# THE ROLE OF CONFORMATIONAL MOBILITY IN THE STEREOSPECIFIC LOSS OF WATER UNDER ELECTRON IMPACT

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*Dedicated to Professor E. Hála on the occasion of his 60th birthday.*

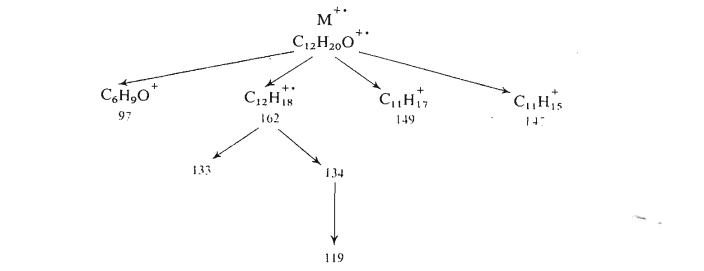
Mass spectra of nine of the sixteen possible diastereoisomeric 7-hydroxytricyclo[7.3.0.0$^{2,6}$]dodecanes are reported. The spectra differ considerably in the extent of water elimination from molecular ions. The diastereoisomers which have conformationally flexible *cis-anti-cis*, *cis-anti-trans* and *cis-syn-trans* skeletons exhibit abundant $(M-H_2O)^{+\cdot}$ ions. Molecular ions of the rigid *trans-anti-trans* isomers lose water to a markedly smaller extent, the main fragmentation proceeding *via* a skeletal cleavage. Effects of conformational mobility are emphasized.

Since the Biemann's pioneering work in the late fifties[1], the stereochemistry of mass spectral fragmentations has attracted considerable interest. The loss of water from cyclic alcohols under electron impact has been investigated extensively because this decomposition has shown a remarkable regio- and stereospecificity. Excellent reviews on the topic are available[2-5]. The elimination of water from a molecular ion of a cyclic alcohol involves the abstraction of γ-, δ- or even more remote hydrogens which are transferred to the hydroxyl group and then lost as water[6-8]. This transfer is not always possible in a ground state conformation, so that conformational flipping may be neccessary[6]. The intramolecular nature of the hydrogen transfer requires both reacting groups to be brought close together. The maximum distance at which a secondary hydrogen can be transferred to hydroxyl in a stereospecific way, *i.e.* without ring opening, has been estimated to be 0·18 nm for a saturated system[9]. Since the mutual accessibility of the hydroxyl group and a hydrogen is governed by the molecular geometry, stereoisomers could differ in the extent of water elimination and, hence, they could be distinguished by means of mass spectrometry. An extensive labelling is usually necessary to determine accurate mechanisms of water loss. In most cases, however, including natural as well as synthetic products, such a labelling is not easily feasible. Therefore it would be desirable to predict the relative

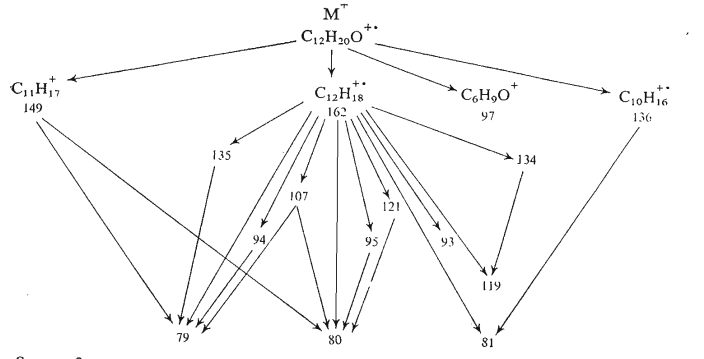
extent of the mass spectral loss of water only on the basis of molecular geometry. For this purpose, investigation of mass spectral behaviour of series of model compounds is of importance. The present paper is aimed at the effects of conformational mobility (or rigidity) on the electron-impact-induced loss of water from 7-hydroxytricyclo[7.3.0.0$^{2,6}$]dodecane diastereoisomers. Although the series is not complete (only nine of the sixteen possible diastereoisomers are reported), it involves skeletons, ranging from a rigid (*trans-anti-trans*) to a freely mobile one (*cis-anti-cis*).

