Baker's Yeast-mediated Transformations of α-Keto Epoxides[1]

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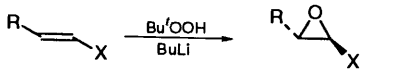
αβ-Epoxy ketones on treatment with baker's yeast yield different types of products depending on their substitution. Small groups such as H or Me attached at the epoxy end protect that end from attack. Thus, 1-acyl epoxides with H, methyl or propyl as the 2-epoxy substituent give solely the epoxy alcohol product with moderate stereoselectivity (13–64% d.e.). With a 2-phenyl substituent the sole product is the 1,2,3-triol as a single racemic diastereoisomer derived by a reduction/hydrolysis sequence involving a *syn* ring-opening of the epoxide. More than one enzyme is probably involved in both of these transformations which tend to favour *S*-reduction. The detailed mechanism of product formation in both processes has been undertaken and the formation of the triols has been shown by ^{18}O labelling studies to involve asymmetric reduction of the ketone and a double inversion during epoxide ring-opening involving a carbocation intermediate.

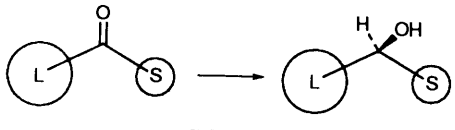
The importance of epoxides in the synthesis of natural products stems primarily from their ready availability as homochiral compounds and their remarkable versatility in specific transformations.[2] The nucleophilic epoxides are those most commonly employed, particularly due to the work of the Sharpless group so that if products bearing electrophilic substituents are required they are generally formed from, for example, allylic epoxides by oxidation. We have undertaken a study of routes to homochiral building blocks by epoxidation of electrophilic alkenes and by the transformation of the epoxides so derived.[3] Thus, the use of lithium *tert*-butyl hydroperoxide allows highly stereocontrolled epoxidation of αβ-unsaturated esters, amides, nitro compounds, sulfones and sulfoximides, whilst excellent and predictable control of the stereochemistry results when a chiral sulfoximide is employed (Scheme 1).



X = CO_2R', $CONR'_2$, NO_2, SO_2R', $SO(NR')R''$

Scheme 1

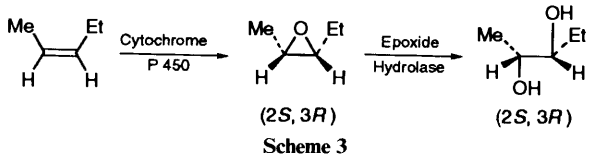
Baker's yeast (*Saccharomyces cerevisiae*) is used in synthesis primarily for its ability to reduce ketones in a predictable way to give asymmetric alcohols utilising one of its oxidoreductase enzymes.[4] The substrate specificity of the principal oxidoreductase in yeast (Yeast alcohol dehydrogenase—YADH) in such reductions is surprisingly limited, the small group of the ketone being limited to H or Me (Scheme 2). In accord with Prelog's rule, hydride is delivered from the back face of the ketone with the small group on the right (Scheme 2).[5]



Scheme 2

That other enzymes are employed in yeast-mediated reductions is indicated by the fact that a wide variety of small and large substituents may be utilised giving alcohols with moderate to high enantioselectivity and that Prelog's rule is not always adhered to. Furthermore, a wide variety of other types of reactions are known to be mediated by yeast.[4] Thus, asymmetric hydrolysis of esters proceeds efficiently as does reduction of αβ-unsaturated carbon–carbon double bonds, both of these reactions having been conducted commercially. Dehydrogenations also proceed to give solely *cis*-double bonds, while epoxysqualene is converted into lanosterol and aldol condensations are catalysed asymmetrically.

Although monooxygenases are known that allow conversion of alkenes into epoxides[6] no application of yeast in this process have been reported to our knowledge. Also, though epoxides are known to be enzymically transformed into diols by epoxide hydrolases,[6,7] we know of no such reactions mediated by baker's yeast. These hydrolases cause *anti*-addition of water as in Scheme 3. In this paper we describe our investigations into the attempted reduction of αβ-epoxy ketones with baker's yeast with a view to generating homochiral building blocks. These reactions are surprising in their variety and when epoxide ring-opening does occur it does so in an unprecedented *syn*-manner.

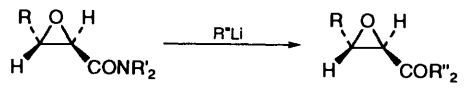


(2*S*, 3*R*) (2*S*, 3*R*)

Scheme 3

Synthesis of αβ-Epoxy Ketones.—The two most common methods for the synthesis of αβ-epoxy ketones, the Darzens reaction (*e.g.* the base-catalysed reaction of an α-halogeno ester with an aldehyde) and the Weitz–Scheffer epoxidation (the base-catalysed reaction of an electrophilic alkene with H_2O_2) are both non-stereospecific processes.[8] Thus, both *cis*- and *trans*-alkenes give the same mixture of epoxides on treatment with alkaline hydrogen peroxide while the application of the Darzens reaction to the synthesis of αβ-epoxy ketones utilising, for example, phenacyl bromide, a strong base and an aldehyde again gives both isomeric epoxides. We have introduced a method whereby the epoxy amides described in Scheme 1, generated in a stereospecific and regiospecific manner, can be readily transformed into epoxy ketones in high yield (Scheme 4). This method is limited to the *trans*-epoxides since the *cis*-analogues yield β-keto amides under these conditions.

Action of Baker's Yeast on αβ-Epoxy Ketones.—Each of the epoxy ketones **1** was treated anaerobically with baker's yeast and sucrose in distilled water at 30 °C. After 24 h a further aliquot of sucrose was added and after 48 h the total mass was extracted continuously with chloroform and the products



1

a R = Ph, R" = Me
b R = Ph, R" = Et
c R = Ph, R" = Pr
d R = Ph, R" = Pr^{i}
e R = Ph, R" = Bu
f R = Ph, R" = Bu^{s}
g R = Ph, R" = Bu^{t}
h R = H, R" = Bu
j R = H, R" = Ph
k R = Me, R" = Bu
m R = Me, R" = Ph
n R = R" = Pr

Scheme 4

examined. The limited water solubility of the substrates did not seem to inhibit the reaction. The products of these transformations are shown in Table 1. A number of interesting points emerge from this work. Small groups such as a hydrogen or methyl attached at the epoxy end appear to protect that end from attack. Otherwise, the epoxide ring is opened to give a diol and the ketone function reduced to give the corresponding alcohol. Thus, epoxy alcohol formation was observed with the mono-substituted epoxides **1h** and **1j** the methyl-substituted epoxides **1k** and **1m** and the propylated derivative **1n**. Large substituents at both ends inhibited the reaction totally. When the epoxy ketones **14a** and **14b** were treated with fermenting yeast, only starting material was isolated (in 66 and 78% yield, respectively) suggesting an upper limit to the steric bulk of the substrates for effective transformations. In one case only, the methyl ketone **1a**, we observed formation of a keto diol (*i.e.* only epoxide ring-opening) this reaction fitting the pattern that small groups protect that end from reaction with baker's yeast. In all other cases we only observed triol formation (*i.e.* the combined effect of reduction of the ketone and hydration of the epoxide). These results are considered separately in the two sections below.

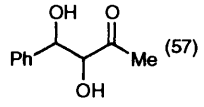
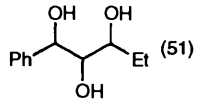
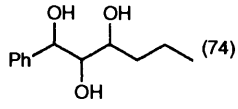
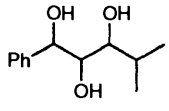
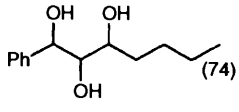
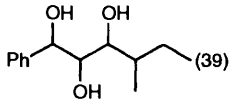
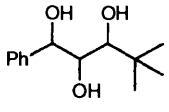
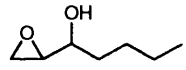
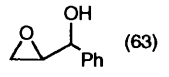
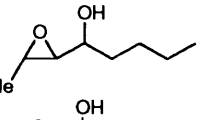
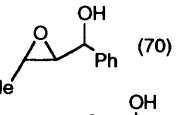
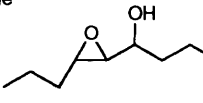
Baker's Yeast-mediated Formation of αβ-Epoxy Alcohols.—(i) *Stereoselectivity in general.* Although yields of reduced product were reasonable (56–67%) the diastereoisomeric excesses (d.e.s) of the product epoxy alcohols were disappointingly low to moderate (13–64%). The highest d.e. was observed for the transformation of *trans*-2,3-epoxyoctan-4-one **1k** (64.3%).

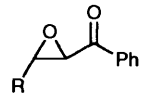
(ii) *The role of the organism/enzyme system.* The fermenting yeast mixture has a pH of 3.5. However, only in one case was a non-enzymatic reaction found to proceed in a similar solution lacking yeast. The epoxy ketone **1a** was slowly transformed into the dihydroxy ketone **2** in a sulfuric acid buffered solution of the medium *lacking* yeast. This compound was, therefore, eliminated from further study.

Freshly cultivated yeast free from other foreign organisms gave similar results to the commercial product when the epoxy ketone **1k** was used (68% yield, 66.5% d.e.). Furthermore, a commercial preparation of YADH (from baker's yeast) had no effect on this epoxy ketone despite adequate added NAD^{+} and ethanol. With the yeast *Hansenula anomala* under the usual conditions a similar yield of the product (64%) was produced, but in a reduced d.e. (27%).

(iii) *How many enzymes are involved in the transformation?* It is possible that the transformations are mediated by one enzyme that can react (i) with both enantiomers of the racemic epoxy ketone (*i.e.* low substrate stereoselectivity) or it can react (ii) to give both *R* and *S* epoxy alcohols from either starting enantiomer (low product stereospecificity). Alternatively, more than one oxidoreductase enzyme may be involved in the transformation (which may have the same or different substrate/product selectivities). Following literature analogies, we have conducted several experiments to clarify the position

Table 1 Transformation of αβ-epoxy ketones with baker's yeast

Epoxy ketone		Product yield (%)	Recov'd 1 [%]	Diastereoisomeric Excess (d.e.)
1a	**2**	 (57)		35.5
1b	**3**	 (51)		one diastereoisomer
1c	**4**	 (74)		one diastereoisomer
1d	**5**	 (22)	[54]	one diastereoisomer
1e	**6**	 (74)		one diastereoisomer
1f	**7**	 (39)	[29]	one diastereoisomer
1g	**8**	 (13)	[67]	one diastereoisomer
1h	**9**	 (56)	[11]	13.0
1j	**10**	 (63)	[6]	16.7
1k	**11**	 (67)	[24]	64.3
1m	**12**	 (70)	[17]	28.6
1n	**13**	 (67)	[17]	23.1



a R = Ph
b R = $(CH_2)_8CH_3$

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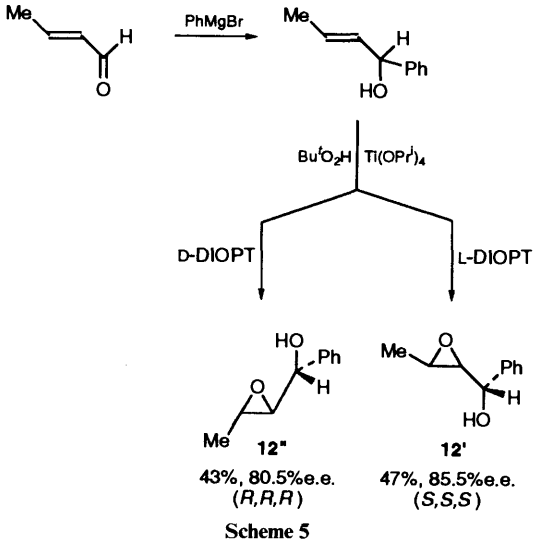
and conclude that more than one oxidoreductase is involved in our reductions.

Two alternative methods have been employed to show up multiple enzyme action in yeast-mediated reductions. (i) Addition of allyl alcohol is known[9] to inhibit specifically the undesired *S*-alcohol oxidoreductase and thus leads to a

significant increase in the *R*-alcohol formation. (ii) Alternatively, elimination of sucrose from the medium has a dramatic effect on the product e.e. in ketone reductions. For example,[10] ethyl 3-oxooctanoate shows an increase from 15% e.e. to >97% e.e. on successive diminution of the added sucrose from 200 to 0 g dm^{-3}. (This effect derives from the optimisation of rate differences in the reduction mediated by the two competing enzymes that produce *R* and *S* alcohols by starving them of ample NADPH. The necessary sugar is only accessible from endogenous carbohydrates which generate NADPH by the pentose phosphate pathway.)

Application of these methods amply supported the role of multiple enzyme action leading to our products. Thus, when the epoxy ketone **1k** was treated in the usual way but with added allyl alcohol the d.e. was *lowered* from 64.3 to 16%. Furthermore, when the ketone **1m** was allowed to react in the absence of added sugar the d.e. *increased* from 28.6 to 64.4%.

