; H, 7.55. $C_{19}N_{24}O_4$ requires C, 72.12; H, 7.64%).

The epoxide (10) (200 mg) and methyl-lithium (7 ml of an 0.55M-solution in ether) at 20 °C for 24 h gave, after aqueous work-up and chromatography, t-6-(3-*benzyloxy*-1-*oxopropyl*)-c-6-*methylcyclohexa*-2,4-*dien*-r-1-*ol ethylene acetal* (11) (140 mg) as a colourless oil, $\nu_{max.}$ (film) 3 500, 3 040, 1 600, 1 450, 1 400, 1 365, 1 250, 1 200, and 1 100 cm^{-1}; δ ($CDCl_3$) 0.96 (3 H, s, Me), 2.15 (2 H, m, OCH_2CH_2), 3.2 (1 H, s, exch. with D_2O, OH), 3.68 (2 H, t, J 7 Hz, OCH_2CH_2), 3.95 (4 H, s, OCH_2CH_2O), 4.50 (2 H, s, CH_2Ph), 4.90 (1 H, br s, $CHOH$), 5.7 (4 H, m, vinylic H), and 7.3 (5 H, m, aromatic H); *m/e* 317 (M^+ + 1).

t-2-(3-*Benzyloxy*-1-*oxopropyl*)-c-2-*methylcyclohex*-3-*en*-r-1-*ol Ethylene Acetal* (12).—The epoxide (10) (3.5 g) in ether (25 ml) was added to a suspension of lithium aluminium hydride (2.0 g) in ether (20 ml), and the mixture was heated under reflux for 6 h. Work-up as above gave the alcohol (12) (3.4 g); a sample was crystallized from ether–light petroleum to give t-2-(3-*benzyloxy*-1-*oxopropyl*)-c-2-*methylcyclohex*-3-*en*-r-1-*ol ethylene acetal* (12), m.p. 54—55 °C; $\nu_{max.}$ ($CHCl_3$) 3 520 and 1 070 cm^{-1}; δ (C_6D_6) 1.10 (3 H, s, Me), 1.69—2.23 (6 H, m, 3 × CH_2), 3.4 (1 H, s, exch. D_2O, OH), 3.50 (6 H, m, 3 × OCH_2), 4.10 (1 H, dd, J 3, 11.7 Hz, $CHOH$), 4.30 (2 H, s, OCH_2Ph), 5.47 and 5.67 (each 1 H, m, vinylic H), and 7.3

(5 H, m, aromatic H) (Found: C, 71.95; H, 7.95. $C_{19}H_{26}O_4$ requires C, 71.67; H, 8.23%).

t-2-(3-*Benzyloxy*-1-*oxopropyl*)-c-3,4-*epoxy*-c-2-*methylcyclohexan*-r-1-*ol Ethylene Acetal* (13).—MCPBA (0.65 g) in chloroform (20 ml) was added to the cyclohexanol (12) (1.0 g) in chloroform at 0 °C, and the mixture stirred for 16 h at 20 °C. The precipitate was filtered off and the filtrate was washed with aqueous sodium sulphite (20 ml), aqueous sodium hydrogen carbonate, and brine, and then dried ($MgSO_4$). Concentration under reduced pressure and crystallization from ether–light petroleum gave the cis-*epoxide* (13) (0.7 g), m.p 82 °C; $\nu_{max.}$ ($CHCl_3$) 3 530 and 1 075 cm^{-1}; δ ($CDCl_3$) 1.02 (3 H, s, Me), 1.34—2.26 (6 H, m, 3 × CH_2), 2.94 (1 H, d, *J* 3.7 Hz, epoxide H), 3.0 (1 H, s, exch. D_2O, OH), 3.09 (1 H, m, epoxide H), 3.54 (2 H, t, *J* 7 Hz, OCH_2), 3.64 (1 H, dd, *J* 3.9, 11.6 Hz, CHOH), 3.95 (4 H, m, OCH_2CH_2O), 4.44 (2 H, s, OCH_2Ph), and 7.27 (5 H, m, aromatic H) (Found: C, 68.45; H, 7.8. $C_{19}H_{26}O_5$ requires C, 68.24; H, 7.84%).

Treatment of the epoxide (13) (200 mg) with methyllithium (2.5 ml of a 1.6M solution in ether) for 60 h at 20 °C gave unchanged epoxide together with *c*-3,4-epoxy-*c*-2-methyl-*t*-2-(1-oxopropen-1-yl)cyclohexan-*r*-1-ol (14) (40 mg) as an oil, $\nu_{max.}$ (film) 3 500 and 1 070 cm^{-1}; δ ($CDCl_3$) 1.1 (3 H, s, Me), 1.3—2.3 (4 H, m, 2 × CH_2), 3.0 (1 H, d, *J* 4 Hz, epoxide H), 2.95 (1 H, s, exch. D_2O, OH), 3.15 (1 H, m, epoxide H), 3.6—4.1 (5 H, m, OCH_2CH_2O and CHOH), and 5.35—6.0 (3 H, m, vinylic H).

Ethyl c-2-*Hydroxy*-1-*methylcyclohex*-5-*ene*-r-1-*carboxylate*.—*c*-2-Hydroxy-1-methylcyclohex-5-ene-*r*-1-carboxylic acid (2 g) [9] and boron trifluoride–ether (1.66 ml) in ethanol (30 ml) were heated under reflux for 3.5 h.[30] Concentration under reduced pressure, dilution with water, and extraction from ether gave *ethyl* c-2-*hydroxy*-1-*methylcyclohex*-5-*ene*-r-1-*carboxylate* (2.08 g) as a colourless oil, $\nu_{max.}$ (film) 3 500, 3 010, 1 760, and 1 730 cm^{-1}; δ ($CDCl_3$) 1.27 (3 H, t, *J* 7 Hz, CH_2CH_3), 1.37 (3 H, s, Me), 1.74—2.4 (4 H, m, 2 × CH_2), 3.31 (1 H, d, exch. D_2O, OH), 3.67 (1 H, m, CHOH), 4.18 (2 H, q, *J* 7 Hz, OCH_2CH_3), and 5.55—5.81 (2 H, m, vinylic H) (Found: M^+ 184.1100. $C_{10}H_{16}O_3$ requires *M* 184.1095).

Preparation and Epoxidation of Ethyl c-6-*Acetoxy*-1-*methylcyclohex*-2-*ene*-r-1-*carboxylate* (19).—Ethyl *c*-2-hydroxy-1-methylcyclohex-5-ene-*r*-1-carboxylate (2.0 g) and acetic anhydride (2.3 g) in anhydrous pyridine (20 ml) were stirred at 20 °C for 16 h and at 80 °C for 3 h. Dilution with water and ether extraction gave the crude ester (19) (2.15 g); a sample was purified by chromatography to give *ethyl* c-6-*acetoxy*-1-*methylcyclohex*-2-*ene*-r-1-*carboxylate* (19) as an oil, $\nu_{max.}$ (film) 3 010, 1 780, 1 733, 1 240, 1 110, and 1 040 cm^{-1}; δ ($CDCl_3$) 1.31 (3 H, s, Me), 1.25 (3 H, t, *J* 7 Hz, CH_2CH_3), 2.01 (3 H, s, CH_3CO), 1.80—2.10 (4 H, m, 2 × CH_2), 4.17 (2 H, q, *J* 7 Hz, OCH_2CH_3), 5.16 (1 H, m, CHOAc), and 5.79 (2 H, m, vinylic H) (Found: M^+ 184.1100. $C_{12}H_{18}O_4$ requires $M - CH_2{=}C{=}O$ 184.1095).

