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The Role of Hydrogen Migration in the Mechanism of Alcohol Elimination from MH^+ Ions of Ethers upon Chemical Ionization

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An enhanced elimination of alcohol under isobutane CI conditions, resulting in highly abundant $[MH - ROH]^+$ ions, has been observed in several primary and secondary ethers having a tertiary β-position (methine), as compared with those with β-methylene. This elimination exhibits a significant degree of stereospecificity in stereoisomeric 2-methyl-1-methoxycyclohexanes 4 and 1-methoxy-*trans*-decalins 7, affording more abundant $[MH - ROH]^+$ ions in the *cis* isomers 4c and 7tc than in their *trans* counterparts 4t and 7tt. These findings suggest involvement of a 1,2-hydride migration from the β- to α-position in the course of the alcohol elimination from the MH^+ ions of the above *cis*-ethers, resulting in tertiary carbocation structures. The proposed mechanism of alcohol elimination is supported by a considerable deuterium isotope effect detected in β-deuterium-labeled *cis*-2-methyl-1-methoxycyclohexane and by a CID study of the structures of $[MH - ROH]^+$ ions obtained from *cis*- and *trans*-1,2-dialkoxycyclohexanes. Ring contraction by a Meerwein-type rearrangement has also been observed in the latter system. © **1997 by John Wiley & Sons, Ltd.**

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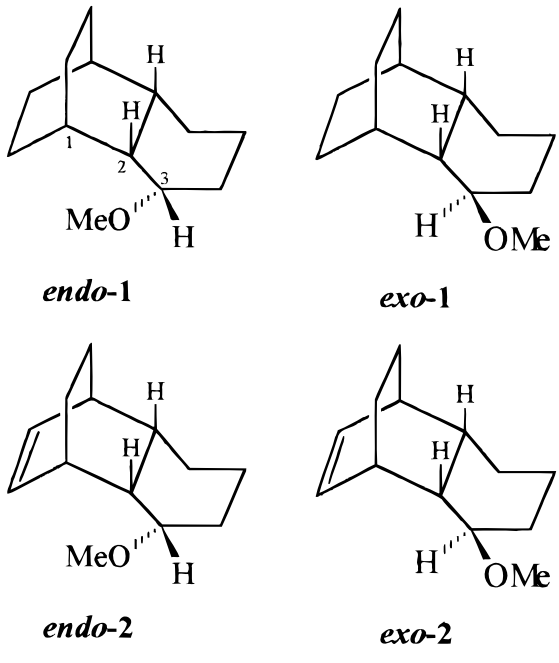
KEYWORDS: hydrogen transfer; stereospecific fragmentation upon chemical ionization (CI); CID; mechanism of alcohol elimination; ethers

INTRODUCTION

The isobutane CI mass spectra of ethers are known to exhibit abundant MH^+ ions, which undergo elimination of alcohol to afford relatively less abundant $[MH - ROH]^+$ ions.[1] For example, the MH^+ ion is the most abundant one (RA 100%) in the i-C_4H_{10} CI mass spectrum of methoxycyclohexane, while the relative abundance of the $[MH - MeOH]^+$ ion is only about 20%.[2] On the other hand, tertiary ethers give rise to very abundant $[MH - ROH]^+$ ions, while MH^+ ions are often absent in their CI mass spectra.[2] This behavior results from the relatively high energy required for the cleavage of the RHO^+—C bond in protonated primary and secondary ethers in contrast with their tertiary analogs.

In the course of our studies on the stereochemistry of organic gas phase ions we have been interested in the effect of configuration and conformation on proton affinities of ethers.[3] To our surprise we found that *endo*- and *exo*-3-methoxytricyclo[6.2.2.0^{2,7}]dodecanes ***endo*-1** and ***exo*-1** do not produce proton-bound dimers upon isobutane CI. The CI measurements also revealed that these ethers afford an extremely low abundance (<1%) of MH^+ ions under isobutane CI conditions. The same was also true for *exo*-3-methoxytricyclo[6.2.2.0^{2,7}]dodeca-9-ene ***exo*-2**: the relative abundance of the MH^+ ion was only 2%. The epimeric *endo*-3-methoxytricyclo[6.2.2.0^{2,7}]dodeca-9-ene ***endo*-2** gave rise to a much more abundant MH^+ ion (44%), presumably because of stabilization by proton bridging involving the double-bond π-electrons.[4,5]

The significant enhancement of the elimination observed in the CI mass spectra of the above secondary



***endo*-1** ***exo*-1** ***endo*-2** ***exo*-2**

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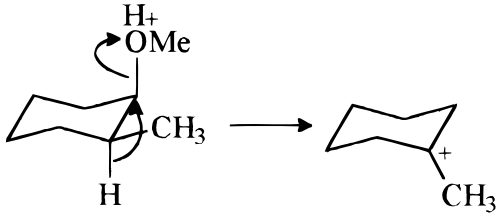
ethers **1** and **2** suggests the presence of an important effect of substitution in the neighborhood of the protonated alkoxy function on the activation energy of the alcohol elimination process. An attempt to understand this effect is the objective of this work.

RESULTS AND DISCUSSION

Primary and secondary carbocations are known to be unstable species. Consequently, it has been established that the elimination of H_2O and ROH from the MH^+ ions of primary and secondary alcohols and ethers affords rearranged tertiary product ions under CI conditions.[6,7] For example, the $C_6H_{11}^+$ ion obtained from cyclohexanol or other cyclohexyl derivatives has been shown to have the methylcyclopentyl carbocation structure.[6–10] This rearrangement preceding the dissociation of the RHO^+—C bond lowers the energy of the elimination process. The high efficiency of alcohol elimination from **1** and **2** as compared with that of methoxycyclohexane suggests possible migration of the hydride from position 2 to C-3 preceding the dissociation, resulting in a tertiary carbocation structure without skeletal rearrangement. In order to investigate this possible pathway, we turned to some simpler model ethers. The isobutane CI mass spectral measurements of these ethers are summarized in Table 1.