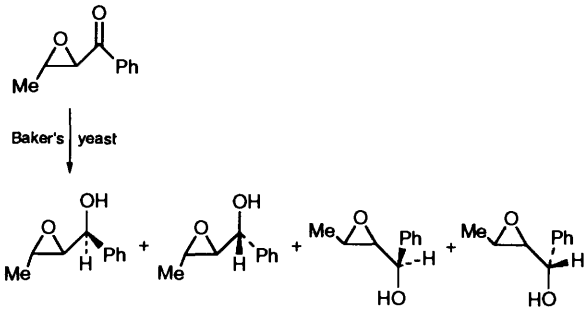
(iv) *Stereochemical outcome of the epoxy alcohol formation.* It is evident that this reduction (asymmetric) also accomplishes the kinetic resolution of the epoxide and thus both diastereoisomeric pairs of product epoxy alcohols could be formed. The degree of stereoselectivity would be indicated by the ratio and optical purity of the two diastereoisomers. All attempts to separate them, however, proved fruitless as did the attempt to prepare and utilise Mosher esters;[11] the esterification of the epoxy alcohol **1m** with (*R*)-(+)-methoxy(trifluoromethyl)-phenylacetyl chloride gave the required esters admixed with Payne rearrangement[12] products (diastereoisomers of 1,2-epoxy-1-phenylbutan-3-ol). We, therefore, resorted to the use of a chiral shift reagent—(+)-[Pr(hfbc)$_3$]. When added to a solution of the epoxy alcohol **1m**, the two distinct doublets for the diastereoisomeric C*H*OH protons only broadened. However, the acetate ester of the mixed epoxy alcohols were effectively resolved into four doublets in two distinct pairs by addition of (+)-[Pr(hfbc)$_3$] with signals at 4.86 and 5.14; 5.49 and 5.58 ppm in the ratio 3.35:1.09:1.00:1.41, respectively. In order to define which signal corresponded to which isomer and, thereby, to prove the degree of stereoselectivity of the yeast-mediated epoxidation, we synthesised two enantiomers of **1m** using the Sharpless method[13] as shown in Scheme 5 starting with crotonaldehyde.



Scheme 5

The enantiomeric purities were found using (+)-[Pr(hfbc)$_3$] on the acetate esters of the two products.

The *erythro*-(*S,S,S*)-isomer **12'** was oxidised to the epoxy ketone **1m'** with pyridinium dichromate {85.4% e.e. by shift reagent assay; the ^{13}C NMR signals for the enantiomeric epoxide ring carbons were also well resolved in the presence of (+)-[Pr(hfbc)$_3$]}. When this ketone was reduced with baker's yeast in the usual way the product epoxy alcohol **12** (55.3%) was obtained as a mixture of the *erythro*-(*S,S,S*) and *threo*-(*S,S,R*)-diastereoisomers in a ratio of 1.7 to 1.0 (25.9% d.e.) indicating an *S*-preference in the yeast reduction. When the enantiomeric epoxy alcohol **12"** was similarly oxidised and the derived ketone (**1m"**, 80.5% e.e.) reduced with yeast the *erythro*-(*R,R,R*)- and *threo*-(*R,R,S*)-epoxy alcohols were obtained in a ratio of 1.3:1.0, again showing a small *S*-preference. These two pairs of epoxy alcohols were acetylated and allowed a definitive characterisation of the four C*H*OAc protons from the product **12** of bakers yeast reduction of the racemic epoxy ketone **1m**, by use of the shift reagent. The results are summarised in Scheme 6. It is evident that Prelog's rule does not hold in this reduction.



	threo *R,R,S*	*erythro* *R,R,R*	*threo* *S,S,R*	*erythro* *S,S,S*
% yield:	14.4%	11.2%	10.2%	34.2%
Ratio:	1.41	1.09	1.00	3.35

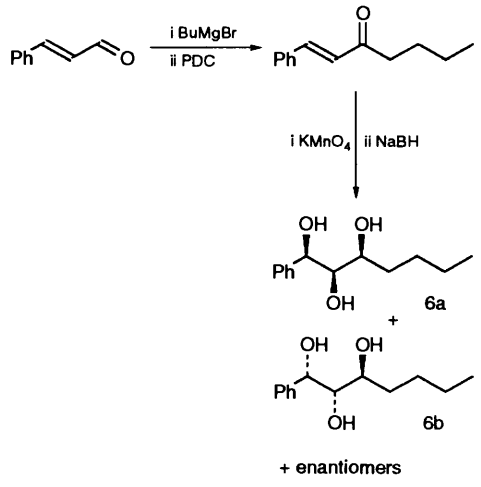
Scheme 6 Ratio *S*/*R* reduction at the carbonyl group = 2.27:1.00. Ratio *erythro*/*threo* = 1.77:1.00.

The chiral discrimination of the oxidoreductases in the epoxy ketone reductions is poor at best and worse in the case of the *R,S*/*S,R* epoxy ketone than in the *R,R*/*S,S*-case. The yeast-mediated reduction of the *R,S*-enantiomer gives the *erythro* and *threo* products in a ratio of 3.35:1, equivalent to an e.e. of 54.6%—and this is the best case, the other enantiomer showing only a 13% e.e. The extent of kinetic resolution of the racemic epoxide is only 26.9% in favour of the *S*-epoxide.

In summary, both enantiomers of the epoxy ketones yield both *R*- and *S*-epoxy alcohols, due to the participation of two (or more) enzymes. A preference for *S*-reduction is observed, the addition of allyl alcohol (known to suppress this process) leading to an understandable diminution of the overall e.e. when the racemic epoxy ketone was reduced.

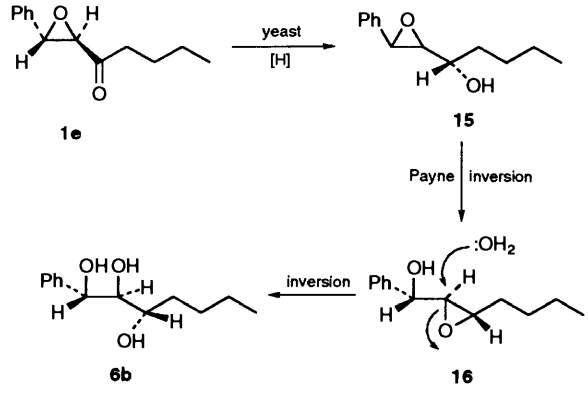
Baker's Yeast-mediated Formation of 1,2,3-*Triols.*—(i) *Overall results.* 1-Phenyl substituted -αβ-epoxy ketones **1b–g** are all transformed into the 1,2,3-triols **3–8**, respectively, on treatment with baker's yeast. All of the products are optically inactive and since the ^{13}C NMR spectra consist solely of one set of peaks in all cases, the triols are evidently only one diastereoisomer. To prove that this was indeed the case we synthesised the two diastereoisomers of the triol **6** as in Scheme 7 and a mixture of the two gave doubled resonances as expected. Furthermore, to prove that this surprising result was not the result of a non-enzymatic ring-opening was shown by control experiments without the yeast. A similar result was also obtained with freshly cultivated pure *Saccharomyces cerevisiae* which transformed the epoxy ketone **1e** into the single diastereomeric triol **6**. The relative configuration of the triol **6** was demonstrated by X-ray crystallography to be the *S,S,S*- and *R,R,R*-pair of enantiomers **6b**.

(ii) *Mechanism of formation of the triols.* It is immediately evident that the formation of the triol **6b** involves a *syn*-ring-



Scheme 7

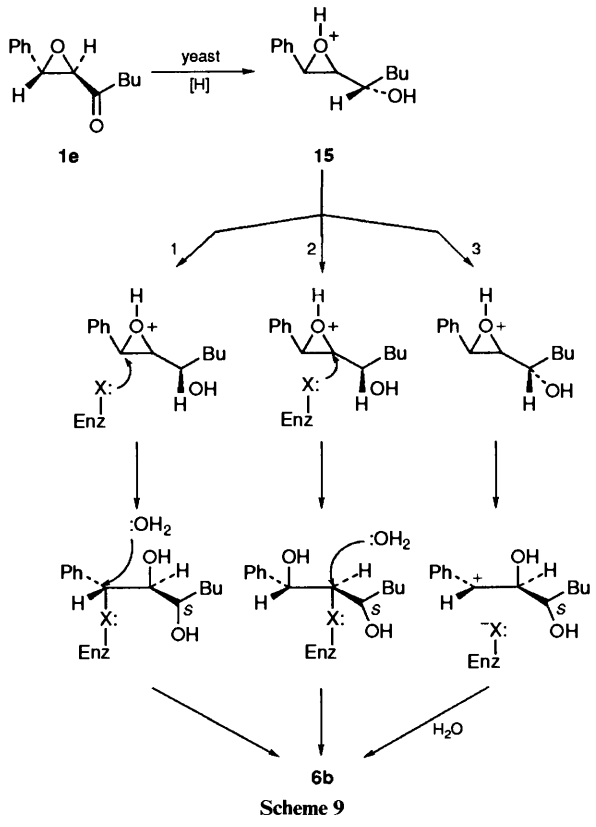
opening of the epoxide ring—an unprecedented scenario. We have considered the following alternative mechanisms: (*a*) Initial ketone reduction (at the *Re* face) of, for example, the 1*S*,2*R*-epoxide **1e** would give the *S*,*S*,*S*-epoxy alcohol **15** (Scheme 8) which could then undergo a Payne rearrangement



Scheme 8

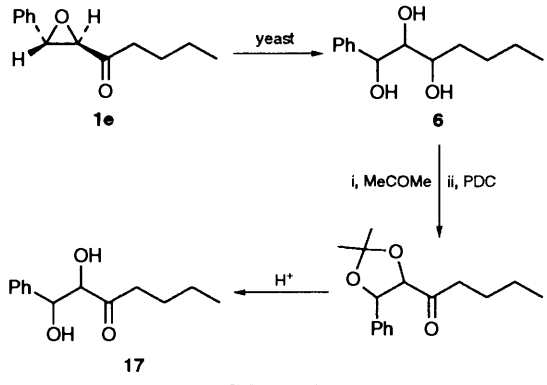
to yield the rearranged (and inverted) epoxide **16** which upon ring-opening in the usual *anti*-manner would result in the *S*,*S*,*S*-triol **6b**. This double inversion would result in retention of the initial epoxide stereochemistry. (Only one of the two possible enantiomeric epoxides **1e** have been considered for clarity.) (*b*) An alternative explanation is described in Scheme 9 wherein asymmetric reduction of the ketone group is followed by an enzyme-mediated double inversion in the ring-opening of the epoxide (paths 1 and 2) or by retention in this step (path c). Paths 1 and 2 involve two consecutive S_N2 reactions at one or other of the epoxide carbons while path 3 requires an ion-pair formation and a non-concerted attack by water on the resonance-stabilised benzylic cation. Unlike the Payne-mediated mechanism, those described in Scheme 9 could equally well proceed by first ring-opening of the epoxide followed by reduction of the oxo-group.

In order to throw light on the sequence of the reactions we conducted several simple experiments. (1) The yeast-mediated reaction of the epoxy ketone **1e** was sampled at intervals of 5 h and the possible appearance of intermediates checked by TLC and gas chromatography. Only starting material and the final triol product **6** was detected. (2) The diastereoisomeric mixture of the epoxy alcohols **15** produced by sodium borohydride reduction of the epoxy ketone **1e**, was subjected to the action of yeast. The triol **6** was, indeed, the sole product (though in reduced yield—62% as against 72% from the epoxy ketone)



Scheme 9

despite the fact that probably only one diastereoisomer of the epoxy alcohol **15** is likely to mediate the conversion of the epoxy ketone into the single diastereoisomeric triol by yeast. (3) The diol ketone **17** was synthesised as shown in Scheme 10 and

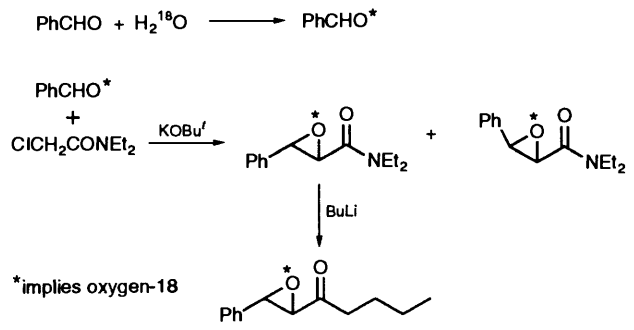


Scheme 10

subjected to yeast treatment. Only starting material was isolated. Taken together these experiments strongly support the reduction of the carbonyl group prior to epoxide hydrolysis to explain the course of triol formation. However, they do not distinguish the mechanism involving the Payne rearrangement from those in Scheme 9.

This key point was clarified by subjecting the epoxy ketone **1e**, labelled with ^{18}O on the epoxy oxygen, to the yeast action. The necessary labelled material was made as in Scheme 11 starting with ^{18}O-labelled benzaldehyde, produced from benzaldehyde and ^{18}O-labelled water. Thus, the labelled benzaldehyde was treated with *N*,*N*-diethyl-2-chloroacetamide in a Darzens condensation and the *trans*-isomer of the product epoxy amide treated with butyllithium (Scheme 11).

