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Mass Spectrometry of Benzo[a]- and Benzo[c]acridines

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The mass spectrograms of fourteen benzo[*a*]- and benzo[*c*]acridines, several of which are carcinogens, have been determined, and the following main features emerge: (a) presence of strong peaks corresponding to several stages of dehydrogenation; (b) very little fragmentation of the polycyclic frame, with, in ethylbenzacridines, a noteworthy splitting of methyl groups; and (c) importance of the double-charged ions, some of which contribute more to the ionic current than do the corresponding single-charged ones. The pattern of the spectrograms can vary considerably with the position of the substituents.

The group of angular benzacridines represents a specially interesting family of heterocycles because it contains numerous carcinogenic compounds (particularly among the benzo[*c*]acridines (1)) and because, in many physical properties (*e.g.* ultraviolet absorption spectra) a close resemblance exists with the isosteric benzo[*a*]anthracenes. In the past few years, much work has been concerned with relationships between molecular structure and various of these physical properties, including behavior in nuclear magnetic resonance spectroscopy (2), Rayleigh diffusion of depolarized light, diamagnetic susceptibilities, etc. The present work is a study of mass spectrometry of several methyl and ethyl homologs in both the benzo[*a*]acridine and benzo[*c*]-acridine series, several of the compounds investigated being actively carcinogenic. From such a study, it was hoped to gather information on certain properties of these molecules: 1) on the ionizability of the benzacridines, which is expressed in the greater or lesser facility with which, under a given voltage, they give molecular ions bearing either a single charge (M/e) or multiple, especially double, charges (M/2e): it is known that polycyclic aromatic hydrocarbons, on the one hand, and nitrogen-containing heterocycles on the other (the benzacridines belong to both groups), readily give such doubly-charged ions; 2) on their stability, which is appreciated by the contribution of their molecular ions to the total ionic current, contribution which is the greater as the molecule is more stable. Apart from the stability of the whole molecule, there is also to be considered the stability of the polyconjugated frame. This is estimated by the importance of fragmentation ions.

It is also hoped, through the study of groups composed each of several isomers, to determine whether behavior in mass spectrometry varies significantly with the position occupied by the substituents, which is known to play so important a role both in the electronic structure and in the carcinogenicity of the benzacridines (3).

We now report on the following 14 benzacridines:
Benzo[*c*]acridine;
5-Methylbenzo[*c*]acridine;
10-Methylbenzo[*a*]acridine;
7, 8-Dimethylbenzo[*c*]acridine;
7, 10-Dimethylbenzo[*c*]acridine;
5, 9-Dimethylbenzo[*c*]acridine;
5, 10-Dimethylbenzo[*c*]acridine;
8, 12-Dimethylbenzo[*a*]acridine;
9, 11-Diethylbenzo[*c*]acridine;
8, 10-Diethylbenzo[*a*]acridine;
9, 11-Diethyl-7-methylbenzo[*c*]acridine;
8, 10-Diethyl-12-methylbenzo[*a*]acridine;
7, 9, 11-Triethylbenzo[*c*]acridine;
and 8, 10, 12-Triethylbenzo[*a*]acridine.

The mass spectrometer used was a German mark Atlas CH4; the temperature of introduction of the substances was 220° and that of ionization was 280°. The most significant peaks for the 13 alkyl-substituted benzacridines, given in Table 1, correspond to mass spectrograms determined at 70 electron-volts (40 mA). Measurements made at lower voltages showed, however, that peaks corresponding to single-charged ions already appear at between 8 and 10 electron-volts, and that the energies requisite for the creation of double-charged ions in significant number are situated at between 22 and 30 electron-volts; this experimental value of 8 eV accords well with values of ionization potentials of benzacridines determined by means of the absorption spectra.

Although this study did not cover molecules tagged with deuterium and/or nitrogen-15 (such a study is under way), and hence does not claim to give any deep insight into the mechanism of formation of many of the ions recorded, it nevertheless establishes the following interesting facts:

1) The importance of dehydrogenation processes.