Cis-2-methyl-1-methoxycyclohexane **4c** undergoes elimination of methanol which is much more efficient than that of the *trans* isomer **4t**. The $[MH - MeOH]^+/MH^+$ ion abundance ratio of **4c** is five times greater than that observed for **4t**. This behavior supports the proposed mechanistic pathway involving hydride transfer in the course of the elimination in **4c**. The stereospecificity of the elimination is consistent with a concerted type of migration of the hydride from C-2 to C-1 and the C—O bond cleavage (see Scheme 1), which is possible only in the *cis* isomer **4c**. The above results do not necessarily lead to the conclusion that *all* the dissociating MH^+ ions undergo the concerted elimination. It is possible that a part of them undergo a non-stereospecific rearrangement to a tertiary substituted cyclopentyl structure in the course of the alcohol elimination.

In contrast with the behavior of 2-methyl-1-methoxycyclohexanes **4c** and **4t**, the stereoisomeric *cis*- and *trans*-3-methyl-1-methoxycyclohexanes **5c** and **5t** and the 4-methyl analogues **6c** and **6t** give rise to similar CI mass spectra. The non-stereospecific behavior of the stereoisomeric pairs **5c**, **5t** and **6c**, **6t** excludes the alternative explanation that the stereochemical effect observed in the **4c**, **4t** pair could be due to the axial isomer **4c** being less thermochemically stable than the diequatorial **4t**.



4c

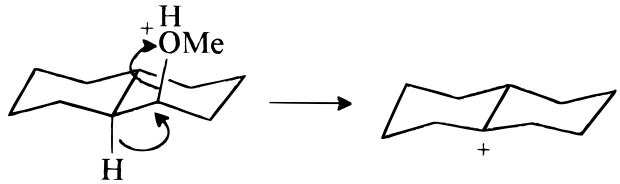
Scheme 1

The stereoisomeric 1-methoxy-*trans*-decalins **7tc** and **7tt** exhibit a similar behavior to that of 2-methyl-1-methoxycyclohexanes **4c** and **4t**. The *trans*, *cis* isomer **7tc** exhibits a greater extent of methanol elimination than the *trans*, *trans* counterpart **7tt**: the ion abundance ratios $[MH - MeOH]^+/MH^+$ are 14 and 2 respectively. This stereospecific behavior suggests here too involvement of hydride migration from C-10 to C-1 in the course of the C—O bond cleavage (see Scheme 2), which is possible only in the *cis* isomer **7tc**.

The two stereoisomeric *cis*-decalin derivatives **7cc** and **7ct** also undergo alcohol elimination to a different extent, as shown in Table 1. However, the difference is less pronounced than that observed in **7tc** and **7tt**: the ion abundance ratios $[MH - MeOH]^+/MH^+$ are 13 and 6 respectively. The lower degree of stereospecificity in these two *cis*-decalin ethers may be explained by the lower stability of the axial methoxy conformer of **7cc**, which is the one that may undergo the lower-energy concerted elimination of MeOH involving the 1,2-hydride migration.

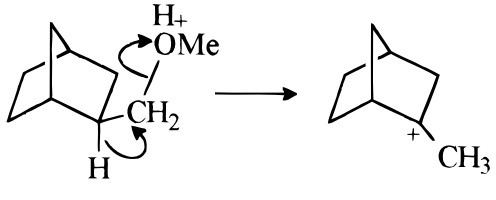
Primary ethers usually undergo very inefficient elimination of alcohol in their isobutane CI mass spectra. It is therefore noteworthy that *exo*- and *endo*-2-methoxymethylnorbornanes ***exo*-9** and ***endo*-9** afford highly abundant $[MH - MeOH]^+$ ions (100% relative abundance) and relatively low-abundance MH^+ ions (12% and 9% respectively). Here again hydride migration in the course of the elimination resulting in a tertiary $[MH - MeOH]^+$ carbocation, shown in Scheme 3 for ***exo*-9**, could explain the high efficiency of this fragmentation process.

Similar behavior has been observed in the isobutane CI mass spectrum of *exo*-5-methoxymethylnorbornene ***exo*-10**: a highly abundant $[MH - MeOH]^+$ ion (100% relative abundance) and a relatively low-abundance (21%) MH^+ ion. Hydride migration, similar to that shown in Scheme 3 for ***exo*-9**, explains here too the high abundance of the $[MH - MeOH]^+$ ion. On the other hand, the epimeric *endo* isomer ***endo*-10** exhibits a lower-abundance $[MH - MeOH]^+$ ion (74%) and the



7tc

Scheme 2



***exo*-9**

Scheme 3

Table 1. Relative abundances (%) of MH^+, $[M - H]^+$ and $[M - ROH]^+$ ions in isobutane CI mass spectra of alicyclic primary and secondary ethers