It was immediately evident that no ^{18}O was lost during the yeast incubation as judged by mass spectral data. ^{18}O causes a small upfield shift of attached α-carbon NMR signals of about



Scheme 11

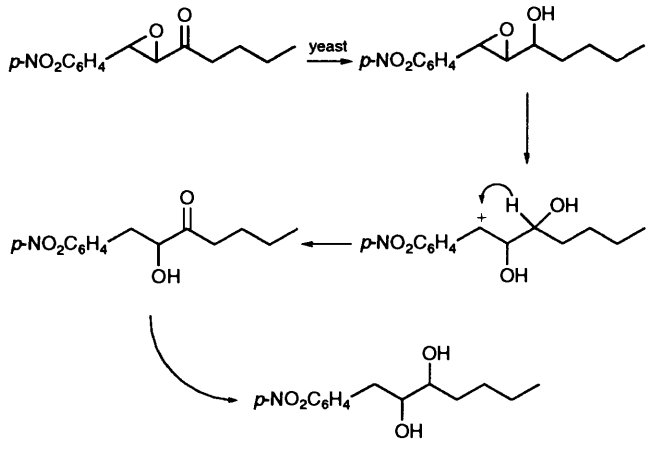
0.2 ppm.[14] Thus, the carbon resonance with attached ^{18}O would appear as a doublet in the ratio of ^{18}O to ^{16}O (the ratio being 43 : 57 respectively). Only the resonance at 78.90 ppm due to the middle C-OH group of the triol showed this doubling. The assignment of the carbon shifts was corroborated by H,C-COSY spectral assignments of the NMR shifts. This result is not compatible with the Payne mechanism but conforms to the pathways 1 or 3 in Scheme 9 indicating either a double inversion or a retention of configuration during epoxide ring-opening.

The NMR evidence was further supported by the mass spectral data of the labelled triol which, although it did not give a molecular ion showed a peak for M − H_2O at *m/z* 208 with complete retention of the label and one at *m/z* 206 for the ^{16}O analogue. Furthermore, a peak at *m/z* 139 (43% of that at 137) characteristic of the ion $PhCHOHCH^{18}OH^+$, but *not* one at *m/z* 109 ($PhCH^{18}OH^+$) supports the above assignment of labelling at the central carbon of the triol.

We have endeavoured to pinpoint the mechanistic detail more exactly by further experiments. The questions still unanswered are: (1) Is the *syn*-epoxide ring-opening due to a double inversion (Scheme 9—1) or retention of configuration? (Scheme 9—3). (2) If more than one enzyme is involved in the formation of the triols how do they operate? (3) Does the epoxide ring-opening involve one epoxy alcohol enantiomer giving one enantiomeric triol while the other enantiomer gives the other enantiomer of the triol? Or are both enantiomeric epoxy alcohols the source of the same triol?

To answer the first question we examined two *para*-substituted analogues of the phenyl pentanoyloxirane **1e**. If the mechanism of epoxide ring-opening involved a carbocation intermediate then a *p*-nitro group on the phenyl ring should inhibit while a *p*-methoxy group should enhance the process (and demonstrate that any lack of reactivity in the *p*-nitro compound was not a steric limitation in the enzyme). The results were unexpected. The *p*-methoxy compound underwent ready epoxide hydrolysis at pH 3.5 *without* added yeast and gave the same dihydroxy ketone with added yeast—clearly a non-enzymic process. The *p*-nitro compound underwent only ketone reduction to give the corresponding epoxy alcohol as the major product, thus supporting the mechanism implying a carbocation intermediate. As a minor product, however, we also observed reduction of both the ketone *and* the epoxide group to give 1-*p*-nitrophenyl-2,3-dihydroxyheptane **18** which, although it showed no optical rotation, was evidently only one diastereoisomer. A possible explanation is shown in Scheme 12 wherein the destabilised carbocation undergoes a 1,2-hydride shift followed by further yeast-mediated reduction. Alternatively, the hydride ion could be delivered by NADPH. We know of no analogues of this process in the literature.

Whether one enzyme or more mediate the triol formation is not certain. The addition of allyl alcohol to the reaction mixture had no effect on the overall stereochemistry of this process. The remarkable conclusion remains, however, that the catalytic efficiency parameters, V_{max}/K_m, of the two antipodal processes



Scheme 12

leading to racemic triol are identical. In other words, the reduction of the epoxy ketone occurs from the *Re*-face of the (1*S*,2*R*) derivative to give (1*S*,2*S*,3*S*)-triol and from the *Si*-face of its enantiomer to give solely the (1*R*,2*R*,3*R*)-triol. Furthermore, the subsequent oxirane hydrolysis is equally stereospecific leading to one diastereoisomeric triol.

To further underline the truth of these conclusions we have conducted one more set of experiments. The homochiral epoxy ketone **1e** (1*S*,2*R*) and the derived homochiral epoxy alcohol **15** (1*S*,2*S*,3*S*) were synthesised [from cinnamaldehyde by sequential treatment with BuMgBr, Sharpless epoxidation with L-(+)-DIPT, and oxidation of the derived epoxy alcohol **15** with PDC] and separately treated with baker's yeast. They gave essentially identical products, the triol **6** (1*S*,2*S*,3*S*), the enantiomer of the same diastereoisomer obtained from racemic epoxy ketone **1e**.

Experimental

Melting points were determined on a Reichert Kofler hot-stage apparatus and are uncorrected. IR spectra were obtained on Perkin-Elmer 257 or 883 instruments as liquid films or Nujol mulls. NMR spectra were recorded in $CDCl_3$ solution with tetramethylsilane as internal standard on a Varian 390 (^1H, 90 MHz), a Varian Gemini 200 (^1H, 200 MHz; ^{13}C, 50 MHz) or a Bruker AM 300 (^{13}C, 75 MHz) or WM 500 (^1H, 500 MHz; ^{13}C, 125 MHz). *J*-Values are in Hz. Mass spectra were obtained with a Varian MAT 212 mass spectrometer and microanalyses were performed by the Microanalytical Laboratory of the CSIR. Specific rotations ($[\alpha]_D$) were determined using a Perkin-Elmer 241 polarimeter and are given in units of 10^{-2} deg cm^2 g^{-1}. Gas chromatography analyses were conducted on a Varian 3400 machine. TLC was performed with Merck silica 60 F254 plates and column chromatography on Merck silica 60 [70–230 mesh or 230–499 mesh (for flash chromatography)].

Light petroleum refers to that of b.p. 60–80 °C and ether implies diethyl ether. Tetrahydrofuran (THF) was distilled from sodium–potassium and benzophenone prior to use. Epoxidations were conducted in oven-dried glassware under nitrogen or argon and followed by TLC using Hammock's[15] spray reagent [4-(4-nitrobenzyl)pyridine] and tetraethylenepentamine to visualise the epoxide spots. Baker's yeast was obtained from the local supermarket (supplied by Anchor) and stored at 0 °C. ^{18}O-Labelled water (97–98 atom% ^{18}O) was obtained from Cambridge Isotope Laboratory and yeast alcohol dehydrogenase (240 U mg^{-1}) was purchased from Sigma Chemical Company. Pure yeast strains, *Saccharomyces cerevisiae* and *Hansenula anomala* were obtained from the Division of Food Science and Technology of the CSIR.

The following compounds were prepared by literature methods: *N,N*-diethyl-2-chloroacetamide,[16] 1,1,1,3,3,3-hexamethyldisilazan-2-yllithium,[17] 1-chlorohexan-2-one,[18] anhydrous *tert*-butyl hydroperoxide (TBHP) in toluene,[19] pyridinium dichromate,[20] (*R*)-(+)-methoxy(trifluoromethyl)phenylacetyl chloride (MTPACl),[11] the amides *trans-N,N*-diethylbut-2-enamide, *trans-N,N*-diethylprop-2-enamide and *N*-(*trans*-3-phenylprop-2-enoyl)pyrrolidine.[3a]

N-(trans-*Hex*-2-*enoyl*)*pyrrolidine*.—This amide was prepared by Meth-Cohn's method[3a] and purified by flash chromatography (ether) to give the title product (95%) as an oil, R_f 0.19; ν_{max}(neat)/cm^{-1} 1660 (C=O) and 1440 (C=C) (Found: M, 167.132. $C_{10}H_{17}NO$ requires *M*, 167.131); *m/z* 70 ($C_4H_8N^+$); δ_H 6.65 (1 H, m, 3-CH), 5.80 (1 H, d, *J* 14.0, 2-CH), 3.18 (4 H, q, *J* 6.0, α-CH_2 of ring), 1.85 (2 H, m, 4-CH_2), 1.60 (4 H, m, β-CH_2 of ring), 1.17 (2 H, m, 5-CH_2) and 0.62 (3 H, t, *J* 7.0, Me); δ_C 164.4 (C=O), 144.8, 121.3 (2-H and 3-H), 45.7 and 44.9 (α-CH_2 of ring), 33.5, 25.2, 23.4 and 20.75 (CH_2) and 12.7 (Me).

Preparation of αβ-*Epoxy Amides*.—*cis*- And *trans-N,N*-diethyl-3-phenyl-2,3-epoxypropinamide were prepared by Darzens condensation.[21] *N*-(*trans*-2-Phenyl-2,3-epoxypropionyl)pyrrolidine, *N,N*-Diethyl-2,3-epoxypropionamide and *trans-N,N*-diethyl-2,3-epoxybutyramide were prepared by Meth-Cohn's method.[3a]

cis- *and* trans-NN-*Diethyl*-3-(p-*methoxyphenyl*)-2,3-*epoxypropionamide*.—The crude oil (13.7 g, 55%) from the Darzens condensation[21] of *p*-methoxybenzaldehyde (13.6 g, 0.10 mol) and 2-chloro-*N,N*-diethylacetamide (14.95 g, 0.10 mol) was purified by flash chromatography (light petroleum–ether, 1:3) to give trans-N,N-*diethyl*-3-(p-*methoxyphenyl*)-2,3-*epoxypropionamide* as a viscous oil (7.22 g, 29%); ν_{max}(neat)/cm^{-1} 1630 (C=O), 1510, 1460 and 1440; [Found: *m/z* 249.137 (M^+); $C_{14}H_{19}NO_3$ requires 249.137]; *m/z* 231 ($M^+ - H_2O$) and 83 ($C_7H_7O^+$); δ_H 7.13 (2 H, d, *J* 8.0, ArH), 6.78 (2 H, d, *J* 8.0, ArH), 3.90 (1 H, d, *J* 2.0, 2-Me), 3.50 (1 H, d, *J* 2.0, 3-CH), 3.68 (3 H, s, OMe), 3.32 (2 H, q, *J* 7.0, CH_2), 3.28 (2 H, q, *J* 7.0, CH_2), 1.08 (3 H, t, *J* 7.0, Me) and 1.05 (3 H, t, *J* 7.0, Me); δ_C 165.8 (C=O), 127.4 (Ar*C*), 126.9, 113.9 (Ar*C*H), 56.7, 54.9 (2-CH and 3-CH), 57.1 (OMe), 41.1 and 40.4 (CH_2), 14.4 and 12.45 (Me).

Further elution with the same solvent (1:4) gave cis-N,N-*diethyl*-3-(p-*methoxyphenyl*)-2,3-*epoxypropionamide* as an oil (5.32 g, 21%); ν_{max}(neat)/cm^{-1} 1635 (C=O) and 1600; [Found: *m/z* 249.136 (M^+); $C_{14}H_{19}NO_3$ requires 249.137]; *m/z* 231 ($M^+ - H_2O$) and 83 ($C_7H_7O^+$); δ_H 7.28 (2 H, d, *J* 8.2, ArH), 6.73 (2 H, d, *J* 8.2, ArH), 4.08 (1 H, d, *J* 5.3, 2-CH), 3.74 (1 H, d, *J* 5.3, 3-CH), 3.68 (3 H, s, 3-CH), 3.05 (2 H, q, *J* 7.0, CH_2), 2.98 (2 H, q, *J* 7.0, CH_2), 0.90 (3 H, t, *J* 7.0, Me) and 0.70 (3 H, t, *J* 7.0, Me); δ_C 164.9 (C=O), 129.6 (Ar*C*), 127.5, 113.4 (Ar*C*H), 57.5, 54.8 (2-CH and 3-CH), 56.7 (OMe), 40.1 and 38.9 (CH_2), 13.5 and 11.9 (Me).

^{18}O-*Labelled* trans-N,N-*Diethyl*-3-*phenyl*-2,3-*epoxypropionamide*.—Benzaldehyde (400 mm^3) in acidic tetrahydrofuran (0.001 mol dm^{-3} HCl; 1 cm^3) and $H_2{}^{18}O$ (200 mm^3) were stored in a stoppered flask at room temperature for 12 h. Further benzaldehyde (600 mm^3) was added to the solution which was then left for a further 1 h. After the mixture had been dried ($MgSO_4$) and filtered it was treated with 2-chloro-*N,N*-diethylacetamide (1.41 g, 9.4 mmol) under the above Darzens conditions to give a crude oil (1.76 g, 85%). This was purified by flash chromatography as above to give the *title compound* as colourless crystals from hexane, m.p. 89–90 °C [Found: C, 71.0; H, 7.7; N, 6.4. $C_{13}H_{17}NOO^*$ (* indicates 43% ^{18}O: 57% ^{16}O) requires C, 70.9; H, 7.8; N, 6.4%]; ν_{max}(Nujol)/cm^{-1} 1650 (C=O), 1475, 1380, 1360 and 1220; the mass spectrum showed 43% incorporation of oxygen-18; *m/z* 219 and 221 (M^+ ratio 1.3:1), 147 and 149 ($M^+ - NEt_2$ ratio 1.3:1), 119 and 121 ($M^+ - CONEt_2$ ratio 1.3:1), 91 ($M^+ - CONEt_2$, −CO ratio 1.3:1) and 77 ($C_6H_5^+$); δ_H 7.5–7.25 (5 H, br, ArH), 4.05 (1 H, d, *J* 2.4, 2-CH), 3.55 (1 H, d, *J* 2.4, 3-CH), 3.45 (4 H, q, *J* 7.1, CH_2), 1.15 (3 H, t, *J* 7.1, Me) and 1.10 (3 H, t, *J* 7.1, Me); δ_C 165.35 (C=O), 135.4 (Ar*C*), 128.4, 128.3 and 125.3 (Ar*C*H), 56.9, 56.5 (2-CH and 3-CH), 40.9 and 40.2 (CH_2), 14.2 and 12.2 (Me).