The crude ester (19) (2.0 g) was treated with MCPBA (1.68 g) in dichloromethane to give a mixture of epoxides (1.97 g) in the ratio (^1H n.m.r.) 85 : 15. Crystallization from ether–light petroleum gave the trans-*epoxide* (25) (1.4 g), m.p. 65.5—66 °C, $\nu_{max.}$ ($CHCl_3$) 1 725 and 1 250 cm^{-1}; δ ($CDCl_3$) 1.25 (3 H, t, *J* 7 Hz, CH_2CH_3), 1.37 (3 H, s, Me), 1.60—2.00 (4 H, m, 2 × CH_2), 1.99 (3 H, s, CH_3CO), 3.34 (1 H, m, epoxide 3-H), 3.63 (1 H, dd, *J* 1, 4 Hz, epoxide 2-H), 4.17 (2 H, q, *J* 7 Hz, CH_2CH_3), and 4.90 (1 H, m, CHOAc) (Found: C, 59.5; H, 7.6. $C_{12}H_{18}O_5$ requires C, 59.48; H, 7.49%). Chromatography of the mother-liquor from the crystallization gave the cis-*epoxide* (31) (0.26 g) as a colourless oil, $\nu_{max.}$ ($CHCl_3$) 1 770, 1 700, and 1 230 cm^{-1}; δ ($CDCl_3$) 1.29 (3 H, t, *J* 7 Hz, CH_2CH_3), 1.37 (3 H, s, Me), 1.59—1.95 (4 H, m, 2 × CH_2), 2.03 (3 H, s, CH_3CO), 3.10 (1 H, d, *J* 3.5 Hz, epoxide 2-H), 3.23 (1 H, m, epoxide 3-H), 4.24 (2 H, q, *J* 7 Hz, OCH_2CH_3), and 4.76 (1 H, m, CHOAc) (Found: M^+ 197.0808. $C_{12}H_{18}O_5$ requires M − OEt 197.0813).

Preparation and Epoxidation of Methyl c-6-*Benzoyloxy*-1-*methylcyclohex*-2-*ene*-r-1-*carboxylate* (20).—Treatment of methyl *c*-6-hydroxy-1-methylcyclohex-2-ene-*r*-1-carboxylate (51) (300 mg) with benzoyl chloride (0.2 ml) in anhydrous pyridine at 20 °C for 17 h gave, after addition of water, ether extraction, and chromatography, *methyl* c-6-*benzoyloxy*-1-*methylcyclohex*-2-*ene*-r-1-*carboxylate* (20) (526 mg) as a colourless oil; $\nu_{max.}$ (film) 1 730, 1 600, and 1 585 cm^{-1}; δ ($CDCl_3$) 1.35 (3 H, s, Me), 2.15 (4 H, m, 2 × CH_2), 3.6 (3 H, s, CO_2Me), 5.4 (1 H, m, CHO), 5.8 (2 H, m, vinylic H), and 7.2—8.2 (5 H, m, aromatic H). Treatment of this ester (0.45 g) with MCPBA (0.35 g) in chloroform gave crude epoxides (0.47 g) which were separated by chromatography. The first eluted product was the trans-*epoxide* (26) (300 mg), a colourless oil; $\nu_{max.}$ (film) 1 740, 1 720, 1 600, 1 270, and 715 cm^{-1}; δ ($CDCl_3$) 1.44 (3 H, s, Me), 1.70—2.05 (4 H, m, 2 × CH_2), 3.5 (1 H, m, epoxide 3-H), 3.61 (3 H, s, CO_2Me), 3.73 (1 H, dd, *J* 1.3, 3.9 Hz, epoxide 2-H), 5.13 (1 H, m, CHO), and 7.28—7.60 (5 H, m, aromatic H) (Found: C, 65.95; H, 6.4. $C_{16}H_{18}O_5$ requires C, 66.20; H, 6.25%). The second eluted product was the cis-*epoxide* (32) (20 mg), a colourless oil, δ ($CDCl_3$) 1.36 (3 H, s, Me), 1.5—2.1 (4 H, m, 2 × CH_2), 3.13 (1 H, d, *J* 3.8 Hz, epoxide 2-H), 3.25 (1 H, m, epoxide 3-H), 3.65 (3 H, s, CO_2Me), 5.0 (1 H, m, CHO), and 7.3—8.1 (5 H, m, aromatic H).

Preparation and Epoxidation of Methyl c-6-p-*Methoxybenzoyloxy*-1-*methylcyclohex*-2-*ene*-r-1-*carboxylate* (21).—Methyl *c*-6-hydroxy-1-methylcyclohex-2-ene-*r*-1-carboxylate (51) (1.0 g) and *p*-methoxybenzoyl chloride (1.1 g) in pyridine (8 ml) at 20 °C for 17 h gave, after isolation as above, *methyl* c-6-p-*methoxybenzoyloxy*-1-*methylcyclohex*-2-*ene*-r-1-*carboxylate* (21) (1.5 g) as a colourless oil; $\nu_{max.}$ (film) 1 735, 1 710, 1 610, 1 580, 1 510, and 1 250 cm^{-1}; δ ($CDCl_3$) 1.35 (3 H, s, Me), 2.15 (4 H, m, 2 × CH_2), 3.61 (3 H, s, OMe), 3.81 (3 H, s, OMe), 5.3 (1 H, m, CHO), 5.8 (2 H, m, vinylic H), and 6.85 and 7.85 (each 2 H, m, aromatic H); *m/e* 305 ($M^+ + 1$). Treatment of this ester (21) (1.5 g) with MCPBA (1.2 g) in chloroform (15 ml) gave a crude mixture of epoxides (1.5 g) which was crystallized from ether–light petroleum to give trans-*epoxide* (27) (1.2 g) as colourless crystals, m.p. 67 °C; $\nu_{max.}$ ($CHCl_3$) 3 010, 1 730, 1 710, 1 610, 1 580, and 1 510 cm^{-1}; δ ($CDCl_3$) 1.36 (3 H, s, Me), 1.7—2.0 (4 H, m, 2 × CH_2), 3.35 (1 H, m, epoxide 3-H), 3.52 (3 H, s, OMe), 3.64 (1 H, dd, *J* 1.3, 3.9 Hz, epoxide 2-H), 3.78 (3 H, s, OMe), 5.01 (1 H, m, CHO), and 6.84 and 7.84 (each 2 H, m, aromatic H); *m/e* 320 (M^+) and 135 (base peak) (Found: C, 63.75; H, 6.2. $C_{17}H_{20}O_6$ requires C, 63.74; H, 6.29%).

