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Mass Spectral Differentiation of Some Unsymmetrically Substituted Isomeric Dihydrobarbiturates

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Recently it has been shown that the sodium borohydride reduction of some unsymmetrically substituted barbituric acid derivatives such as 1-methyl-5-ethyl-5-phenylbarbituric acid (MEPBA, *1*) leads to the formation of two different dihydrobarbiturates.[1] From a mass spectral investigation of the products formed it was found that mass spectrometry provides a method by which they can be easily distinguished. In the present communication we describe the results mainly obtained using the dihydrobarbiturates *2* and *3*, derived from *1*.

The mass spectral fragmentation of unreduced barbituric acid derivatives is well-known and it has been shown that the preferential fragmentation is strongly influenced by the nature of the C-5 substituents.[2-4] See also Refs. 5–11.

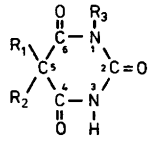
Fig. 1 shows the mass spectrum of 1-methyl-5-ethyl-5-phenyl-6-dihydrobarbiturate *2*. The fragmentation is strongly dominated by the formation of an abundant ion corresponding to *m/e* 146 (base peak). Its formation and further fragmentation are depicted in Scheme 1. The loss of water from the molecular ion has also taken place to a certain extent.

Fig. 2 shows the mass spectrum of 1-methyl-5-ethyl-5-phenyl-4-dihydrobarbiturate *3*. The formation of the base peak at *m/e* 146 can be depicted in a manner analogous to the previous case (Scheme 2, Route A). The elimination of water leads to the ion of *m/e* 230* which may fragment to the ion of *m/e* 146. However, its main fragmentation path is of *retro*-Diels-Alder type, leading to an abundant ion of *m/e* 173. Its formation and further fragmentation are depicted in Scheme 2 (Route B).

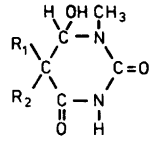
It is worthy of note that the McLafferty rearrangement of the C-5 ethyl substituent, dominating the mass spectral fragmentation of similar unreduced barbituric acid derivatives (*e.g.* 5-ethyl-5-phenylbarbituric acid, Luminal® *4*),[3] is not present in any appreciable amount in either case.

The importance of the *retro*-Diels-Alder process in the mass spectral behaviour of *3*, in all probability due to the vicinity of the OH- and NH-groups permitting the thermal 1,2-elimination of water (*vide supra*), can be used successfully to differentiate between *2* and *3*. In an analogous manner, the peaks at *m/e* 159 and *m/e* 149 in the mass spectra of *6* and *8*, respectively, permit the differentiation of *6* and *8*

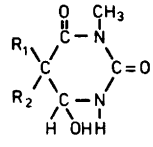
* The peak at *m/e* 230 (*vide supra*) is, in all evidence, due mainly to the molecular ion of the olefin produced by thermal loss of water prior to ionization.



1. $R_1 = C_6H_5$; $R_2 = C_2H_5$; $R_3 = CH_3$
4. $R_1 = C_6H_5$; $R_2 = C_2H_5$; $R_3 = H$



2. $R_1 = C_6H_5$; $R_2 = C_2H_5$
5. $R_1 = C_6H_5$; $R_2 = CH_3$
7. $R_1 = R_2 = CH_2{=}CH{-}CH_2$



3. $R_1 = C_6H_5$; $R_2 = C_2H_5$
6. $R_1 = C_6H_5$; $R_2 = CH_3$
8. $R_1 = R_2 = CH_2{=}CH{-}CH_2$

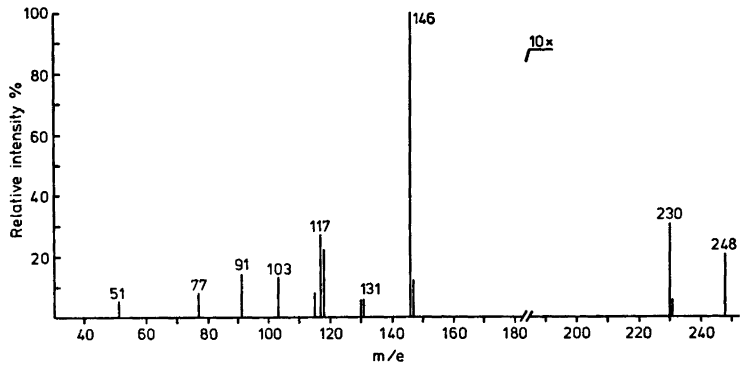


Fig. 1. Mass spectrum (70 eV) of 1-methyl-5-ethyl-5-phenyl-6-dihydrobarbiturate *2*.