N-(trans-2,3-*Epoxyhexanoyl*)*pyrrolidine*.—The compound was prepared according to the method of Meth-Cohn[3a] and purified by flash chromatography (ether) to give the *title product* as an oil (5.92 g, 90%); ν_{max}($CHCl_3$)/cm^{-1} 1650 (C=O) and 1230 (C–O); [Found: *m/z* 183.125 (M^+). $C_{10}H_{17}NO_2$ requires 183.126; 165 ($M^+ - H_2O$)]; *m/z* 70 ($C_4H_8N^+$); δ_H 4.25 (1 H, d, *J* 3.5, 2-CH), 3.95 (1 H, br t, 3-CH), 3.50 (4 H, m, α-CH_2 of ring), 1.90 (4 H, m, β-CH_2 of ring), 1.78–1.25 (4 H, m, CH_2) and 0.90 (3 H, t, *J* 7.0, 6-Me); δ_C 170.4 (C=O), 73.0 and 62.6 (2-CH and 3-CH) 46.5 and 46.1 (α-CH_2), 34.75 and 18.95 (CH_2) 25.7 and 23.75 (β-CH_2) and 13.2 (Me).

Preparation of the Epoxy Ketones **1**.—*trans*-1-Phenyl-2,3-epoxypropan-1-one **1j**, *trans*-1,3-diphenyl-2,3-epoxypropan-1-one **13a** and *trans*-1,2-epoxyheptan-3-one **1h** were prepared according to our previously described method.[3a]

trans-1-*Phenyl*-1,2-*epoxybutan*-3-*one* **1a**. A solution of *trans-N,N*-diethyl-3-phenyl-2,3-epoxypropionamide (0.73 g, 3.34 mmol) in dry THF (100 cm^3) −78 °C under nitrogen was treated with methyllithium (1.39 mol dm^{-3} solution; 36 cm^3, 4.51 mmol). The solution was stirred for 30 min at −78 °C and then warmed to ambient temperature when it was treated with water (100 cm^3) and extracted with ether. The extract was dried ($MgSO_4$) and evaporated and the residue purified by flash chromatography (light petroleum–ether, 1:1) to give the *title product* (0.53 g, 98.5%) as colourless crystals from hexane, m.p. 56–57 °C; R_F 0.25 (Found: C, 74.0; H, 6.1. $C_{10}H_{10}O_2$ requires C, 74.1; H, 6.2%); ν_{max}($CHCl_3$) cm^{-1} 1720 (C=O) and 1610, 1500, 1420 and 1255 (C–O); *m/z* 162 (M^+), 144 ($M^+ - H_2O$) and 77 ($C_6H_5^+$); δ_H 7.4–7.2 (5 H, m, ArH), 3.98 (1 H, d, *J* 2.5, 2-CH), 3.45 (1 H, d, *J* 2.5, 1-CH) and 2.15 (3 H, s, 4-Me); δ_C 204.1 (C=O), 135.1 (ArC), 128.9, 128.6, 125.6 (ArCH), 63.1 and 57.4 (2-CH and 1-CH) and 24.3 (Me).

trans-1-*Phenyl*-2,3-*epoxydecan*-1-*one* **13b**. The crude oil (40%) obtained from a Darzens condensation[21] of decanal (5.15 g, 0.03 mol) and 2-bromoacetophenone (6.5 g, 0.03 mol) was purified by flash chromatography (light petroleum–ether, 1:1) to give the *title compound* **13b** (2.86 g, 32%) as a white solid from hexane, m.p. 93–94 °C (Found: C, 78.9; H, 9.3. $C_{18}H_{26}O_2$ requires C, 78.8; H, 9.55%); ν_{max}(Nujol)/cm^{-1} 1700 (C=O), 1600, 1440, 1410 and 1220 (C–O); *m/z* 274 (M^+), 256 ($M - H_2O$) and 77 ($C_6H_5^+$); δ_H 8.15–7.35 (5 H, m, ArH), 4.00 (1 H, d, *J* 2.4, 2-CH), 3.15 (1 H, dt, *J* 2.3 and 6.0, 3-CH), 1.90–1.05 (16 H, m, CH_2) and 0.90 (3 H, t, *J* 7.0, Me); δ_C 194.7 (C=O), 135.6 (ArC), 133.7, 128.7, 128.2 (ArCH), 60.0 and 57.45 (2-CH and 3-CH), 31.95, 31.8, 29.4, 29.3, 29.2, 25.8, 22.6 (CH_2) and 14.05 (Me).

trans-4-*Methyl*-1-*phenyl*-1,2-*epoxypentan*-3-*one* **1d**. Following the above method but using 1-bromo-3-methylbutan-2-one (22.2 g, 0.14 mol) and benzaldehyde (14.3 g, 0.14 mol) as reactants, the crude epoxy ketone (22.0 g, 83%) was purified by flash chromatography (light petroleum–ether, 1:1) to give the *title compound* **1d** (15.56 g, 58.5%) as an oil (Found: C, 75.6; H, 7.3. $C_{12}H_{14}O_2$ requires C, 75.8; H, 7.4%); ν_{max}(neat)/cm^{-1} 1715 (C=O), 1615, 1520 and 1464; *m/z* 190 (M^+), 147 ($M^+ - C_3H_7$), 119 ($M^+ - C_3H_7 - CO$) and 77 ($C_6H_5^+$); δ_H 7.45–7.15 (5 H, br, ArH), 3.90 (1 H, d, *J* 1.5, 2-CH), 3.58 (1 H, d, *J* 1.5, 3-CH), 2.80 (1 H, m, 4-CH) and 1.10 (6 H, d, *J* 6.9, Me); δ_C

208.0 (C=O), 134.9 (ArC), 128.0, 128.2, 125.2 (ArCH), 61.3 and 57.8 (2-CH) and 1-CH, 36.4 (4-CH), 17.5 and 16.8 (Me).

1-(4-*Nitrophenyl*)-1,2-*epoxyheptan*-3-*one*. The crude oil obtained after the usual Darzens condensation[21] of *p*-nitrobenzaldehyde (3.80 g, 0.03 mol) and 1-chlorohexan-2-one (3.40 g, 0.03 mol) was purified by flash chromatography (light petroleum–ether, 1:1) to give the title compound (1.26 g, 20%) as an oil; ν_{max}(neat)/cm^{-1} 1720 (C=O), 1600, 1520, 1460 and 860; *m*/*z* 249 (M^+), 231 ($M - H_2O$), 185 ($M - H_2O - NO_2$) and 77 ($C_6H_5^+$); δ_H 8.15–7.35 (5 H, m, ArH), 4.00 (1 H, d, *J* 2.4, 2-CH), 3.15 (1 H, dt, *J* 2.3 and 6.0, 3-CH), 1.90–1.05 (16 H, m, CH_2) and 0.90 (3 H, t, *J* 7.0, Me); δ_C 194.7 (C=O), 135.6 (ArC), 133.7, 128.7, 128.2 (ArCH), 60.0 and 57.45 (2-CH and 3-CH), 31.95, 31.8, 29.4, 29.3, 29.2, 25.8, 22.6 (CH_2) and 14.05 (Me).

trans-1-*Phenyl*-2,3-*epoxybutan*-1-*one* **1m**. α-Bromoacetophenone (13.90 g, 0.07 mol) in THF (40 cm^3) was added dropwise to a solution of lithium bis(trimethylsilyl)amide (0.6 mol dm^{-3}; 140 cm^3) amd THF (50 cm^3) at −78 °C under nitrogen. After the mixture had been stirred for a further 10 min at this temperature acetaldehyde (3.00 g, 0.07 mol) in THF (10 cm^3) was added to it and stirring continued for a further 20 min at −78 °C. The mixture was then diluted first with water and then ether after which the organic phase was separated, washed with dilute hydrochloric acid and then water, dried ($MgSO_4$) and evaporated. Flash chromatography (light petroleum–ether, 3:1) of the residue gave the *title product* (7.61 g, 67.4%) as colourless crystals from light petroleum, m.p. 65–66 °C (Found: C, 74.0; H, 6.3. $C_{10}H_{10}O_2$ requires C, 74.1; H, 6.2%); ν_{max}(Nujol)/cm^{-1} 1700 (C=O), 1600, 1580, 1450 and 1420; *m*/*z* 162 (M^+), 144 ($M^+ - H_2O$) and 77 ($C_6H_5^+$); δ_H 8.1–7.9 (2 H, m, ArH), 7.65–7.35 (3 H, m, ArH), 3.95 (1 H, d, *J* 1.9, 2-CH), 3.20 (1 H, dq, *J* 1.9 and 5.4, 3-CH) and 1.48 (3 H, d, *J* 5.6, Me); δ_C 194.9 (C=O), 135.7 (ArC), 133.8, 128.9, 128.4 (ArCH), 58.2 and 55.8 (2-CH and 3-CH) and 17.4 (Me).

Other epoxides prepared in this way, together with their properties, were as follows. trans-1-*Phenyl*-1,2-*epoxypentan*-3-*one* **1b** (78%) as colourless crystals from hexane, m.p. 43–44 °C (Found: C, 74.9; H, 6.9. $C_{11}H_{11}O_2$ requires C, 75.0; H, 6.9%); ν_{max}(Nujol)/cm^{-1} 1715 (C=O), 1500, 1460, 1410 and 1216 (C–O); *m*/*z* 176 (M^+), 147 (M^+ − Et) and 77 ($C_6H_5^+$); δ_H 7.45–7.15 (5 H, br, ArH), 3.95 (1 H, d, *J* 2.5, 2-CH), 3.48 (1 H, d, *J* 2.5, 1-CH), 2.48 (2 H, t, *J* 7.0, CH_2) and 1.02 (3 H, t, *J* 7.0, Me); δ_C 206.3 (C=O), 135.2 (ArC), 128.9, 128.6, 125.6 (ArCH), 63.0 and 58.0 (2-CH and 1-CH), 31.05 (4-CH_2) and 7.0 (Me).

trans-1-*Phenyl*-1,2-*epoxyhexan*-3-*one* **1c** (70%) as colourless crystals from hexane, m.p. 45–46 °C (Found: C, 76.7; H, 7.5. $C_{12}H_{14}O_2$ requires C, 75.8; H, 7.4%); ν_{max}(Nujol)/cm^{-1} 1705 (C=O), 1500, 1460, 1415 and 1220 (C–O); *m*/*z* 190 (M^+), 147 (M^+ − Pr), 119 (147 − CO), 77 ($C_6H_5^+$) and 43 (Pr^+); δ_H 7.50–7.20 (5 H, m, ArH), 3.95 (1 H, d, *J* 2.4, 2-CH), 3.50 (1 H, d, *J* 2.4, 1-CH), 2.45 (2 H, t, *J* 7.0, 4-CH_2), 1.65 (2 H, sex, *J* 7.0, 5-CH_2) and 0.95 (3 H, t, *J* 7.0, Me); δ_C 205.8 (C=O), 135.25 (ArC), 128.9, 128.6, 125.7 (ArCH), 63.1 and 57.9 (2-CH and 1-CH), 39.6 (4-CH_2), 16.6 (5-CH_2) and 13.7 (Me).

trans-1-*Phenyl*-1,2-*epoxyheptan*-3-*one* **1e** (84%) as colourless crystals from hexane, m.p. 47–48 °C (Found: C, 76.5; H, 7.8. $C_{13}H_{16}O_2$ requires C, 76.4; H, 7.9%); ν_{max}(Nujol)/cm^{-1} 1710 (C=O), 1490, 1465, 1415 and 1260 (C–O); *m*/*z* 204 (M^+), 147 (M^+ − Bu), 119 (147 − CO) and 77 ($C_6H_5^+$); δ_H 7.35–7.00 (5 H, m, ArH), 3.90 (1 H, d, *J* 2.0, 2-CH), 3.40 (1 H, d, *J* 2.0, 1-CH), 2.54–2.20 (2 H, t, *J* 7.0, 4-CH_2), 1.75–1.07 (4 H, m, 5- and 6-CH_2) and 0.90 (3 H, t, *J* 7.0, Me); δ_C 206.0 (C=O), 135.25 (ArC), 128.9, 128.6, 125.7 (ArCH), 63.1 and 57.9 (2-CH and 1-CH), 37.4, 25.2, 22.2 (CH_2) and 13.7 (Me).

