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# Conformational Dependence of Mass Spectral Fragmentation of Pinane Derivatives

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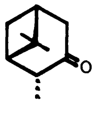
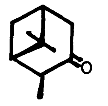
The major fragmentation pathway for pinane derivatives on electron impact involves cleavage of the cyclobutane bond which is part of a boat-cyclohexane. This trend is followed by ketones, alcohols, and hydrocarbons of the same skeleton.

Stereochemical correlation of mass spectrometric fragmentations has been investigated by many chemists.[1] While the majority of the reported data is concerned with the differences arising from configuration variation of functional groups, the effects of molecular conformations on the fragmentation pathways remain a subject of great interest but insufficient inquiry. The reason for this apparent lack of activity in the area is two fold: general consensus indicates that highly energetic species are generated in the mass spectrometer and the decomposition of these species must be accompanied by the destruction of conformational integrity of the original molecules; more importantly, adequate conformational isomers are difficult to identify.

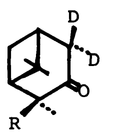
We are convinced that the electron impact-induced fragmentation of a molecule must be biased by conformational factors. For studying this possibility we chose the diastereoisomeric 3-pinanones, i.e., pinocamphone (*trans*-3-pinanone (**1**)) and isopinocamphone (*cis*-3-pinanone (**2**)). They are a pair of stable compounds which can be regarded as closest to being conformationally isomeric.[2] Thus, if we ignore the methylene bridge of the bicyclic structure, pinocamphone is reduced to 2,4,4-trimethylcyclohexanone in a flattened chair form, whereas isopinocamphone, that a flattened boat.



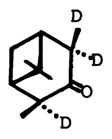
(**1**)



(**2**)



(**1**-$d_3$) R=D
(**1**-$d_2$) R=H



(**2**-$d_3$)

Since both ketones contain an equatorial α-methyl group, there is only a conformational difference between the two with respect to the cyclohexanone moiety. As ionization in the mass spectrometer of such ketones is commonly localized at the carbonyl group, factors affecting their fragmentation pathways other than the conformations must be the same. The pairwise comparison of the principal peaks in their mass spectra should then provide clues to the conformational influence on the fragmentation of the 3-pinanones.

In the electron impact mass spectra of the 3-pinanones the relative intensities of ions $m/z$ 83 and 55 are reversed (see Figs. 1 and 2). The $m/z$ 83 ion is stronger and $m/z$ 55 ion is weaker in the spectrum of **1**, and the opposite is true for that of **2**. These results are clear-cut and reproducible under GC-MS conditions. With the help of high resolution mass analysis and by examination of the corresponding deuterated ketones, Schemes 1 and 2 can be postulated to account for the differences.

The rationale is supported by spectral analysis of pinocamphone-2,4,4-$d_3$ (**1**-$d_3$), pinocamphone-4,4-$d_2$ (**1**-$d_2$), and isopinocamphone-2,4,4-$d_3$ (**2**-$d_3$). The following mass shifts were observed: with the trideuterated ketones— $m/z$ 83→84, 69→71, 55→56, and 41→43. Furthermore, the negligible 55→56 shift in the spectrum of **1**-$d_2$ and the much lower intensity of $m/z$ 84 in the same spectrum confirm the assignment of the ion structure.

While these ions are actually doublets, invariably the hydrocarbon species are in much higher abundance, therefore there is no possibility of misinterpreting the trends. The ratios of the hydrocarbon ions to acylium ions for **1** are 10.63 for $m/z$ 83, 8.28 for $m/z$ 69, 64.91 for $m/z$ 55, and those for **2** are 4.74 ($m/z$ 83), 10.85 ($m/z$ 69), 29.33 ($m/z$ 55) as determined by high resolution scans.

