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MASS SPECTROMETRIC STUDIES OF DITERPENES
4[1]-AROMATIC DITERPENES

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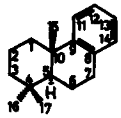
The vast majority of aromatic diterpenes so far isolated from natural sources are of podocarpa-8,11,13-triene type (I). A study of this group of compounds has been undertaken as part of a systematic mass spectrometric investigation of diterpenes[2-4]. This paper describes the fragmentation reactions of podocarpa-8,11,13-triene derivatives lacking oxygenation in the saturated part of the molecule and differing in aromatic substitution as shown by the partial structures given below. An account of earlier mass spectrometric work on terpenes has recently been given by Budzikiewicz, Djerassi and Williams[5].



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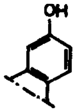
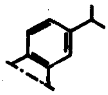
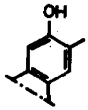
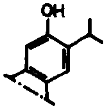
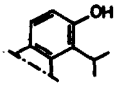


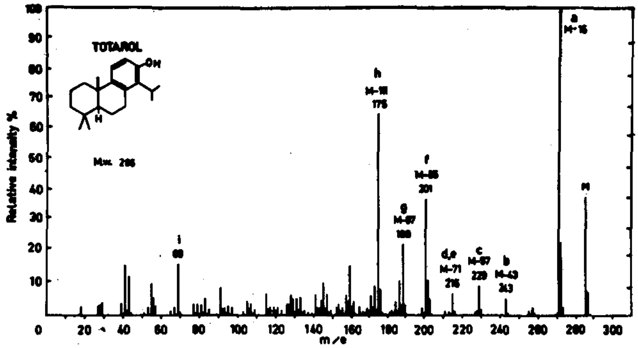








The differences in aromatic substitution do not alter the main paths of fragmentation, but cause certain variations in intensity, noticeably of the M and M-15 peaks. These latter variations are consistent with a stabilising effect on the molecular ions by oxygenation at C(12) and on the M-15 ions by the various C(13) substituents. Since the M-15 ions arise almost exclusively by elimination of the methyl group attached to C(10) which is para to C(13) the variations are in agreement with expectation. It is therefore sufficient to consider here one example, totarol, the spectrum of which is given below.

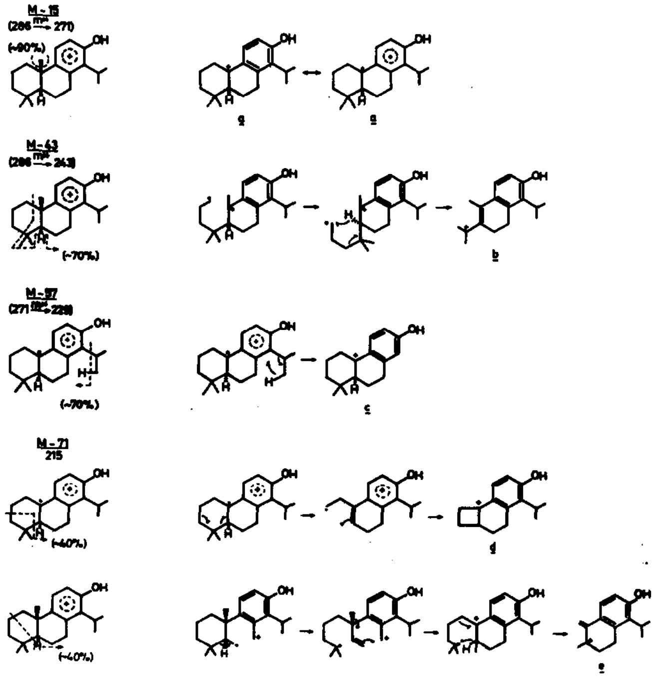


An interpretation of the fragmentation reactions of totarol, based on studies of compounds deuterated at positions 2, 3, 5, 6, 7, 11, 12, 16, 17 and 20[3] and of diffuse peaks due to metastable ions $(m^*)^4$, is outlined in the schemes below. These summarise on the left, the results obtained and on the right the probable mechanisms involved in the formation of the ion under consideration. The dotted lines represent the cleavages required by the deuterium labelling results, and the percentage figures, the estimated extent to which the ion formed according to this cleavage contributes to the peak of appropriate mass number. Canonical formulae, such as the two given for ion a, are used in the diagrams in spite of considerable charge delocalisation.

