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REACTIONS OF EPOXIDES—VI[1]

A CONFORMATIONAL ANALYSIS OF REARRANGEMENTS OF TETRA-SUBSTITUTED EPOXIDES

M. P. HARTSHORN and D. N. KIRK
University of Canterbury, Christchurch, New Zealand

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Abstract—A conformational analysis of the rearrangements of a model 1,2-dialkyl-epoxycyclohexane with BF_3 suggests two possible modes of cleavage of the epoxide to give carbonium ions which may subsequently rearrange to form ketones. "Axial cleavage" of the epoxide is defined, and shown to be preferred over "equatorial cleavage" by a conformational analysis of rearrangements of twelve steroidal epoxides.

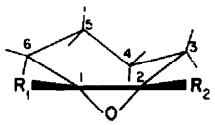
A SURVEY of the rearrangement reactions of 4,5-epoxy-4-methyl[2,3] and 5,6-epoxy-6-methyl steroids[1] reveals a complexity of behaviour which cannot adequately be explained in terms of the simple principles underlying the reactions of trisubstituted epoxides.[4] This paper represents an attempt to analyse the conformational and electronic factors which control the rearrangement reactions of tetra-substituted epoxides leading to ketonic products. We also hoped to account for the large variations in total yields of ketonic products (as distinct from hydroxylic and olefinic products), ranging from zero to over 90% for the different epoxides we have examined.

The rearrangement reactions of twelve tetra-substituted epoxides have been described in our earlier papers, and the ketonic products are summarized in the Table. Few regularities were apparent from a direct study of these results, and it was found more profitable to base their interpretation upon a conformational analysis of a hypothetical monocyclic epoxycyclohexane. Dreiding molecular models were used throughout this work.

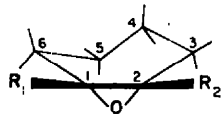
Conformation analysis of epoxy-cyclohexanes

A molecular model of a 1,2-dialkyl-1,2-epoxy-cyclohexane can exist in one of two favourable conformations. These are designated for convenience as the R- and L-forms (Fig. 1), and correspond to the stable "half-chair" conformations of cyclohexene.[5] Substituents on adjacent ring-carbon atoms are in fully staggered conformations of minimum energy, with the exception of one pair (R_1 and the *cis*-related group at C-6 in the R-form; R_2 and the *cis*-related group at C-3 in the L-form) which are nearly eclipsed in the model. The resulting strain may be partially relieved in the actual molecule by slight distortions elsewhere in the ring.

[1] Part V, J. W. Blunt, M. P. Hartshorn and D. N. Kirk, *Tetrahedron* **21**, 559 (1965).
[2] Part I, J. M. Coxon, M. P. Hartshorn and D. N. Kirk, *Tetrahedron* **20**, 2531 (1964).
[3] Part IV, M. P. Hartshorn and D. N. Kirk, *Tetrahedron* **20**, 2943 (1964).
[4] H. B. Henbest and T. I. Wrigley, *J. Chem. Soc.* 4765 (1957); see also Ref. 8.
[5] B. Ottar, *Acta Chem. Scand.* **1**, 283 (1947).



R - conformation



L - conformation

The distribution of the epoxide among various reaction products must be determined initially by the energy levels of the corresponding transition states, and may also be influenced by the relative populations of R- and L- forms for any particular epoxide. These factors will determine the composition of the final mixture of products provided that the rearrangement reactions are effectively irreversible, that is, where the products are not subject to equilibration under thermodynamic control. Such systems represent a separate problem which will be discussed later.

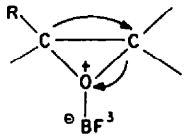
TABLE 1. YIELDS OF KETONES FROM REARRANGEMENTS OF EPOXIDES WITH BORON TRIFLUORIDE

EPOXIDE		Product of: Methyl migration[a]	Ketones (% yield) Ring contraction[b]	Skeletal rearrangement[c]	Total ketones
4-Methylcholestane derivatives:					
	4α,5α-epoxide	(42[d])	—	84	84
3-Keto–	4α,5α-epoxide	16	9	—	25
3β-AcO–	4α,5α-epoxide	10	—	26	36
3α-AcO	4α,5α-epoxide	—	—	—	0
	4β,5β-epoxide	40	6	—	46
3-Keto	4β,5β-epoxide	39	39	—	78
3β-AcO–	4β,5β-epoxide	10	—	—	10
3α,AcO–	4β,5β-epoxide	29	—	—	29
6-Methylcholestane derivatives:					
	5α,6α-epoxide	(30[d])	—	75	75
3β-AcO–	5α,6α-epoxide	—	—	85	85
	5β,6β-epoxide	16	23	—	39
3β-AcO–	5β,6β-epoxide	12	3	23	38