It appears then the α-cleavage at the C(2)–C(3) bond of the ketones is rapidly followed by a rupture of the four-membered ring, with the latter fragmentation displaying a remarkable degree of selectivity. It may be concluded that the cyclobutane bond which also constitutes a part of the boat-shaped cyclohexanone, and the one subtended by it, break preferentially. This process, but not the alternative mode of cleavage,

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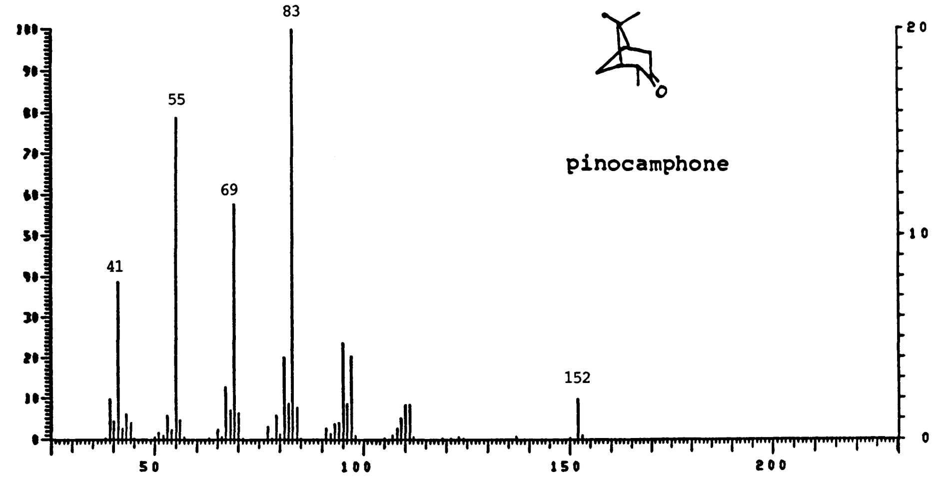


Fig. 1.