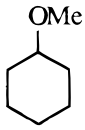
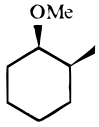
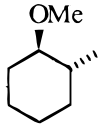
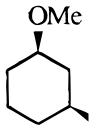
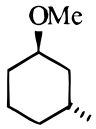
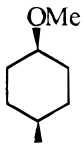
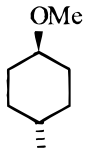
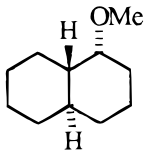
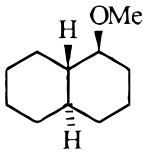
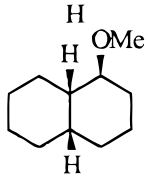
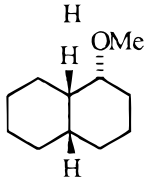
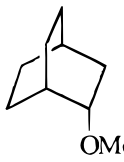
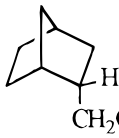
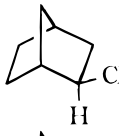
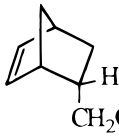
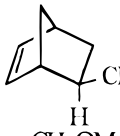
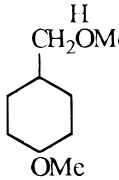
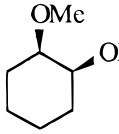
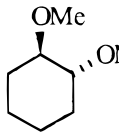
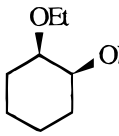
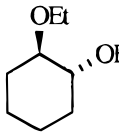
	$[MH]^+$	$[M-H]^+$	$[MH-ROH]^+$
***exo*-1**	<1	4	100
***endo*-1**	<1	12	100
***exo*-2**	2	4	100
***endo*-2**	44	4	100
 **(3)**	100	2	21
 **(4c)**	7	2	100
 **(4t)**	33	2	100
 **(5c)**	41	<1	100
 **(5t)**	49	1	100
 **(6c)**	51	2	100
 **(6t)**	59	2	100
 **(7tc)**	7	11	100
 **(7tt)**	49	9	100
 **(7ct)**[a]	17	9	100
 **(7cc)**[a]	8	9	100

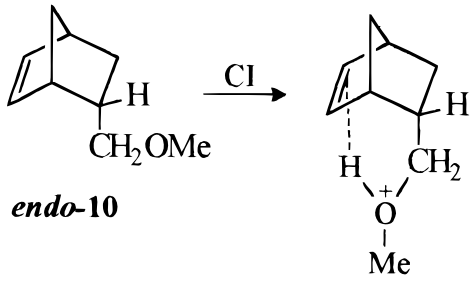
Table 1. Continued

	[MH]$^+$	[M − H]$^+$	[MH − ROH]$^+$
 **(8)**	35	4	100
 ***(endo*-9)**	9	3	100
 ***(exo*-9)**	12	2	100
 ***(endo*-10)**	100	<1	74
 ***(exo*-10)**	21	<1	100
 **(11)**	85	4	100
 **(12c)**	100	>1	93
 **(12t)**	72	2	100
 **(13c)**	100	1	27
 **(13t)**	100	2	53

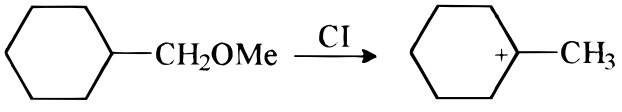
[a] Configurational assingment of the two *cis*-decalin ethers is based on the CI mass spectral evidence

MH^+ ion is the most abundant one (100% relative abundance) in the isobutane CI mass spectrum. This behavior of ***endo*-10** indicates stabilization of its MH^+ ion by proton bridging involving the double-bond π-electrons (Scheme 4).[4,5]

Methoxymethylcyclohexane **11**, which is another example of a primary ether with a disubstituted β-C atom, shows a most abundant $[MH - MeOH]^+$ in its CI mass spectrum, suggesting again a hydride transfer in the course of this elimination (Scheme 5). It is noteworthy that the MH^+ ion of **11** is significantly more abundant than those of ***endo*-9**, ***exo*-9** and ***exo*-10** (85% *vs.* 9%, 12% and 21% respectively). This difference in the ion abundances of the MH^+ ions may suggest possible skeletal rearrangements in addition to the hydride migration process in the bicyclic systems **9** and **10**,



Scheme 4



Scheme 5

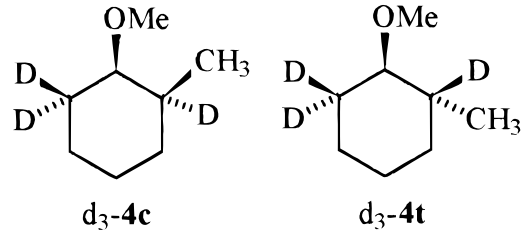
which would result in enhanced dissociation in the two latter systems.

Isotope effect

Attempts have been made to find support for the concerted mechanism of alcohol elimination beyond the stereospecificity evidence presented above. A deuterium isotope effect is expected in ethers, where the presumably migrating hydrogen atom is replaced by deuterium if C2—H bond cleavage occurs in the transition state, as shown in Scheme 1. *Cis*- and *trans*-2-methyl-2,5,5-d_3-methoxycyclohexanes d_3-**4c** and d_3-**4t** were prepared for this examination. The ion abundance ratio $[MH - MeOH]^+/MH^+$ is indeed lower for d_3-**4c** than that observed for **4c**, indicating an isotope effect $k_H/k_D = 1.3 \pm 0.1$ (average of three independent measurements) if it is assumed that *all* the MH^+ ions eliminate MeOH via the hydride transfer-assisted pathway. If only a part of the MH^+ ions dissociate via this route, the isotope effect of the concerted elimination involving 1,2-hydride migration will be considerably higher. On the other hand, the ion abundance ratio $[MH - MeOH]^+/MH^+$ measured for d_3-**4t** is similar to that observed in the CI mass spectrum of **4t** (the ratio of **4t** to d_3-**4t** is 1.1 ± 0.1), in agreement with the proposed non-occurrence of the concerted hydride transfer in the course of methanol elimination in this particular stereoisomer. The above value of the measured k_H/k_D ratio of **4c** (1.3) is similar to that reported for the McLafferty rearrangement and related processes (k_H/k_D = 1.09–1.15,[11] 1.3–1.9,[12] 1.4[13]), but lower than that observed for the intermolecular hydride transfer from 1,1-dimethylcyclohexane to the *t*-butyl cation under radiolytic conditions at close to atmospheric pressure ($k_H/k_D = 1.89$).[14] These results are in agreement with the mechanistic pathway involving hydride transfer from position 2 to 1 (at least in a part of the dissociating MH^+ ions), proposed in Scheme 1 for the CI-induced elimination of methanol from *cis*-2-methyl-methoxycyclohexanol **4c**.