All the benzacridines investigated, including the non-substituted benzo[*c*]acridine, show pronounced peaks corresponding to the loss of one or several hydrogen atoms. This loss can occur through two

different processes: (a) through α-fission, *i.e.* abstraction of hydrogen atoms from nuclear =CH- groups (this process being, of course, the only operative one in the case of benzo[c]acridine); and (b) through β-fission, *i.e.* abstraction of hydrogen atoms from methyl and/or methylene groups attached to the nucleus; in the thirteen substituted benzacridines investigated, this takes place along with α-fission. And in fact, the contribution to the total ionic current of the ions M-1 and M-2 (singly and doubly charged) is considerable in all the substances examined, and in several cases (dimethylbenzacridines) the peaks corresponding to the M-3 ions are also quite high. The importance of hydrogen abstraction is particularly marked in the substances containing ethyl groups, the peaks corresponding to the M-7 ions still being important in the two triethyl compounds investigated; this extensive dehydrogenation must occur for a significant part on the side chains. As regards α-fission, it can be seen from Table 2 that nuclear dehydrogenation is more pronounced in the case of benzo[c]acridine than with either the isosteric benzo[a]anthracene or with acridine itself; it is possible that the M-2 ions correspond to species containing a benzyne ring, by analogy with the formation of benzyne ions in the fragmentation of 1,4-naphthoquinone and anthraquinone (4).

2) The stability of the benzacridine polyconjugated frame.

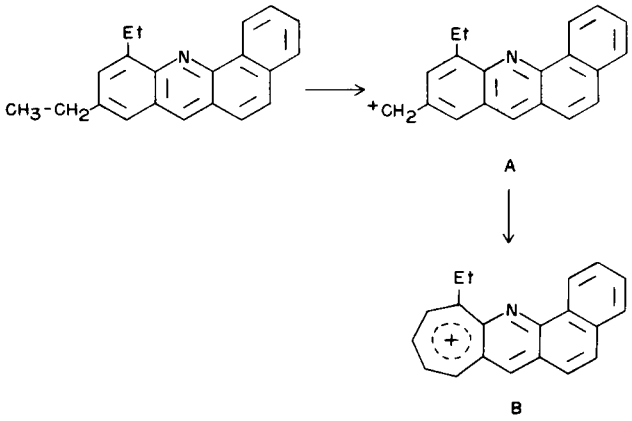
This is demonstrated by the fact that, in all the substances investigated, the molecular peak M/e is the most important, and the contribution to the total ionic current of ions arising from the fragmentation of the skeleton (*e.g.* splitting off of acetylene or hydrogen cyanide) is relatively unimportant. The stability of benzo[a]- and benzo[c]acridines under electron-impact is analogous to that observed in the case of the isosteric benzo[a]anthracene structure. On the other hand, certain fragmentation processes affecting the side chains are significant in both methylated and ethylated benzacridines. (a) Although α-fission of one methyl group occurs to a very small extent in the two monomethylbenzacridines examined, it becomes much more pronounced in the dimethyl compounds, the isomer which most easily loses one methyl group being 7,10-dimethylbenzo[c]acridine: if we add together in each case the relative values of peak (M-15)/e and peak (M-15)/2e, we get the following results:

7,8-dimethylbenzo[c]acridine : 8.5% (of base peak)
7,10-dimethylbenzo[c]acridine : 15.4%
5,9-dimethylbenzo[c]acridine : 5%
5,10-dimethylbenzo[c]acridine : 7.8%
8,12-dimethylbenzo[a]acridine : 8.8%

Loss of both methyl groups (M-30, singly and doubly charged peaks) is observed in all five dimethyl compounds; likewise, with the diethyl and triethyl compounds loss of two ethyl groups (M-58) is important, especially among the trisubstituted benzacridines, although no significant peaks corresponding to loss of three ethyl groups in the two triethyl compounds are discernible. For example, adding together the relative values of peak (M-58)/e and peak (M-58)/2e gives the following:

7,9,11-triethylbenzo[c]acridine : 35.5% (of base peak)
8,10,12-triethylbenzo[a]acridine : 25%

(b) β-Fission of one methyl group occurs in the ethylated benzacridines, this event giving species analogous to benzyl cations and therefore possibly involves tetracyclic tropylium ions, through ring expansion (6), as for instance:



Although highly probable, this ring expansion process in benzacridines needs confirmation through the study of deuterated molecules. So does the loss of acetylene by tropylium species such as [B] and its lower homologs, although the occurrence of metastable ions confirms the existence of this latter process; however, the peaks corresponding to this event (M $\longrightarrow$ M-27) are the same as for M-HCN, event that is characteristic of the fragmentation of many nitrogen-containing heterocycles (7): in the case of quinoline, for instance, the peak m/e = 102 (M-HCN) is 22.5% of the molecular base peak, and with acridine itself the peak m/e = 152 (M-HCN) is 6.64% (5). It is therefore difficult to assess the contribution of each event to the total peak (see Fig. 1). This is a point which the study of benzacridines containing N-15 should settle.

3) The importance of double charged ions.

The mass spectrograms of aromatic polycyclic structures on the one hand, and of nitrogen-containing heterocycles on the other, are known to give significant peaks corresponding to double charged ions; benzacridines, being a combination of the two, not surprisingly show this characteristic to a considerable degree. In some instances, a doubly charged ion is represented by a peak that is markedly higher than that corresponding to the singly charged ion; in such cases, fragmentation with loss of two