trans-4-*Methyl*-1-*phenyl*-1,2-*epoxyhexan*-3-*one* **1f** (53%) as a colourless oil; ν_{max}(Nujol)/cm^{-1} 1715 (C=O), 1610, 1500, 1460 and 1415; *m*/*z* 204.116 (M^+; $C_{13}H_{16}O_2$ requires 204.115), 147 (M^+ − Bu) and 77 ($C_6H_5^+$); δ_H 7.50–7.15 (5 H, m, ArH), 3.92 (1 H, d, *J* 2.5, 2-CH), 3.58 (1 H, d, *J* 2.5, 1-CH), 2.65 (1 H, m, 4-CH), 2.00–1.70 (2 H, m, 5-CH_2), 1.15 (3 H, d, *J* 7.0, Me) and 0.85 (3 H, d, *J* 7.0, Me); δ_C 208.5 (C=O), 135.3 (ArC), 128.8, 128.6, 125.6 (ArCH), 62.1 and 58.0 (2-CH and 1-CH), 43.7 (4-CH), 25.0 (CH_2), 15.9 and 11.4 (Me).

trans-4,4-*Dimethyl*-1-*phenyl*-1,2-*epoxypentan*-3-*one* **1g** (71%) as colourless crystals from hexane, m.p. 104–105 °C (Found: C, 76.3; H, 8.0. $C_{13}H_{16}O_2$ requires C, 76.4; H, 7.9%); ν_{max}(Nujol)/cm^{-1} 1720 (C=O), 1480, 1455, 1410 and 1200; *m*/*z* 204 (M^+), 147 (M^+ − Bu^t), and 77 ($C_6H_5^+$); δ_H 7.48–7.15 (5 H, m, ArH), 3.83 (2 H, br, 2-CH and 1-CH) and 1.20 (9 H, s, 1-Me); δ_C 208.0 (C=O), 135.6 (ArC), 128.8, 128.7, 125.6 (ArCH), 59.3 and 59.1 (2-CH and 1-CH), 43.5 (4-C) and 25.7 (Me).

trans-2,3-*Epoxyoctan*-4-*one* **1k** (70%) as a colourless oil; ν_{max}(Nujol)/cm^{-1} 1710 (C=O) and 1490, 1465, 1415 and 1260 (C–O); *m*/*z* 142.098 (M^+; $C_8H_{14}O_2$ requires 142.099), 124 ($M^+ - H_2O$) and 57 (Bu^+); δ_H 3.05 (1 H, d, *J* 2.4, 3-CH), 2.25 (1 H, m, 2-CH), 1.45 (2 H, t, *J* 6.5, 5-CH_2), 1.30 (3 H, d, *J* 6.1, 1-Me), 1.35–1.10 (4 H, m, CH_2) and 0.78 (3 H, t, *J* 7.0, Me); δ_C 207.9 (C=O), 60.3, 54.0 (3- and 2-CH) 36.5, 24.8, 21.9, 17.2 and 13.4.

trans-(4-*Methoxyphenyl*)-1,2-*epoxyheptan*-3-*one* (25%) as a colourless oil; ν_{max}(Nujol)/cm^{-1} 1720 (C=O) and 1610, 1520, 1460 and 1250; *m*/*z* 234.1260 (M^+; $C_{14}H_{18}O_3$ requires 234.1267), 216 ($M^+ - H_2O$) and 107 ($C_7H_7O^+$); δ_H 7.22–7.10 (2 H, m, ArH), 6.95–6.80 (2 H, m, ArH), 3.88 (1 H, d, *J* 1.8, 2-CH), 3.48 (1 H, d, *J* 1.8, 1-CH), 3.75 (3 H, s, OMe), 2.60–2.30 (2 H, m, 4-CH_2), 1.67–1.10 (4 H, m, CH_2) and 0.85 (3 H, d, *J* 6.8, Me); δ_C 206.7 (C=O), 160.45 (ArC), 127.2, 114.2 (ArCH), 63.05 (OMe) and 57.9 and 55.2 (2-CH and 1-CH), 25.0 and 22.1 (CH_2) and 13.6 (Me).

trans-4,5-*Epoxyoctan*-6-*one* **1n** (27%) as a colourless oil; ν_{max}(Nujol)/cm^{-1} 1680 (C=O) and 1220 (C–O); *m*/*z* 156.114 (M^+; $C_9H_{16}O_2$ requires 156.115) and 138 ($M^+ - H_2O$); δ_H 3.15 (1 H, br, 5-CH), 3.00 (1 H, m, 4-CH), 1.80–1.02 (8 H, m, CH_2) and 1.00–0.70 (6 H, m Me); δ_C 207.9 (C=O), 59.4, 57.9 (5- and 4-CH) 38.7, 33.6, 18.85, 16.3, 13.4 and 13.3.

Oxygen-18 *labelled* trans-1-*phenyl*-1,2-*epoxyheptan*-3-*one*. This epoxide was prepared in the above manner and the crude oily product (70%) purified by flash chromatography (light petroleum–ether, 1:1) to give the title product (0.38 g, 65.1%) as a white solid from hexane, m.p. 47–48 °C.

Reaction of Epoxy Ketones with Baker's Yeast.—General method. Baker's yeast (12.5 g), sucrose (20.0 g) and water (200 cm^3) were stirred at 30 °C in a 500 cm^3 round-bottomed flask fitted with a gas trap. After 30 min the epoxy ketone was added to the mixture which was then stirred for 24 h before further sucrose (20 g) was added to it. After a further 24 h the suspension was subjected to continuous extraction with chloroform (6 h) and the organic extract dried ($MgSO_4$) and evaporated. The crude product was either recrystallised directly or purified by flash column chromatography on silica gel.

Control experiment with trans-1-*phenyl*-1,2-*epoxybutan*-3-*one* **1b** *as substrate*. The pH of a solution of sucrose (20 g) in water (200 cm^3) was adjusted to 3.5 by addition of dilute sulfuric acid. The title epoxide (1.00 g) was added to the solution which was then stirred for 2 days and worked up as above. Chromatography (ether–light petroleum, 1:1) gave unchanged material (0.62 g) together with 1-phenyl-1,2-dihydroxybutan-3-one **2** (0.24 g, 21.6%; *erythro*:*threo* ratio 1.6:1.0).

Formation of Epoxy Alcohols.—From trans-1-*phenyl*-1,2-*epoxybutan*-1-*one* **1b**. Chromatography (ether–light petroleum 1:1) gave unchanged material (17%) followed by 1-phenyl-1,2-epoxybutan-1-ol **12** as an oil (70%; *erythro*:*threo* ratio 1.8:1.0;

d.e. 28.6%) (Found: C, 74.0; H, 7.4. $C_{10}H_{12}O_2$ requires C, 73.15; H, 7.4%); ν_{max}(Nujol)/cm^{-1} 3435 (br, OH), 1505, 1450 and 1390; *m/z* 164 (M^+), 146 ($M^+ - H_2O$) and 77 ($C_6H_5^+$); *threo*-epoxy alcohol; δ_H 7.40–7.20 (5 H, m, ArH), 4.43 (1 H, br, *J* 6.0, 1-CH), 4.75 (1 H, br s, OH), 3.08 (1 H, dq, *J* 3.2 and 6.3, 3-H), 2.90 (1 H, dd, *J* 3.1 and 6.2, 2-CH) and 1.25 (3 H, d, *J* 6.2, Me); δ_C 140.3 (ArC), 128.4, 126.2, 126.2 (ArCH), 73.8, 63.2 and 53.2 (CH) and 17.0 (Me).

From (2S,3R)-1-*phenyl*-1,2-*epoxybutan*-1-*one* **1b**. Chromatography (ether–light petroleum, 1:1) gave unchanged material (4%) followed by 1-phenyl-1,2-epoxybutan-1-ol **12** as an oil (45%); *erythro*:*threo* ratio 1.3:1.0; d.e. 13%; $[\alpha]_D^{25}$ +11.84 (*c* 0.9, $CHCl_3$).

From (2R,3S)-1-*phenyl*-1,2-*epoxybutan*-1-*one* **1b**. Chromatography (ether–light petroleum, 1:1) gave unchanged material (22.4%) followed by 1-phenyl-1,2-epoxybutan-1-ol **12** as an oil (55%); *erythro*:*threo* ratio 1.7:1.0; d.e. 25.9%; +1.2 (*c* 0.3, $CHCl_3$).

From trans-1,2-*epoxyheptan*-3-*one* **1h**. Chromatography (ether–light petroleum, 1:1) gave unchanged material (24%) followed by 1,2-epoxheptan-3-ol **9** as an oil (56%, d.e. 13%); ν_{max}(Nujol)/cm^{-1} 3440br (OH) and 1220; *m/z* 130.099 (M^+; $C_7H_{14}O_2$ requires 130.099) 112 ($M^+ - H_2O$) and 57 (Bu^+); δ_H (minor diastereoisomer indicated with asterisk) 4.20 (1 H, m, 3-CH), 3.60*, 3.35 (1 H, m, 2-CH), 3.15 (2 H, br d, *J* 4.2, 1-CH_2), 2.60 (2 H, m, 4-CH_2) 2.10–1.45 (4 H, m, CH_2) and 1.35 (3 H, t, *J* 7.0, Me); δ_C 71.7*, 68.6, 55.4*, 54.6, 45.1*, 43.4 (1-CH_2 and CH), 34.0*, 33.2, 27.4, 22.6 (CH_2) and 13.9 (Me).

From 2,3-*epoxyoctan*-4-*one* **1k**. Chromatography (ether–light petroleum, 1:1) gave unchanged material (24%) followed by 2,3-epoxyoctan-4-ol **11** as an oil (67%, d.e. 64%); ν_{max}(Nujol)/cm^{-1} 3440br (OH); *m/z* 144.114 (M^+; $C_8H_{16}O_2$ requires 144.115) and 126 ($M^+ - H_2O$); δ_H(minor diastereoisomer indicated with asterisk) 3.78 (1 H, m, 4-CH), 3.40 (1 H, br s, OH), 3.08 and 2.95* (1 H, dq, *J* 3.0 and 6.7, 3-H), 2.70 (1 H, m, 3-CH) and 1.70–1.20 (6 H, m, CH_2), 1.30 (3 H, d, *J* 6.7, Me) and 0.90/0.80* (3 H, t, *J* 7.0, Me); δ_C 71.3*, 68.6, 62.7*, 61.9, 52.75*, 50.9 (2-, 3- and 4-CH), 33.9*, 33.1, 27.3, 27.2, 22.6*, 22.5, 17.0 and 13.75 (CH_2 and Me).

From 1-*phenyl*-2,3-*epoxypropan*-1-*one* **1j**. Chromatography (ether–light petroleum, 1:1) gave unchanged material (6%) followed by 1-*phenyl*-2,3-*epoxypropan*-1-*ol* **10** as an oil (63%; d.e. 16.7%); ν_{max}(Nujol)/cm^{-1} 3420br (OH), 1500 and 1450; *m/z* 150.068 (M^+; $C_9H_{10}O_2$ requires 150.068), 107 ($M^+ - C_2H_3O$) and 77 ($C_6H_5^+$); δ_H(*indicates minor diastereoisomer) 7.50–7.15 (5 H, m, ArH), 5.90* (1 H, d, *J* 3.0, 1-CH), 4.47 (1 H, d, *J* 6.0, 1-CH), 3.25 (1 H, m, 2-H) and 2.85 (2 H, m, 3-CH_2); δ_C 140.1, 139.5* (ArC); 128.5, 128.4*; 128.0, 128.0*; 126.3, 126.2* (ArCH), 74.4, 70.9*; 56.0, 55.0*; 45.3 and 43.6* (CH_2 and CH).

From trans-4,5-*epoxynonan*-6-*one* **1n**. Chromatography (ether–light petroleum, 1:1) gave unchanged material (17%) followed by 2,3-epoxyoctan-4-ol **11** as an oil (67%, d.e. 23%); ν_{max}(Nujol)/cm^{-1} 3430br (OH) and 1220; *m/z* 158.130 (M^+; $C_9H_{18}O_2$ requires 158.131) and 140 ($M^+ - H_2O$) and 115 ($M^+ - Pr$); δ_H 3.82 (1 H, m, 6-CH), 2.90 (1 H, m, 4-H), 2.72 (1 H, br d, *J* 6.2, 5-H), 3.46 (1 H, br, OH) and 1.75–1.12 (8 H, m, CH_2) and 0.90 (6 H, m, Me); δ_C (minor diastereoisomer indicated with asterisk) 71.2*, 68.3; 61.8, 60.9*; 56.7, 54.7* (CH), 36.3, 33.5, 19.1, 18.4 (CH_2), 13.9 and 13.7 (Me).

Formation of Triols.—*From* trans-1-*phenyl*-1,2-*epoxypentan*-3-*one* **1b**. 1-*Phenylpentane*-1,2,3-*triol* **3** (51%) was obtained as white crystals from ethyl acetate–hexane, m.p. 154–155 °C (Found: C, 67.0; H, 8.3. $C_{11}H_{16}O_3$ requires C, 67.3; H, 8.2%); ν_{max}(Nujol)/cm^{-1} 3450br (OH), 1485, 1450 and 1370; *m/z* 178 ($M^+ - H_2O$), 149 (178 – Et) and 77 ($C_6H_5^+$); δ_H 7.65–7.28 (5 H, m, ArH), 4.85 (1 H, br, *J* 4.1, 1-CH), 4.50 (3 H, br, OH), 4.00 (1 H, m, 3-CH), 3.70 (1 H, m, 2-CH), 2.10–1.40 (2 H, m, CH_2) and 1.10 (3 H, t, *J* 7.0, Me); δ_C 144.4 (ArC), 128.5, 127.45, 127.3 (ArCH), 78.5, 74.1 and 73.3 (CH), 268.8 (CH_2) and 10.3 (Me).