Structural evidence

Structural assignment of the $[MH - MeOH]^+$ ions obtained from stereoisomeric 2-methyl-1-methoxy-

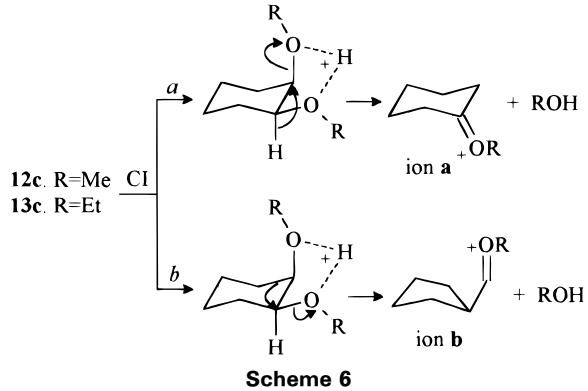


cyclohexanes **4c** and **4t** by comparative studies of their low-energy CID spectra is not easy, because these spectra do not exhibit considerably different features and both are quite similar to that of 1-methylcyclohexyl cation. *Cis*- and *trans*-1,2-dimethoxy- and diethoxycyclohexanes **12c**, **12t**, **13c** and **13t** were prepared with the hope for possible differentiation of their low-energy CID spectra and their comparison with suitable models.

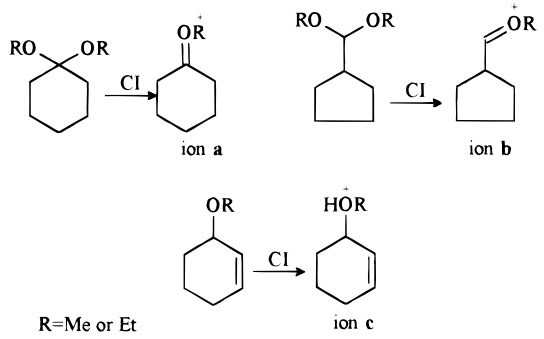
The results of the isobutane CI measurements of **12c**, **12t**, **13c** and **13t** are listed in Table 1. The MH^+ ions, particularly those of the *cis* isomers, are highly abundant in the CI mass spectra, in keeping with the expected stabilization by internal proton bridging between the two alkoxyls, which is possible in both stereoisomers. In analogy to the reported behavior of 1,2-cyclohexanediols,[15,16] two pathways may be expected for the elimination of ROH from the MH^+ ions of **12c** and **13c**: (i) involving a 1,2-hydride transfer, analogous to those proposed above in Schemes 1, 2, 3 and 5, followed by loss of the axial alkoxyl, leading to *O*-alkylcyclohexanone ions **a** (see route *a* in Scheme 6); (ii) involving Meerwein-type rearrangement resulting in ring contraction and loss of the equatorial alkoxyl, leading to *O*-alkylcyclopentanecarbaldehyde ions **b** (see route *b* in Scheme 6).

The model ions **a** and **b** (R ≡ Me and Et) were prepared by CI-induced dissociation of 1,1-dimethoxy- and diethoxycyclohexanes and of dimethoxy- and diethoxymethylcyclopentanes (Scheme 7) respectively. Protonated 3-methoxy- and 3-ethoxycyclohexenes (ions **c**, R ≡ Me and Et) were also used in the comparative study.

The CID spectra of the three model ions **a**, **b** and **c** are shown in Figs 1 (R ≡ Me, *m/z* 113) and 2 (R ≡ Et, *m/z* 127). The *m/z* 113 ions **a** and **b** exhibit two fragments at *m/z* 81 and 45 ($[P - MeOH]^+$ and $MeOCH_2^+$) differing in their relative abundances. The CID spectrum of ion **c** shows only the *m/z* 81 $[P - MeOH]^+$ ion as the major fragment; the *m/z* 45 ion is of negligible abundance and an additional *m/z* 41 ion is of minor importance.



Scheme 6



Scheme 7

Much more distinct features were found in the CID spectra of the *m/z* 127 ions **a** and **b** (R ≡ Et): (i) the $[P - C_2H_4]^+/[P - EtOH]^+$ ion abundance ratio is much greater for ion **a** than for **b**; (ii) the *m/z* 59

