Some Epoxy-olefin Cyclisations

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Summary It is shown that certain alk-2-enyl-2,3-epoxy-3-methylcyclohexanones can be cyclised in good yield with some Lewis acids to decalone derivatives, but use of weak Lewis acids and/or nonpolar solvents leads to ring contraction.

THE elegant work of Johnson[1] has established cation-induced cyclisation of polyenes as a viable synthetic method for the preparation of certain types of alicycles. Useful yields generally result only when a stable carbonium ion, *e.g.* tetra-alkylallyl or oxonium, is used to initiate cyclisation.

Use of co-ordinated epoxide to initiate cyclisation has given valuable results[2] which have an important bearing on terpene biosynthesis but as a synthetic method it leaves something to be desired. Previously we have shown that a tetrasubstituted cyclohexene epoxide could be cyclised[3] in good yield. In order to examine the generality and usefulness of this as a preparative method we have examined epoxy-olefins with varied double bond substitution.

The substrates for cyclisation [(**1**)—(**7**)] were synthesised[4] by alkylation of Hagemann's ester with appropriate halide or tosylate, followed by hydrolysis, decarboxylation, and epoxidation of the cyclohexenone with $NaOH–H_2O_2$. Cyclisation ($TiCl_4$, CH_2Cl_2) of (**1**) gave (**8**) (30%) and (**11**)† (25%). Spectroscopic data for (**8**) [ν_{max} (CCl_4) 3495 and 1715 cm^{-1}; τ ($CDCl_3$; 300 MHz) 5·23 (1H, m), 5·28 (1H, m), and 9·15 (3H, s)] established part structure (A) for (**8**) where C* is either C-1, -2, -3, or -10; (**8**) was assigned on the basis of mechanism and the degradation of related cyclisation products. With other Lewis acids (**8**) was also formed together with varying amounts[5] of (**12**) [ν_{max} ($CHCl_3$) 1745 and 1715 cm^{-1}; τ ($CDCl_3$) 4·3 (1H, m), 5·1 (2H, m), and 8·7 (3H, s)] which on alkaline hydrolysis gave the acid (**14**). If it is accepted that gas-phase metal–oxygen bond strengths[6] give a rough measure of Lewis acidity for oxygen for a series of chlorides then it is apparent from the Table that

TABLE

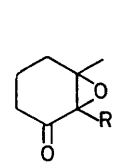
Lewis acid	Solvent	Ratio (**8**) : (**12**)
$TiCl_4$	CH_2Cl_2	∞
$AlCl_3$	"	3·0
$FeCl_3$	"	1·1
$SnCl_4$	"	0·6
$ZnCl_2$	"	0·3
$BF_3.OEt$	"	0·8
"	C_6H_6	0·6
"	Et_2O	0·1
$ZnCl_2$	"	0·1

[a] Ratios determined by g.l.c.

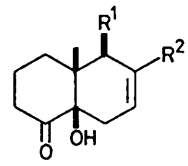
increased Lewis acid strength favours cyclisation over ring-contraction. This could arise from C–O–metal bonds being formed in the cyclisation transition state, whereas C=O-metal bonds result from ring contraction; while both systems would be lowered in energy by increasing bond strengths the latter might be relatively less stabilised owing to a consequent reduction in resonance stabilisation. It is also clear from the Table that decreasing solvent polarity favours ring contraction.

Reaction of (**2**) with Lewis acids ($BF_3.OEt_2$, $SnCl_4$, or BCl_3) gave (**9**) [τ (CCl_4), 4·3 (2H, m), 9·0 (3H, d, J 7 Hz), and 9·15 (3H, s)] and (**10**) [τ (CCl_4), 4·63 (1H, m), 8·35 (3H, br. s), and 9·1 (3H, s)] as major products (> 60%). The ketone (**10**) was reduced by $NaBH_4$ to a mixture of diols which on cleavage with periodate gave a keto-aldehyde, the spectroscopic properties of which [ν_{max} ($CHCl_3$) 1730 and 1715 cm^{-1}; τ(CCl_4) 4·3 (1H, m), 8·3 (3H, br. s), and 8·84 (3H, s)] demonstrated that the double bond was not allylic to the hydroxy-group of (**10**).‡ Only small amounts of ring contraction product were formed in these cyclisations probably because the more nucleophilic disubstituted double bond increases the rate of cyclisation[7] while the rate of ring contraction is independent of double bond substitution. It was therefore surprising that we were unable to obtain any well defined cyclisation products from (**3**).