Preparation and Epoxidation of Ethyl c-6-p-*Methoxybenzoyloxy*-1-*methylcyclohex*-2-*ene*-r-1-*carboxylate* (22).—Ethyl *c*-2-hydroxy-1-methylcyclohex-5-ene-*r*-1-carboxylate (1.08 g) and *p*-methoxybenzoyl chloride (1.1 g) in pyridine (8 ml) at 20 °C for 16 h gave, after isolation as above and chromatography, *ethyl* c-6-p-*methoxybenzoyloxy*-1-*methylcyclohex*-2-*ene*-r-1-*carboxylate* (22) (1.64 g) as a colourless oil; $\nu_{max.}$ (film) 1 740, 1 710, 1 610, 1 580, and 1 510 cm^{-1}; δ ($CDCl_3$) 1.1 (3 H, t, *J* 7 Hz, CH_2CH_3), 1.35 (3 H, s, Me), 2.1 (4 H, m, 2 × CH_2), 3.8 (3 H, s, OMe), 4.05 (2 H, q, *J* 7 Hz, OCH_2CH_3), 5.3 (1 H, m, CHO), 5.82 (2 H, m, vinylic H), and 6.85 and 7.85 (each 2 H, m, aromatic H); *m/e* 319 ($M^+ + 1$) and 135 (base

peak). This ester (3.0 g) and MCPBA (2.3 g) in chloroform (30 ml) gave a mixture of epoxides (2.9 g) in the ratio 88 : 12 (^{1}H n.m.r.). Column chromatography on silica gave as the first eluted product the trans-*epoxide* (28) as colourless crystals, m.p. 66—67 °C; $\nu_{max.}$ ($CHCl_3$) 1 730, 1 710, 1 610, 1 510, and 910 cm^{-1}; δ ($CDCl_3$) 1.08 (3 H, t, *J* 7 Hz, CH_2CH_3), 1.42 (3 H, s, Me), 1.6—2.0 (4 H, m, 2 × CH_2), 3.42 (1 H, m, epoxide 3-H), 3.74 (1 H, dd, *J* 1.3, 3.9 Hz, epoxide 2-H), 3.86 (3 H, s, OMe), 4.05 (2 H, q, *J* 7 Hz, OCH_2CH_3), 5.12 (1 H, m, C*H*O), and 6.81 and 7.90 (each 2 H, m, aromatic H); *m/e* 335 ($M^+ + 1$) (Found: C, 64.5; H, 6.55. $C_{18}H_{22}O_6$ requires C, 64.65; H, 6.63%). The second eluted product was the cis-*epoxide* (34) (0.2 g), a colourless oil, $\nu_{max.}$ (film) 1 740, 1 710, 1 610, 1 582, and 1 515 cm^{-1}; δ ($CDCl_3$) 1.08 (3 H, t, *J* 7 Hz, CH_2CH_3), 1.32 (3 H, s, Me), 1.5—2.05 (4 H, m, 2 × CH_2), 3.15 (1 H, d, *J* 3.7 Hz, epoxide 2-H), 3.21 (1 H, m, epoxide 3-H), 3.75 (3 H, s, OMe), 4.07 (2 H, q, *J* 7 Hz, OCH_2CH_3), 5.0 (1 H, m, C*H*O), and 6.81 and 7.90 (each 2 H, m, aromatic H); *m/e* 335 ($M^+ + 1$) and 135 (base peak).

Preparation and Epoxidation of Methyl c-6-*Benzyloxy*-1-*methylcyclohex*-2-*ene*-r-1-*carboxylate* (23).—Methyl *c*-6-hydroxy-1-methylcyclohex-2-ene-*r*-1-carboxylate (51) (300 mg), sodium hydride (130 mg, 50% dispersion in oil, washed with ether), and benzyl bromide (0.4 ml), in THF (7 ml), at 60—70 °C for 2 h gave, after aqueous work-up and chromatography, *methyl* c-6-*benzyloxy*-1-*methylcyclohex*-2-*ene*-r-1-*carboxylate* (23) as a colourless oil; $\nu_{max.}$ (film) 1 730, 1 250, and 1 110 cm^{-1}; δ ($CDCl_3$) 1.25 (3 H, s, Me), 2.0 (4 H, m, 2 × CH_2), 3.61 (3 H, s, OMe), 3.7 (1 H, m, C*H*O), 4.48 and 4.60 (each 1 H, d, *J* 12 Hz, CH_2Ph), 5.73 (2 H, m, vinylic H), and 7.23 (5 H, m, aromatic H); *m/e* 169 ($M^+ - PhCH_2$) and 91 (base peak). Treatment of this ester (300 mg) with MCPBA (330 mg) in chloroform gave an oily product which was chromatographed on silica. The first eluted product was the trans-*epoxide* (29) (185 mg), a colourless oil, $\nu_{max.}$ (film) 1 730 and 1 265 cm^{-1}; δ ($CDCl_3$) 1.32 (3 H, s, Me), 1.5—2.15 (4 H, m, 2 × CH_2), 3.32 (1 H, m, epoxide 3-H), 3.49 (1 H, m, C*H*O), 3.63 (1 H, dd, *J* 1, 4 Hz, epoxide 2-H), 3.67 (3 H, s, OMe), 4.32 and 4.51 (each 1 H, d, *J* 11.6 Hz, OCH_2Ph), and 7.27 (5 H, m, aromatic H); *m/e* 185 ($M^+ - PhCH_2$). The second eluted product was the cis-*epoxide* (35) (55 mg), a colourless oil, $\nu_{max.}$ (film) 1 730 and 1 270 cm^{-1}; δ ($CDCl_3$) 1.32 (3 H, s, Me), 1.42—2.2 (4 H, m, 2 × CH_2), 3.01 (1 H, d, *J* 3.7 Hz, epoxide 2-H), 3.18 (1 H, m, epoxide 3-H), 3.36 (1 H, m, C*H*O), 3.74 (3 H, s, OMe), 4.43 and 4.56 (each 1 H, d, *J* 12.4 Hz, OCH_2Ph), and 7.29 (5 H, m, aromatic H); *m/e* 170 ($M^+ - PhCH_2O$).

Opening of Epoxides with Lithium Dimethylcuprate.—Methyl *c*-6-benzyloxy-*t*-2,3-epoxy-1-methylcyclohexane-*r*-1-carboxylate (29) (140 mg) in ether was added to a solution of lithium dimethylcuprate (from 6.4 ml of 0.75M methyllithium and 490 mg CuI) in ether under nitrogen at 0 °C and and the mixture was stirred for 18 h at 20 °C. Addition of saturated aqueous ammonium chloride and extraction from ether gave *methyl* c-6-*benzyloxy*-t-2-*hydroxy*-1,c-3-*dimethylcyclohexane*-r-1-*carboxylate* (37) (125 mg) as a colourless oil, $\nu_{max.}$ (film) 3 560, 1 720, 1 270, and 1 060 cm^{-1}; δ ($CDCl_3$) 1.05 (3 H, d, *J* 6 Hz, $CHCH_3$), 1.20 (3 H, s, Me), 1.46—1.89 (5 H, m, 2 × CH_2 and C*H*Me), 2.99 (1 H, d, *J* 2.9 Hz, OH), 3.64 (3 H, s, OMe), 3.87 (1 H, m, C*H*O), 3.98 (1 H, dd, *J* 2.9, 10.7 Hz, C*H*OH), 4.28 and 4.52 (each 1 H, d, *J* 11.7 Hz, CH_2Ph), and 7.28 (5 H, m, aromatic H).