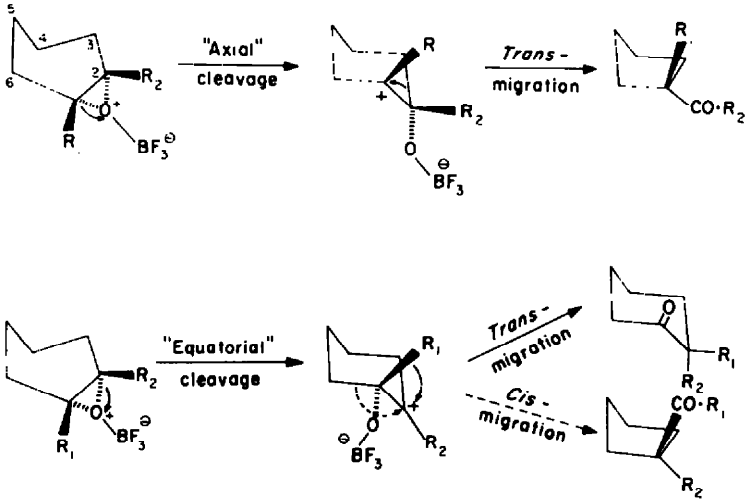
[a] 5-methyl-4- or 6-ketones.
[b] 5-Acetyl-A-nor- or 5-acetyl-B-nor-cholestanes.
[c] A-nor-B-homo-6-ketones or A-homo-B-nor-4a-ketones.
[d] Final product of thermodynamically controlled rearrangement.

We shall now consider the transition states which can arise for our hypothetical 1,2-dialkyl-epoxycyclohexane, and their relative energy levels. The boron trifluoride-catalysed rearrangement of an epoxide is believed to proceed through a transition state of considerable ionic character,[6] although the degree of development of positive charge at the reaction centre probably varies for different epoxides and reaction paths. When the stereochemistry of the epoxide permits migration of a group to be concerted with rupture of the epoxide the transition state need not involve a fully developed

[6] D. J. Goldsmith, *J. Amer. Chem. Soc.* **84**, 3913 (1962).

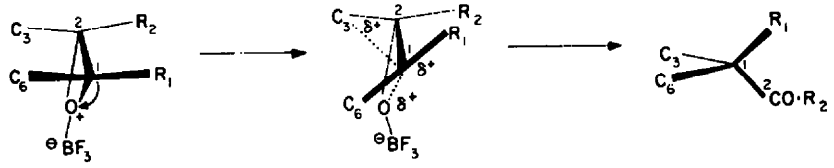


carbonium ion. This situation should be strongly preferred over a non-concerted process requiring a discrete carbonium ion at a *secondary* carbon atom. It is well established, however, that a trisubstituted epoxide will rearrange preferentially by cleavage at the *tertiary* centre where carbonium ion development is relatively favourable.[4] In a tetrasubstituted epoxide a concerted rearrangement would still be expected to proceed in preference to one requiring full charge development, but this preference should be much less marked, and may be overcome in certain situations by steric factors unfavourable to rearrangement by a concerted pathway.

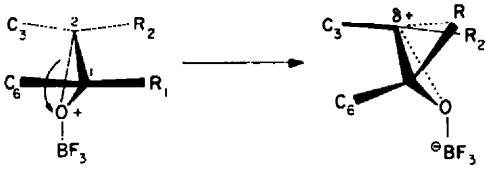


The most probable reaction pathway from a tetra-substituted epoxide to a ketone is therefore considered to be one in which migration of a group is concerted with the breaking of the epoxide bond, with the important additional requirement that the transition state should involve the minimum of unfavourable non-bonded interactions. Fig. 2 illustrates the two modes of reaction of an epoxy-cyclohexanone (in its R-conformation) which seem best to satisfy these requirements. The two ionic species shown will be referred to as the products of "axial" and "equatorial" cleavage respectively, depending upon the conformation of the oxygen atom. In both cases the ring assumes the "chair" conformation closest to the conformation of the epoxy-compound, so that non-bonded interactions are minimised. The rotation of groups about the 1,2-bond during this initial step should determine which group will migrate. Axial cleavage (Fig. 3) would permit *trans*- attack by C-3 upon the reaction centre, with ring contraction. Equatorial cleavage (Fig. 4) should favour *trans*-migration of the group R_1, giving a dialkyl-cyclohexanone, although the alternative of ring contraction by *cis*- attack upon the carbonium ion can be envisaged if the nature of

R_1 makes its migration particularly unfavourable. Instances of both modes of reaction following equatorial cleavage were found in our subsequent analysis of rearrangements of steroid epoxides.