From trans-1-*phenyl*-1,2-*epoxyhexan*-3-*one* **1c**. 1-Phenylhexane-1,2,3-triol **4** (74%) was obtained as white crystals from chloroform–hexane, m.p. 157–158 °C (Found: C, 68.4; H, 8.9. $C_{12}H_{18}O_3$ requires C, 68.55; H, 8.6%); ν_{max}(Nujol)/cm^{-1} 3360 (br, OH), 1460 and 1375; *m/z* 192 ($M^+ - H_2O$), 135 (192 – Bu) and 77 ($C_6H_5^+$); δ_H 7.60–7.15 (5 H, m, ArH), 4.75 (1 H, br, *J* 4.7, 1-CH), 3.95 (1 H, m, 3-CH), 3.70 (3 H, br, OH), 3.50 (1 H, m, 2-CH), 1.70–1.10 (4 H, m, CH_2) and 0.09 (3 H, t, *J* 7.0, Me); δ_C 144.4 (ArC), 128.6, 127.5, 127.4 (ArCH), 78.9, 73.4 and 72.6 (CH), 36.3, 19.5 (CH_2) and 14.5 (Me).

From trans-4-*methyl*-1-*phenyl*-1,2-*epoxypentan*-3-*one* **1d**. 4-*Methyl*-1-*phenylpentane*-1,2,3-*triol* **5** (22%) was obtained as an oil; ν_{max}(Nujol)/cm^{-1} 3480 (br, OH), 1565 and 1430; *m/z* 192 ($M^+ - H_2O$), 149 (192 – Pr) and 77 ($C_6H_5^+$); δ_H 7.50–7.2 (5 H, m, ArH), 4.95 (1 H, br d, *J* 5.1, 1-CH), 3.83 (1 H, m, 3-CH), 4.76 and 3.65 (2 H, br, OH), 3.60 (1 H, m, 2-CH), 1.95 (1 H, m, 4-CH) and 0.90 (6 H, d, *J* 6.5, 6-Me); δ_C 143.9 (ArC), 128.95, 128.5, 127.1 (ArCH), 78.8, 75.6 and 73.0 (CH), 33.7 (4-CH), 15.9 and 15.9 (Me). Starting material was also isolated (54%).

From trans-1-*phenyl*-1,2-*epoxyheptan*-3-*one* **1e**. 1-*Phenylheptane*-1,2,3,-*triol* **6** (74%) was obtained as white crystals from chloroform–hexane, m.p. 156–157 °C (Found: C, 69.8; H, 8.75. $C_{13}H_{20}O_3$ requires C, 69.6; H, 9.0%); ν_{max}(Nujol)/cm^{-1} 3250br (OH), 1565, 1460 and 1170; *m/z* 206 ($M^+ - H_2O$), 167 ($M^+ - Bu$), (206 – Bu), 137 ($PhC_2H_4O_2^+$), 107 ($PhCHOH^+$) and 77 ($C_6H_5^+$); δ_H 7.40–7.15 (5 H, m, ArH), 4.91 (1 H, br d, *J* 5.8 OH), 4.85 (1 H, dd, *J* 5.2 and 5.8, 1-CH), 4.44 (1 H, d, *J* 6.3, OH), 3.43 (1 H, m, 3-CH), 3.31 (1 H, m, 2-CH), 1.70–1.20 (6 H, m, CH_2) and 0.89 (3 H, t, *J* 7.0, Me); δ_C 144.4 (ArC), 128.6, 127.5, 127.4 (ArCH), 78.9 (2-CH), 73.4 (1-CH), 72.9 (3-CH), 33.8, 28.7 and 23.4 (CH_2) 14.4 (Me).

From trans-4-*methyl*-1-*phenyl*-1,2-*epoxyhexan*-3-*one* **1f**. 4-*Methyl*-1-*phenylhexane*-1,2,3-*triol***7** (39%) was obtained as white crystals from chloroform–hexane, m.p. 193–195 °C (Found: C, 69.7; H, 8.8. $C_{13}H_{20}O_3$ requires C, 69.6; H, 9.0%); ν_{max}(Nujol)/cm^{-1} 3470 (br, OH), 1565, and 1540 and 1460; *m/z* 206 ($M^+ - H_2O$), 149 (206 – Bu), 107 ($PhCHOH^+$) and 77 ($C_6H_5^+$); δ_H 7.50–7.2 (5 H, m, ArH), 4.95 (1 H, br d, *J* 3.6, 1-CH), 3.68 (1 H, m, 3-CH), 3.55 (1 H, m, 2-CH), 2.95 (3 H, br, OH), 2.02 (3 H, d, *J* 6.6, Me), 1.78 (1 H, m, 4-CH), 1.55–1.20 (2 H, m, 5-CH_2) and 0.09 (3 H, t, *J* 7.0, 6-Me); δ_C 145.0 (ArC), 128.5, 127.3, 127.2 (ArCH), 76.1, 73.9 and 73.0 (CH), 36.5, 27.7 (CH and CH_2) 12.8 and 12.45 (Me). Starting material was also isolated (29%).

From trans-4,4-*dimethyl*-1-*phenyl*-1,2-*epoxypentan*-3-*one* **1g**. 4,4-*Dimethyl*-1-*phenylhexane*-1,2,3-*triol* **8** (13%) was obtained as an oil; ν_{max}(Nujol)/cm^{-1} 3480br (OH), 1520, 1490 and 1450; *m/z* 206.130 ($M^+ - H_2O$. $C_{13}H_{18}O_2$ requires 206.131), 149 (206 – Bu), 107 ($PhCHOH^+$) and 77 ($C_6H_5^+$); δ_H 7.45 (5 H, br, ArH), 5.25 (1 H, br d, *J* 4.5, 1-CH), 4.25 (1 H, br d, *J* 4.5, 3-CH), 2.80 (1 H, br t, *J* 6.0, 2-CH), 4.20 (3 H, br, OH) and 1.05 (9 H, s, Me); δ_C 140.0 (ArC), 128.45, 128.0, 125.6 (ArCH), 94.1, 86.7 and 73.9 (CH), 33.9 (4-C) and 24.75 (Me). Starting material was also isolated (67%).

From oxygen-18 *labelled* trans-1-*phenyl*-1,2-*epoxyheptane*-3-*one* **1e**. 1-*Phenylheptane*-1,2,3-*triol* **6** (74%) was obtained from the title epoxide (0.50 g) as white needles from chloroform–hexane, m.p. 156–157 °C (Found: C, 69.45; H, 9.0. $C_{13}H_{20}O_2{}^{18}O$ requires C, 69.35; H, 8.95%); ν_{max}(Nujol)/cm^{-1} 3250 (br, OH), 1565, 1460 and 1170; *m/z* 206/208 (1.3:1.0 = 43.2% ^{18}O; this ratio was seen in the remaining doubled peaks) ($M^+ - H_2O$), 167/169 ($M^+ - Bu$), (206 – Bu), 137/139 ($PhC_2H_4O_2^+$), 107 (base peak, $PhCHOH^+$) and 77 ($C_6H_5^+$); δ_H 7.40–7.15 (5 H, m, ArH), 4.91 (1 H, br d, *J* 5.8, OH), 4.85 (1 H, dd, *J* 5.2 and 5.8, 1-CH), 4.44 (1 H, d, *J* 6.3, OH), 3.43 (1 H, m, 3-CH), 3.31 (1 H, m, 2-CH), 1.70–1.20 (6 H, m, CH_2) and 0.89 (3 H, t, *J* 7.0, Me);

δ_C 144.4 (ArC), 128.6, 127.5, 127.4 (ArCH), 78.90 and 78.88* (2-CH; asterisk indicates ^{18}O label), 73.4 (1-CH), 72.9 (3-CH), 33.8, 28.7 and 23.4 (CH_2) 14.4 (Me).

From homochiral (1S,2R)-trans-1-*phenyl*-1,2-*epoxyheptan*-3-*one* **1e**. 1-Phenylheptane-1,2,3-triol **6** (74%) was obtained as white crystals from chloroform–hexane, $[\alpha]_D^{25}$ −5.44 (*c* 2.8, ethyl acetate).

From (1S,2R)-erythro-trans-1-*phenyl*-1,2-*epoxyheptan*-3-*one* **1e**. 1-*Phenylheptane*-1,2,3-*triol* **6** (74%) was obtained as white crystals from chloroform–hexane, $[\alpha]_D^{25}$ −5.31 (*c* 1.1, ethyl acetate).

From trans-1-*phenyl*-1,2-*epoxyheptan*-3-*ol* **15**. 1-Phenylheptane-1,2,3-triol **6** (71%) was obtained as white crystals from chloroform–hexane, $[\alpha]_D^{25}$ +0.24 (*c* 0.5, ethyl acetate).

Other Products from Baker's Yeast Treatment of Epoxy Ketones.—From trans-1-*phenyl*-1,2-*epoxybutanone*. From the title epoxide (1.00 g) was obtained 1,2-*dihydroxy*-1-*phenylbutan*-3-*one* **2** as a colourless oil (0.63 g, 57%; *erythro*:*threo* ratio 2.1:1), $[\alpha]_D^{25}$ +21.5 (*c* 0.47 dichloromethane) (Found: C, 64.6; H, 7.5. $C_{10}H_{12}O_3$ requires C, 66.65; H, 6.7%); ν_{max}(Nujol)/cm^{-1} 3460 (br, OH), 1710 (C=O), 1510, 1450 and 1400; *m*/*z* 180 (M^+), 162 ($M^+ - H_2O$), 119 (162 − Ac), 107 (base peak, $PhCHOH^+$); δ_H of *erythro*-diol: 7.45–7.25 (5 H, m, ArH), 5.00 (1 H, br d, *J* 4.0, 1-CH), 4.35 (1 H, br d, *J* 4.0, 2-CH), 3.75 (1 H, br, OH) and 2.20 (3 H, s, Me); δ_C of *threo*-diol: 208.2 (C=O), 139.9 (ArC), 128.4, 128.0, 126.2 (ArCH), 80.6, 73.9 (CH) and 26.3 (Me); of *threo*-diol: 208.3 (C=O), 139.0 (ArC), 128.4, 128.0, 126.2 (ArCH), 81.0, 74.8 (CH) and 27.5 (Me).

From trans-1-(4-*methoxyphenyl*)-1,2-*epoxyheptan*-3-*one*. 1-(4-*Methoxyphenyl*)-1,2-*dihydroxyhexan*-3-*one* (79%) was obtained as an oil; ν_{max}(Nujol)/cm^{-1} 3430 (br, OH), 1710 (C=O), 1620, 1520 and 1460; *m*/*z* 252.134 (M^+, $C_{14}H_{20}O_3$ requires 252.136) 234 ($M^+ - H_2O$), 107 ($PhCHOH^+$) and 57 (Bu^+); δ_H 7.25–6.80 (4 H, m, ArH), 4.82 (1 H, d, *J* 4.0, 2-CH), 4.20 (1 H, d, *J* 4.0, 3-CH), 4.50 (2 H, br OH), 3.70 (3 H, s, OMe), 1.60–1.00 (6 H, m, CH_2) and 0.80 (3 H, t, *J* 7.0, Me); δ_C 211.2 (C=O), 159.3 (ArC), 132.2, 127.6, 113.7 (ArCH), 80.3, 73.7 and 73.0 (CH), 54.9 (OMe), 38.75, 24.95 and 21.8 (CH_2) and 13.4 (Me).