Similarly methyl *c*-6-benzoyloxy-1-methyl-*t*-2,3-epoxycyclohexane-*r*-1-carboxylate (26) (160 mg) gave, after chromatography, *methyl* c-6-*benzoyloxy*-t-2-*hydroxy*-1,c-3-*dimethylcyclohexane*-r-1-*carboxylate* (38) (75 mg) as a colouress oil, $\nu_{max.}$ (film) 3 540, 1 720, 1 600, and 1 270 cm^{-1}; δ ($CDCl_3$) 1.1 (3 H, d, *J* 6 Hz, $CHCH_3$), 1.32 (3 H, s, Me), 1.2—2.0 (5 H, m, 2 × CH_2 and C*H*Me), 3.15 (1 H, s, OH), 3.65 (3 H, s, OMe), 4.1 (1 H, d, *J* 12 Hz, C*H*OH), 5.45 (1 H, m, C*H*O), and 7.3—8.0 (5 H, m, aromatic H); *m/e* 307 ($M^+ + 1$), 289 ($M^+ + 1 - H_2O$), and 275 base peak).

Similarly methyl *t*-2,3-epoxy-*c*-6-(*p*-methoxybenzoyloxy)-1-methylcyclohexane-*r*-1-carboxylate (27) (190 mg) gave after chromatography, *methyl* t-2-*hydroxy*-c-6-p-*methoxybenzoyloxy*-1,c-3-*dimethylcyclohexane*-r-1-*carboxylate* (39) (110 mg) as colourless crystals, m.p. 100 °C; $\nu_{max.}$ ($CHCl_3$) 3 560, 3 050, 1 710, 1 610, 1 580, 1 510, 1 275, 1 260, and 1 170 cm^{-1}; δ ($CDCl_3$) 1.2 (3 H, d, *J* 6.3 Hz, $CHCH_3$), 1.33 (3 H, s, Me), 1.55—2.0 (5 H, m, 2 × CH_2 and C*H*Me), 3.17 (1 H, d, *J* 2.7 Hz, OH), 3.57 (3 H, s, OMe), 3.86 (3 H, s, OMe), 4.08 (1 H, dd, *J* 2.7, 12.2 Hz, C*H*OH), 5.41 (1 H, m, C*H*O), and 6.93 and 7.91 (each 2 H, m, aromatic H); *m/e* 337 ($M^+ + 1$), 319 ($M^+ + 1 - H_2O$), 305 ($M^+ + 1 -$ MeOH), and 135 (base peak) (Found: C, 64.35; H, 7.15. $C_{18}H_{24}O_6$ requires C, 64.27; H, 7.19%).

Opening of Epoxides with Sodium Phenylselenide.—Diphenyl diselenide (2.0 g) and hypophosphorous acid (17 ml; 30%) in THF were heated under nitrogen under reflux for 1 h.[12] The mixture was then extracted into benzene, dried ($MgSO_4$), and concentrated under reduced pressure to give the phenylselenol. This was dissolved in benzene (10 ml) and added to sodium hydride (60 mg, 80% suspension in oil); methyl *c*-6-acetoxy-*t*-2,3-epoxy-1-methylcyclohexane-*r*-1-carboxylate (24) (1.0 g) was then added and the mixture heated under reflux for 48 h. Removal of the benzene under reduced pressure, and partitioning of the residue between water and ether, gave the crude selenide (40) (1.3 g). Acidification of the aqueous layer and extraction from ether gave the selenide acid (41) which was esterified with diazomethane. The samples of ester selenide (40) were combined, and crystallized from ether–light petroleum to give *methyl* c-6-*acetoxy*-2-t-*hydroxy*-1-*methyl*-c-3-*phenylselenocyclohexane*-r-1-*carboxylate* (40) (1.3 g), m.p. 114 °C; $\nu_{max.}$ ($CHCl_3$) 3 550, 1 725, 1 575, and 1 240 cm^{-1}; δ ($CDCl_3$) 1.29 (3 H, s, Me), 1.65—1.80 (4 H, m, 2 × CH_2), 1.93 (3 H, s, COMe), 3.4 (1 H, m, C*H*SePh), 3.32 (1 H, d, *J* 2.9 Hz, exch. D_2O, OH), 3.68 (3 H, s, OMe), 4.33 (1 H, dd, *J* 2.9, 11.2 Hz, C*H*OH), 5.18 (1 H, m, C*H*OAc), and 7.25—7.69 (5 H, m, aromatic H) (Found: C, 53.15; H, 5.85. $C_{17}H_{22}O_5Se$ requires C, 52.97; H, 5.76%).

Similarly the ethyl acetoxy *trans*-epoxide (25) (0.45 g), phenylselenol (from 1 g diphenyl diselenide), and sodium hydride (40 mg, 80% dispersion in oil) in toluene (30 ml) were heated under reflux under nitrogen for 24 h. Dilution with water and extraction with ether gave, after crystallization from ether–light petroleum, *ethyl* c-6-*acetoxy*-t-2-*hydroxy*-1-*methyl*-c-3-*phenylselenocyclohexane*-r-1-*carboxylate* (42) (0.6 g) as colourless crystals, m.p. 86—87 °C; $\nu_{max.}$ ($CHCl_3$) 3 520, 1 735, 1 575, and 1 220 cm^{-1}; δ ($CDCl_3$) 1.22 (3 H, t, *J* 7 Hz, CH_2CH_3), 1.29 (3 H, s, Me), 1.63—1.75 (4 H, m, 2 × CH_2), 1.94 (3 H, s, MeCO), 3.38 (1 H, m, C*H*SePh), 3.41 (1 H, d, *J* 2.6 Hz, exch. D_2O, OH), 4.16 (2 H, m, OCH_2CH_3), 4.31 (1 H, dd, *J* 2.6, 10.9 Hz, C*H*OH), 5.21 (1 H, m, C*H*OAc), and 7.26—7.67 (5 H, m, aromatic H); *m/e* 490 (M^+) (Found: C, 54.15; H, 6.1. $C_{18}H_{24}O_5Se$ requires C, 54.12; H, 6.06%).

Similarly the ethyl *p*-methoxybenzoyloxy *trans*-epoxide (28) (1.0 g), phenylselenol (from 1.2 g diphenyl diselenide), and sodium hydride (150 mg), in toluene (40 ml) were heated under reflux under nitrogen for 48 h. Work-up as above and recrystallization from ether–light petroleum gave *ethyl* t-2-*hydroxy*-c-6-p-*methoxybenzoyloxy*-1-*methyl*-c-3-*phenylselenocyclohexane*-r-1-*carboxylate* (43) (1.17 g), m.p. 112 °C; $\nu_{max.}$ ($CHCl_3$) 3 550, 1 710, 1 608, 1 580, 1 510, 1 255, 1 170,

and 1 090 cm^{-1}; δ ($CDCl_3$) 1.03 (3 H, t, *J* 7.2 Hz, CH_2CH_3), 1.36 (3 H, s, Me), 1.75—1.90 (4 H, m, 2 × CH_2), 3.32 (1 H, m, C*H*SePh), 3.50 (1 H, d, *J* 2.8 Hz, exch. D_2O, OH), 3.87 (3 H, s, OMe), 4.05 (2 H, m, OCH_2CH_3), 4.42 (1 H, dd, *J* 2.8, 11.2 Hz, C*H*OH), 5.41 (1 H, m, C*H*O), 6.88 (2 H, m, aromatic H), 7.3 (3 H, m, aromatic H), and 7.7 (4 H, m, aromatic H) (Found: C, 58.85; H, 5.55. $C_{24}H_{26}O_6Se$ requires C, 58.89; H, 5.35%).