The foregoing arguments refer to the R-conformation of the epoxide, but it will be apparent that similar conclusions may be derived for the L-form. In the discussion which follows, the transition state will be represented as a carbonium ion for convenience in discussion and diagrammatic presentation. It is to be understood that full developement of a positive charge is not necessarily implied, except in cases of *cis*- replacement of the oxygen atom.



It will now be shown that the rearrangement reactions of the twelve epoxides studied may be interpreted on the presupposition that "axial cleavage" of an epoxide presents a reaction pathway having lower energy requirements than "equatorial cleavage", unless special structural features are present which specifically oppose the axial mode of cleavage of a particular epoxide. The preference for axial cleavage may be regarded as an extension of the generalization that nucleophilic attack upon an epoxy-cyclohexane (or a protonated or Lewis acid-coordinated epoxy-cyclohexane) gives the products of diaxial opening of the epoxide.[7]

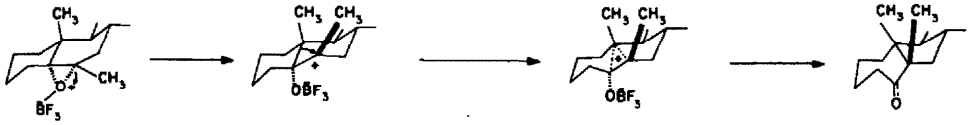
Rearrangements of steroid epoxides

In order to extend the discussion to our tetrasubstituted steroid epoxides, one of the alkyl groups (R_1 or R_2) in the model monocyclic compound is considered to be a methyl group, and the other becomes a part of the adjoining ring of the steroid skeleton. An examination of models of the 4α,5α-epoxy-4β-methyl- and 5α,6α-epoxy-6β-methyl compounds (I and II) shows that the epoxide-bearing rings are in the R- and L-conformation respectively in the stable conformations of the epoxides. Reactions initiated by axial cleavage lead in each case to the observed products of skeletal rearrangement. Thus the 4α,5α-epoxide (I) gives a C-4 carbonium ion rotating to allow a concerted *trans*- attack by the 10,5 bond. The 5α,6α-epoxide (II) similarly gives a C-6 carbonium ion, oriented for *trans*- attack by the 10,5- bond. An additional factor probably favouring these skeletal rearrangements is the quaternary substitution

[7] *Steric Effects in Organic Chemistry* (Edited by M. S. Newman) p. 130. J. Wiley, New York (1956).

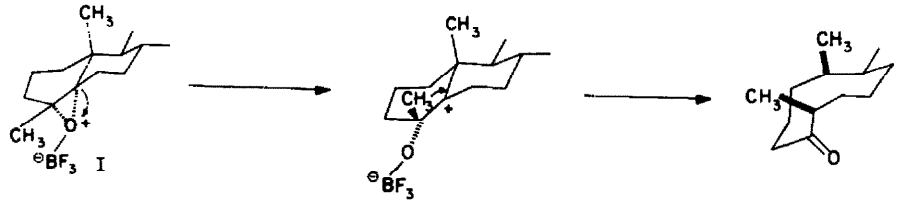
at C-10, which should facilitate its participation in the non-classical carbonium ion in the transition state.

I



II

The less favourable alternative of equatorial cleavage would afford a C-5 carbonium ion from each of the α-epoxides. The concomitant rotation of groups about the ring carbon atom (C-4 or C-6) which retains the oxygen substituent places the 4β- or 6β-methyl group in position for a *trans*- attack upon C-5, resulting in the corresponding 5β-methyl ketones. We have shown[1,3] that these ketones are the ultimate



