THE MASS SPECTRA OF DIMETHOXYAMPHETAMINE HYDROCHLORIDES

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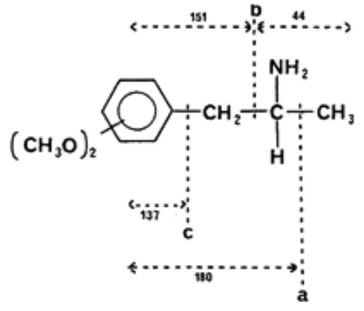
Anal. Chim. Acta 60, 287-292 (1972)

The mass spectra of several derivatives of phenethylamine have been reported[1-4]. Bellman[3] described the spectra of the hallucinogenic methoxylated derivatives 3,4,5-trimethoxyphenethylamine (mescaline) and 2,5-dimethoxy-4-methylamphetamine (DOM or STP) and accounted for their principal fragmentation pathways. The "β-fission" process (β to the amino function and to the benzene ring) is the common and major cleavage mode of amphetamines[1-4]. In the present work, the effect of the aromatic substitution pattern on the fragmentation of dimethoxyamphetamines was examined, and the mass spectra were studied for their suitability for identification and differentiation of these hallucinogenic[5] compounds.

The normalized mass spectra obtained from the six possible dimethoxyamphetamine hydrochlorides (these salts are more easily maintained in a pure state than are the free bases) are presented in Figs. 1–6. All have *m/e* 44 as the base peak, a weak parent ion at *m/e* 195 equivalent to that from the free amine, and only two or three other peaks greater than 5%. Thus it is important to know that the mass spectrometer does not show signals from residual substances. The spectra, although weak and similar, seem to be characteristic, but observations made at such low relative abundances require careful assessment.

The side-chain cleavage modes shown in the scheme were proposed by Beckett *et al.*[1] but no metastable ions supporting these contentions were reported.



Cleavage *a* to give *m*-15 probably occurs weakly in all, but the corresponding metastable ion at *m/e* 166.2 was not observed for any isomer. Bellman[3] considered that *m*-15 in DOM probably arose by loss of the aromatic methyl rather than cleavage *a*. Loss of a methyl radical from a methoxy group might be more favoured in the 2,3- 2,5- and 3,4-isomers since these could form quinoid-stabilized ionic species[6].

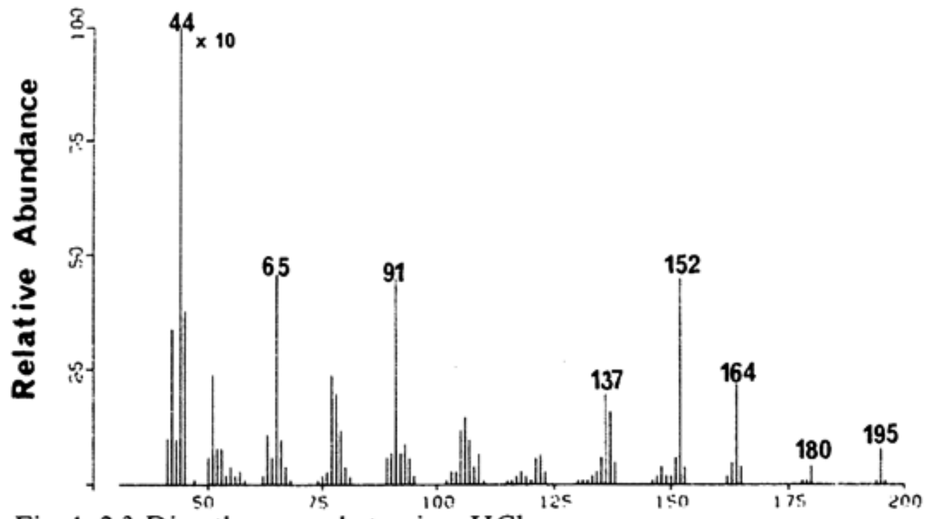


Fig. 1. 2,3-Dimethoxyamphetamine · HCl.

