Institut de Chimie des Substances Naturelles du C.N.R.S.

# Electron-impact Fragmentation of 7-Chloro- and 7-Methyl-7,12-dihydrobenzo[c]phenarsazine and of 12-Chloro-7,12-dihydrobenzo[a]phenarsazine

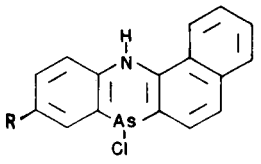
N. P. Buu-Hoï, M. Mangane and P. Jacquignon

7-Chloro-7,12-dihydrobenzo[c]phenarsazine (I) and its derivatives have been intensively investigated in our laboratory for many years, because of the tumor-producing activity of some members of this group (1). Another interesting biological feature, which these compounds share with the isomeric 12-chloro-7,12-dihydrobenzo[a]phenarsazines (*e.g.* III), is their strong sternutatory and mucous-membrane irritating properties; in this, they resemble the tricyclic 10-chloro-5,10-dihydrophenarsazine (Adamsite).

In a recent paper, we reported an investigation on the structure and stability of Adamsite by means of the electron-impact fragmentation method (2), and the present paper records a similar study with compounds I, II and III, and with 7-methyl-7,12-dihydrobenzo[c]phenarsazine (IV), which was prepared by the reaction of methylmagnesium iodide on compound I (3). The electron-impact fragmentation of substances I to IV was investigated with an Atlas CH 4 mass-spectrometer (70 electron-volts; 40 $\mu$ A; ionisation temperature: 230°). The presence in these various molecules of the arsenic atom on the one hand, and of the chlorine atom (with its two isotopes $^{35}Cl$ and $^{37}Cl$) on the other, makes for a relatively facile interpretation of the mass spectrograms obtained, which, furthermore, were remarkably simple, as was the case with Adamsite.

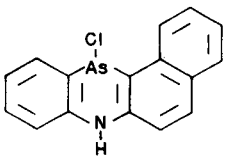
Compound I.

The mass spectrogram of this compound, shown in Fig. 1, calls for the following comments. - a) the ease with which I undergoes electron impact fragmentation is manifest in the practical absence of molecular peaks (these, corresponding to the $^{35}Cl$ and $^{37}Cl$ isotopes, together account for only 1.2% of the base peak); b) the most important peak, which serves as base peak, is the one (m/e = 291) corresponding to the hitherto unreported benzo[c]-phenarsazine species (V), which was formed from compound I by abstraction of chlorine and one atom of hydrogen; the presence of this species is also shown by the peak 145.5, which corresponds to a doubly charged ion. The loss by V of further hydrogen is shown by peaks 290 (15.2% of base peak) and 289 (19.5%); c) Abstraction of chlorine alone from compound V is also a notable feature of the fragmentation of compound I, the peak m/e = 292 being the second most important one (60.5%), and the peak 146, corresponding to the doubly charged ion, representing as much as 32% of the base peak; d) the formation of the benzo[a]carbazole species (VII) is shown by the peak 217 (10%); the peaks 216



I, R = H

II, R = $CH_3$



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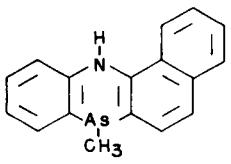

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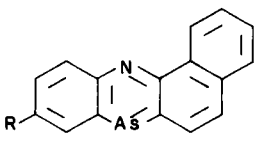
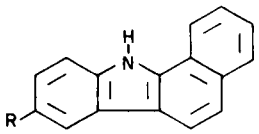


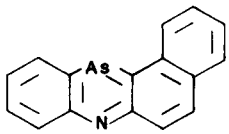
V, R = H

VI, R = $CH_3$



VII, R = H

VIII, R = $CH_3$



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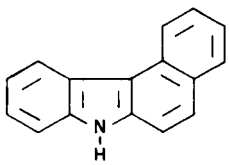
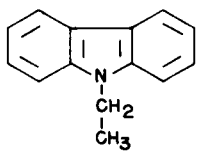