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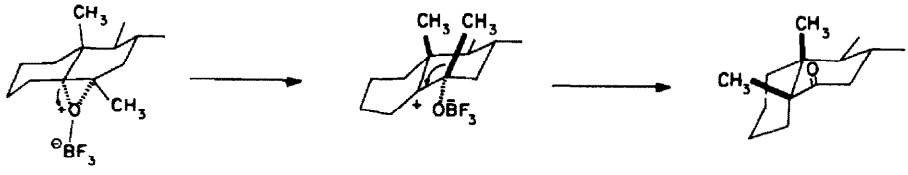
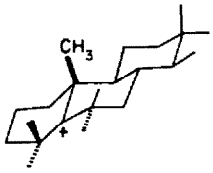


II

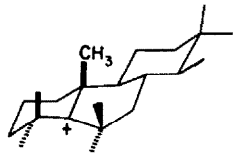
ketonic products of thermodynamically controlled rearrangements starting either from the α-epoxides or from the skeletally rearranged homo-nor ketones. It does not necessarily follow, although it seems probable, that the epoxides are intermediates in the ketone isomerization reactions.

The behaviour of the 4β,5β- and 5β,6β-epoxides with boron trifluoride requires a more subtle interpretation. The bicyclic analogues (rings A and B only) would

clearly be enantiomeric, and should afford structurally identical (through enantiomeric) products of rearrangement. In fact two ketones were formed from each steroidal β-epoxide, but in significantly different ratios from the two epoxides. The $4\beta,5\beta$-epoxide gave predominantly the product of methyl-group migration, the 5α-methyl-4-ketone, while ring contraction was the major ketone-forming reaction of the $5\beta,6\beta$-epoxide, the main product in this case being 5β-acetyl-B-norcholestane. These ketones all arise from epoxide cleavage at C-5, as required by the axial-cleavage postulate. The differences between the subsequent reactions of the C-5 carbonium ions from the two β-epoxides may be interpreted in terms of the conformational restraint imposed upon the carbonium ions by the presence of rings C and D. Inspection of a model of the C-5 carbonium ion reveals two extreme conformations (P and Q).

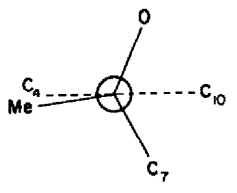


P

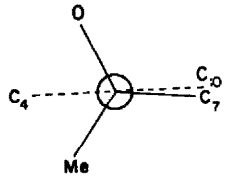


Q

Structure P permits the existence of ring B in a strain-free conformation, the intrinsic strain in the model being absorbed by the relatively mobile ring A. Structure Q involves unfavourable interactions, including a partial eclipsing about the 7,8-bond, and twisting of the 9,10-bond, which forces the C-19 angular methyl group towards C-11. Thus it seems appropriate to consider the rearrangements of the C-5 carbonium ions derived from the two β-epoxides in terms of a preference for conformation P over conformation Q. The behaviour of the $5\beta,6\beta$-epoxide can then be seen as a normal axial cleavage to give a C-5 carbonium ion in conformation P, with contraction of ring B to give the 5β-acetyl-B-nor product. The essential features of the transition state are represented in a Newman projection in Fig. 5a. The model is viewed along

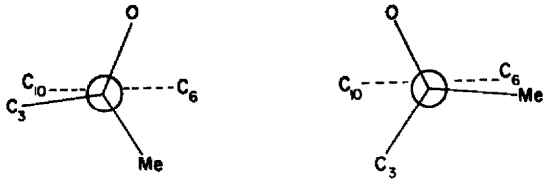


(a)



(b)

the C_6-C_5 bond, and is seen to be suitably oriented for *trans*-migration of C-7. The minor product, the 5α-methyl-6-ketone, would be derived from conformation Q, represented by Fig. 5b. A similar analysis of the C-5 carbonium ion derived from the $4\beta,5\beta$-epoxide gives the transition states represented by Figs. 6a and 6b, corresponding to conformations P and Q respectively. (The projections are along the 4,5-bond in this case). The preference for conformation P results in methyl migration, the "normal" ring-contracted product being formed in only 6% yield in this case.



The extension of this analysis to the 3β-acetoxy-5α,6α- and 5β,6β-epoxides was straightforward. The 3β-acetoxy group must exert its -I effect more strongly at C-5 than at C-6, and does not prevent the normal C-6 cleavage of the 5α-6α-epoxide. A 5β-methyl-A-homo-B-nor-4a-ketone therefore results from the rearrangement of a 5α,6α-epoxy-6β-methyl steroid, irrespective of the presence or absence of a -I substituent at C-3 (3β-acetoxy[1] or 3,3-ethylenedioxy[8]).