The simplest fragmentation of the molecular ion is the elimination of the methyl group attached to the benzylic quarternary carbon with the formation of ion a. This is almost the sole contributor to the M-15 peak, as shown by the shift of this peak to higher mass number in the spectra of all labelled compounds. It represents the most important intermidiate in the further fragmentation.

The M-15 peak is at descending mass numbers followed by three characteristic peaks of fairly low intensity, M-43, M-57 and M-71, which for reasons discussed below are of limited diagnostic value. The first of these is found to be due mainly to ion b, formed from the molecular ion by elimination of a C(1)-C(3) fragment together with the C(5) hydrogen, since this peak in the spectra of the 2,2,3,3-d_4- and 5-d_1-derivatives occurs mainly at the same mass number, but in the spectra of the other deuterio derivatives it is shifted to higher mass numbers.

In the spectra of the compounds carrying an isopropyl group the M-57 peak is due mainly to ion c, formed from ion a by elimination of the isopropyl group with back-transfer of one of its hydrogens, since on labelling of the isopropyl group there is no significant shift of this peak. However, the M-57 peak is also present in the spectra of compounds lacking an isopropyl substituent and is here due to ions formed by routes which are less favoured in the isopropyl derivatives[6].

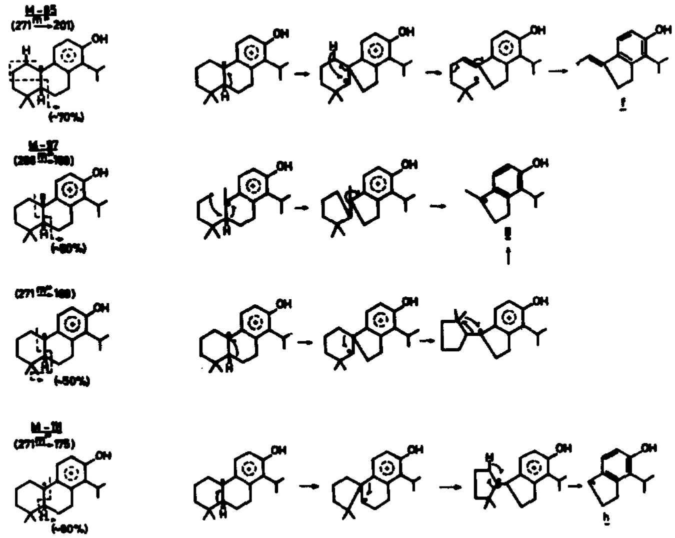


There are no diffuse peaks to indicate the origin of the ions giving rise to the M-71 peak, but from the labelling results it is obvious that it is due to at least two species, which may be formulated as ions d and e. On the basis of the assumption that fragmentation in this series of compounds is initiated by cleavage of benzylic bonds, the formation of these ions may be accounted for as shown above. Although methyl migration is not frequently encountered it has been proved to occur in analogous systems[7].

The most characteristic feature in the spectra of this series of compounds is the group of three prominent peaks at M-85, M-97 and M-111. The M-85 peak, according to deuterium labelling results and diffuse peaks, is due mainly to ion f arising from ion a by cleavage of the C(2)-C(3), C(5)-C(10) and C(5)-C(6) bonds. The only simpler alternative fragmentation of ion a, the elimination of a C(2)-C(4) fragment with substituents, can be disregarded, since it would require a specific and highly impropable transfer of four hydrogens, i.e. the interchange of two of the four C(2) and C(3) hydrogens with the C(5) and one of the C(1) hydrogens.