X



XI

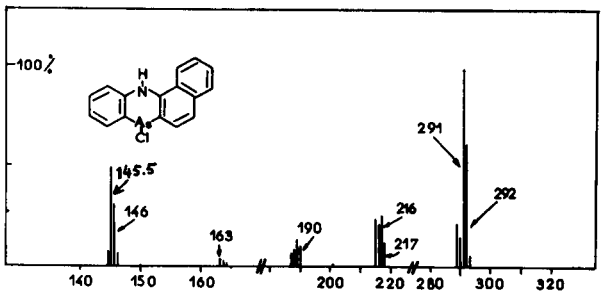



Fig. 1

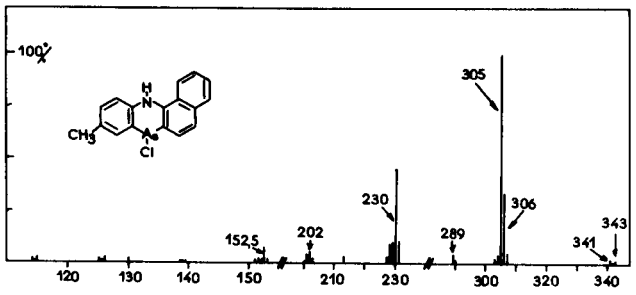



Fig. 2

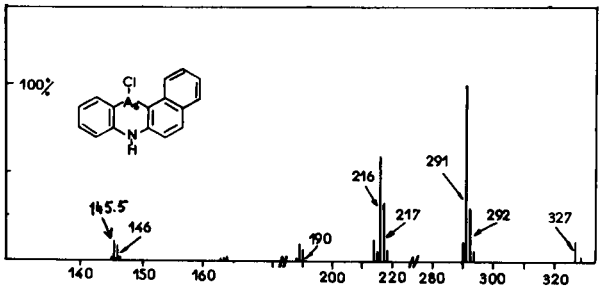



Fig. 3

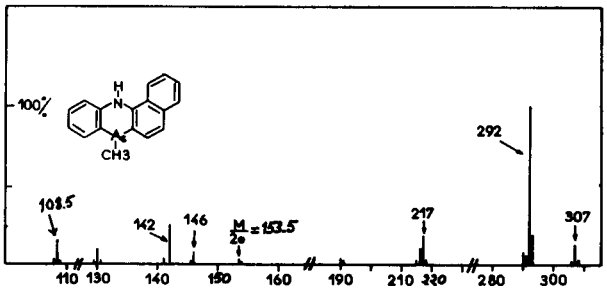



Fig. 4

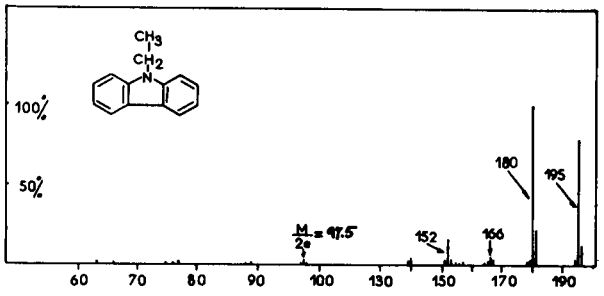



Fig. 5

(25.8%), 215 (20.2%) and 214 (25.7%) correspond to three stages in the dehydrogenation of benzo[a]-carbazole; e) lastly, the small peaks 190 and 189 represent the abstraction, along with As-Cl, of HCN and $H_2CN$ respectively, from compound I; this behavior is quite similar to that of the previously investigated Adamsite.

7-Chloro-9-methyl-7,12-dihydrobenzo[c]phenarsazine (II).

The mass spectrogram of this compound (Fig. 2) shows an electron impact fragmentation that is very similar to that of the non-methylated compound (I); extremely weak molecular peaks, these (341 and 343) together representing only 4.2% of the base peak; ready formation of 9-methylbenzo[c]phenarsazine (VI), corresponding to peak 305 (base peak), and to peak 152.5 (6.7%) which represents the doubly charged ion; abstraction of chlorine alone is also important and is represented by the peak 306 (34.2%). The formation of 8-methylbenzo[a]carbazole (VIII) is shown by the peak 231 (11.8%), with the peaks 230 (47.2%), 229 (11.7%) and 228 (8.5%) representing stages in dehydrogenation of the species VIII.

Compound III.