In the case of the 5β,6β-epoxide, however a -I substituent at C-3 opposes the normal formation of a C-5 carbonium ion. The initial formation of a fluorohydrin, by attack of F^- (or its equivalent[9]) upon C-5 can occur by a synchronous mechanism to give the product of diaxial opening of the epoxide, and is apparently preferred over the alternative of equatorial cleavage at C-6. We have already proposed a mechanism for the subsequent slow conversion of the fluorohydrin into a mixture of ketonic products, postulating the intermediacy of the boron trifluoride-complex of the 5β,6β-epoxide. It is now possible to consider the relatively high energy transition states leading to the ketones, and to account for the differences between the ketonic products obtained from the 3β-acetoxy- and 3-deoxy-5β,6β-epoxides.

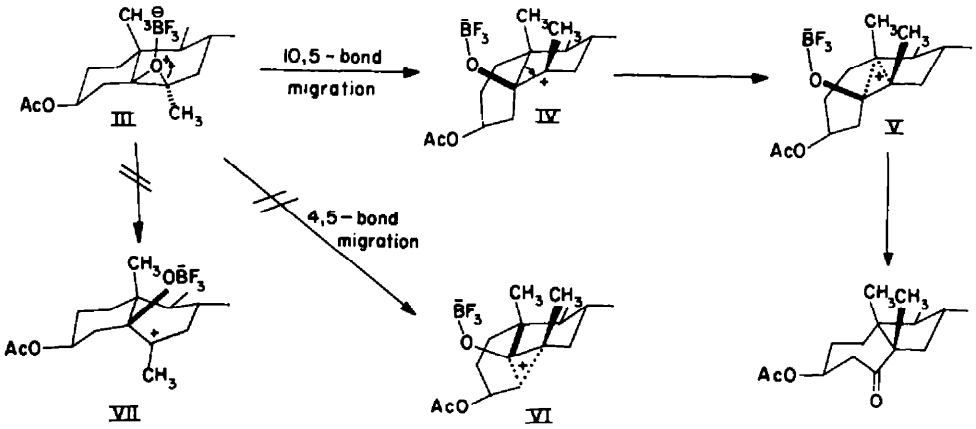
The -I effect of the 3β-acetoxy group, by opposing C-5 (axial) cleavage, enforces a considerable proportion of C-6 (equatorial) cleavage. By analogy with the monocyclic model epoxide (L-form), the carbonium ion produced by equatorial cleavage of 3β-acetoxy-5,6β-epoxy-6α-methyl-5β-cholestane (III) should have structure (IV) (The conformation of ring A is uncertain). Two possibilities are apparent for rearrangement of the carbonium ion (IV), involving migration of the 10,5- (*cis*) or the 4,5- (*trans*) bond respectively. Only the product of 10,5-bond migration was formed. This is probably due, at least in part, to the favourable participation of the quaternary (C-10) centre in the non-classical carbonium ion (V). The corresponding transition state (VI) for migration of the 4,5-bond should be distinctly less stable, for the secondary C-4 group, already under the -I influence of the 3β-acetoxy substituent, would need to share the positive charge at the reaction centre.

The carbonium ion at C-6 might conceivably react in the alternative conformation (VII), which would lead to a 5α-methyl-A-homo-B-nor-4a-ketone. This can, however, be discounted from examination of a model. Conformation (VII) is destabilised by the near-eclipsing of substituents about the 7-8, 5-10, and 9-10 bonds, as well as a strong non-bonded repulsion between the 3α-H and the 6-methyl group. No *trans*-fused homo-nor steroids were found in the present work.

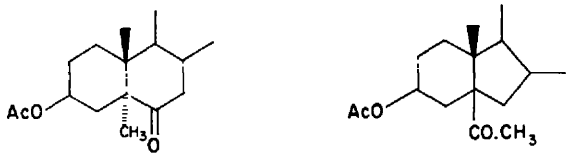
The formation of a little 3β-acetoxy-5-methyl-5α-cholestan-6-one (VIII) indicates that the normal axial cleavage (at C-5) of the 5β-6β-epoxide is not entirely prevented

[8] A. Bowers, L. Ibáñez and H. J. Ringold, *Tetrahedron* **7**, 138 (1959).