TABLE I

Peaks Representing 1% and More of Base Peak

m/e	5-Methyl-benzo[c]-	10-Methyl-benzo[a]-	7,8-Dimethyl-benzo[c]-	8,12-Dimethyl-benzo[a]-	7,10-Dimethyl-benzo[c]-	5,9-Dimethyl-benzo[c]-	5,10-Dimethyl-benzo[c]-	9,11-Diethyl-benzo[c]-	8,10-Diethyl-benzo[a]-	9,11-Diethyl-7-methylbenzo[c]-	8,10-Diethyl-12-methylbenzo[a]-	7,9,11-Triethyl-benzo[c]-	8,10,12-Triethyl-benzo[a]-
94.5	2.4	3.0	1.2	-	-	-	-	-	-	-	-	-	-
107	-	-	3.1	5.8	2.0	-	1.0	3.0	3.0	2.2	-	3.0	3.5
107.5	5.4	3.6	2.1	1.5	1.8	2.5	-	2.0	3.0	1.0	1.0	3.0	3.0
108	2.0	2.5	-	5.8	2.0	2.0	1.0	6.0	7.0	2.2	3.0	7.0	3.0
108.5	12.2	7.8	2.0	2.8	-	2.5	1.5	-	-	-	-	-	-
112.5	-	-	-	3.0	-	2.5	3.5	-	-	-	-	-	-
113	-	1.2	2.8	3.6	3.6	4.5	3.0	-	-	-	-	-	-
113.5	1.1	-	2.2	-	1.0	5.0	7.0	-	-	-	-	-	-
114	1.0	2.0	6.1	1.6	4.2	5.5	6.0	6.2	7.0	6.0	5.0	7.0	5.0
114.5	1.2	-	3.8	2.4	1.2	4.5	4.8	-	-	-	-	-	-
119.5	2.5	2.3	2.2	7.4	1.0	1.5	4.8	-	-	-	-	-	-
120	1.4	1.9	1.8	7.5	1.9	2.5	-	-	-	-	-	-	-
120.5	8.5	8.5	12.5	-	5.2	3.8	-	6.8	8.3	4.2	-	2.3	-
121	2.0	4.2	8.0	2.6	4.9	4.0	1.8	2.0	6.0	9.0	5.0	9.5	6.5
121.5	7.3	11.5	1.3	5.0	-	1.0	1.1	-	10.0	6.0	5.2	4.3	2.0
122	-	-	-	-	-	-	-	11.4	3.0	4.0	1.0	9.0	4.0
126	-	7.5	7.5	3.0	3.4	1.0	6.3	-	-	-	-	-	-
126.5	-	6.0	6.0	3.2	2.6	-	3.1	3.8	5.5	5.0	13.9	7.0	3.0
127	-	-	14.0	8.0	6.3	3.5	2.2	5.8	4.5	11.0	13.0	8.0	8.0
127.5	-	-	11.5	6.2	4.4	4.5	4.1	6.6	-	7.5	5.0	9.5	7.0
128	-	-	5.0	4.8	2.7	3.7	5.2	5.8	7.0	4.5	1.0	9.0	2.0
128.5	-	-	20.5	8.1	8.0	10.0	8.0	-	-	-	-	-	-
132.5	-	-	-	-	-	-	-	6.7	5.0	7.0	7.5	8.5	1.0
133	-	-	-	-	-	-	-	9.8	4.0	7.5	6.0	4.0	1.1
133.5	-	-	-	-	-	-	-	10.2	9.0	14.0	11.0	5.0	5.5
134	-	-	-	-	-	-	-	5.8	6.0	9.0	9.0	7.5	7.0
134.5	-	-	-	-	-	-	-	6.6	13.0	9.0	10.5	8.0	6.9
135	-	-	-	-	-	-	-	1.0	7.0	5.0	5.8	6.0	1.9
139	-	-	-	-	-	-	-	-	-	6.0	3.4	4.0	1.0
139.5	-	-	-	-	-	-	-	3.0	1.0	2.0	3.0	4.0	2.0
140	-	-	-	-	-	-	-	2.8	-	3.0	3.4	5.5	10.5
140.5	-	-	-	-	-	-	-	2.0	-	2.5	3.0	5.0	7.0
141	-	-	-	-	-	-	-	2.2	-	2.8	5.0	3.0	3.5
141.5	-	-	-	-	-	-	-	4.0	1.0	9.5	12.0	3.5	6.0
142	-	-	-	-	-	-	-	2.9	1.0	4.3	4.9	2.0	2.2
142.5	-	-	-	-	-	-	-	9.0	7.0	-	-	-	-
148	-	-	-	-	-	-	-	-	-	3.0	3.0	4.5	-
149	-	-	-	-	-	-	-	8.0	6.0	4.0	2.0	4.0	2.0
149.5	-	-	-	-	-	-	-	-	-	5.0	9.0	2.0	1.8
150	-	-	1.0	2.0	1.5	2.0	-	-	-	-	-	-	-
151	-	-	3.0	3.0	2.0	3.0	1.0	-	-	-	-	-	-
152	-	-	2.0	2.5	3.0	3.2	-	-	-	-	-	-	-
153	-	-	1.0	1.5	2.0	-	1.2	-	-	-	-	-	-