Oxidative Elimination of Hydroxy-selenides.—30% Aqueous hydrogen peroxide (7 ml) was added to a solution of the acetoxy-hydroxyselenide (40) (2.45 g) in THF at 0 °C, and the mixture heated under reflux for 2 h, cooled, and more hydrogen peroxide (7 ml) added. This cycle was repeated three times. Dilution with water, and extraction into chloroform, gave, after column chromatography, *methyl* c-6-*acetoxy*-t-2-*hydroxy*-1-*methylcyclohex*-3-*ene*-r-1-*carboxylate* (44) (0.93 g) as a colourless oil, $\nu_{max.}$ (film) 3 560, 1 730, and 1 240 cm^{-1}; δ ($CDCl_3$) 1.12 (3 H, s, Me), 1.92 (3 H, s, CH_3CO), 2.25 (2 H, m, CH_2), 2.81 (1 H, d, *J* 3.8 Hz, exch. D_2O, OH), 3.66 (3 H, s, OMe), 4.83 (1 H, m, C*H*OAc), 5.28 (1 H, m, C*H*OH), and 5.57 (2 H, m, vinylic H) (Found: M^+ 197.0804. $C_{11}H_{16}O_5$ requires *M* − OMe, 197.0813).

Similarly the ethyl hydroxyselenide (42) (400 mg) gave, after chromatography, *ethyl* c-6-*acetoxy*-t-2-*hydroxy*-1-*methylcyclohex*-3-*ene*-r-1-*carboxylate* (45) (160 mg) as colourless crystals, m.p. 82 °C; $\nu_{max.}$ ($CHCl_3$) 3 550, 1 720, and 1 250 cm^{-1}; δ ($CDCl_3$) 1.19 (3 H, s, Me), 1.25 (3 H, t, *J* 7 Hz, CH_2CH_3), 1.99 (3 H, s, MeCO), 2.17—2.38 (2 H, m, CH_2), 3.02 (1 H, d, *J* 3.5 Hz, exch. D_2O, OH), 4.24 (2 H, m, OCH_2CH_3), 4.90 (1 H, m, C*H*OAc), 5.36 (1 H, m, C*H*OH), and 5.63 (2 H, m, vinylic H) (Found: C, 59.35; H, 7.6. $C_{12}H_{18}O_5$ requires C, 59.48; H, 7.49%).

MCPBA (0.5 g) was added to the ethyl *p*-methoxybenzoyloxy-hydroxyselenide (43) (1.2 g) in dichloromethane (10 ml) at 0 °C. After 5 min, triethylamine (0.5 g) was added, and the mixture added to carbon tetrachloride (30 ml) under reflux. The mixture was heated under reflux for 5 h, the solvent evaporated under reduced pressure, and the residue partitioned between water and dichloromethane. The organic extracts weer combined and chromatographed on silica. The first eluted product was identified as r-6-*ethoxycarbonyl*-c-5-p-*methoxybenzoyloxy*-6-*methylcyclohex*-2-*en*-1-*one* (77 mg), obtained as a colourless oil; $\nu_{max.}$ (film) 1 715, 1 680, 1 610, 1 580, and 1 515 cm^{-1}; δ ($CDCl_3$) 1.23 (3 H, t, *J* 7 Hz, CH_2CH_3), 1.47 (3 H, s, Me), 2.85 (2 H, m, CH_2), 3.84 (3 H, s, OMe), 4.21 (2 H, q, *J* 7 Hz, OCH_2CH_3), 5.35 (1 H, m, C*H*O), 6.15 and 6.95 (each 1 H, m, vinylic H), and 6.95 and 7.95 (each 2 H, m, aromatic H); *m/e* 332 (M^+) and 135 (base peak). The second eluted product was *ethyl* t-2-*hydroxy*-c-6-p-*methoxybenzoyloxy*-1-*methylcyclohex*-3-*ene*-r-1-*carboxylate* (46) (0.52 g), a colourless oil, $\nu_{max.}$ (film) 3 540, 3 040, 1 720, 1 610, 1 585, 1 515, 1 260, and 1 170 cm^{-1}; δ ($CDCl_3$) 1.1 (3 H, t, *J* 7 Hz, CH_2CH_3), 1.25 (3 H, s, Me), 1.32—1.63 (2 H, m, CH_2), 3.1 (1 H, br s, O*H*), 3.86 (3 H, s, OMe), 4.13 (2 H, m, OCH_2CH_3), 5.1 (1 H, m, C*H*O), 5.57—5.80 (3 H, m, vinylic H and C*H*OH), and 6.9 and 7.9 (each 2 H, m, aromatic H); *m/e* 335 ($M^+ + 1$) and 317 ($M^+ + 1 - H_2O$).

Epoxidation of Ethyl t-2-*Hydroxy*-c-6-p-*methoxybenzoyloxy*-1-*methylcyclohex*-3-*ene*-r-1-*carboxylate* (46).—The allylic alcohol (46) (100 mg) and MCPBA (100 mg) in chloroform gave a mixture of epoxides (90 mg) in the ratio 70 : 30 (^1H n.m.r.). Column chromatography on silica gave as the first eluted product *ethyl* t-3,4-*epoxy*-t-2-*hydroxy*-c-6-p-*methoxybenzoyloxy*-1-*methylcyclohexane*-r-1-*carboxylate* (48) (11 mg) as a colourless oil, δ ($CDCl_3$) 1.11 (3 H, t, *J* 7 Hz, CH_2CH_3), 1.42 (3 H, s, Me), 2.18—2.46 (2 H, m, CH_2), 3.01 (1 H, d, *J* 5.5 Hz, OH), 3.34 and 3.56 (each 1 H, m, epoxide H), 3.87 (3 H, s, OMe), 4.10 (2 H, m, OCH_2CH_3), 4.83 (1 H, dd, *J* 3.0, 5.5 Hz, C*H*OH), 5.41 (1 H, m, C*H*O), and 6.93 and 7.92 (each 2 H, m, aromatic H). After a mixed fraction (25 mg), the second eluted product was *ethyl* c-3,4-*epoxy*-t-2-*hydroxy*-c-6-p-*methoxybenzoyloxy*-1-*methylcyclohexane*-r-1-*carboxylate* (47) (36 mg), crystallized from ether–light petroleum, m.p. 82 °C; $\nu_{max.}$ ($CHCl_3$) 3 560, 3 050, 1 710, 1 608, 1 580, 1 510, 1 260, and 1 170 cm^{-1}; δ ($CDCl_3$) 1.10 (3 H, t, *J* 7.1 Hz, CH_2CH_3), 1.26 (3 H, s, Me), 2.20—2.50 (2 H, m, CH_2), 3.15 (1 H, d, *J* 3.5 Hz, exch. with D_2O, OH), 3.25 (1 H, d, *J* 3.7 Hz, epoxide 3-H), 3.28 (1 H, m, epoxide 4-H), 3.85 (3 H, s, OMe), 4.10 (2 H, m, OCH_2CH_3), 4.72 (1 H, d, *J* 3.5 Hz, collapsed to s on D_2O exch., C*H*OH), 5.47 (1 H, dd, *J* 2, 5 Hz, C*H*O), and 6.90 and 7.93 (each 2 H, m, aromatic H); *m/e* 351 ($M^+ + 1$) and 135 (base peak) (Found: C, 61.85; H, 6.3. $C_{18}H_{22}O_7$ requires C, 61.70; H, 6.33%).