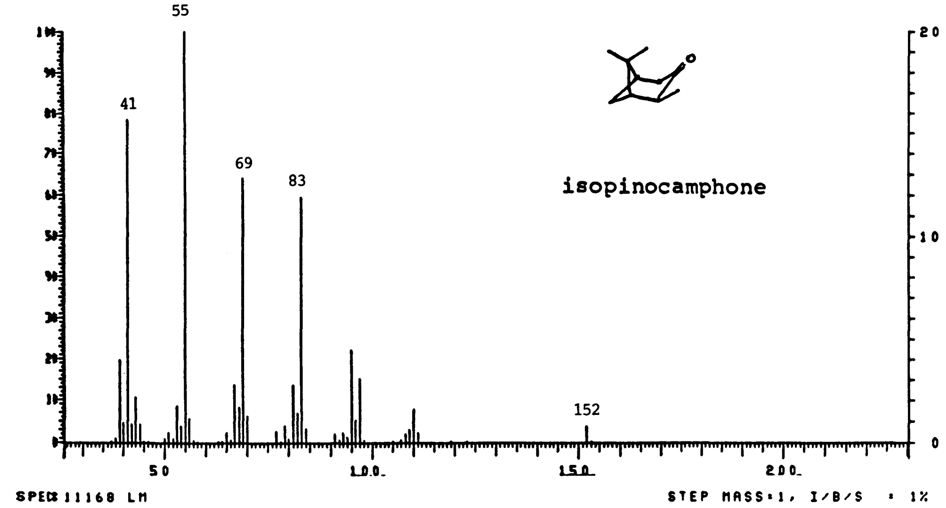
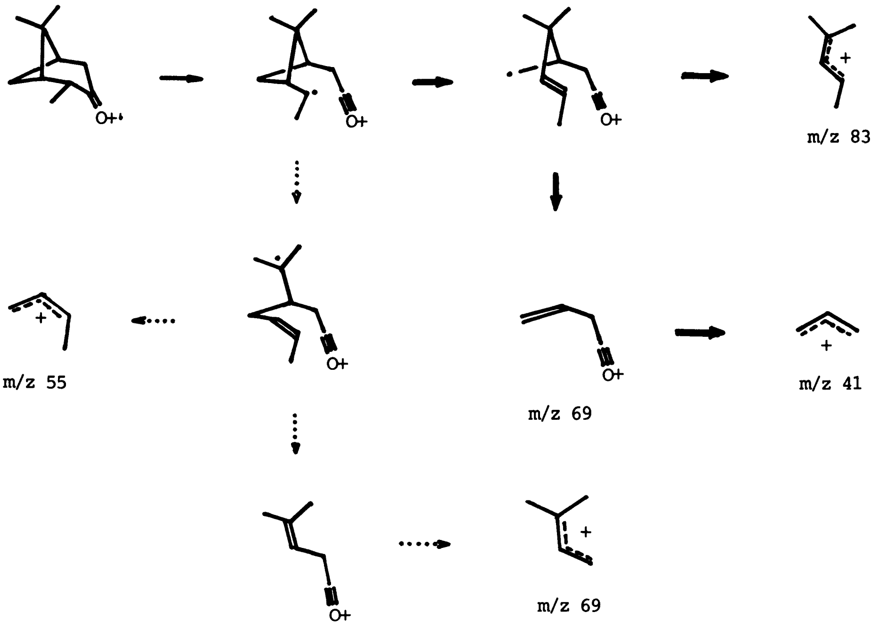
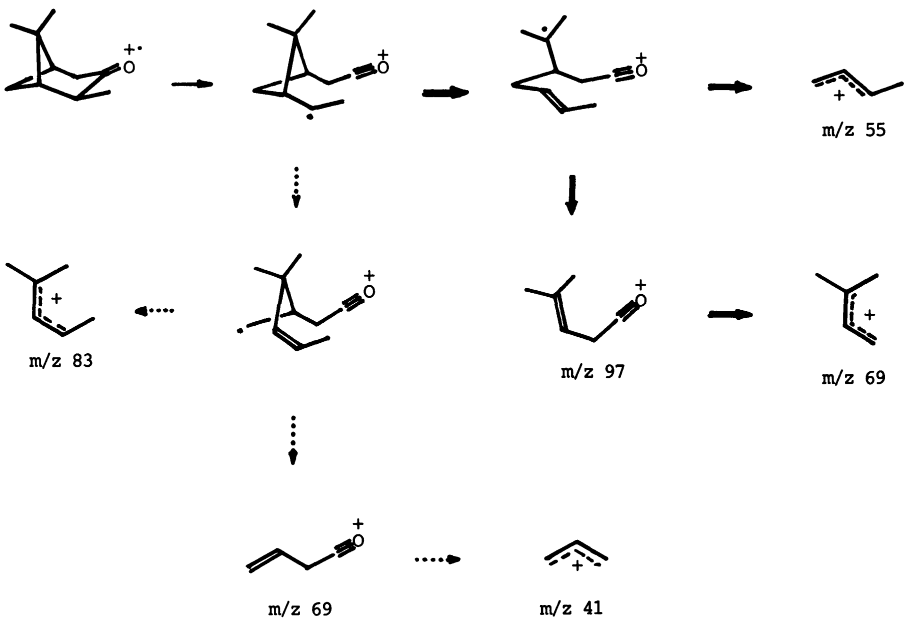


Fig. 2.



Scheme 1.



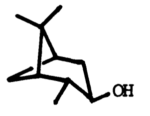
Scheme 2.

relieves a larger portion of the inherent strain of the molecule.

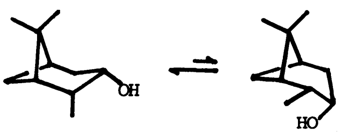
While the strain relief must play a contributory role in the selective fragmentation, the more important factor may be related to the Principle of Least Motion. Newman projections along the C(2)-C(1) bond of the ketones clearly show a smaller dihedral angle subtended by C(3) and C(7) than that subtended by C(3) and C(6) in pinocamphone (**1**) and a larger dihedral angle in isopinocamphone (**2**). Cyclobutane cleavage of the 2,3-seco radical ion is favored at the bond nearly parallel to the original C(2)-C(3) bond for easier development of a double bond involving the empty orbital C(2)$^+$ or radical C(2)$^{\cdot}$. This preference for bond cleavage finds analogy in the E2 elimination which is least favored when the departing groups are close to being orthogonal and becomes progressively more favorable as the dihedral angle narrowed or widened, maximizing at 0° or 180°.