154	-	-	1.0	1.0	1.0	1.0	1.3	-	-	-	-	-	-
155.5	-	-	-	-	-	-	-	-	-	-	-	1.0	1.0
156	-	-	-	-	-	-	-	-	-	-	-	1.5	1.0
156.5	-	-	-	-	-	-	-	-	-	-	-	5.9	5.9
213	-	-	2.0	2.0	2.0	2.0	1.8	-	-	-	-	-	-
214	3.0	3.2	1.0	1.5	2.0	3.0	1.9	-	3.5	2.0	1.5	4.0	1.5
215	3.1	4.5	2.0	2.5	3.0	3.0	1.9	-	3.1	-	1.5	6.0	1.5
216	3.5	2.9	1.0	1.5	2.0	2.0	1.5	-	3.0	-	1.5	7.0	1.5
217	-	-	-	1.2	2.0	1.9	1.5	2.0	3.1	1.0	2.0	8.0	1.5
218	-	-	-	-	-	-	-	2.0	-	1.5	2.0	8.0	1.5
219	-	-	-	-	-	-	-	-	-	-	2.0	11.0	1.5
220	-	-	-	-	-	-	-	-	-	-	-	5.0	1.5
223	-	-	-	1.5	1.0	-	2.6	-	-	-	-	-	-
224	-	-	-	2.6	1.0	-	3.2	-	-	-	-	-	-
225	-	-	2.0	3.5	2.0	-	3.6	-	-	-	-	-	-
226	-	-	3.0	4.0	2.5	3.5	1.8	-	-	-	-	-	-
227	1.1	3.4	3.6	2.5	3.0	5.0	3.4	-	7.2	1.5	2.0	-	1.0
228	-	1.8	2.0	2.5	2.1	4.0	2.0	-	7.0	1.5	2.0	-	3.0
229	-	-	1.2	2.1	1.0	1.8	4.5	1.0	6.0	1.0	2.0	-	3.0
230	-	-	1.3	2.0	1.0	2.0	3.8	2.0	-	1.0	2.2	-	3.0
231	-	-	-	-	-	-	-	3.2	-	1.0	2.0	-	1.5
232	-	-	-	-	-	-	-	2.5	-	-	1.5	-	1.5
238	-	-	4.5	-	-	8.0	-	-	-	-	-	-	-
239	1.0	-	7.5	2.0	2.0	15.0	2.5	-	-	-	-	-	-
240	7.0	7.5	13.5	7.5	5.3	16.0	4.5	-	-	-	-	-	-
241	17.0	15.5	2.7	12.0	8.7	3.0	7.0	2.0	15.0	6.0	5.4	8.0	1.0
242	25.0	26.0	-	6.2	10.5	1.0	6.0	2.4	8.0	4.1	4.2	13.0	2.0
243	100	100	-	3.5	1.5	-	4.0	5.0	2.0	2.8	2.5	14.5	3.5
244	19.6	19.7	-	2.5	-	-	4.0	4.0	-	6.0	2.0	11.0	5.0
245			-	-	-	-	-	5.5	-	5.0	-	7.0	3.0
252			1.5	2.7	1.0	6.0	-	-	-	-	-	-	-
253			2.0	2.6	1.5	5.0	-	-	-	-	-	-	-
254			9.0	8.6	7.5	12.0	6.0	10.2	3.0	14.0	9.5	7.5	10.0
255			5.5	10.0	6.8	16.0	5.5	6.2	7.0	5.5	4.0	26.0	18.0
256			13.5	22.5	12.5	28.6	10.0	6.9	3.0	10.0	5.0	15.0	18.0
257			100	100	100	100	100	12.8	9.0	-	-	24.0	20.0
258			20.5	20.4	20.5	20.4	20.4	7.2	7.0	-	-	-	-
264								-	-	-	-	-	9.5
265								-	-	-	-	6.5	12.5
266								-	-	-	-	12.2	18.0
267								-	-	-	-	21.0	13.6
268								-	-	-	-	28.0	5.0
269								8.8	8.0	20.0	9.0	21.7	3.0
270								17.3	18.0	10.0	8.5	22.0	2.0
271								-	5.0	35.0	20.0	20.0	3.0
272								-	-	12.0	9.0	-	-
283								7.0	7.0	22.0	9.0	15.0	74.0
284								70.0	79.0	14.0	6.0	25.0	21.0
285								100	100	-	-	43.0	3.0
286										-	-	17.0	4.2
296										19.0	7.0	62.0	12.0
297										12.0	7.8	10.0	4.0
298										82.0	76.0	26.0	22.0
299										100	100	27.0	1.0
310												4.0	43.5
311												10.8	67.0
312												46.0	77.9
313												100	100