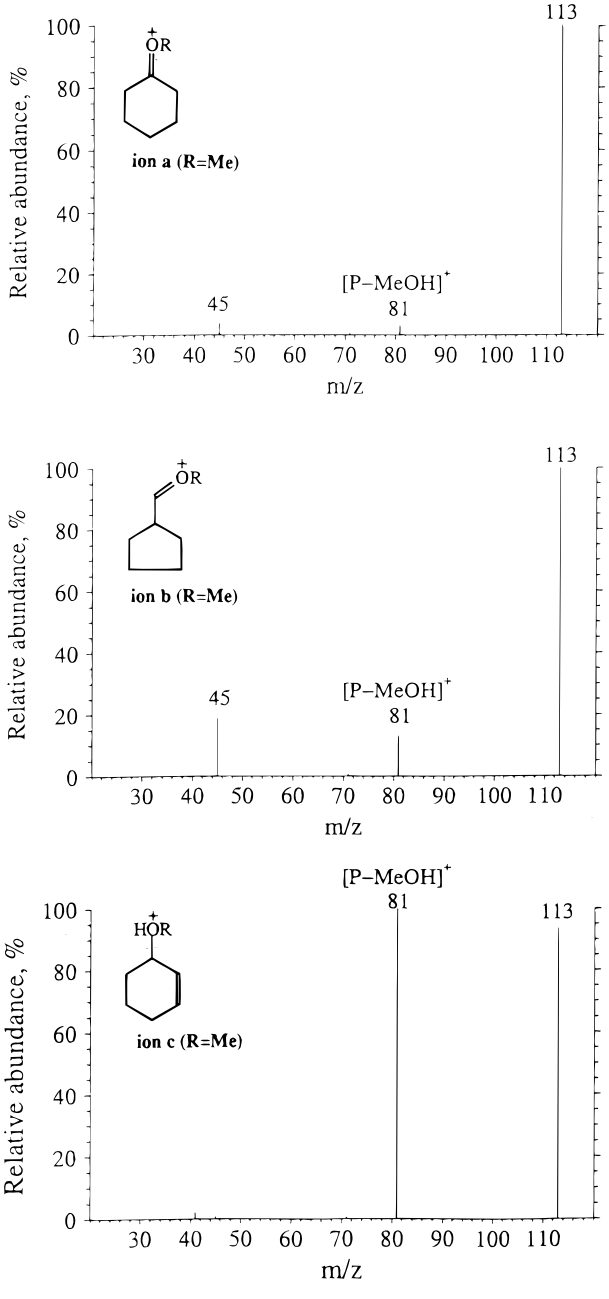


Figure 1. CID spectra (50 eV collision energy) of *m/z* 113 ions **a**, **b** and **c** (R ≡ Me).

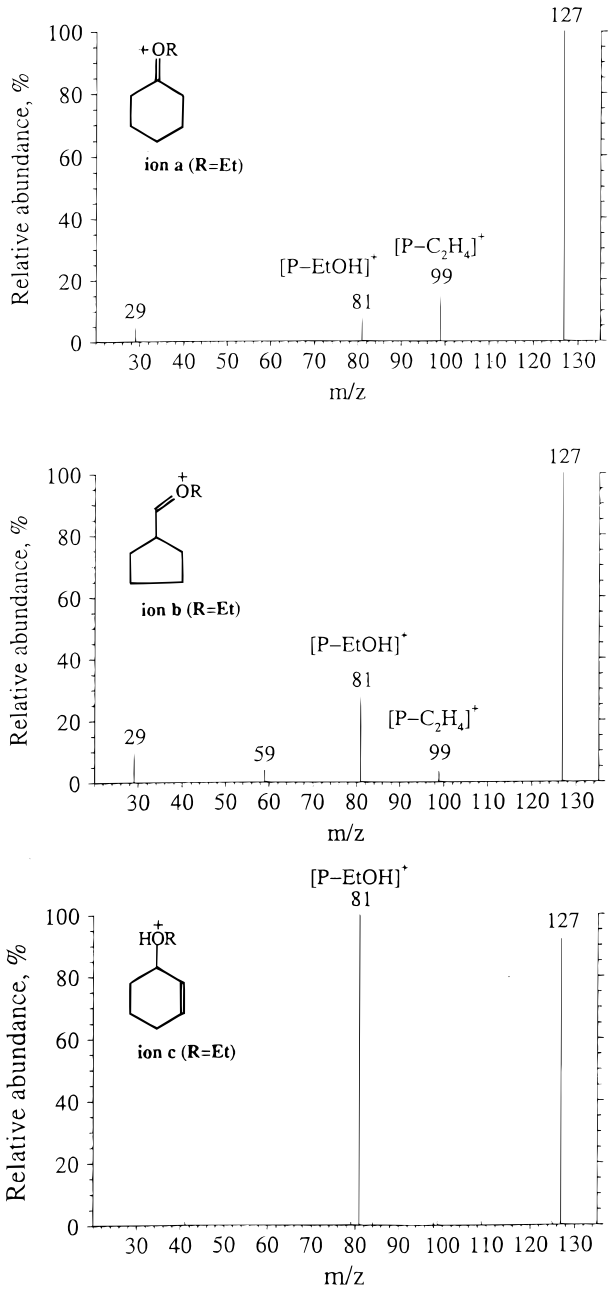


Figure 2. CID spectra (50 eV collision energy) of *m/z* 127 ions **a**, **b** and **c** (R ≡ Et).

$EtOCH_2^+$ ion is observed only in the CID spectrum of ion **b**. Ion **c** (R ≡ Et) affords the *m/z* 81 $[P - EtOH]^+$ ion as a practically single product of dissociation. These results suggest higher reliability for a comparative study using the ethoxy derivatives.

The CID spectra of the *m/z* 113 and 127 $[MH - ROH]^+$ ions obtained from **12c** and **13c** are shown in Fig. 3 and the results of the computer-aided analyses[17] are outlined in Scheme 8. These analyses indicate comparable formation of ions **a** and **b** from the MH^+ ions of the *cis*-dialkoxycyclohexanes and a minor contribution of ion **c**. This result is in full agreement with the predicted mechanistic pathway for the alcohol elimination from **12c** and **13c** upon CI, proposed above in Scheme 6. Two competing processes give rise to the