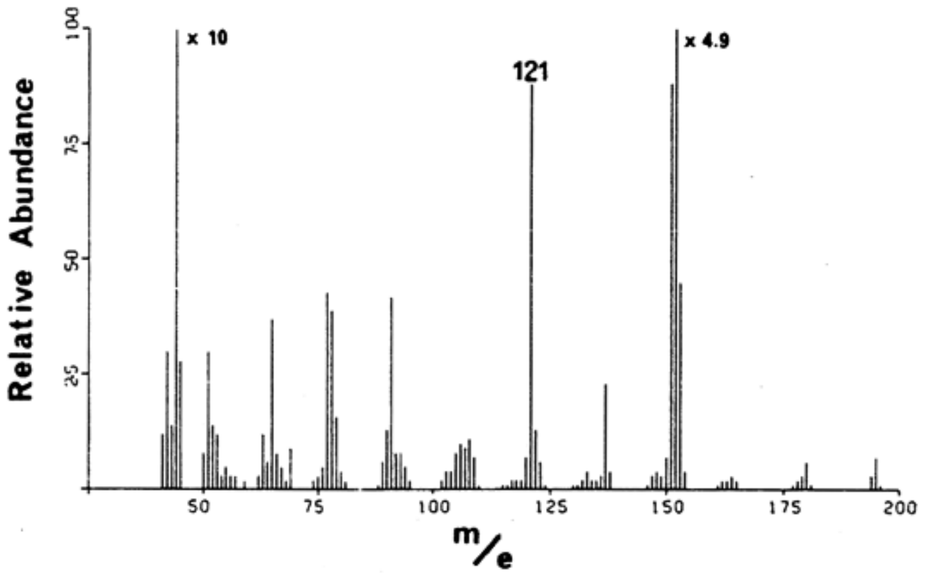


Fig. 2. 2,4-Dimethoxyamphetamine · HCl.

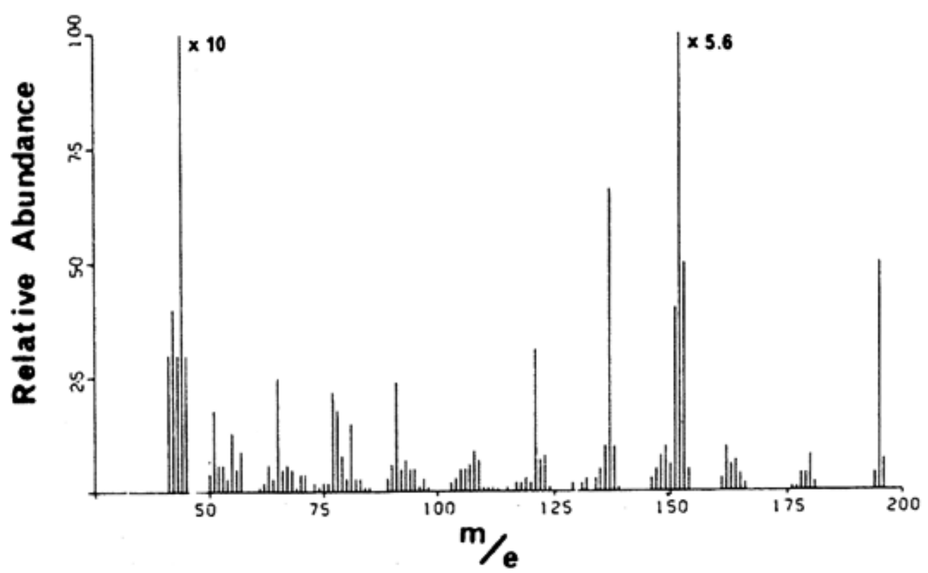


Fig. 3. 2,5-Dimethoxyamphetamine · HCl.

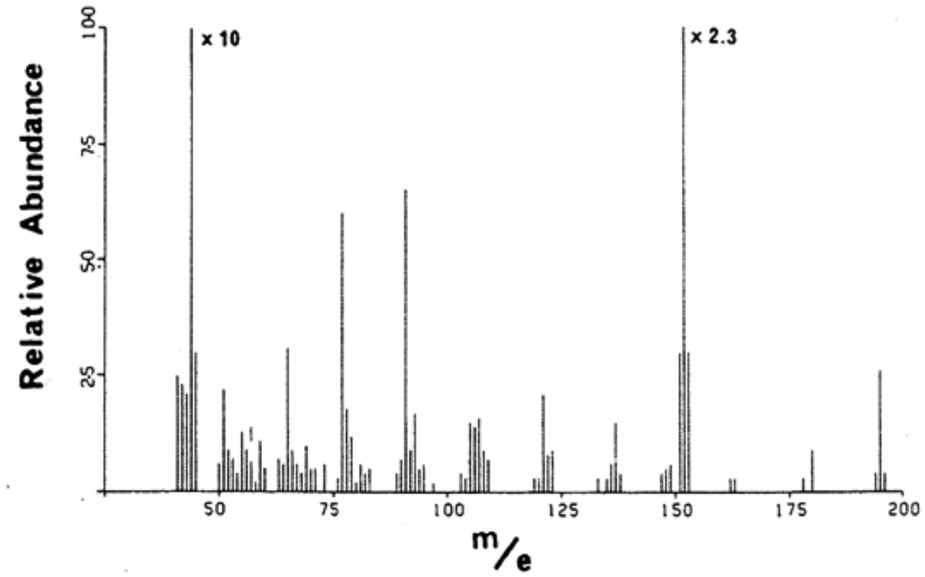


Fig. 4. 2,6-Dimethoxyamphetamine · HCl.