## RESULTS AND DISCUSSION

Mass spectra of the *trans-anti-trans* isomers *I* and *II* differ markedly from those of the other isomers *III*–*IX*. The elemental composition and origin of abundant ions are visualized in fragmentation maps (Scheme 1 and 2). The spectra of *I* and *II* show

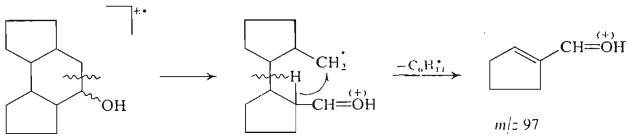



SCHEME 1




SCHEME 2

prominent $C_6H_9O^+$ ions, $m/z$ 97 (Scheme 3). As determined from the spectrum of the labelled derivative *Ia*, the hydrogen, transferred to the neutral $C_6H_{11}$ fragment, originates from $C_{(6)}$, the regiospecificity being about 80%. The abundances of the $C_6H_9O^+$ ions in *I–IX* are summarized in Table I. It follows that formation of the $C_6H_9O^+$ ions is enhanced only if the hydrogen at $C_{(6)}$ is fixed in the axial position (isomers *I*, *II*, *VI* and *VII*). Thus, the skeletal cleavage shows a remarkable stereospecificity. Similar effects of the configuration at the annulation site have been described for 3,6,20β-trihydroxypregnanes[10] and 6-hydroxycholestanes[11].




SCHEME 3

The spectra of *I* and *II* also differ from those of *III–IX* in the abundance of the $(M - H_2O)^{+\bullet}$ ions, $m/z$ 162. In order to express the extent of water elimination quantitatively, the abundances of $(M - H_2O)^{+\bullet}$, related to the total ion current, and/or the abundance ratios $(M - H_2O)^{+\bullet}/M^{+\bullet}$ have been employed[12]. Both these values for *I–IX* are summarized in Table II. The hydrogens accessible to the hydroxyl group (Table II) were found by inspection of Dreiding models. In *I* and *II* which have the rigid skeleton, there are no γ- or δ-hydrogens directly available to the hydroxyl

TABLE I

Abundances of $C_6H_9O^+$ Ions and Configurations at $C_{(6)}$

| Compound | *I* | *II* | *III* | *IV* | *V* | *VI* | *VII* | *VIII* | *IX* |
|---|---|---|---|---|---|---|---|---|---|
| Position of hydrogen[a] at $C_{(6)}$ | *a* | *a* | *e* | *e* | *e* | *a* | *a* | *e* | *e,a* |
| $(C_6H_9O)^+/\Sigma_{26}$, % | 15·0 | 15·1 | — | 1·32 | 0·63 | 2·27 | 4·72 | 0·60 | 1·35 |
| $(C_6H_9O)^+/M^{+\bullet}$ | 12·9 | 16·1 | — | 17·5 | 27·5 | 22·8 | 116·6 | 8·6 | 58·7 |

[a] Axial, [e] equatorial.

group within the 0·18 nm limit. In the equatorial isomer *I*, the distance between hydroxyl and the nearest hydrogen at $C_{(5)}$ was found to be 0·30 nm. In the axial isomer *II*, the distance between hydroxyl and the nearest hydrogen at $C_{(2)}$ is 0·25 nm (Fig. 1). However, any distance measured on the molecular models should be applied carefully to molecular ions[9]. In the ionised state, the bond angles and bond lengths can be altered so that the ground state geometry represents only a rough approximation. Moreover, since the molecular ion is vibrationally excited, its internal energy is sufficient to make two groups accessible by bending the corresponding bonds. If such a skeletal deformation is neccessary to enable the hydrogen transfer, the corresponding strain energy makes a significant contribution to the activation energy of the water loss, decreasing the reaction rate of the latter and lowering the relative abundance of the $(M - H_2O)^{+\cdot}$ ions. As *I* and *II* have the rigid *trans-anti-trans* skeleton, there is no low-energy path available (*e.g.* chair-to-boat flipping) to bring the skeletal hydrogens to the hydroxyl group. Accordingly, the molecular ions of *I* and *II* decompose mainly *via* the competing skeletal cleavage leading to the $C_6H_9O^+$ ions. The easier loss of water from the axial alcohol *II* than from the equatorial isomer *I* can be explained in terms of the preceding considerations: bending of the cyclohexane ring in *II* brings the axial hydrogen at $C_{(2)}$ closer to the axial hydroxyl group, while in *I* the distance between the equatorial hydroxyl and the nearest hydrogen at $C_{(4)}$ remains unchanged. The activation energy of water elimination in *II* could also be modulated by a release of the non-bonding strain due to interaction between two axial substituents.

