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A Reasonable Accounting for Mass Spectral Stereoisomeric Effects in Substituted Cyclohexanols

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A large stereochemical bias against *cis*-isomers for electron impact-induced water elimination from the epimers of both 4- and 3-t-butylcyclohexanols has been reported.[1,2] Further, the 4-t-butyl group is at least ten times more effective in promoting the isomer differences.[2]

These stereochemical effects are only consistent[1,2] with substantial abstraction of the available tertiary hydrogen in the *trans*-isomer. Since both 1,4- and 1,3-modes of elimination are available in cyclohexanol,[3] this implies that in the 4-t-butylcyclohexanol the 1,4-elimination in the *trans*-isomer must be faster than the 1,3-elimination in the *cis*-isomer whereas in the 3-substituted case the opposite must be true. That the eliminations in the *cis*- are slower than those in the *trans*-isomers can be theoretically justified, since the *cis*-isomers must lose secondary hydrogens, while the *trans*-isomers can readily lose tertiary ones. The suppression of the secondary hydrogen eliminations in the *cis*-isomers, where no tertiary hydrogens are available, is clearly not justified in view of the classical steric role of the t-butyl group.

Cleavage of the t-butyl group in competition with water elimination nealty accounts for the observed isomeric differences and these implications. Such pre-emptive cleavage could block the slower secondary hydrogen eliminations in the *cis*-isomers, allowing only the faster tertiary hydrogen abstractions in the *trans*-epimers. Since the 1,4-elimination is faster than its 1,3-counterpart,[4] the latter would be more effectively interrupted and a larger difference for the 4-substituted isomers would be found, as is the case.[1,2] This explanation demands that the *trans*/*cis* difference for loss of water in isomeric substituted cyclohexanols decrease as the substituent group (R) presents lower order bonds for cleavage, in contrast to the hypothesis[1,2] which only invokes availability of a tertiary hydrogen in the *trans*-isomers.

The mass spectra of the *cis*- and *trans*-isomers of various alkylcyclohexanols (Scheme, Table) both support our hypothesis and reveal an additional feature of the role of the t-butyl group. The requirements that the stereochemical difference be largest for the t-butyl substituents in each series (*i.e.*, 1,3 or 1,4) and that the 4-substituents be most effective in promoting the isomeric differences are met† (except for R = Pr^i, see below) (Table) and support the special role for the alkyl group discussed above.

TABLE*

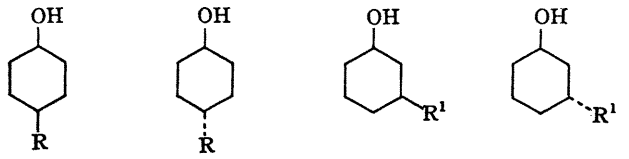
	$(A)_{trans}/(A)_{cis}$			
	Me	Et	Pr^i	Bu^t
R^1	1·0	1·1	2·0	3·6
R^2	13	5·0	1·3	340

* $A = M - H_2O/M$. Each value is the average of at least three determinations. The scatter was *ca.* 10%. The spectra were taken on a MAT Atlas CH-4 mass spectrometer by adsorbing samples on charcoal in the direct-inlet system (TO-4). Electron energy was 70 v, ionizing current 5·4 μA and source temperature <70°.

The remarkable decrease in the *trans* : *cis* ratios in the 1,4- series from methyl to isopropyl, may be justified in the light of the mass spectra of *cis*- and *trans*-1,4-cyclohexanediol.[6] Not only does the *trans*-diol eliminates water more readily than its *cis*-epimer but further, the compound with deuteriated hydroxy-groups shows that most of the loss of water in the *cis*-isomer occurs by elimination of D_2O. These results offer us an attractive explanation. If loss of hydrogen from the R group is important in the 1,4-series

† (a) Any diminution of the isomeric molecular ions due to relative thermodynamic stabilities would act to enhance the *trans* : *cis* ratio in the 3 series and decrease the ratio in the 4 series in opposition to the trends observed. (b) An assumption inherent in this interpretation of these data is that the $M - H_2O$ ion from the *cis*- and *trans*-isomers (for each R group) further decomposes to approximately the same extent.

as well as in the diols studied earlier,[6] this loss would be facilitated in going from methyl to isopropyl since the abstracted hydrogens progress from primary to tertiary. Further, the t-butyl group has no α-hydrogen and thereby is most similar to methyl in this respect, as indicated experimentally by the progression in the 1,4-series. Loss of hydrogen from the 3-substituent would be expected to be of less importance for isomeric differences in this series, owing to the availability of other ring hydrogens (*i.e.*, C-4) already suppressing these isomer differences.



SCHEME

$R^1 = R^2 =$ Me, Et, Pr^i, Bu^t

All isomers were obtained by preparative v.p.c. on either 10 ft. 20% Diglycerol or 10 ft. 20% Carbowax 20M on 60–80 Chromosorb W. Stereochemical assignments were made from the relative retention times from the ratio of isomers produced by lithium aluminium hydride reduction of the derived keytones.[5] The latter compounds in every case were converted into derivatives with properties in agreement with values in the literature.

It is significant that our proposal requires that even in those molecules where the overall isomer differences are small or non-existant the eliminations will be highly stereospecific, although this will not be apparent in the absence of labelling. Nevertheless this work, and the work of others[1,2,6] indicates that a non-empirical approach may fulfil the expected[7] potential of mass spectrometry for stereochemical studies in these, and related alicyclic molecules.

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