From trans-1-(4-*nitrophenyl*)-1,2-*epoxyheptan*-3-*one*. The crude product from the title epoxy ketone (0.50 g) was flash chromatographed to give (light petroleum) starting material (0.10 g, 19%) followed by (ether) trans-1-(4-*nitrophenyl*)-1,2-*epoxyhexan*-3-*ol* (0.16 g, 32%; d.e. 62%), as an oil; $[\alpha]_D^{25}$ +1.61 (*c* 0.62 chloroform); ν_{max}(Nujol)/cm^{-1} 3430 (br, OH), 1710 (C=O), 1620, 1520 and 1460; *m*/*z* 252.134 (M^+; $C_{14}H_{20}O_3$ requires 252.136) 234 ($M^+ - H_2O$), 107 ($PhCHOH^+$) and 57 (Bu^+); δ_H 8.18 (2 H, d, *J* 8.2, ArH), 7.42 (2 H, d, *J* 8.2, ArH), 4.05 (1 H, d, *J* 2.0, 1-H), 3.95 (1 H, m, 3-CH), 3.00 (1 H, dd, *J* 2.0 and 4.1, 2-CH), 2.76 (1 H, br, OH), 1.75–1.00 (6 H, m, CH_2) 0.90 (3 H, t, *J* 7.0, Me); δ_C (minor diastereoisomer indicated with asterisk) 148.0*, 145.0 (ArC), 126.5, 123.9 (ArCH), 70.5*, 68.5, 66.2*, 55.2*, 53.65 (CH), 34.1*, 33.0, 27.3*, 27.2 and 22.5 (CH_2) and 13.7 (Me). Further elution with ether gave 1-(4-*nitrophenyl*)-2,3-*dihydroheptane* **18** (0.06 g, 12%) as white needles from ethyl acetate–light petroleum, m.p. 144–145 °C; $[\alpha]_D^{25}$ 0 (*c* 1.3 chloroform); ν_{max}(Nujol)/cm^{-1} 3400 and 3280 (br, OH), 1610, 1600 and 1520; *m*/*z* 207.138 ($M^+ - NO_2$. $C_{13}H_{19}O_2$ requires 207.139), 150 (207 − Bu), 132 (150 − H_2O) and 137 ($C_7H_7NO_2^+$, base peak) and 122 ($C_6H_4NO_2^+$); δ_H 8.15 (2 H, d, *J* 9.5, ArH), 7.40 (2 H, d, *J* 9.5, ArH), 4.72 (2 H, br, OH), 3.80 (1 H, m, 2-CH), 3.68 (1 H, m, 3-CH), 2.87 (2 H, m, 1-CH_2), 1.60–1.10 (6 H, m, CH_2) 0.90 (3 H, t, *J* 7.0, Me); δ_C 147.1 (ArC), 130.4, 123.8 (ArCH), 75.0 (2-CH), 74.3 (3-CH), 37.5 (1-CH_2), 31.5, 27.9 and 22.5 (CH_2) and 13.8 (Me).

From trans-1,3-*diphenyl*-1,2-*epoxypropan*-3-*one* **13a** *and from* trans-1-*phenyl*-2,3-*epoxydodecan*-1-*one* **13b**. The title epoxides gave solely unchanged material (66% and 78% respectively).

From trans-2,3-*epoxyoctan*-4-*one* **1k** *with Hansenula anomala*. Using the same conditions as for baker's yeast the title epoxide gave the same epoxy alcohol **11** (64%) with a d.e. 27.2%, $[\alpha]_D^{25}$ −1.46 (*c* 3.4, chloroform).

From trans-2,3-*epoxyoctan*-4-*one* **1k** *with added allyl alcohol*. Using the general method but with allyl alcohol (0.5 g) added after the yeast had fermented for 10 min followed by a further aliquot 20 min before addition of the title epoxide, gave after work-up unchanged epoxide (22%) and 2,3-epoxyoctano-4-ol (47%, d.e. 16%).

From trans-1-*phenyl*-2,3-*epoxybutan*-1-*one* **1m** *without sucrose*. Using the general method but without sucrose, gave after work-up unchanged epoxide {56%, $[\alpha]_D^{25}$ −4.0 (*c* 2.5 chloroform)} and 1-phenyl-2,3-epoxybutan-1-ol {22%, d.e. 64%, $[\alpha]_D^{25}$ −39.1 (*c* 0.5, chloroform)}.

From trans-2,3-*epoxyoctan*-4-*one* **1k** *with yeast alcohol dehydrogenase*. The title ketone (10.01 mg, 0.01 mmol) was added to a suspension of yeast alcohol dehydrogenase (2.0 mg, 480 U), NAD^+ (1.00 mg) and ethanol (0.2 cm^3) in glycine buffer (pH 9.3, 0.5 mol dm^{-3}; 5 cm^3) at 30 °C. After 48 h of swirling additional enzyme (2.0 mg) was added to the reaction mixture and the swirling continued for a further 24 h at 30 °C. After work-up only starting material was isolated (9.8 mg, 98%).

Epoxidations using the Sharpless Method.—(i) *Preparation of* (S,S,S)-(+)-erythro-trans-1-*phenyl*-2,3-*epoxybutan*-1-*ol*. 1-Hydroxy-1-phenylbut-2-ene (9.00 g, 0.06 mol) and (+)-diisopropyl tartrate (2.14 g, 9.14 mol) were treated under the Sharpless kinetic resolution conditions[23] for 15 h at −20 °C. Flash chromatography (hexane–ether, 1:1) of the crude product (4.79 g, 48%) gave (S,S,S)-(+)-erythro-trans-1-*phenyl*-2,3-*epoxybutan*-1-*ol* **12′** (4.63 g, 47%) as an oil, $[\alpha]_D^{25}$ +26.0 (*c* 1.41, dichloromethane); ν_{max}(Nujol)/cm^{-1} 3430br (OH), 1500, 1455 and 1385; *m*/*z* 164.083 (M^+, $C_{10}H_{12}O_2$ requires 164.084), 146 ($M^+ - H_2O$) and 77 ($C_6H_5^+$); δ_H 7.40–7.20 (5 H, m, ArH), 4.75 (1 H, br d, *J* 3.6, 1-CH), 3.18 (1 H, m, 3-CH), 3.05 (1 H, br, OH) and 2.88 (1 H, *J* 3.5 and 2.6, 2-CH) and 1.25 (3 H, d, *J* 5.2, Me); δ_C 139.75 (ArC), 128.4, 128.0, 126.4 (ArCH), 71.1, 62.2 and 51.4 (CH) and 17.0 (Me).

(ii) *Preparation of* (R,R,R)-(−)-erythro-trans-1-*phenyl*-2,3-*epoxybutan*-1-*ol* **12″**. 1-Hydroxy-1-phenylbut-2-ene (9.00 g, 0.06 mol) and (−)-diisopropyltartrate (2.14 g, 9.14 mol) were treated under the Sharpless kinetic resolution conditions[22] for 15 h at −20 °C and worked up as above. The crude product (4.43 g, 45%) yielded (R,R,R)-(−)-erythro-trans-1-*phenyl*-2,3-*epoxybutan*-1-*ol* **12″** (4.24 g, 43%), which was isolated as an oil, $[\alpha]_D^{25}$ −24.5 (*c* 1.1, chloroform); ν_{max}(Nujol)/cm^{-1} 3430br (OH), 1500, 1455 and 1385; *m*/*z* 164.084 (M^+, $C_{10}H_{12}O_2$ requires 164.084), 146 ($M^+ - H_2O$) and 77 ($C_6H_5^+$); δ_H 7.40–7.20 (5 H, m, ArH), 4.75 (1 H, br d, *J* 3.6, 1-CH), 3.18 (1 H, m, 3-CH), 3.05 (1 H, br, OH) and 2.88 (1 H, *J* 3.5 and 2.6, 2-CH) and 1.25 (3 H, d, *J* 5.2, Me); δ_C 139.75 (ArC), 128.4, 128.0, 126.4 (ArCH), 71.1, 62.2 and 51.4 (CH) and 17.0 (Me).

(iii) *Preparation of* (−)-erythro-trans-1-*phenyl*-1,2-*epoxyheptan*-1-*ol* **15**. To an oven-dried 3-necked 1 dm^3 flask was added magnesium (14.00 g, 0.58 mol), anhydrous ether (50 cm^3) and a few iodine crystals. A small portion of a solution of butyl bromide (77.84 g, 0.57 mol) in dry ether (150 cm^3) was added to the mixture under argon and after the reaction had commenced the remaining material was added dropwise so as to maintain reflux. After completion of the addition the mixture was stirred for a further 15 min and then cooled in an ice-bath and cinnamaldehyde (50.00 g, 0.38 mol) was added dropwise to it over 1 h. The solution was stirred overnight at ambient temperature and then poured into cold saturated aqueous ammonium chloride, extracted with ether and the extract dried

($MgSO_4$) and evaporated. The residue was distilled to give trans-3-*hydroxy*-1-*phenylhept*-1-*ene* (60.50 g, 84%), b.p. 145–148 °C at 4 mmHg; ν_{max}(Nujol)/cm^{-1} 3380br (OH), 2980 and 1650; δ_H 7.50–7.15 (5 H, m, ArH), 6.57 (1 H, d, *J* 14.0, 1-CH), 6.25 (1 H, dd, *J* 14.0 and 7.0, 2-CH), 4.28 (1 H, m, 3-CH), 2.18 (1 H, br, OH), 1.80–1.20 (6 H, m, CH_2) and 0.95 (3 H, t, *J* 7.0, Me); δ_C 136.9 (ArC), 132.8, 130.2, 128.6, 127.6 and 126.5 (ArCH and 1- and 2-CH) 72.9 (3-CH) 36.9, 27.4, 22.4 (CH_2) and 13.8 (Me).

trans-3-*Hydroxy*-1-*phenylhept*-1-*ene* (20.00 g, 0.11 mol) and (+)-diisopropyl tartrate (3.70 g, 15.6 mol) were treated under the Sharpless kinetic resolution conditions[22] for 3 h. Flash chromatography (hexane–ether, 1:1) of the crude product (11.1 g, 49%) gave (−)-erythro-trans-1-*phenyl*-1,2-*epoxyheptan*-3-*ol* (10.67 g, 47%) as an oil, $[\alpha]_D^{25}$ −27.4 (*c* 2.0, chloroform); ν_{max}(Nujol)/cm^{-1} 3440 br (OH), 1500, 1460 and 1049; *m/z* 206.130 (M^+, $C_{13}H_{18}O_2$ requires 206.131), 188 ($M^+ - H_2O$), 131 (188 − Bu), 107 ($C_6H_5CHOH^+$, base peak) and 77 ($C_6H_5^+$) and 57 (Bu^+); δ_H 7.40–7.22 (5 H, m, ArH), 3.98 (1 H, d, *J* 2.0, 1-CH), 3.90 (1 H, m, 3-CH), 3.05 (1 H, dd, *J* 2.0 and 3.7, 2-CH), 2.70 (1 H, br, OH), 1.70–1.25 (6 H, m, CH_2) and 0.90 (3 H, t, *J* 7.0, Me); δ_C 137.1 (ArC) 128.5, 128.2, 125.7 (ArCH) 68.6, 64.9 and 54.7 (CH) 32.9, 27.1, 22.4 (CH_2) and 13.7 (Me).

Non-enzymatic Transformations.—(i) *Mosher esters of epoxybutanols. trans*-1-Phenyl-2,3-epoxybutan-1-ol **12** (0.24 g, 1.48 mmol) and distilled (*R*)-(+)-2-methoxy-2-trifluoromethylphenacetyl chloride (0.38 g, 1.50 mmol) were mixed in carbon tetrachloride (5 cm^3) and dry pyridine (0.2 cm^3) and stored in a stoppered flask for 12 h. The mixture was diluted with water (1 cm^3) and extracted with ether (50 cm^3) and the extract was washed successively with 2 mol dm^{-3} hydrochloric acid, water and saturated aqueous sodium carbonate. The dried ($MgSO_4$) solution was evaporated and the crude product purified by flash chromatography (light petroleum–ether, 1:1) to give as the major product, 1-*phenyl*-1,2-*epoxybutan*-3-*ol* (0.06 g, 25%), $[\alpha]_D^{25}$ −13.45 (*c* 2.3, chloroform); ν_{max}(Nujol)/cm^{-1} 3480br (OH), 1540, 1500, 1460 and 1235; *m/z* 164.083 (M^+, $C_{10}H_{12}O_2$ requires 164.084), 146 ($M^+ - H_2O$) and 77 ($C_6H_5^+$); δ_H 7.50–7.15 (5 H, m, ArH), 4.85 (1 H, br t, *J* 5.5, 2-CH), 4.10–3.80 (2 H, m, 1-CH and 3-CH), 2.80 (1 H, br, OH) and 1.50 (3 H, d, *J* 6.0, Me); δ_C (minor diastereoisomer is shown with an asterisk) 140.65, 140.2* (ArC), 129.0*, 128.8; 128.7, 128.5*; 127.2*, 126.5 (ArCH), 79.5*, 78.2; 74.3*, 73.1; 58.4*, 58.0 (CH) and 19.6, 19.2* (Me).

(ii) *Acetylation of* erythro-trans-1-*phenyl*-2,3-*epoxybutan*-1-*ol* **12′**. A solution of the title alcohol (0.24 g, 1.45 mmol) in dry dichloromethane (5 cm^3) at 0 °C was treated with acetyl chloride (0.17 g, 2.18 mmol) and dry triethylamine (0.29 g, 2.91 mmol) and stored in a stoppered flask overnight at 0 °C. The mixture was diluted with ether (40 cm^3) washed with water (×3), dried and evaporated to give a crude oil which when flash chromatographed (light petroleum–ether, 1:1) afforded erythro-trans-1-*phenyl*-2,3-*epoxybutyl acetate* **12′** as an oil (0.29 g, 97%), $[\alpha]_D^{25}$ +19.55 (*c* 1.3, chloroform); ν_{max}(Nujol)/cm^{-1} 1740 (C=O), 1500, 1370 and 1225; *m/z* 206.093 (M^+, $C_{12}H_{14}O_3$ requires 206.094), 188 ($M^+ - H_2O$) and 77 ($C_6H_5^+$); δ_H 7.48–7.20 (5 H, m, ArH), 5.80 (1 H, d, *J* 4.4, 1-CH), 3.00 (2 H, m, 2-CH and 3-CH), 2.10 (3 H, s, OCOMe), 1.30 (3 H, d, *J* 5.3, Me); δ_C 169.9 (C=O), 136.5 (ArC), 128.6, 127.4 (ArCH), 73.9 (1-CH), 52.4 (2- and 3-CH) and 20.7, 16.75 (Me).