TABLE II

Abundances of $(M-H_2O)^{+\cdot}$ and Accessibilities of Skeletal Hydrogens

| Compound | $M^{+\cdot}/\Sigma_{26}$ % | $(M - H_2O)^{+\cdot}/\Sigma_{26}$ % | $(M - H_2O)^{+\cdot}/M^{+\cdot}$ | Positions of accessible hydrogens |
|---|---|---|---|---|
| *I* | 1·16 | 2·69 | 2·33 | none |
| *II* | 0·94 | 3·76 | 4·00 | $C_{(5)}$ |
| *III* | 0·03 | 5·53 | 97·1 | $C_{(1)}$, $C_{(3)}$, $C_{(4)}$, $C_{(5)}$ |
| *IV* | 0·07 | 5·69 | 75·0 | $C_{(5)}$, $C_{(9)}$ |
| *V* | 0·02 | 4·95 | 218·5 | $C_{(1)}$ |
| *VI* | 0·10 | 4·99 | 50·0 | $C_{(2)}$, $C_{(5)}$ |
| *VII* | 0·04 | 4·31 | 107·6 | $C_{(10)}$, $C_{(11)}$, $C_{(12)}$ |
| *VIII* | 0·07 | 4·89 | 69·9 | $C_{(3)}$, $C_{(4)}$, $C_{(5)}$, $C_{(9)}$ |
| *IX* | 0·02 | 5·63 | 244·3 | $C_{(1)}$, $C_{(3)}$, $C_{(4)}$, $C_{(5)}$, $C_{(9)}$ |

The isomers *III*–*IX*, which have conformationally mobile skeletons, show the abundance ratios $(M - H_2O)^+/M^{+\cdot}$ of one to two orders of magnitude higher than those observed with *I* and *II*. Of course, neither the abundance of the $(M - H_2O)^{+\cdot}$ ion nor the abundance ratio $(M - H_2O)^{+\cdot}/M^{+\cdot}$ reflect only the rates of formation of the $(M - H_2O)^{+\cdot}$ ions. Both these values depend also on the rates of all decompositions of the ions involved. Table II shows that the $(M - H_2O)^{+\cdot}/M^{+\cdot}$ values depend on the molecular geometry in a different way than the $(M - H_2O)^{+\cdot}$ abundances do. Clearly, the latter values cannot be used when comparing isomers with different skeletons because of a different tendency of the $(M - H_2O)^{+\cdot}$ ions to skeletal fragmentations. The $(M - H_2O)^{+\cdot}/M^{+\cdot}$ ratios give more regular values than the abundances of $(M - H_2O)^{+\cdot}$, and also the sensitivity of the former to the configurational variations is better when compared with the latter term. The $(M - H_2O)^{+\cdot}/M^{+\cdot}$ ratio also reflects the stability of $M^{+\cdot}$. Assuming that the energy transferred during ionisation does not depend on the molecular geometry in *I*–*IX*, the high abundance of $M^{+\cdot}$ in the spectra of *I* and *II* indicates that the overall rates of decomposition of these ions are substantially lower than those of *III*–*IX*. Fragmentation maps (Schemes 1 and 2) show that most of the abundant ions in the spectra of *I* and *II* originate from $M^{+\cdot}$, while with *III*–*IX* the abundant fragment ions are formed from the $(M - H_2O)^{+\cdot}$ ions. Hence it follows that the molecular ions of *III*–*IX* decompose predominantly *via* loss of water.

The $(M - H_2O)^{+\cdot}/M^{+\cdot}$ values of *III*–*IX* can be related to the nature of accessible hydrogens – and thus to the configurations at asymmetric centers – if the conformational mobility of the skeletons is taken into consideration. It can be inferred from Table II that the isomers *III*, *V*, *VII* and *IX* which have accessible δ-hydrogens lose water most easily. In these isomers the δ-hydrogens become accessible to the hydroxyl group during chair-to-boat flipping of the cyclohexane ring (Fig. 2 and 3) as has been described earlier for other cyclic systems[6,13]. The excess energy in the molecular ion is in part consumed by the conformational inversion of the skeleton.