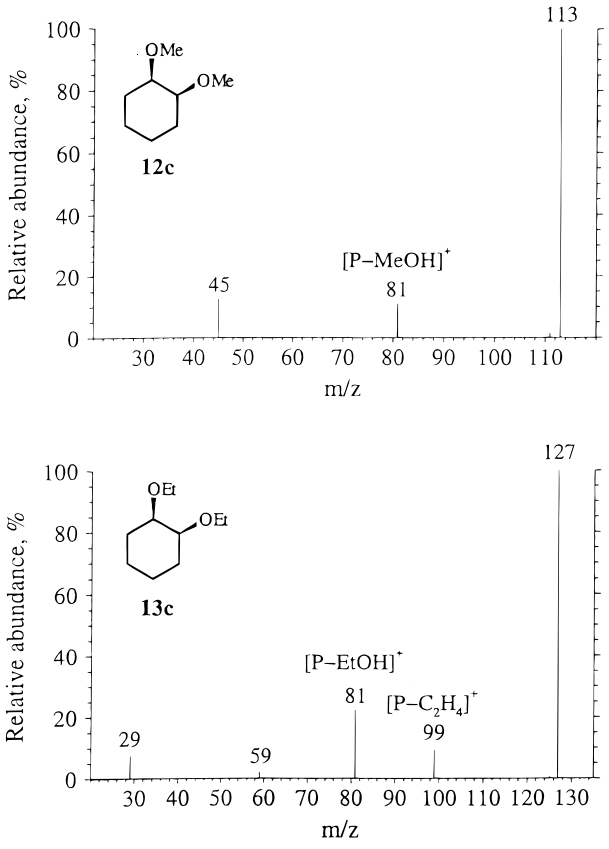


Figure 3. CID spectra (50 eV collision energy) of $[MH - ROH]^+$ ions of **12c** (R ≡ Me, *m/z* 113) and **13c** (R ≡ Et, *m/z* 127).

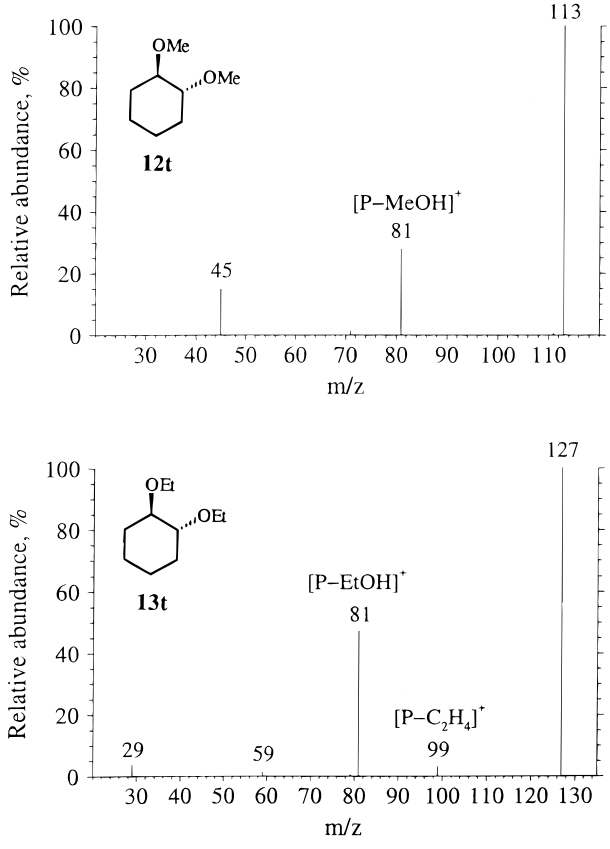
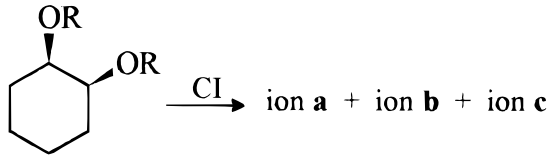


Figure 4. CID spectra (50 eV collision energy) of $[MH - ROH]^+$ ions of **12t** (R ≡ Me, *m/z* 113) and **13t** (R ≡ Et, *m/z* 127).

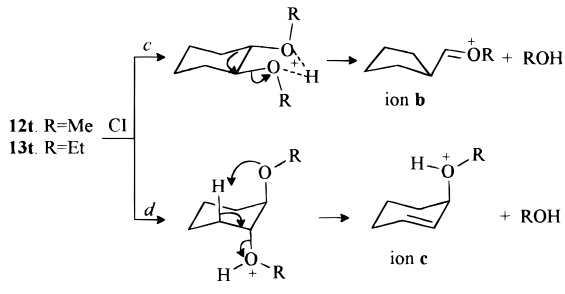
two major product ions: (i) involving a 1,2-hydride transfer and loss of the axial alkoxyl, leading to ions **a** (route *a* in Scheme 6); (ii) involving ring contraction and loss of the equatorial alkoxyl, affording ions **b** (route *b* in Scheme 6).

The configuration of *trans*-dialkoxycyclohexanes **12t** and **13t** suggests the ring contraction mechanism, leading to ions **b** (route *c* in Scheme 9), as the lowest-energy pathway of alcohol elimination from their MH^+ ions under CI conditions. The concerted elimination



12c. R=Me	40 %	58%	2%
13c. R=Et	47.5%	47.5%	5%

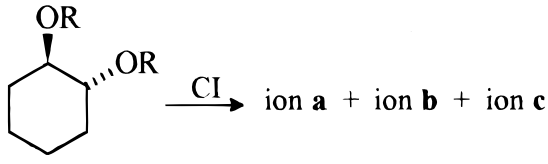
Scheme 8



Scheme 9

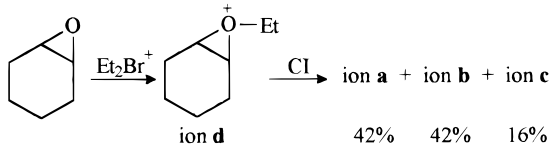
channel involving the 1,2-hydride migration, which would afford ions **a**, is not available in the *trans* isomers.