c-5-*Acetoxy*-r-6-*methoxycarbonyl*-6-*methylcyclohex*-2-*en*-1-*one* (49).—A 70% aqueous solution of t-butyl hydroperoxide (150 mg) was added to the allylic alcohol (44) (180 mg) and $Mo(CO)_6$ (5 mg) in benzene, and the mixture was heated under reflux for 4 h.[17] Dilution with water and extraction with chloroform gave, after washing with aqueous sodium hydrogen carbonate and brine, a residue which was chromatographed on silica to give c-5-*acetoxy*-r-6-*methoxycarbonyl*-6-*methylcyclohex*-2-*en*-1-*one* (49) (100 mg) as a colourless oil, $\nu_{max.}$ (film) 3 010, 1 740, and 1 670 cm^{-1}; δ ($CDCl_3$) 1.43 (3 H, s, Me), 2.09 (3 H, s, MeCO), 2.75 (2 H, m, CH_2), 3.72 (3 H, s, OMe), 5.19 (1 H, t, *J* 7 Hz, C*H*O), 6.12 (1 H, dt, *J* 10.3, 1 Hz, vinylic H), and 6.92 (1 H, dt, *J* 10.3, 4 Hz, vinylic H) (Found: M^+ 226.0842. $C_{11}H_{18}O_5$ requires *M* 226.0841).

c-5-*Acetoxy*-r-6-*ethoxycarbonyl*-6-*methylcyclohex*-2-*en*-1-*one* (50).—A 70% aqueous solution of t-butyl hydroperoxide (74 mg) was added to the allylic alcohol (45) (100 mg) and $VO(acac)_2$ (5 mg) in benzene at 0 °C.[17] After 17 h at 20 °C the mixture was filtered, concentrated under reduced pressure, and chromatographed to give c-5-*acetoxy*-r-6-*ethoxycarbonyl*-6-*methylcyclohex*-2-*en*-1-*one* (50) (80 mg) as a colourless oil; $\nu_{max.}$ ($CHCl_3$) 3 020, 1 740, and 1 678 cm^{-1}; δ ($CDCl_3$) 1.25 (3 H, t, *J* 7 Hz, CH_2CH_3), 1.42 (3 H, s, Me), 2.09 (3 H, s, MeCO), 2.75 (2 H, m, CH_2), 4.18 (2 H, q, *J* 7 Hz, OCH_2CH_3), 5.19 (1 H, t, *J* 7 Hz, C*H*O), 6.14 (1 H, dt, *J* 10, 2 Hz, vinylic H), and 6.93 (1 H, dt, *J* 10, 4 Hz, vinylic H) (Found: M^+ 240.0998. $C_{12}H_{16}O_5$ requires *M* 240.0977).

Methyl c-6-*Hydroxy*-c-4-*methoxy*-1-*methylcyclohex*-2-*ene*-r-1-*carboxylate* (53).—Methyl *c*-6-hydroxy-1-methylcyclohex-2-ene-*r*-1-carboxylate (51) (500 mg) and *N*-bromosuccinimide (580 mg) in carbon tetrachloride (10 ml) were heated under reflux for 18 h. Filtration and concentration under reduced pressure gave the bromides (52) (0.68 g) as an oil, δ ($CDCl_3$) 1.42 (3 H, s, Me), 2.4 (2 H, m, CH_2), 3.5 (1 H, s, OH), 3.69 and 3.71 (3 H, s, OMe of each isomer), 4.0 (1 H, m, C*H*OH), 4.75 (1 H, m, C*H*Br), and 5.5—6.1 (2 H, m, vinylic H). This crude bromide mixture and potassium carbonate (0.42 g) in methanol (8 ml) were stirred at 20 °C for 18 h. Concentration under reduced pressure and partitioning of the residue between water and ether gave a brown oil which was chromatographed on silica to give *methyl* c-6-*hydroxy*-c-4-*methoxy*-1-*methylcyclohex*-2-*ene*-r-1-*carboxylate* (53) (180 mg) as a colourless oil; $\nu_{max.}$ (film) 3 470, 3 030, 1 735, 1 105, and 1 070 cm^{-1}; δ ($CDCl_3$) 1.33 (3 H, s, Me), 2.0—2.2 (2 H, m, CH_2), 3.38 (3 H, s, OMe), 3.73 (3 H, s, OMe), 3.80 (3 H, m, C*H*OMe and C*H*OH), and 5.91 (2 H, m, vinylic H); *m/e* 201 ($M^+ + 1$) and 169 ($M^+ + 1 - MeOH$).

p-Methoxybenzoyl chloride (30 mg) was added to the

hydroxy-ester (53) (30 mg) in anhydrous pyridine at 0 °C. After 18 h at 20 °C addition of water, and extraction with ether gave the p-*methoxybenzoate* (54) (40 mg) as an oil; $\nu_{max.}$ (film) 1 720, 1 610, 1 580, 1 510, 1 255, 1 170, 1 100, 1 030, 850, and 775 cm^{-1}; δ ($CDCl_3$) 1.26 (3 H, s, Me), 2.27 (2 H, m, CH_2), 3.28 (3 H, s, OMe), 3.67 (3 H, s, OMe), 3.77 (3 H, s, OMe), 3.97 (1 H, m, C*H*OMe), 5.02 (1 H, dd, *J* 4.6, 9.7 Hz, C*H*O), 5.64 (1 H, dd, *J* 1.8, 10.3 Hz, vinylic H), 5.85 (1 H, dd, *J* 2.2, 10.3 Hz, vinylic H), and 6.82 and 7.86 (each 2 H, m, aromatic H).

Methyl c-6-*Benzyloxy*-t-2,3-*epoxy*-c-4-*methoxy*-1-*methylcyclohexane*-r-1-*carboxylate* (56).—Hydroxy-ester (53) (200 mg), benzyl bromide (340 mg), and sodium hydride (58 mg, 50% dispersion in oil) in anhydrous THF (8 ml) at 70 °C for 2 h gave, after addition of water, ether extraction, and chromatography, the *benzyl ether* (55) (150 mg) as a colourless oil, $\nu_{max.}$ (film) 3 040, 1 735, and 1 200 cm^{-1}; δ ($CDCl_3$) 1.3 (3 H, s, Me), 2.23 (2 H, m, CH_2), 3.39 (3 H, s, OMe), 3.44 (1 H, dd, *J* 8.0, 5.5 Hz, C*H*OCH_2Ph), 3.68 (3 H, s, OMe), 3.87 (1 H, m, C*H*OMe), 4.49 and 4.70 (each 1 H, d, *J* 12 Hz, OCH_2Ph), 5.60 (1 H, dd, *J* 1.9, 10.5 Hz, vinylic H), 5.85 (1 H, dd, *J* 2.2, 10.5 Hz, vinylic H), and 7.27 (5 H, m, aromatic H); *m/e* 291 ($M^+ + 1$) and 259 ($M + 1 -$ MeOH).