[9] A. Bowers and H. J. Ringold, U.S. 3, 115, 492 (1963); *Chem. Abstr.* **61**, 3179h (1964); see also Ref. 4.



by the 3β-acetoxy group. The analysis of the reactions of the 3-deoxy-5β,6β-epoxide, presented above, suggested that C-5 cleavage, if it occurred, should afford not only the 5α-methyl-6-ketone (VIII) but also the 5β-acetyl-B-nor-compound (IX). A search was therefore made in the mother-liquors from the crystallisation of the two major ketonic products.[1] A band at 1356 cm^{-1} in the IR spectra of residues from the purification of 3β-acetoxy-5-methyl-A-homo-B-nor-5β-cholestane indicated the presence of some of the 5β-acetyl-B-nor isomer (IX). This was confirmed, after vigorous alkaline hydrolysis of the 3β-acetoxy group, by the presence of a signal at τ7·77 in



VIII IX

the NMR spectrum of the sample. The yield of 5β-acetyl compound was estimated as ca. 3%. Compared with the 3-deoxy-5β,6β-epoxide, the reversal of the relative yields of the 5α-methyl-6-ketone and the 5β-acetyl-B-nor-compound can be seen as the combined consequence of a slight destabilisation of conformation P of the C-5 carbonium ion, as a result of the tendency of the 3β-acetoxy group to retain an equatorial conformation in a pure chair-form of ring A, and resistance to the assumption of a 5β-configuration, with the resulting steric compression between the axial 3β- and 5β- substituents.

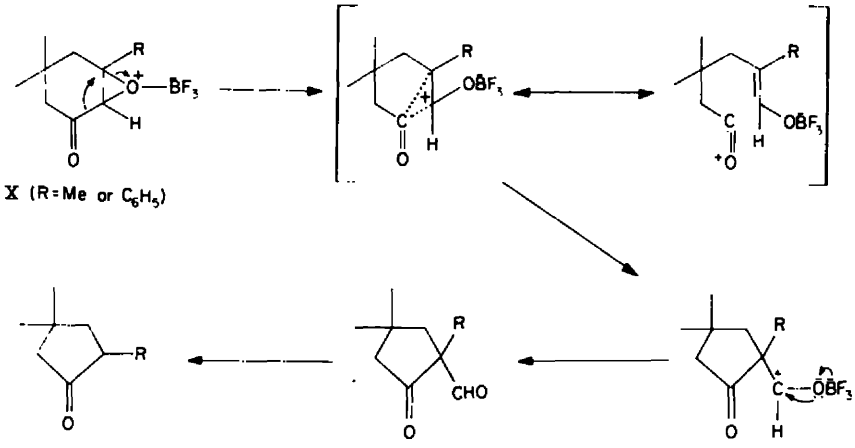
Finally, the formation of the three ketonic products which, on conformational arguments, might be expected from the 3β-acetoxy-5β,6β-epoxide, is regarded as strengthening our belief[1] that the epoxide is, in fact, the common intermediate in the formation of the three ketones from the initially formed fluorohydrin.

Rearrangements of 3-substituted-4,5-epoxides

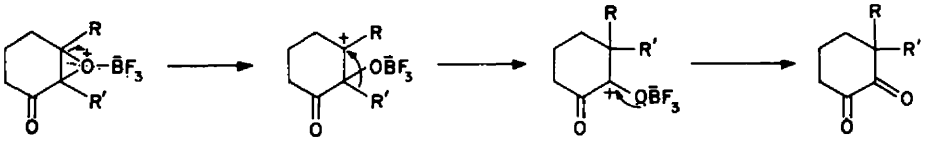
The behaviour of the 3-substituted-4,5-epoxy-4-methyl steroids is analysed in terms of deviations from the reactions of the 3-deoxy-epoxides caused by the presence of the C-3 substituent. In general, a -I group at C-3 should alter profoundly the reactions of a 4α,5α-epoxide, by opposing the normal axial cleavage at C-4 and

compelling alternative reactions. The effect of a C-3 substituent on a 4β,5β-epoxide should not change the preference for cleavage at C-5 observed in the 3-deoxy-compound.

The 3-keto-4,5-epoxides will be considered first. Here an additional factor becomes important. House[10] has demonstrated convincingly that acyl-group migration to an electron-deficient centre is strongly preferred over H- or alkyl-migration, in the absence of over-riding steric or other complications. It was shown, for example, that the 3-methyl(or phenyl)-2,3-epoxycyclohexanones (X) undergo predominant ring contraction with boron trifluoride. House has interpreted the ease of acyl migration in terms of the ability of the carbonyl group to share the positive charge in the transition state, which may be represented as a resonance hybrid involving structures of the type shown. Acyl-group migration also leads to localisation of positive