The analysis of the results of the CID measurements of the $[MH - ROH]^+$ ions obtained upon isobutane CI from **12t** and **13t** (Fig. 4 and Scheme 10) supports the above conclusion. The *O*-methyl- and *O*-ethylcyclopentanecarbaldehyde ions **b** are indeed the major products of alcohol elimination from the MH^+ ions of **12t** and **13t**, while ions **a** are of least importance. The latter may be formed by a higher-energy stepwise process. The results of the CID study suggest considerable contribution of an additional route *d*, leading to the formation of ions **c** (protonated 3-alkoxycyclohexenes) from the *trans*-diethers. Formation of protonated 3-alkoxycyclohexenes has been previously proposed as the major pathway of alcohol elimination from the MH^+ ions of *cis*-1,4-dialkoxycyclohexanes, in



12t. R=Me	6%	77%	17%
13t. R=Et	22%	47%	31%

Scheme 10



Scheme 11

contrast with the *trans* isomers which undergo an anchimerically assisted elimination affording *O*-alkyl-7-oxa[2.2.1]bicycloheptane cations.[18]

CONCLUSION

The results of this study indicate the important role of 1,2-hydride shifts in the mechanism of alcohol elimination from the MH^+ ions of primary and secondary ethers having a tertiary β-position under isobutane CI. The mechanistic conclusions are based on (i) the enhanced elimination observed in such ethers as compared with analogs having a secondary β-position (β-methylene instead of methine), (ii) the stereospecificity of such eliminations (preferential elimination when the migrating β-H and the alkoxyl are antiperiplanar), (iii) isotope effect evidence and (iv) a comparative structural CID study of the $[MH - ROH]^+$ ions obtained from *cis*- and *trans*-1,2-dimethoxy- and diethoxycyclohexanes **12** and **13**.

The last investigation was possible owing to the distinctive features of the low-energy CID spectra of *O*-alkylcyclohexanone ions **a**, *O*-alkylcyclopentanecarbaldehyde ions **b** and protonated 3-alkoxycyclohexenes ions **c**. These distinctive features may be applied to other structural and mechanistic problems in gas phase ion chemistry. An example of such an application is the behavior of the *m/z* 127 product of *O*-ethylation of cyclohexene oxide in the gas phase (ion **d**). The CID spectrum of this ion suggests isomerization to the above three ions **a**, **b** and **c** (see Scheme 11), which indicates that the behavior of the ethyl-substituted epoxide is different from that of the protonated analogue.[19]

EXPERIMENTAL

Mass spectrometry

The CI–GC–MS analyses and CID measurements were carried out on a Finnigan TSQ-70B triple-stage quadrupole mass spectrometer. The stereoisomeric pairs were introduced as mixtures, and separations were performed on a DB-5 (0.25 μm film thickness) capillary column (30 m × 0.25 mm i.d.). The *cis*/*trans* pairs of **4**, **5** and **6** were measured under isothermal conditions. For the measurements of all other stereoisomers the temperature was programmed from 60 to 200 °C at 5–10 °C min^{-1}. The scan rate was 1 scan s^{-1}.

CI measurements were performed at 150 °C ion source temperature and 0.4 Torr (indicated) reagent gas pressure. Isobutane was used as protonation reagent. CID measurements were performed with argon as target gas (0.3 mTorr indicated) at 50 eV collision energy (indicated).

Materials

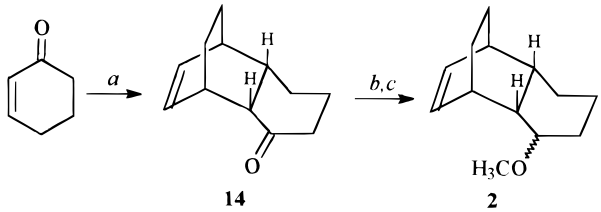
Stereoisomeric ethers ***endo*-2** and ***exo*-2** were prepared by the route outlined in Scheme 12.

Tricyclo[6.2.2.0^{2,7}]dodeca-9-en-3-one, 14. The Diels–Alder reaction (route *a*) of 1,3-cyclohexadiene (1.5 g, 0.015 mol) with 2-cyclohexene-1-one (1 g, 0.01 mol) was carried out in 100 ml of dry CH_2Cl_2 in the presence of $AlCl_3$ (0.26 g). The reaction mixture was stirred at room temperature for 24 h and poured into ice water. The aqueous layer was extracted with CH_2Cl_2 and the organic phase was washed with saturated $NaHCO_3$ solution. Solvent evaporation followed by chromatographic purification on a silica gel column [hexane–ethyl acetate (15:1)] yielded 65% of **14**.

3-Methoxytricyclo[6.2.2.0^{2,7}]dodeca-9-en-ene, mixture of *endo*-2 and *exo*-2. 3-Hydroxytricyclo[6.2.2.0^{2,7}]dodeca-9-ene (mixture of *endo* and *exo* isomers) was prepared from **14** by route *b*. **14** (0.5 g, 2.84 mmol) dissolved in dry diethyl ether (3 ml) was added dropwise to a refluxed suspension of $LiAlH_4$ (0.21 g, 5.53 mmol) in ether. The mixture was refluxed for 1 h and carefully quenched with EtOAc. The resulting suspension was filtered through Celite. Evaporation of the solvent yielded 95% of the product.