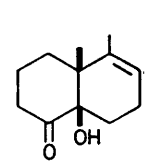
In line with Baldwin's view[8] that 5-*endo* trigonal cyclisations are disfavoured we obtained only ring contraction products from reaction of (**5**) and (**6**) with the common Lewis acids. Reaction of (**5**) with $TiCl_4$ gave the ether (**15**) [τ (CCl_4) 2·5—3·9 (3H, m), 7·1 (2H, s), 7·8 (3H, s), and 8·6 (6H, s); λ_{max} (EtOH) 280 nm (ϵ 2200)]. Attempts to generate a seven-membered ring by cyclisation of (**4**) led to ring contraction.



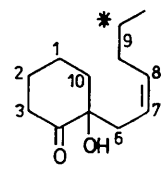
(1) R = –$[CH_2]_2CH=CH_2$
(2) R = –$[CH_2]_2CH=\overset{t}{C}HMe$
(3) R = –$[CH_2]_2C(Me)=CH_2$
(4) R = –$[CH_2]_3CH=CH_2$
(5) R = $CH_2C(Me)=CH_2$
(6) R = $CH_2CH=CH_2$
(7) R = $CH_2CH_2C_6H_4OMe$-*p*



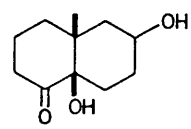
(8) $R^1 = R^2 = H$
(9) R^1 = Me, R^2 = H



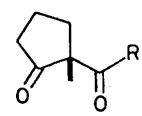
(10)



(A)



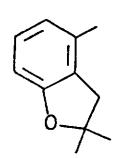
(11)



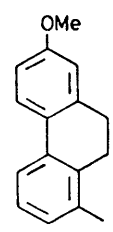
(12) R = –$[CH_2]_2CH=CH_2$
(13) R = $CH_2CH=CH_2$

$HO_2C[CH_2]_2CH(Me)CO•[CH_2]_2CH=CH_2$

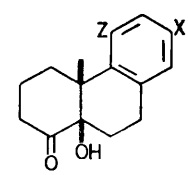
(14)



(15)



(16)



(17) X = H, Z = OMe
(18) X = OMe, Z = H

† Normal precautions to exclude moisture were taken. This compound is not found to any major extent in other cyclisations.

‡ This excludes the possibility that the product is arising by an 'ene' process followed by rearrangement which has been observed in one special case (see following communications) and which would put the double bond and substituent in the 6,7- rather than the 8,9-positions.

Reaction of the anisole (**7**) with $BF_3.OEt_2$ or $SnCl_4$ gave (**17**) (45%) [τ ($CDCl_3$) 2·95 (1H, m), 3·3 (2H, m), and 8·63 (3H, s)] and (**18**) (45%) [τ 2·9 (1H, d, J 7 Hz), 3·3 (2H, m), and 8·75 (3H, s)] which could be readily separated. The mixture of (**17**) and (**18**) was reduced with $NaBH_4$ and the diols cleaved with HIO_4 to the corresponding keto-aldehydes which were separated and characterised; spectral data established that the carbonyl groups were not conjugated to the anisole ring. With $TiCl_4$ (**7**) gave (**17**) and (**18**) as minor products and the dihydrophenanthrene (**16**) (50%) [τ ($CDCl_3$) 2·4 (2H, dt), 2·9 (2H, m), 3·2 (2H, m), 6·2 (3H, s), 7·2 (4H, s), and 7·65 (3H, s); λ_{max} (EtOH), 278 nm (ϵ 29,800)] as the major one.

cis-Stereochemistry is assigned to all the decalones since they exhibit intramolecular hydrogen bonding which is possible only in the 'non-steroid' *cis*-decalin conformation; such bonding is not observed in the 5α- and 5β-hydroxycholestan-4-ones.

These results suggest that such cyclisations could be developed for preparative use if proton elimination could be directed, *e.g.* by use of silyl substituents, and that polyolefinic cyclisations might be possible. Such experiments are now under way.

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