As well as similarities with that of its isomer (I), the mass spectrogram of this compound (Fig. 3) shows an interesting difference. The base peak corresponds to the completely conjugated benzo[a]-phenarsazine species (IX), which is further represented by the peak 145.5 of the doubly charged ion (12.7%); as with benzo[c]phenarsazine, the stability of the conjugated framework is manifest in the presence of a dehydrogenated ion (peak 290 = 11.8%). Once more, abstraction of chlorine alone from III is an important event (peak 292 = 49.2% and peak 146 = 10.2% corresponding to the doubly charged ion). Lastly, the formation of benzo[c]carbazole (X) (peak 217 = 40%), and its various stages of dehydrogenation (peak 216 = 59.4%, peak 215 = 7.7%, and peak 214 = 12.7%) are important here, too. But, for this compound, the molecular peaks are much more pronounced and represent 15.2% of the base peak; this shows that compound III is relatively more stable toward electron impact fragmentation than compound I, in which the positions of the two heteroatoms are reversed.

Compound IV.

As in the case of Adamsite, the replacement of the As-Cl linkage in compound I by an $As-CH_3$ linkage increases the molecular stability, and the mass spectrogram of compound IV (Fig. 4) shows thus relatively few important fragmentations. Although the main peak (292; base peak) corresponds to the abstraction of the methyl group (this event is also manifested by the presence of the peak 146, corresponding to the doubly charged ion), the molecular peak (307) represents as much as 13% of the base peak and is noticeably accompanied by the peak 153.5 (3.8%) corresponding to the doubly charged molecular

ion. The peak 291 (8.3%) corresponds to the formation of the benzo[c]phenarsazine species; and lastly, the formation of benzo[a]carbazole is shown by the peak 217 (18%), and by the peak 108.5 (15.2%) which corresponds to the doubly charged ion.

## DISCUSSION

From the mass spectrograms of the three tetracyclic analogs of Adamsite investigated, it is clear that the driving force in their electron impact fragmentation is the tendency to assume the fully conjugated benzophenarsazine systems V, VI and IX, which have so far resisted chemical preparation; in all three cases, the main contribution to the ionic current comes from the ions derived from these nuclei. The fragility of the bond linking the arsenic heteroatom to the chlorine (compounds I, II and III) or to a $CH_3$ group (compound IV) is evidenced by the importance of the ions formed by the splitting of this linkage.

Another important feature is the tendency of all four compounds investigated to undergo conversion into the corresponding carbazoles, which belong to a chemical group that is particularly stable both toward heat and toward electron impact fragmentation. As a comparison, Fig. 5 gives the mass spectrogram, taken under similar conditions, of an *N*-alkylated carbazole (9-ethylcarbazole (XI)), which shows very few significant peaks apart from the base peak m/e = 180 (corresponding to the abstraction of a methyl group) and the peak m/e = 195 which is the molecular peak (76.5%).

In conclusion, it can be said that the electron impact fragmentation of compounds I, II, and III gives predominantly singly or doubly charged ions of the corresponding benzophenarsazines, other significant fragments being M-Cl and benzocarbazole ions; in other respects, however, the mass spectrograms of the two isomers I and III are unalike, reflecting structural differences. The fragmentation of compound IV affects predominantly the As-$CH_3$ bond, and also leads to benzo[a]carbazole ions.

## EXPERIMENTAL

Preparation of Compounds.

Compounds I, II and III were obtained in over 80% yield, by refluxing for 4 to 5 hours a solution of arsenic trichloride (1 mole) and 1.1 mole of *N*-phenyl-$\alpha$-naphthylamine, *N*-*p*-tolyl-$\alpha$-naphthylamine, or *N*-phenyl-$\beta$-naphthylamine in the minimum of anhydrous *o*-dichlorobenzene, according to Burton and Gibson (4); after cooling, the precipitate was collected, washed with benzene, and recrystallized from xylene.

Compound IV was prepared in almost quantitative yield, by the reaction of compound I (1 mole) with methylmagnesium iodide (2.5 moles), according to Buu-Hoi *et al.* (3), and the reaction-product recrystallized from a mixture of ether and hexane.

The mass spectrograms were determined in the Dept. of Mass Spectroscopy of this Institute, and we thank the scientists in charge.

## REFERENCES

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(3) N. P. Buu-Hoï, Hiong-Ki-Wei and R. Royer, *Rev. Sci.*, 82, 453 (1944).

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