TABLE II

Relative Importance of Dehydrogenation Peaks

Benzo[*c*]acridine			Acridine (a)			Benzo[*a*]anthracene		
m	ion	%	m	ion	%	m	ion	%
229	M/e	100	179	M/e	100	228	M/e	100
228	(M-1)/e	25	178	(M-1)/e	14.2	227	(M-1)/e	4.9
227	(M-2)/e	7	177	(M-2)/e	7.3	226	(M-2)/e	19.1
114.5	M/2e	13	89.5	M/2e	11.1	114	M/2e	17.8
114	(M-1)/2e	15.1	89	(M-1)/2e	11.8	113.5	(M-1)/2e	2.9
113.5	(M-2)/2e	6.1	88.5	(M-2)/2e	2.9	113	(M-2)/2e	12.9
113	(M-3)/2e	6.0	88	(M-3)/2e	1.1	112.5	(M-3)/2e	0.0

(a) Data taken from published mass spectrogram (5).

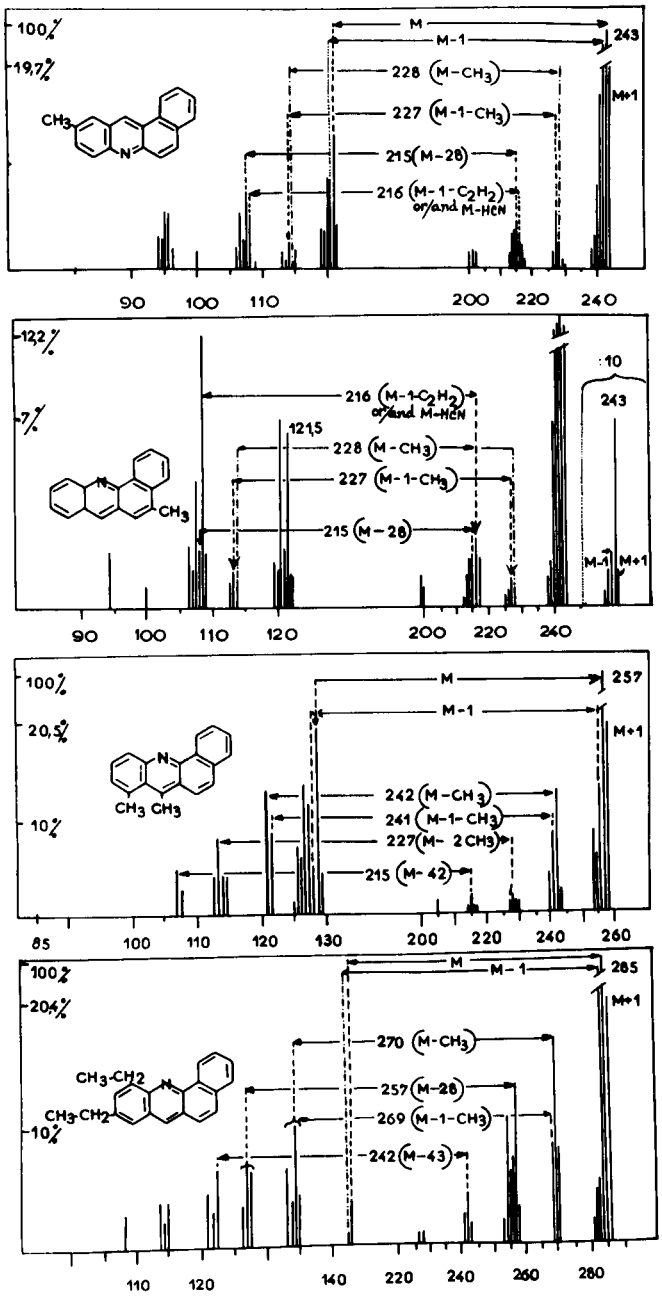


Figure 1

electrons is, energetically, favored over fragmentation with loss of a single electron, and this phenomenon is analogous to the known fragmentation of simple biatomic molecules such as N_2, P_2, Sb_2, Bi_2, etc. (8).

The overall profile of the significant peaks corresponding to doubly charged ions varies with molecular structure, as shown in Fig. 2. Ions with a triple charge are also present, although the corresponding peaks generally represent less than 0.1% of the base peaks.