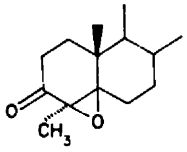
charge at the carbon atom which finally becomes the site of the new carbonyl group. This charge transfer to a position β- to the original ketone should be preferred over the localization of positive charge α- to the ketone, which occurs in the formation of an α-diketone by the alternative migration of an alkyl substituent from the C-2 position. This additional influence in favour of acyl migration should operate in the



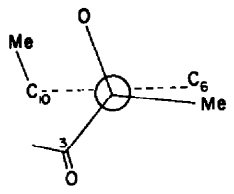
case of 2,3-dialkyl-2,3-epoxycyclohexanones, but is probably not important in the rearrangement of the 3-alkyl-compounds (X) which are believed to afford the enol of the α-diketone by direct elimination of the C-2 proton from the initial C-3 carbonium ion.

In the rearrangement of the 4β,5β-epoxy-ketone (XI), ring contraction (acyl migration) should become relatively more important than in the 3-deoxy β-epoxide, where it was only just detectable. Although extensive ring contraction was observed

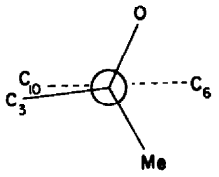
[10] H. O. House and D. J. Reif, *J. Amer. Chem. Soc.* **77**, 6525 (1955).



XI



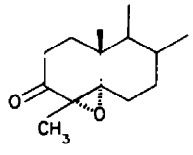
(a)



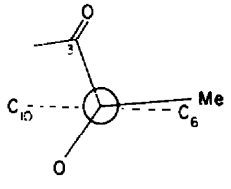
(b)

in the β-epoxyketone (XI), various conformational factors prevent the reaction from becoming dominant. An examination of a Dreiding model of the C-5 carbonium ion derived from the β-epoxyketone revealed that the transition state for migration of the C-3 carbonyl group requires eclipsing of the 4-methyl substituent and the C-6 methylene group (Fig. 7a), and close approach of the 4β-oxygen atom to the 19-methyl group. The tendency, noted earlier, for the C-5 carbonium ion to assume conformation P, with clockwise rotation of the C-4 substituents (viewed along $C_4 - C_5$), also favours 4-methyl migration (Fig. 7b). The counterbalancing of these various effects results in equal yields of the two ketonic products.

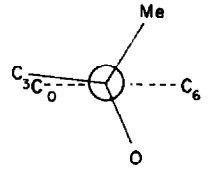
The α-epoxyketone (XII), compelled by the -I effect of the carbonyl group to undergo abnormal cleavage at C-5, affords the 4,6-dienone as the major product. This elimination reaction is perhaps more favourable than in other similar epoxides because of the *trans*- planar relationship of the 6β-proton to the epoxide ring, and the driving force of conjugation in the product. Rearrangements leading to ketones involve either 3,4-bond (acyl group) migration to C-5 (Fig. 8a), or 4-methyl group migration (Fig. 8b). The former reaction not only requires near eclipsing of the 4-methyl group with C-6, but also leads to a strained *trans*- junction between the 5-



XII



(a)



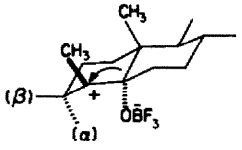
(b)

membered ring A and 6-membered ring B. The latter reaction results in a strained *cis*-decalin type of structure, rendered even less favourable by the skew interaction between the 5β-methyl substituent and the 19-methyl group. Both ketonic products are formed, but in modest yields compared with the epimeric diketones derived from the β-epoxyketone.

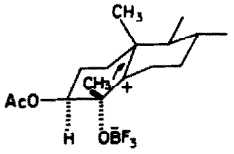
The resonance-stabilized cationic structure (Xa), which can explain the ring contraction of epoxy-ketones, has no counterpart when the C-3 substituent is an acetoxy group, for the -I effect of the acetoxy-carbonyl moiety opposes participation of p-electrons on the ether-linked oxygen of the acetoxy group in a comparable resonance hybrid. The reactions of the 3-acetoxy-4,5-epoxides must therefore be

analysed in terms of the -I effect of the 3-substituent, but without any likelihood of ring contraction occurring. An additional restraint is imposed on these compounds by the conformational preference of the acetoxy group. An examination of models shows that two or more conformations of ring A must be considered for each 3-acetoxy-epoxide, and for each derived C-5 carbonium ion. The relative stabilities of these conformations should be determined by the non-bonded interactions involved, particularly those to which the 3-acetoxy group contributes.