Perhaps it should be emphasized that the fragmentation of the 2,3-seco radical ions is instantaneous such that their intermediacy is unnecessary. In other words, acyclic species could have been generated more or less directly. This transiency explains the maintenance of the original conformations and their influence on the fragmentation pathways.

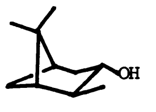
It may be interesting to speculate also that molecular conformations have subtle effects on the initial cleavage sites. Undoubtedly the more highly substituted C(2)-C(3) bond is the preferred locale of fragmentation, but this mode is not to the exclusion of the C(3)-C(4) bond fission, as evinced by the appearance of $C_5H_7O^+$ and $C_3H_3O^+$ ions. An increased percentage of the C(3)-C(4) bond cleavage in **2** relative to that in **1** is apparent from examination of the $C_nH_{2n-1}^+/C_nH_mO^+$ ratio of the twin peaks at *m/z* 83 and 55.



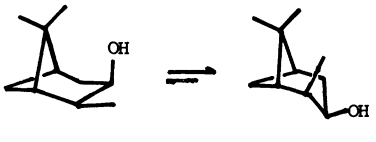
pinocampheol (3)



neopinocampheol (4)



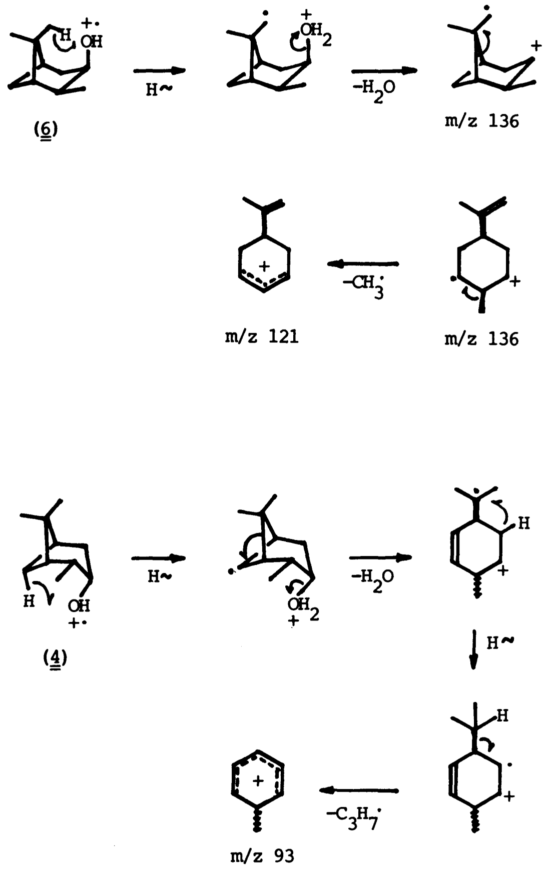
isopinocampheol (5)



neoisopinocampheol (6)

The four stereoisomeric 3-pinanols[3] also exhibit discernible intensity variations in a number of fragments. The members of the neo alcohols, each being capable of assuming a conformation in which the hydroxyl group is axially oriented and juxtaposed to a remote hydrogen atom, give rise to more abundant (M$-H_2O$) and (M$-H_2O-CH_3$) peaks— *m/z* 136: neopinocampheol (**4**) 6%, neoisopinocampheol (**6**) 5%, pinocampheol (**3**) 3%, isopinocampheol (**5**) 2%; *m/z* 121: **4** 9%, **6** 14%, **3** 0.5%, **5** 1%. On the other hand, the normal/iso compounds, having equatorial hydroxyl groups, display considerably stronger ions at *m/z* 43: **3** 85%, **5** 82%, **4** 40%, **6** 46%. Based on the conformations of the four alcohols (Fig. 3) the more facile dehydration and the tandem demethylation of the neo alcohols becomes clear (Scheme 3).