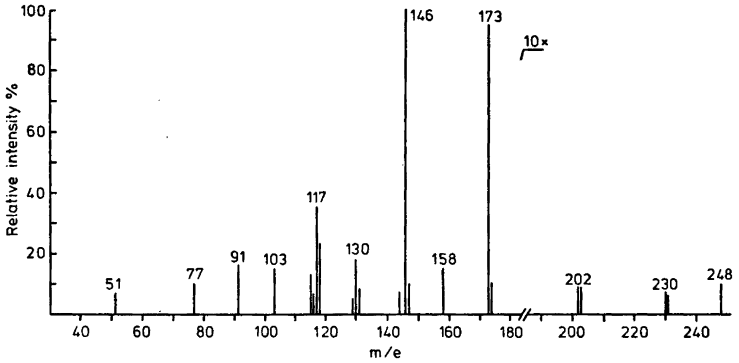
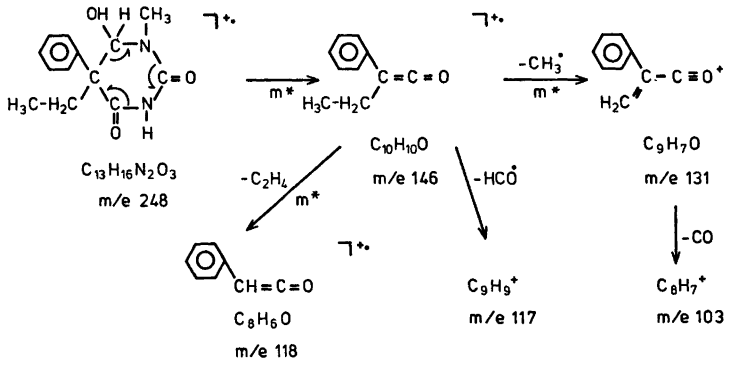
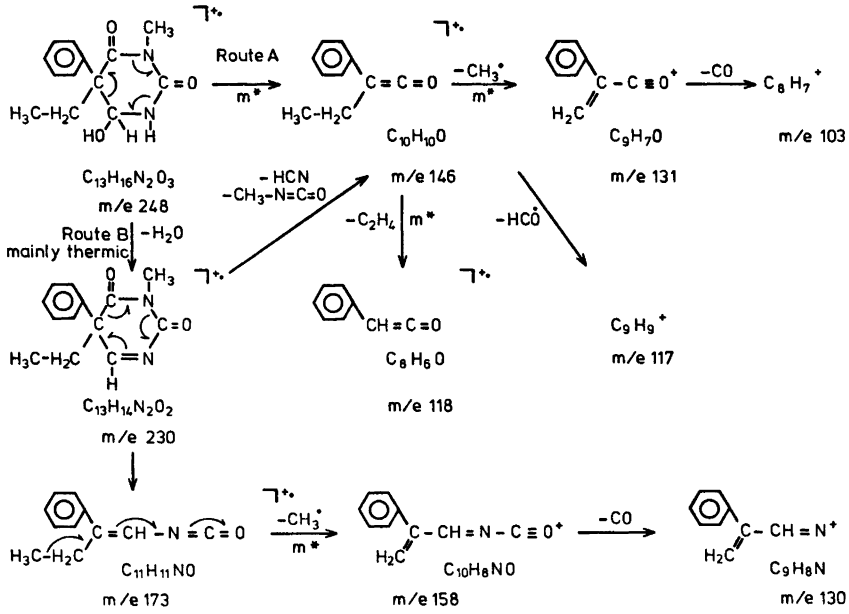


Fig. 2. Mass spectrum (70 eV) of 1-methyl-5-ethyl-5-phenyl-4-dihydrobarbiturate *3*.



Scheme 1.



Scheme 2.

from their corresponding C-6-OH isomers *5* and *7*.

Experimental. The preparation of dihydrobarbiturates *2*, *3*, *5*, *6*, *7* and *8* has been described earlier.[1] The mass spectra were recorded on a Jeol JMS-D-100 Mass Spectrometer at 70 eV using direct sample insertion into the ion source, whose temperature was 110–120 °C. The presence of metastable ions, when indicated, was confirmed by measurements performed using a Hitachi Perkin-Elmer RMU 6E instrument.

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