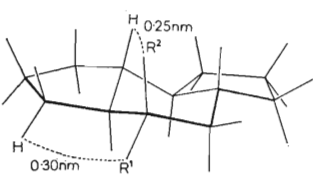
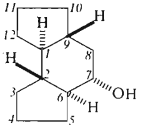
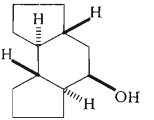


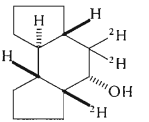

FIG. 1
Conformation of Alcohols *I* and *II*
*I*: $R^1 = OH$; $R^2 = H$
*II*: $R^1 = H$; $R^2 = OH$



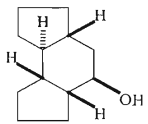
*I*,
*Ia*, 6-$^2H_1$



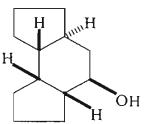
*II*



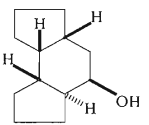
*III*



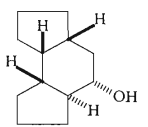
*IV*



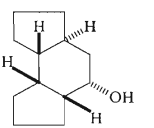
*V*



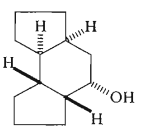
*VI*



*VII*



*VIII*



*IX*

The axial isomer *VIII* furnishes a striking example of the conformational effects. Although in *VIII* there are δ-hydrogens at $C_{(3)}$ and $C_{(4)}$ which could be made accessible to the hydroxyl group by twisting the flexible *cis-syn-trans* skeleton, the conformational excitation leads to a quite opposite intramolecular motion by which the hydroxyl group is removed from the formerly accessible hydrogens (Fig. 3). In such a way, the loss of water from the molecular ion of *VIII* is somewhat hampered and the competing loss of $CH_2{=}CH{-}OH$, leading to ions *m/e* 136, becomes more abundant. Similar competitive losses of water and vinyl alcohol have been observed earlier with 1,4-dihydroxy-$\Delta^{6,7}$-octalins[14].

As the conformational mobility or rigidity are intrinsic features of any cyclic system, the mass spectra of diastereoisomeric alcohols, differing in mobility of the skeletons, differ in their $(M - H_2O)^{+\cdot}/M^{+\cdot}$ ratios. These considerations can be applied to 1,4-dihydroxydecalins whose mass spectra have been reported by Grützmacher and Fechner[13]. It follows from the published spectra of diastereoisomers which have the same relative configurations of the hydroxyl groups but differ in the

annulation of rings that the flexible *cis*-annulated isomers exhibit the abundance ratios $(M - H_2O)^{+\cdot}/M^{+\cdot}$ three to four times higher than observed with the more rigid *trans*-annulated isomers. Although the cyclohexane rings of both *cis* and *trans*-annulated decalins can be inverted to a twisted boat conformation[13], in *cis*-isomers a mere conformational motion approaches the hydroxyl to accessible hydrogens, while an additional strain is neccessary to approach the reacting groups in the *trans*-annulated isomers. Similar results have been reported[14] for 1,4-dihydroxyoctalins, although in this case the mechanisms of water elimination have been shown to depend on configurations of the hydroxyl groups. A further evidence stems from the comparison of mass spectra of 3-hydroxycholestanes with those of 3-hydroxycoprostanes[15].

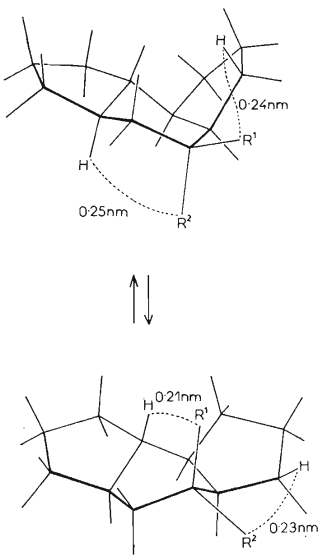



FIG. 2

Conformations of Alcohols *III* and *IV*
*III*: $R^1 = OH$; $R^2 = H$
*IV*: $R^1 = H$; $R^2 = OH$