The *m/z* 55 fragment is the base peak of pinocampheol **3**. In the spectra of the other isomers this fragment is approximately half as intense. The appearance of *m/z* 56 as the major peak in the cluster of the surrounding region in the mass spectrum of the 2,4,4-trideuterated alcohols suggests its main component as a crotyl cation composing of a carbon segment of C(7,1,2,10) (Scheme 4).

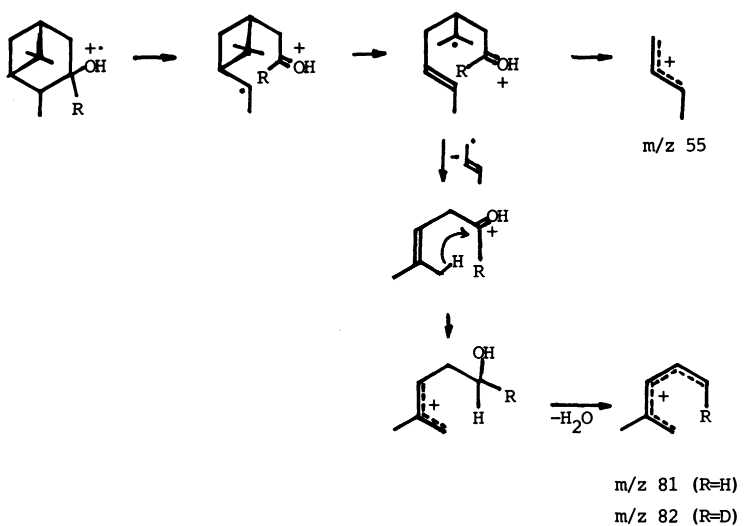


Scheme 3.

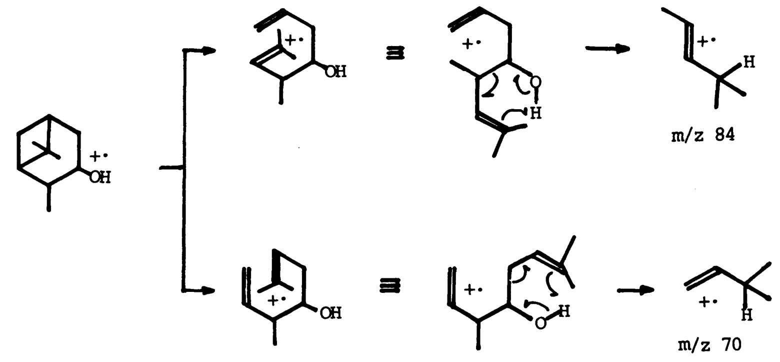
The most noticeable peak shift in the spectra of the 3-deuterio alcohols is *m/z* 81→82, in addition to the $(M-H_2O)$ and $(M-H_2O-CH_3)$ ions. Thus the *m/z* 81 ion could arise from the same seco species by losing a crotyl radical, and subsequent dehydration.

It is likely that *m/z* 84 and 70 are interrelated. Both peaks are derivable from the molecular ions via analogous processes albeit involving scission of different bonds. The relative intensities of *m/z* 84 are in the descending order of **4**>**3**≃**6**>**5**, whereas those of *m/z* 70 are **5**≃**6**>**3**>**4**. The trends are most satisfactorily explained by Scheme 5 in which a preferential ring fission involving C(1)-C(7) and C(5)-C(6) bonds when the compound contains a chair-like trimethylcyclohexane and cleavage at C(1)-C(6) and C(5)-C(7) bonds when the trimethylcyclohexane moiety is forced into a boat-like conformation is indicated. Assignment of the fragment is also consistent with the observed mass shifts of *m/z* 70→72 and 84→85 in the 2,4,4-trideuterio alcohols. Mass shift is absent with regard to these two ions in the 3-deuterio alcohols.