MCPBA (140 mg) and the benzyl ether (55) (150 mg) in chloroform (3 ml) gave, after chromatography, the trans-*epoxide* (56) (70 mg) as a colourless oil, homogeneous by t.l.c.; $\nu_{max.}$ (film) 1 740, 1 500, and 1 200 cm^{-1}; δ ($CDCl_3$) 1.33 (3 H, s, Me), 1.77—2.00 (2 H, m, CH_2), 3.24 (3 H, m, 2 × epoxide H and C*H*OMe), 3.38 (3 H, s, OMe), 3.5 (1 H, dd, *J* 5.5, 8.0 Hz, C*H*OCH_2Ph), 3.65 (3 H, s, OMe), 4.32 and 4.54 (each 1 H, d, *J* 12.0 Hz, CH_2Ph), and 7.22 (5 H, m, aromatic H); *m/e* 307 ($M^+ + 1$) and 135 (base peak).

Methyl c-6-*Benzyloxy*-t-2-*hydroxy*-c-4-*methoxy*-1,c-3-*dimethylcyclohexane*-r-1-*carboxylate* (57).—The epoxide (56) (80 mg) in ether (3 ml) was added to lithium dimethylcuprate (from 3.92 ml of 0.75M-methyl-lithium and 280 mg of CuI) in ether at 0 °C under nitrogen, and the mixture stirred for 48 h at 20 °C. Work-up as above and chromatography gave the unchanged epoxide (56) (15 mg) and *methyl* c-6-*benzyloxy*-t-2-*hydroxy*-c-4-*methoxy*-1,c-3-*dimethylcyclohexane*-r-1-*carboxylate* (57) (25 mg) as a colourless oil; $\nu_{max.}$ (film) 3 560, 1 720, 1 280, 1 132, 1 095, 1 060, 740, and 700 cm^{-1}; δ ($CDCl_3$) 1.16 (3 H, d, *J* 6.6 Hz, CHCH_3), 1.20 (3 H, s, Me), 1.44 (1 H, dt, *J* 15.8, 3.3 Hz, methylene H), 1.77 (1 H, m, C*H*Me), 2.34 (1 H, dt, *J* 15.8, 2.6 Hz, methylene H), 2.99 (1 H, d, *J* 2.9 Hz, OH), 3.31 (3 H, s, OMe), 3.31 (1 H, m, C*H*OMe), 3.61 (3 H, s, OMe), 3.85 (1 H, m, C*H*OCH_2Ph), 4.37 (1 H, dd, *J* 2.9, 11.8 Hz, C*H*OH), 4.31 and 4.58 (each 1 H, d, *J* 12.0 Hz, CH_2Ph), and 7.28 (5 H, m, aromatic H); *m/e* 323 ($M^+ + 1$) and 91 (base peak).

c-5-p-*Methoxybenzoyloxy*-r-4-*methoxycarbonyl*-4-*methylcyclohex*-2-*en*-1-*one* (58).—3,5-Dimethylpyrazole (6.72 g) was added to chromium trioxide (7.0 g) in dichloromethane (30 ml) at −20 °C.[20] Methyl *c*-6-*p*-methoxybenzoyloxy-1-methylcyclohex-2-ene-*r*-1-carboxylate (21) (0.99 g) in dichloromethane (20 ml) was added after 0.5 h, and stirred at −10 to −20 °C for 24 h. Addition of dilute hydrochloric acid and ether extraction gave a crude product which was filtered through silica twice to remove tar and crystallized from ether–light petroleum to give c-5-p-*methoxybenzoyloxy*-r-4-*methoxycarbonyl*-4-*methylcyclohex*-2-*en*-1-*one* (58) (390 mg), m.p. 104 °C; $\nu_{max.}$ ($CHCl_3$) 1 737, 1 710, 1 687, 1 610, and 1 583 cm^{-1}; δ ($CDCl_3$) 1.55 (3 H, s, Me), 2.9 (2 H, m, CH_2), 3.67 (3 H, s, OMe), 3.85 (3 H, s, OMe), 5.7 (1 H, m, C*H*O), 6.15 (1 H, d, *J* 10.3 Hz, vinylic H), 6.88 (2 H, m, aromatic H), 7.20 (1 H, dd, *J* 1.8, 10.3 Hz, vinylic H), and 7.85 (2 H, m, aromatic H) (Found: C, 63.9; H, 5.75. $C_{17}H_{18}O_6$ requires C, 64.15; H, 5.70%).

Methyl c-2,3-*Epoxy*-c-4-*hydroxy*-c-6-*p-methoxybenzoyloxy*-1-*methylcyclohexane*-r-1-*carboxylate* (60).—The enone (58) (300 mg) in methanol (5 ml) was added to sodium borohydride (50 mg) in methanol at −5 °C. After 0.5 h the methanol was evaporated off and the residue partitioned between water and ether. Chromatography of the product gave the *cyclohexenol* (59) (260 mg) as a colourless oil, homogeneous by t.l.c.; $\nu_{max.}$ (film) 3 480, 1 720, 1 615, 1 590, 1 520, 1 265, 1 175, 1 110, and 775 cm^{-1}; δ ($CDCl_3$) 1.34 (3 H, s, Me), 1.87 (1 H, br d, *J* 9.4 Hz, exch. D_2O, OH), 2.31 (2 H, m, CH_2), 3.66 (3 H, s, OMe), 3.85 (3 H, s, OMe), 4.28 (1 H, m, C*H*OH), 5.37 (1 H, dd, *J* 2.7, 7.2 Hz, C*H*O), 5.95 (1 H, d, *J* 10.2 Hz, vinylic H), 6.01 (1 H, dd, *J* 3.1, 10.2 Hz, vinylic H), and 6.91 and 7.90 (each 2 H, m, aromatic H). This alcohol (59) (260 mg) and MCPBA (200 mg) in chloroform (10 ml) gave the crude epoxide (250 mg), crystallized from ether–light petroleum to give *methyl* c-2,3-*epoxy*-c-4-*hydroxy*-c-6-p-*methoxybenzoyloxy*-1-*methylcyclohexane*-r-1-*carboxylate* (60) as colourless crystals, m.p. 117 °C; $\nu_{max.}$ ($CHCl_3$) 3 580, 3 010, 1 740, 1 710, 1 610, 1 585, 1 510, 1 210, 1 170, and 850 cm^{-1}; δ ($CDCl_3$) 1.39 (3 H, s, Me), 1.95 (1 H, m, methylene H), 2.13 (1 H, d, *J* 10.9 Hz, exch. D_2O, O*H*), 2.25 (1 H, m, methylene H), 3.44 (1 H, d, *J* 3.7 Hz, epoxide H), 3.54 (1 H, t, *J* 3.7 Hz, epoxide H), 3.72 (3 H, s, OMe), 3.86 (3 H, s, OMe), 4.23 (1 H, m, C*H*OH), 5.10 (1 H, dd, *J* 2.8, 7.5 Hz, C*H*O), and 6.91 and 7.95 (each 2 H, m, aromatic H) (Found: C, 60.7; H, 5.9. $C_{17}H_{20}O_7$ requires C, 60.70; H, 5.99%).