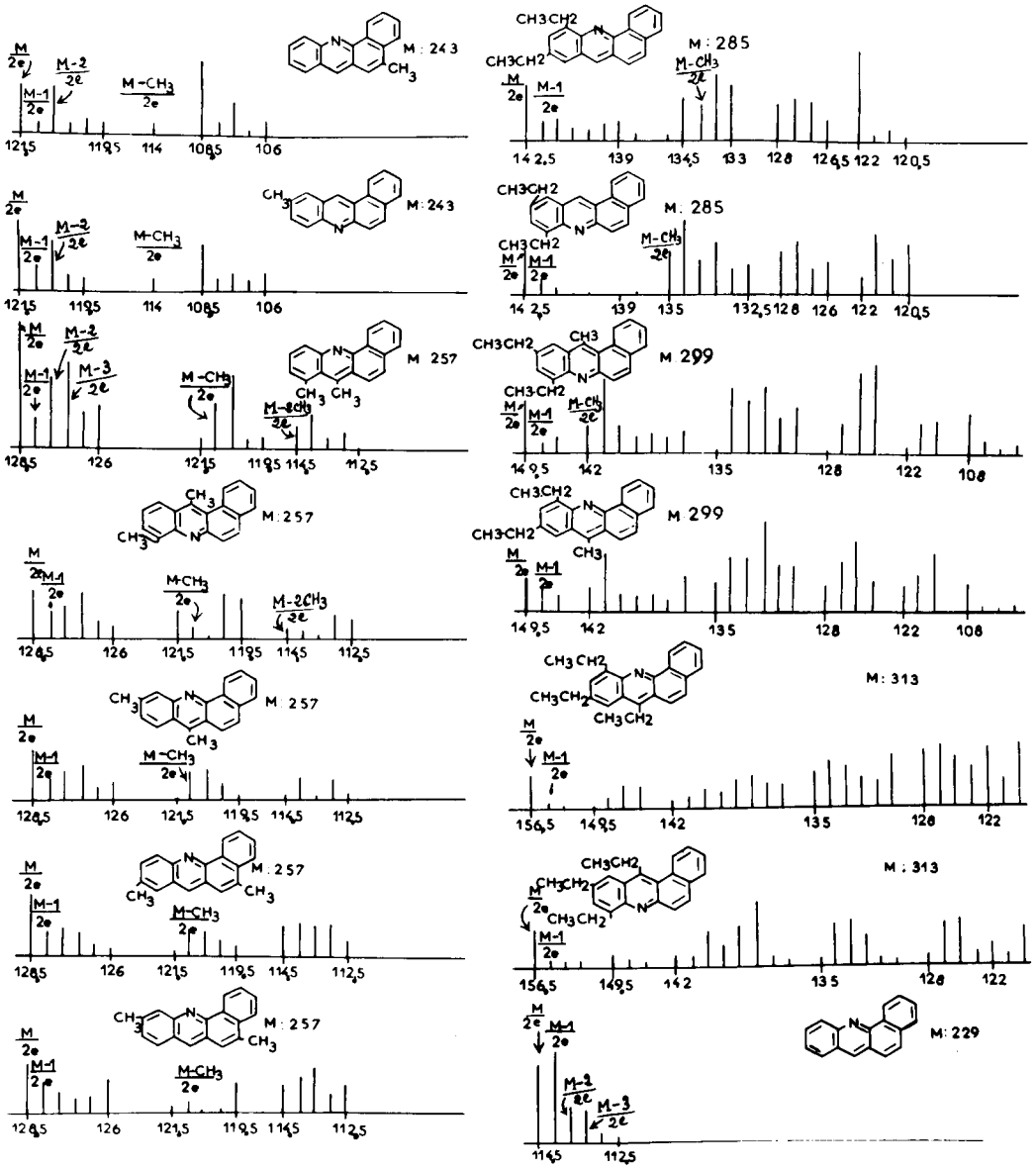


Figure 2

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