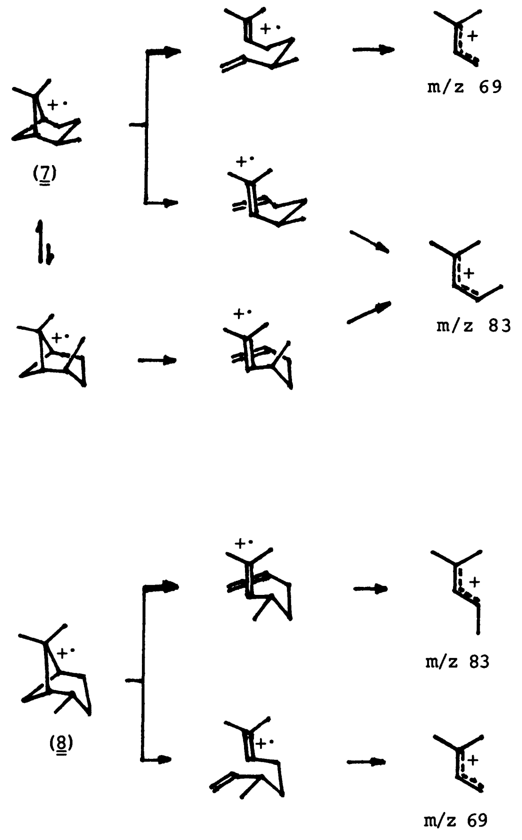
The major direction of cyclobutane ring cleavage for the alcohols follows the two ketones. Remarkably, even the parent hydrocarbons *cis*-pinane (**7**) and *trans*-pinane (**8**) manifest parallel intensity differences in the relevant peaks. While we observed approximately equal intensity of the *m/z* 83 and 69 ions for **7** at ca. 54%, the corresponding peaks registered at 63% and 48%, respectively, in **8**. The coincidental balance of the fragmentation pathways for *cis*-pinane may be actually due to further conformational modification or flattening of the boat-shaped trimethylcyclohexane ring as flagpole interaction between the axial hydrogen at C(3) and the syn-methyl group at C(6) is rather severe. Scheme 6 showing two extreme conformational isomers is only presented for the sake of clarity. It should also be stated that the seco ions indicated



Scheme 4.



Scheme 5.



Scheme 6.

in Schemes 5 and 6 could be generated in a stepwise manner instead of a synchronous process.

The recognizable differences in the mass fragmentation of pinane derivatives are hardly fortuitous. As the only dissimilarity among members of the three series of compounds is in their conformations, it seems that the fragmentation pathways are indeed affected to a large extent by those factors.

The origin of the conformational preferences of the compounds discussed above can be traced to the secondary methyl group. It appears that this group has an additional effect in causing the cyclobutane bond nearest to dihedrally orthogonal to it to undergo rupture preferentially. The destabilization of that cyclobutane bond and/or slight stabilization of the antiperiplanar counterpart may be expected on the basis of an electronic transmission which is operated in the three-bond spin-spin coupling (Karplus relationship).

## Experimental

All known compounds were prepared according to literature methods.[3] Deuteration of **1** and **2** were carried out in a mixture of dioxane and deuterium oxide in the presence of sodium methoxide at room temperature. The alcohols were obtained by reduction of the ketones with either sodium borohydride or lithium aluminum deuteride.

Mass spectra were measured in a Finnigan MAT 112 mass spectrometer connected to a Perkin Elmer Sigma gas chromatograph which was equipped with a DX-4 column (30 m×0.246 mm) and temperature-programmed at 4 °C $\mathrm{min}^{-1}$ from 60 to 250 °C using helium as carrier gas.

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### References

1) S. Meyerson and A. W. Weitkamp, *Org. Mass Spectrom.*, **1**, 659 (1968); M. M. Green, *Topics in Stereochem.*, **9**, 35 (1976); *Tetrahedron*, **36**, 2687 (1980); A. Mandelbaum, *Mass Spectrom. Rev.*, **2**, 223 (1983); A. F. Thomas and B. Wilhalm, *Helv. Chim. Acta*, **50**, 826 (1967).

2) M. V. Bhatt, *Chem. Ind.*, **1959**, 1452; Y. Bessiere-Chretien and C. Grison, *Bull. Soc. Chim. Fr.*, **1971**, 1454.

3) H. Schmidt, *Chem. Ber.*, **77**, 544 (1944).