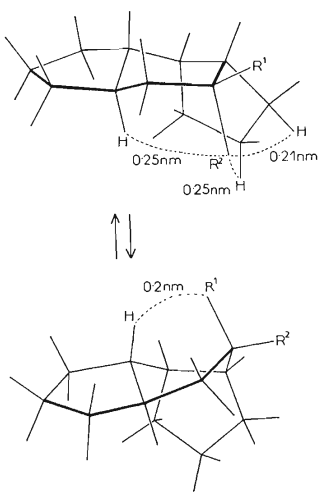



FIG. 3

Conformations of Alcohols *V* and *VIII*
*V*: $R^1 = OH$; $R^2 = H$
*VIII*: $R^1 = H$; $R^2 = OH$

Although the elimination of water from a cyclic alcohol seems to be governed mainly by both the nature and the number of accessible hydrogens, other factors cannot be *a priori* excluded. The *trans*-annulated decalins[16,17] and octalins[18] are known to be more stable than the corresponding *cis*-annulated isomers. The abundance of $M^{+\cdot}$ follows the stability of the ground state[19] in that the more stable *trans*-isomers give more abundant molecular ions[2]. A lower stability of $M^{+\cdot}$ could lead to its diminished abundance, increasing thus the $(M - H_2O)^{+\cdot}/M^{+\cdot}$ ratio for the less stable isomer. The stability of $M^{+\cdot}$ plays only a minor role in systems which contain the annulation of six- and five-membered rings. The *cis*-annulated bicyclo[4·3·0]-3--nonen-8-ol exhibits the $(M - H_2O)^{+\cdot}$ to $M^{+\cdot}$ ratio about twenty times higher than the *trans*-annulated isomer[20]. In this case, the *cis*- and *trans*-annulated skeletons are of comparable stability[21]. Another striking example of the effects of conformational mobility is provided by the spectra of *III*, *IV* and *IX* reported in the present paper: The isomer *IX* shows the highest $(M - H_2O)^{+\cdot}/M^{+\cdot}$ ratio of all alcohols under investigation, although its *cis-anti-cis* skeleton is known[22] to be more stable than the *cis-anti-trans* one of *III* and *IV*. This can be attributed unambigously to an enhanced conformational mobility of *IX*.

It follows from the preceding discussion that mass spectra could provide valuable information concerning both the geometric and conformational properties of cyclic skeletons. The electron-impact-induced loss of water is easy in conformationally mobile stereoisomers in which the approach of the hydroxyl to skeletal hydrogens is not accompanied by additional strain.

## EXPERIMENTAL

The mass spectra were recorded on a JEOL JMS D-100 spectrometer operating at 14—75 eV. The samples were introduced using direct inlet at 50—60°C, the source temperature was maintained at 140°C. Decompositions of metastable ions in the first field-free region were detected by using the accelerating voltage scan method. The mass spectral data are available from the authors (F. T., V. H.). $^1$H-NMR spectra ($\delta$, ppm) were measured on a Tesla B-576 (60 MHz) instrument in deuteriochloroform with tetramethylsilane as internal standard. The synthesis of *I*, *Ia*, *II*, *III* and *IV* has been described earlier[23]. The alcohols *V*, *VI*, *VII* and *VIII* were prepared by lithium aluminium hydride reduction of the corresponding tricyclo[7.3.0.0$^{2,6}$]-7-dodecanones[22]. The diastereoisomers were separated on a silica gel column (elution with hexane–ether, 2 : 1). Compound *V*: m.p. 58—59°C (pentane); $^1$H-NMR: 1·67 m (peak of OH at $\delta$ = 1·46 ppm), 17 H; 3·32 m ($W$ = 20 Hz), 1 H. *VI*: m.p. 57—58°C (pentane); $^1$H-NMR: 1·50 m, 17 H; 4·02 m ($W$ = 6·8 Hz), 1 H. *VII*: m.p. 52—53°C; $^1$H-NMR: 1·54 m (peak of OH at $\delta$ = 1·69 ppm), 17 H; 3·33 m ($W$ = 21 Hz), 1 H. *VIII* (oil); $^1$H-NMR: 1·66 m (peak of OH at $\delta$ = 1·30 ppm), 17 H; 3·93 m ($W$ = 8·8 Hz), 1 H. The isomer *IX* has been described earlier[22].

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