c-2-*Hydroxy*-1,t-3-*dimethyl*-c-6-p-*methoxybenzoyloxycyclohexane*-r-1,4-*carbolactone* (61).—Methyl-lithium (2.25 ml of a 1.05M solution in ether) was added to anhydrous copper(I) iodide (280 mg) in ether (7 ml) under nitrogen at 0 °C. After 40 min at 0 °C, the epoxide (60) (45 mg) in ether (8 ml) was added dropwise. The mixture was then stirred at 0 °C for 20 h before being poured into saturated aqueous ammonium chloride–ammonia (*d* 0.880) (95 : 5). Separation and extraction into dichloromethane gave an oil (30 mg) which was chromatographed on silica ($CHCl_3$–CH_2Cl_2) to give the *lactone* (61) (10 mg); this was recrystallized from benzene, m.p. 185—186 °C; $\nu_{max.}$ ($CHCl_3$) 1 755, 1 710, 1 605, and 1 170 cm^{-1}; δ ($CDCl_3$) 1.195 (3 H, d, *J* 7 Hz, CHCH_3), 1.34 (3 H, s, CH_3), 1.94 (1 H, d, *J* 5 Hz, exch. with D_2O, OH), 1.96 and 2.57 (each 1 H, m, methylene H), 2.14 (1 H, m, C*H*CH_3), 3.49 (1 H, m, C*H*OH), 3.87 (3 H, s, OCH_3), 4.48 (1 H, m, HCOCO), 5.08 (1 H, dd, *J* 3, 9 Hz, $CH_3OC_6H_4CO_2CH$), and 6.92 and 7.97 (each 2 H, m, aromatic H); *m/e* 321 ($M^+ + 1$) and 135 (base peak) (Found: C, 63.8; H, 6.2. $C_{16}H_{20}O_6$ requires C, 63.75; H, 6.30%).

Crystal Structure Determination for the Epoxide (28).—$C_{18}H_{22}O_6$, $M_r = 332.4$. Triclinic, space group *P*1, $Z = 2$, $a = 8.860(3)$, $b = 9.998(3)$, $c = 12.439(4)$ Å, $\alpha = 63.54(3)$, $\beta = 67.18(3)$, $\gamma = 68.65(3)°$, 1 604 unique reflections with $I \geqslant 3\alpha(I)$, final *R*-value 0.056. Preliminary Weissenberg photography showed the crystal system to be triclinic. The crystal was transferred to an Enraf Nonius CAD4-F four-circle diffractomer and accurate cell parameters determined. Diffraction intensities were measured by an ω/2θ scan in ZIGZAG mode with periodic re-measurement of the orientation and intensity of three standard reflections. The space group *P*1 was assumed. The data was transferred to the Chemical Crystallography Laboratory's VAX II 750 computer on which all subsequent computing was performed. Lorentz and polarisation corrections were applied and equivalent reflections merged to give 2 454 unique reflections. The structure was solved with Multan 80[31] (but only after

inclusion of the molecular scattering factors for epoxide, ethyl ester and *p*-methoxybenzoyloxy-groups in the calculation of *E*'s) yielding all but one of the non-hydrogen atoms. The missing atom was subsequently located from a difference Fourier synthesis. The structure was refined, including isotropic temperature factors, against the 1 604 reflections with $I \geqslant 3\sigma(I)$ using the CRYSTALS [32] package. All hydrogen positions were calculated except the two at the fusion of the epoxide ring which were deliberately taken from a difference Fourier synthesis. They were all assigned an isotropic temperature factor of 0.06 and were not included in further refinements which proceeded with blocked-matrix least-squares with non-hydrogen atoms assigned anisotropic temperature factors. After inclusion of a weighting scheme derived from the Chebyshev series ($\omega = [414.8\ t_0\ (X) + 558.0\ t_1\ (X) + 148.0\ t_2\ (X)]^{-1}$ where $(X) = F_o/F_{max.}$) [33] the refinement converged at $R = 0.056$. Final atomic co-ordinates, are given in Table 3. Anisotropic temperature factors and tables of structure factors are available as a Supplementary publication (SUP No. 23407, 20 pages).* The value of equivalent isotropic temperature factors for non-hydrogen atoms vary from 0.045 to 0.089, except for C(10) which is 0.116.

Table 3. Fractional atomic co-ordinates for the epoxide (28)

Atom	*x/a*	*y/b*	*z/c*	U_{iso}
O(1)	1.2297(3)	0.4558(3)	0.2160(3)	0.0740
O(2)	0.7404(4)	0.5338(3)	0.2125(3)	0.0838
O(3)	0.6825(3)	0.3455(3)	0.3953(2)	0.0733
O(4)	0.9622(3)	0.1833(2)	0.2512(2)	0.0485
O(5)	0.9479(4)	−0.0602(3)	0.3702(2)	0.0649
O(6)	0.6853(3)	0.0563(3)	−0.0770(2)	0.0724
C(1)	1.2380(5)	0.3817(5)	0.1381(4)	0.0721
C(2)	1.0775(5)	0.4585(4)	0.1992(3)	0.0612
C(3)	0.9595(4)	0.3711(3)	0.3167(3)	0.0494
C(4)	1.0142(4)	0.1984(3)	0.3407(3)	0.0458
C(5)	1.2014(4)	0.1373(4)	0.3208(3)	0.0580
C(6)	1.2973(5)	0.2102(5)	0.1853(4)	0.0750
C(7)	0.9515(5)	0.4024(4)	0.4283(3)	0.0631
C(8)	0.7853(5)	0.4289(4)	0.2988(3)	0.0620
C(9)	0.5131(5)	0.3748(6)	0.3908(5)	0.0890
C(10)	0.4402(7)	0.2500(8)	0.4931(6)	0.1162
C(11)	0.9249(4)	0.0507(3)	0.2790(3)	0.0486
C(12)	0.8578(4)	0.0587(3)	0.1855(3)	0.0451
C(13)	0.8411(4)	−0.0757(4)	0.1882(3)	0.0555
C(14)	0.7835(4)	−0.0733(4)	0.1003(3)	0.0610
C(15)	0.7375(4)	0.0654(4)	0.0072(3)	0.0519
C(16)	0.7495(4)	0.1997(4)	0.0058(3)	0.0531
C(17)	0.8099(4)	0.1960(3)	0.0932(3)	0.0494
C(18)	0.6295(6)	0.1940(5)	−0.1699(4)	0.0844
H(11)	1.2918	0.4309	0.0415	0.0600
H(21)	1.0221	0.5662	0.1458	0.0600
H(41)	0.9591	0.1354	0.4298	0.0600
H(51)	1.2388	0.1574	0.3783	0.0600
H(52)	1.2291	0.0210	0.3446	0.0600
H(61)	1.4245	0.1826	0.1777	0.0600
H(62)	1.2857	0.1684	0.1295	0.0600
H(71)	1.0659	0.3666	0.4435	0.0600
H(72)	0.9114	0.5166	0.4132	0.0600
H(73)	0.8714	0.3487	0.5063	0.0600
H(91)	0.4439	0.4773	0.3998	0.0600
H(92)	0.5121	0.3789	0.3081	0.0600
H(101)	0.3206	0.2622	0.4964	0.0600
H(102)	0.4400	0.2465	0.5757	0.0600
H(103)	0.5083	0.1481	0.4840	0.0600
H(131)	0.8749	−0.1760	0.2551	0.0600
H(141)	0.7715	−0.1727	0.1027	0.0600
H(161)	0.7123	0.2998	−0.0615	0.0600
H(171)	0.7968	0.3134	0.0980	0.0600
H(181)	0.5929	0.1737	−0.2264	0.0600
H(182)	0.7200	0.2528	−0.2204	0.0600
H(183)	0.5286	0.2628	−0.1284	0.0600

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