(iii) *Acetylation of* erythro-trans-1-*phenyl*-2,3-*epoxybutan*-1-*ol* **12″**. A solution of the title alcohol (0.24 g, 1.45 mmol) in dry dichloromethane (5 cm^3) at 0 °C was treated as above to give erythro-trans-1-*phenyl*-2,3-*epoxybutyl acetate* **12″** as an oil (0.29 g, 97%), $[\alpha]_D^{25}$ −17.3 (*c* 1.0, chloroform); ν_{max}(Nujol)/cm^{-1} 1740 (C=O), 1500, 1370 and 1225; *m/z* 206.093 (M^+, $C_{12}H_{14}O_3$ requires 206.094), 188 ($M^+ - H_2O$) and 77 ($C_6H_5^+$); δ_H 7.48–7.20 (5 H, m, ArH), 5.80 (1 H, d, *J* 4.4, 1-CH), 3.00 (2 H, m, 2-CH and 3-CH), 2.10 (3 H, s, OCOMe) and 1.30 (3 H, d, *J* 5.3, Me); δ_C 169.9 (C=O), 136.5 (ArC), 128.6, 127.4 (ArCH), 75.9 (1-CH), 60.3, 52.7 (2- and 3-CH) and 20.7, 16.75 (Me).

(iii) *Acetylation of* threo-trans-1-*phenyl*-2,3-*epoxybutan*-1-*ol* **12**. A solution of the mixture of diastereoisomeric title alcohols obtained by the action of yeast on the optically active (2*R*,3*S*)-*trans*-1-phenyl-epoxybutan-1-one was treated as above to give the *title acetate* (95%) which was used without further purification; δ_H 7.48–7.20 (5 H, m, ArH), 5.52 (1 H, d, *J* 6.6, 1-CH), 3.00 (2 H, m, 2-CH and 3-CH), 2.10 (3 H, s, OCOMe) and 1.30 (3 H, d, *J* 5.3, Me); δ_C 169.9 (C=O), 136.5 (ArC), 128.6, 127.4 (ArCH), 75.9 (1-CH), 60.3, 52.7 (2- and 3-CH) and 20.7, 16.75 (Me).

Sodium Tetrahydroborate Reductions of Ketones.—Reduction of trans-1-*phenyl*-1,2-*epoxyheptan*-3-*one*. Sodium tetrahydroborate (0.07 g, 1.84 mmol) in ethanol (10 cm^3) was stirred at 0 °C under argon whilst *trans*-1-phenyl-1,2-epoxyheptan-3-one (1.00 g, 4.90 mmol) was added to it. The mixture was stirred for a further 1 h at 0 °C after which it was treated with saturated brine (5 cm^3) and continuously extracted with chloroform for 4 h. The dried organic phase was evaporated and the residue flash chromatographed (light petroleum–ether, 1:1) to give trans-1-*phenyl*-1,2-*epoxyheptan*-3-*ol* **15** as an oil (0.62 g, 62%; d.e. 54.6%); ν_{max}(Nujol)/cm^{-1} 3440br (OH) 1500, 1460 and 1049; *m/z* 206.130 (M^+, $C_{13}H_{18}O_2$ requires 206.131), 188 ($M^+ - H_2O$) 131 (188 − Bu) 107 ($PhCHOH^+$, base peak) 77 ($C_6H_5^+$) and 57 (Bu); δ_H(minor diastereoisomer is shown with an asterisk) 7.40–7.22 (5 H, m, ArH), 3.98 (1 H, d, *J* 2.0, 1-CH) 3.85* (1 H, d, *J* 4.0, 1-CH); 3.90 (1 H, m, 3-CH), 3.05, 3.00* (1 H, m, 2-CH), 2.70 (1 H, br, OH), 1.70–1.25 (6 H, m, CH_2) and 1.30 (3 H, d, *J* 7.0, Me); δ_C(minor diastereoisomer is shown with an asterisk) 137.1, 136.9* (ArC), 128.5, 128.2, 125.7 (ArCH), 71.1*, 68.6; 65.7*, 64.9; 56.5*, 54.7 (CH), 33.8*, 32.9; 27.2*, 27.1; 22.4, 22.4* and 13.7 (Me).

Reduction of threo-1,2-*dihydroxy*-1-*phenylheptan*-3-*one*. To *threo*-1,2-dihydroxy-1-phenylheptan-3-one (90 mg, 0.41 mmol) in ethanol (1 cm^3) was added dropwise at 0 °C, sodium tetrahydroborate (15.4 mg) in ethanol (0.5 cm^3) and the mixture was stirred overnight. It was then filtered through silica (chloroform–acetone, 3:1) and the organic phase was evaporated to give the diastereoisomeric mixture of 1,2,3-*trihydroxy*-1-*phenylheptanes* **6** as an oil (88 mg, 97%; 3.1:1); δ_C([$^2H_6$]DMSO) (minor diastereoisomer is shown with an asterisk) 144.3, 143.2* (ArC), 127.5, 126.5, 126.3 (ArCH), 77.9, 77.1*; 73.8*; 70.4; 70.1* (CHs) 33.3*, 32.6; 27.6*, 27.4; 22.3, 22.2* and 14.0, 13.9 (Me).

Preparation of trans-1-*Phenylhept*-1-*en*-3-*one.—trans*-1-Phenylhept-1-en-3-ol was oxidised using pyridinium dichromate according to Stevens[23] to give trans-1-*phenylhept*-1-*en*-3-*one* as a white solid from ether–hexane, m.p. 45–46 °C (Found: C, 82.8; H, 8.6. $C_{13}H_{16}O$ requires C, 82.9; H, 8.6%); ν_{max}(Nujol)/cm^{-1} 3020 (C=C), 1620 (C=O), 1570, 1500 and 1450; *m/z* 188 (M^+), 131 (M^+ − Bu), 77 ($C_6H_5^+$); δ_H 7.60–6.66 (7 H, m, ArH and 1-H, 2-H), 2.65 (2 H, t, *J* 7.5, 4-CH_2) 1.75–1.05 (4 H, m, CH_2) and 0.93 (3 H, t, *J* 7.0, Me); δ_C 200.9 (C=O), 142.4 (ArC), 134.7, 130.4, 129.0, 128.3, 126.35 (ArH and 1-H, 2-H), 40.9, 26.3, 22.2 (CH_2) and 13.7 (Me).

Preparation of (2R,3S)-1-*Phenyl*-2,3-*epoxybutan*-1-*one* **1m′**.—(1*S*,2*S*,3*S*)-1-Phenyl-2,3-epoxybutanol **12′** (2.00 g, 0.01 mol) was oxidised using pyridinium dichromate according to Stevens[23] to give the title compound **1m′** (1.22 g, 62%), $[\alpha]_D^{25}$ +8.5 (*c* 1.8, chloroform). Other details are as for the racemic compound **1m**.

Preparation of (2S,3R)-1-*Phenyl*-2,3-*epoxybutan*-1-*one* **1m'**.—(1*R*,2*R*,3*R*)-1-Phenyl-2,3-epoxybutanol **12''** was oxidised using pyridinium dichromate according to Stevens[23] to give the title compound **1m'** (75%), $[\alpha]_D^{25}$ −8.4 (*c* 1.7, chloroform). Other details are as for the racemic compound **1m**.

Preparation of (1R,2S)-1-*Phenyl*-1,2-*epoxyheptan*-3-*one* **1e'**.—(1*S*,2*S*,3*S*)-1-Phenyl-1,2-epoxyheptan-3-ol **15** was oxidised using pyridinium dichromate according to Stevens[23] to give the title compound **1e'** (75%), [α] −8.4 (*c* 1.7, chloroform). Other details are as for the racemic compound **1e**.

Preparation of Racemic threo-1,2-*Dihydroxy*-1-*phenylheptan*-3-*one* **17**.—*trans*-1-Phenylhept-1-en-3-one (2.22 g, 0.01 mol) in ethanol was cooled to −40 °C and a solution of potassium permanganate (1.80 g, 0.01 mol) and magnesium sulfate heptahydrate (2.00 g, 8.00 mmol) in water (60 cm^3) was added dropwise to it at −40 °C. After addition was complete the mixture was allowed to warm to ambient temperature when it was filtered and the residue washed with ether. The organic phase was dried ($MgSO_4$) and evaporated to give an oil, flash chromatography of which (light petroleum–ether, 1:4) gave the title compound **17** (0.81 g, 31%) as a white solid, m.p. 55–56 °C (Found: C, 70.1; H, 8.3. $C_{13}H_{18}O_3$ requires C, 70.2; H, 8.2%); ν_{max}(Nujol)/cm^{-1} 3450br (OH), 1720 (C=O), 1600, 1460 and 1400; *m*/*z* 204 ($M^+ - H_2O$), 119 (204 − BuCO), 107 ($PhCHOH^+$, base peak) 77 ($C_6H_5^+$) and 57 (Bu); δ_H 7.40–7.18 (5 H, m, ArH), 4.92 (1 H, br d, *J* 4.3, 2-CH), 4.30 (1 H, br d, *J* 4.3, 1-CH_2), 3.25 (2 H, br, OH), 2.45 (2 H, br d, *J* 7.2, 4-CH_2), 1.65–1.15 (4 H, m, CH_2) and 0.90 (3 H, t, *J* 7.2, Me); δ_C 210.9 (C=O), 140.3 (ArC), 128.6, 128.1, 126.4 (ArCH), 80.25, 74.1 (2-CH) and 1-CH), 38.65, 25.2, 22.0 (CH_2) and 13.5 (Me).

Preparation of 1,2-*Dihydroxy*-1-*phenylheptan*-3-*one from the Triol* **6** (*obtained by Baker's Yeast Treatment of the Epoxy Ketone* **1e**).—The title triol **6** (0.23 g, 0.13 mmol), toluene-*p*-sulfonic acid monohydrate (25 mg), acetone (25 cm^3) and light petroleum (b.p. 30–50 °C; 90 cm^3) were mixed and heated under reflux for 36 h. Sodium acetate (1 g) was added to the cooled solution and which after being stirred for 30 min was filtered and evaporated. The residue was continuously extracted with chloroform for 4 h after which the extract was dried, and evaporated to give an oil. Flash chromatography of this (light petroleum–ether, 1:1) gave 4-(1-*hydroxypentyl*)-2,2-*dimethyl*-5-*phenyldioxolane* (0.25 g, 92%) as white needles from chloroform–hexane, m.p. 153–154 °C (Found: C, 72.5; H, 9.15. $C_{16}H_{24}O_3$ requires C, 72.7; H, 9.15%); ν_{max}(Nujol)/cm^{-1} 3460br (OH), 1450 and 1250; *m*/*z* 264 (M^+), 246 ($M^+ - H_2O$), 77 ($C_6H_5^+$); δ_H 7.36–7.21 (5 H, m, ArH), 4.95 (1 H, d, *J* 8.3, 1-CH), 3.92 (1 H, dd, *J* 8.4 and 8.0, 2-CH), 3.82 (1 H, m, 3-CH), 2.23 (1 H, br, OH), 1.55 (3 H, s, Me) and 1.48 (3 H, s, Me); δ_C 138.5 (ArC) 128.4, 128.3, 127.7 (ArCH), 108.8 (C), 85.3, 78.7, 70.7 (CH), 32.1, 27.7, 27.3, 27.0, 22.3 and 13.7 (CH_2 and Me).

This dioxolane (0.20 g, 0.88 mmol) was oxidised using pyridinium dichromate according to Stevens method[23] and the crude oil flash chromatographed (hexane–ether, 1:1) to give 2,2-*dimethyl*-4-*pentanoyl*-5-*phenyldioxolane* (0.14 g, 68%) as an oil; ν_{max}(Nujol)/cm^{-1} 1680 (C=O), 1600, 1450, 1385 and 1050; *m*/*z* 262.156 (M^+, $C_{16}H_{22}O_3$ requires 262.157), 244 ($M^+ - H_2O$), 77 ($C_6H_5^+$) and 57 (Bu^+); δ_H 7.80–7.15 (5 H, m, ArH), 5.03 (1 H, d, *J* 7.3, 2-CH), 4.25 (1 H, d, *J* 7.3, 1-CH), 2.56 (2 H, br t, *J* 7.3, 4-CH), 1.70–1.10 (4 H, m, CH_2) and 1.55 (3 H, s, Me), 1.45 (3 H, s, Me) and 0.85 (3 H, t, *J* 7.0, Me); δ_C 138.3 (ArC), 128.65, 128.6, 126.65 (ArCH), 110.9 (C), 87.0, 79.6 (2- and 1-CH), 38.85, 26.6, 26.0, 24.8, 22.3 and 13.55 (CH_2 and Me).

The keto dioxolane (0.10 g, 0.44 mmol) in acetone (5 cm^3) was treated with water (2 cm^3) and aqueous sulfuric acid (2 mol dm^{-3}; 0.5 cm^3) and the solution heated for 48 h, cooled and extracted with chloroform continuously for 6 h. The extract was dried and evaporated and the residual oil purified by flash chromatography (light petroleum–ether, 1:1) to give the diol ketone **17** (0.07 g, 73%) identical with that described above.

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