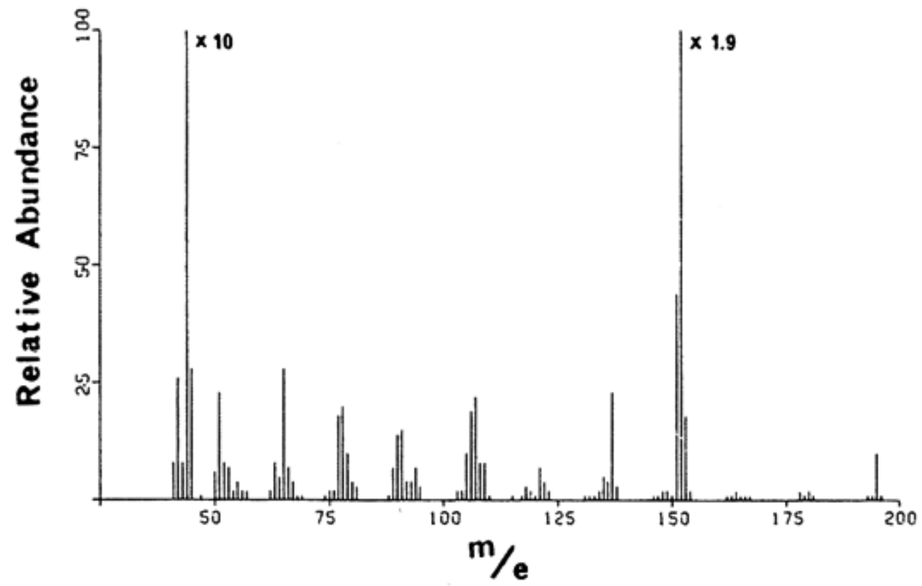


Fig. 5. 3,4-Dimethoxyamphetamine · HCl.

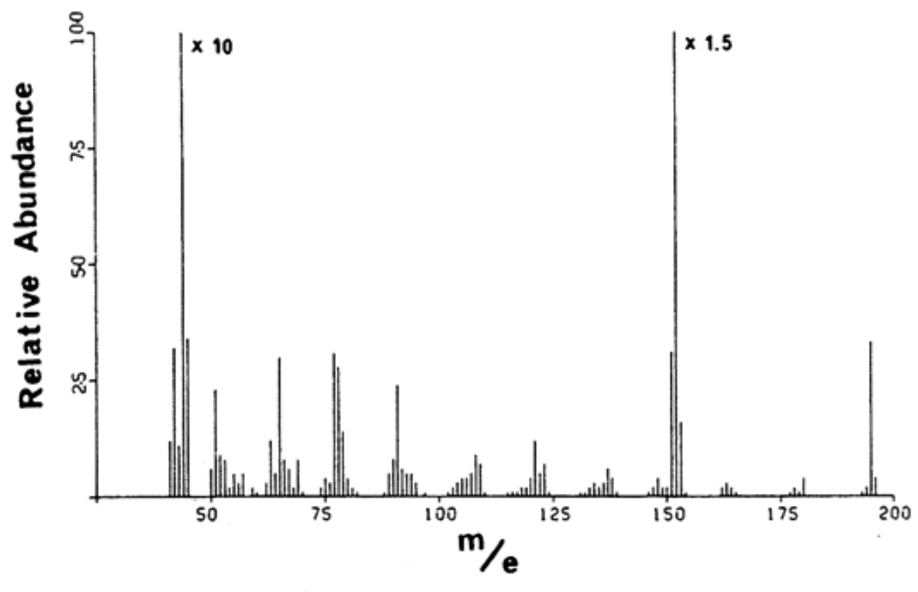


Fig. 6. 3,5-Dimethoxyamphetamine · HCl.

The similar relative intensities of *m/e* 180 peaks in the spectra offer no evidence for this.

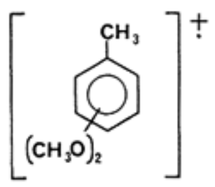
Cleavage *b* is the dominant fragmentation process and is responsible for the base peak at *m/e* 44. The positive charge lies with the *m/e* 151 dimethoxytropylium fragment in the 2,4-isomer more than in the others.