The mixture of *endo*-**2** and *exo*-**2** was prepared by route *c*. 3-Hydroxytricyclo[6.2.2.0^{2,7}]dodeca-9-ene (0.2 g, 1.13 mmol, in 3 ml of dry THF) was added to stirred NaH (55 mg, 2.83 mmol, 50% in oil, washed with hexane) in THF (7 ml). The reaction mixture was maintained at 40 °C for 0.5 hr, then MeI (0.73 g, 5.15 mmol) was added, followed by further heating for 5 h. The cooled reaction mixture was hydrolyzed by dropwise addition of water. Extraction with ether and evaporation followed by chromatographic purification on a silica gel column [hexane–ethyl acetate (30:1)] yielded 85% of the product (70% ***endo*-2**, 30% ***exo*-2**). The configuration assignment of the isomers was based upon CIMS analysis. The *endo* isomer exhibits a greater abundance of MH^+ ion (44%) than the *exo* counterpart (2%), which is consistent with the expected stabilization of its MH^+ ions by proton bridging with the double-bond π-electrons.[4,5] The GC elution sequence was ***endo*-2**, ***exo*-2**.

3-Methoxytricyclo[6.2.2.0^{2,7}]dodecane, mixture of *endo*-1 and *exo*-1. The mixture of ***endo*-1** and ***exo*-1** (70:30 concentration ratio) was obtained from **2** by catalytic hydrogenation with 5% Pd/C in ethyl acetate. The isomer



14 **2**

(*a*) 1,3-Cyclohexadiene, $AlCl_3$; (*b*) $LiAlH_4$; (*c*) NaH, MeI

Scheme 12

configuration was established by GCMS. The elution sequence was *exo*-**1**, *endo*-**1**.

2-Methoxymethylnorbornane, mixture of *endo*-9 and *exo*-9. The mixture of ***endo*-9** and ***exo*-9** was obtained from **10** by catalytic hydrogenation with 5% Pd/C in ethyl acetate.

Ethers **3**, **4**, **5**, **6**, **10** and **11** were synthesized from commercially available (Aldrich) starting alcohols by route *c*. Diethers **12t**, **13t**, **12c** and **13c** were prepared from *trans*- and *cis*-1,2-cyclohexanediol[20,21] in the same manner (route *c*). Ethers **7** and **8** were obtained by reduction of 1-decalone (Aldrich) and bicyclo[2.2.2] octan-2-one[22] respectively with $NaBH_4$ in ethanol to the corresponding alcohols, followed by etherification via route *c*.

Acknowledgements

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REFERENCES

1. A. G. Harrison, *Chemical Ionization Mass Spectrometry*, 2nd edn, p. 77 and references cited therein. CRC Press, Boca Raton, FL (1992).
2. C. Denekamp and A. Mandelbaum, *J. Mass Spectrom.* **30**, 1421 (1995).
3. C. Denekamp, A. Etinger, R. H. Fokken, N. Khaselev, A. Mandelbaum and N. M. M. Nibbering, *J. Mass Spectrom.* **30**, 1174 (1995).
4. (a) J. Jalonen and J. J. Taskinen, *J. Chem. Soc., Perkin Trans.* 2 1833 (1988); (b) B. Manson, Feng Ta-Min, H. D. Ward and R. K. Marray, *Org. Mass. Spectrom.* **22**, 606 (1987).
5. N. Morlender-Vais and A. Mandelbaum, *Int. J. Mass Spectrom. Ion Process*. in press (1997).
6. S. G. Lias, D. M. Shold and P. Ausloos, *J. Am. Chem. Soc.* **102**, 2540 (1980).
7. H. Vancik and E. Sunko, *J. Am. Chem. Soc.* **111**, 3742 (1989).
8. P. M. Viruela-Martin, I. Nebot, R. Viruela-Martin and J. Phanelles, *J. Chem. Soc., Perkin Trans.* 2 49 (1986).
9. M. Attina, F. Cacace and A. Marzio, *J. Am. Chem. Soc.* **111**, 6004 (1989) and references cited therein.
10. P. Cecchi, R. Cipollini, A. Pizzabiocca, G. Renzi and M. Speranza, *Tetrahedron* **44**, 4847 (1988).
11. H. Budzikiewicz, C. Djerassi and D. H. Williams, *Mass Spectrometry of Organic Compounds*, p. 156 and references cited therein. Holden-Day, San Francisco, CA (1967).
12. (a) F. M. Benoit and A. G. Harrison, *Org. Mass. Spectrom.* **11**, 599 (1976); (b) F. M. Benoit and A. G. Harrison, *Org. Mass. Spectrom.* **13**, 128 (1978).
13. M. M. Green, G. J. Mayotte, L. Meites and D. Forsyth, *J. Am. Chem. Soc.* **102**, 1464 (1980).
14. M. E. Crestoni, S. Fornarini, M. Lentini and M. Speranza, *J. Phys. Chem.* **100**, 8285 (1996).
15. R. Wolfschütz, H. Schwarz, W. Blum and W. J. Richter, *Org. Mass. Spectrom.* **13**, 697 (1978).
16. R. Wolfschütz, H. Schwarz, W. Blum and W. J. Richter, *Org. Mass. Spectrom.* **14**, 462 (1979).
17. M. Edelson-Averbukh and A. Mandelbaum, *J. Mass Spectrom.* **32**, 515 (1997).
18. R. Shvily, T. Müller, Y. Apeloig and A. Mandelbaum, *J. Chem. Soc., Perkin Trans.* **2**, 1221 (1997) and references cited therein.
19. H. I. Kenttamaa, R. R. Pachuta, A. P. Rothwell and R. G. Cooks, *J. Am. Chem. Soc.* **111**, 1654 (1989).
20. L. Mangoni, M. Adinolfi, G. Bargone and M. Parrilli, *Tetrahedron Lett.* **45**, 4485 (1973).
21. A. Roebuck and H. Adkins, *Org. Synth., Coll.* **III**, 217 (1955).
22. O. Diels and K. Alder, *Ann. Chem.* **478**, 137 (1930).