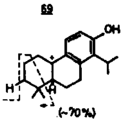
Diffuse peaks and the partial shift of the M-97 peak by two mass units on introduction of two deuteriums in either of the C(4) methyl groups demonstrate that the corresponding ion originates both from the molecular ion and ion a. The lack of shift of the M-97 peak on deuteration at C(2), C(3) and C(5) and the almost complete shift on deuteration at C(6), C(7), C(11), C(12) and C(20) are best explained by the cleavages indicated by the dotted lines in the parent ions. The only alternative fragmentation of any reasonable probability, the cleavage of the C(4)-C(5), C(5)-C(10) and C(9)-C(10) bonds with transfer of the C(5) hydrogen to the neutral fragment and one of the C(4) methyl groups to the charged fragment, is more complex.

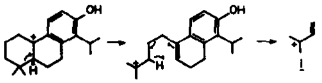
Furthermore it would only explain the formation of an ion containing a C(4) methyl group. Any alternative formation of an ion not containing a C(4) methyl group would require highly improbable and specific shifts of no less than four hydrogens. The main contributor to the M-97 peak may therefore be formulated as ion g, in which the origin of the methyl group attached to the five-membered ring is not the same in all cases. Like ion f, it probably arises by contraction of ring B and possesses an indene skeleton. In arriving at ion g from the molecular ion, methyl migration from C(4) to C(5) may occur instead of C(1) to C(5) bond formation, but the neutral fragment formed in the reaction shown, a dimethyl cyclopentyl radical, should be more stable.



The M-111 peak occurs at the same mass number on deuteration at C(2), C(3), C(16) and C(17), but is almost completely shifted in the spectra of the other deuterio derivatives. The corresponding ion, which according to diffuse peaks originates from ion a, must hence be formed either by the cleavage indicated by the dotted line or by rupture of the C(1)-C(10), C(5)-C(10) and C(5)-C(6) bonds with transfer of the C(5) hydrogen to the charged fragment. The former fragmentation may be visulised as shown and the latter by a reaction in which the first two steps are the same as in the ion a to ion g reaction; the terminating steps would involve transfer of the C(5) hydrogen to the charged fragment and subsequent rupture of the C(5)-C(10) bond accompanied by hydrogen or methyl migration in the neutral fragment. Both processes lead to the formation of ion h and although the reaction shown is preferred since it involves fewer steps an unequivocal choice would require ^{14}C-labelling of C(5) or C(10).

The most charateristic feature in the fragmentation of this series of compounds is the contraction of ring B with the formation of indanyl ions. Support for a more general occurence of such reactions comes from a very recent study[8] of ring B aromatic steroids and 6-azasteroids, which provides evidence for the formation of analogous ions by contraction of ring C. Moreover, the indanyl ions formed in the reactions discussed here appear to be of very high stability; the peaks at descending mass numbers are of low intensity and the only product ions observed originate from the f, g and h ions carrying an isopropyl group, which eliminate this group with back-transfer of a hydrogen. The peaks corresponding to the ions formed by this elimination are often somewhat higher than surrounding peaks, but still of low intensity and partly due to other ions. Hence, they appear to be of little use for structural elucidation purposes.





The peak at m/e 69 is the most prominent peak in the lower part of the majority of the spectra under consideration. It is almost completely shifted to higher mass numbers on deuteration at C(2), C(3), C(16) and C(17) but not on isotopic labelling of the other positions. The corresponding ion must therefore comprise of a C(2)-C(4) fragment with substituents and may accordingly be formulated as ion i or the corresponding cyclised derivative, the dimethyl cyclopropylium ion. Although the appropriate diffuse peaks could not be observed it seems likely that ion i, like the majority of the ions discussed, originates from ion a.

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5. H. Budzikiewicz, C. Djerassi and D.H. Williams, *Structure Elucidation of Natural Products by Mass Spectrometry,* Vol. 2, Chap. 24. Holden-Day, San Francisco (1964).
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