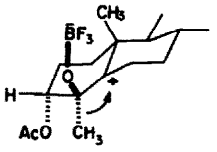
The "normal" axial cleavage of a 4α,5α-epoxide at C-4 is apparently so facile as to occur even when opposed by the -I effect of the 3β-acetoxy group, which must be weaker than that of a 3-ketone. It becomes clear from examination of a model that the *conformational* changes involved in skeletal rearrangement of the C-4 carbonium ion should not be influenced by the presence of a 3β-acetoxy substituent (diagram XIII). The 3α-acetoxy-4α,5α-epoxide, in contrast, cannot assume the conformation (XIII) necessary for skeletal rearrangement without introducing steric and dipolar repulsions between the 3α-acetoxy and 5α-oxygen groups.



XIII



XIV



XV

The only other ketone-forming process open to the 3-acetoxy-4,5-epoxides is the one proceeding by C-5 cleavage and migration of the 4-methyl group. The facility of this process for any particular epoxide clearly depends upon the stereochemistry of the corresponding C-5 carbonium ion. In the 3β-acetoxy-4α,5α-epoxide the process of equatorial cleavage at C-5 and 4-methyl migration (XIV), observed for the 3-deoxy compound (I), can occur with only moderate interference by the 3β-acetoxy group, which becomes axially opposed to the 5β-methyl group in the resulting 4-ketone. The 3α-epimer cannot easily undergo a similar rearrangement for the acetoxy group would be forced into a pseudo-axial conformation, and dipole interaction with the 4α-oxygen substituent would also contribute to raising the energy level of a C-5 carbonium ion of conformation similar to (XIV). It is unfortunately not possible to attempt a full account of the observed behaviour of the 3α-acetoxy-4α,5α-epoxide as the structure of the only reaction product (an unsaturated hydroxy-acetate[2]) is unknown. It is clear that all routes to ketones are blocked for this compound by the combined conformational and inductive effects of the 3α-acetoxy group.

Methyl-group migration is assisted in the 3α-acetoxy-4β,5β-epoxide by the conformational effect of the acetoxy group. An upward rotation (diagram XV) of the C-3 substituents, which tends to relieve steric interactions between the 3α-acetoxy group and the 1α-H and 4α-methyl substituents, rotates the 4-methyl group downwards into position for attack upon the α-face of the C-5 carbonium ion. A 3β-acetoxy group, however, appears to exert some opposition to 4-methyl migration, which occurs only to a minor extent. Here the acetoxy group will tend, by its steric effect and its dipolar interaction with the 4β-oxygen atom, to prevent the downward rotation of the C-4 substituents necessary for methyl migration.

Finally, it is worth noting that both the 3α- and 3β-acetoxy-4β,5β-epoxides undergo elimination reactions to a marked extent, the 3α-epimer giving the Δ^5-4β-alcohol, and the 3β-epimer giving, very remarkably, the $\Delta^{3,5}$-enol acetate of 4-methylcholest-4-en-3-one. It is clear that formation of the Δ^3-unsaturated bond only in the latter case must be a consequence of the *trans*-diaxial relationship of the 3α-H and 4β-oxygen functions. We have reported in Part IV[3] that the 3-deoxy-4β,5β-epoxide gave a non-polar gum as a significant proportion (47%) of the product. A further examination of this material has shown it to contain 78% of 4-methylcholesta-3,5-diene, which was ultimately obtained crystalline and characterized by its UV and IR spectra, and by comparison with an authentic sample.[11] It is clear, therefore, that elimination is an important reaction of the 4β,5β-epoxide system, despite the non-planarity of either of the C-6 hydrogen atoms with the epoxy oxygen. The elimination is probably initiated by formation of the C-5 carbonium ion in conformation P (see above), followed by loss of the 6β-proton.

CONCLUSION

The foregoing analysis has provided a qualitative interpretation of many of the main features of the rearrangement reactions of the epoxides. It is obviously desirable to put this interpretation on a quantitative basis, by determining the contributions of the various conformational and electronic factors to the energy levels of the transition states leading to different products. Further work is in progress, employing other epoxy compounds, to gain a deeper understanding of the quantitative aspects of the behaviour of epoxides with boron trifluoride.

Acknowledgement—The authors acknowledge grants from the Research Committee of the New Zealand Universities Grants Committee.

[11] S. Julia and J-P. Lavaux, *Bull. Soc. Chim. Fr.*, 1231 (1963).