Cleavage *c* would give the dimethoxyphenyl ion with *m/e* 137. In no case was the corresponding metastable ion (calculated *m/e* 96.3) observed, but the metastable ion at *m/e* 123.5 seen in every spectrum is appropriate for the production of *m/e* 137 from *m/e* 152. The weakness of *m/e* 137 and of the metastable ion at 123.5 in the 3,5-isomer perhaps reflects the inability of the oxygen atoms in these positions to stabilize the positive charge developed on C_1.

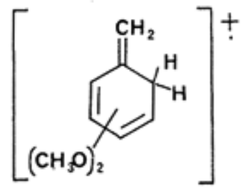
The remaining important fragmentation processes involve the aromatic ring substituents and rearrangement processes:

m/e 164. This is comparatively abundant in the 2,3-isomer and here only was a (weak) metastable ion at 138.0 (as calculated for *m*-31) seen. It is tentatively suggested that bond-strains associated with 1,2,3-trisubstitution of the benzene ring are responsible for this difference, although *m/e* 164 is very weak in the 2,6-isomer. The 3-methoxy radical may be the one mostly expelled since this would give an *ortho* substituted ion. Only the 2,3-isomer exhibited a metastable ion at *m/e* 136.4; the position calculated for 195 fragmenting to *m/e* 163 (loss of CH_3OH) is 136.3.

m/e 152. This is the second most important signal in the spectra. It corresponds with protonated dimethoxytropylium or dimethoxybenzyl ion, and the metastable ion at *m/e* 118.4 for *m*-43 (loss of $CH_3CH{=}NH$) was observed in every spectrum. Bellman proposed[3] that such ions arose by amino proton transfer to the benzylic position, giving a structure such as



There is no evidence for the alternative McLafferty arrangement to a species such as



since the 2,6-isomer appears to be unexceptional, and a subsequent breakdown path is the loss of 15 mass units (CH_3) to give *m/e* 137 as described earlier. In the 2,4- and 2,5-isomers the *m/e* 152 ion is particularly abundant.

m/e 121. This corresponds with loss of 31 (CH_3O) from *m/e* 152 or of 43 ($CH_3CH{=}NH$) from *m/e* 164, but metastable ions at the calculated positions (96.3 and 89.3 respectively) were not observed. A metastable ion at 97.0 was seen in the

2,4- and 2,5-isomers and weakly in the 2,6- and 3,5-isomers and not in the 2,3- or 3,4-isomers *i.e.*, in a strength roughly proportional to the intensity of the *m/e* 121 peak. The calculated position for a metastable ion associated with the production of *m/e* 121 from 151 is 97.0. A metastable ion was noted at *m/e* 75.3 in the 2,5- and at 75.6 in the 2,3-, 2,4-, and 2,6-isomers. Breakdown of the molecular ion to *m/e* 121 would have the metastable ion at (calculated) 75.1; loss of a nitrogen-containing fragment of 74 mass units (C_3H_8NO?) indicates a process involving the side chain and methoxyl moieties. However, the fragmentations *m/e* 109 to *m/e* 91 and *m/e* 108 to *m/e* 90 have metastable positions calculated at 76.0 and 75.0 respectively.

m/e 91. The production of the tropylium ion *m/e* 91 by loss of 30 mass units (CH_2O) from *m/e* 121 is normal, and the corresponding metastable ion was observed at 68.5 for all but the 2,3-isomer which has a very weak *m/e* 121. The breakdown of tropylium is well established[7].

The broad, weak, overlapping metastable ions seen in every case at *m/e* 86.5–87.5 are probably associated with fission of the fragments around *m/e* 137 to those around 109.

In conclusion, the mass spectra of the dimethoxyamphetamine hydrochlorides offer a ready method for determining the character of a substance to be that of a dimethoxyamphetamine, and spectral differences indicate that substituent randomization is not too significant. However, their general weakness does not support confidence in mass spectrometry alone for unequivocal identification of the individual isomers, especially if small quantities of extraneous substances with possibly strong spectra are present in the sample or residual in the spectrometer. It seems very desirable that the investigator have authentic material for simultaneous comparison on the same spectrometer.

EXPERIMENTAL

Mass spectra were recorded on an A.E.I. MS 12 with an ionization voltage of 70 eV and a probe temperature between 120 and 140°. The salts described here were synthesized by standard procedures and recrystallized from isopropanol–hexane to constant m.p.

SUMMARY

The six dimethoxyamphetamine hydrochlorides give weak but distinguishable mass spectra useful for analytical purposes. The principal fragmentation pathways are discussed in terms of the changing aromatic substitution pattern.

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