Apodinine a new alkaloid from Tabernaemontana Apoda Wr ex Sauv. (Peschiera Apoda Markgraf) (Tabernaemontana Armeniaca Areces)*

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ABSTRACT. A new alkaloid apodinine has been isolated from Tabernaemontana Apoda. On the basis of the spectral properties of this alkaloid, and those of their derivatives, particularly of its mass spectra, structure I is proposed.

RESUMEN. Un alcaloide nuevo apodinina se ha aislado de la Tabernaemontana Apoda. En base a sus propiedades espectrales y las de sus derivados, particularmente las de sus espectros de masas, se propone la estructura I.

INTRODUCTION

In our continuing programme, of research into the biological activity of Cuban flora, a new alkaloid, "apodinine", has been isolated from T. Apoda.

RESULTS AND DISCUSSION

Extraction of 1,6 kg of powder from the leaves in the usual from[1] produced 10.7 grams of crude base mixture which was chromatographed on alumina column (act II-III) using benzene and mixtures of benzene chloroform as eluents. The fractions 19 to 25 eluted with 40% Cl_3CH produced two new alkaloids which were called apodine[1] and desoxoapodine.[2]

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A third alkaloid, which precipitates the crude base mixture when it is dissolved in benzene, was also new and called apodinine.

The determination of its structure has been the objetc of the present work. It's U.V. spectrum shows a β anyline acryl ester chromophore with maxima at 223, 297 and 325 (log ε, 3.96, 3.88 and 3.25).

It's I.R spectrum in KBr shows bands at 3370, 1680, 1610 and 1200 cm^{-1}, confirming the presence of a β anyline acryl ester chromophore.

Besides a band at 1780 cm^{-1} is present also in apodine[1] attributable to a γ lactone.

Further direct comparison of the I.R. spectrum of apodine and apodinine shows the two to be almost identical. A shoulder at 3450 cm^{-1} and little difference in the C–O stretching region, pointed to an OH group present in apodinine.

Apodinine is not substituted at the indol moiety as shows the N.M.R. spectrum in hexafluor isopropanol. (T.M.S. as standard), 4 aromatic protons at 7.3 p.p.m. (multiplet), and the strong I.R. band at 750 cm^{-1}. The presence of a γ lactone is confirmed as in apodine by the signal at 3.95 p.p.m. (1 proton singlet).

The mass spectrum shows the following main peaks: m/e 364, 320, 319, 261, 228, 214, 168 and 154.

It seems at firts glance that m/e 364 corresponds to the molecular ion.

If this were true apodinine it would be a dehydroapodine but high m.p. (> 350°), low volatility and the differences shown in the I.R. spectrum pointed to its being a hydroxyapodine and so, m/e 364 corresponds to ($M^{+\cdot} - H_2O$) and actually, the mass spectrum shows no $M^{+\cdot}$ peak. On the other hand, peaks at 214 and 168 (Fig. 1) correspond to the normal cleavage in apodinine. The peak at m/e 214 is also present in the mass spectrum of apodine, desoxoapodine and others[1–3]. The peak at m/e 168 is the corresponding ion to m/e 152 in apodine[1], 138 in desoxoapodine[2], 124 in vinkadifformine[3] and it is displaced 16 mass units of the 152 peak in apodine. Confirming the OH presence in the allycyclic moiety. So m/e 228 and, 154 are homologous ions, and the sum of 214 + 168 or 228 + 154 gives us 382 as the molecular weight for this compound.

Further more, m/e 320 should be $(M\text{-}H_2O - CO_2)^+$; CO_2 lost from the lactone ring and, m/e 261 should be $(M\text{-}H_2O - CO_2 - COOMe)^+$:. "Unprecedental" loss of CO_2 from the lactone ring and further processes could be adscribe the peculiar features of the structure of the ion to $(M - H_2O)^{+\cdot}$[4].

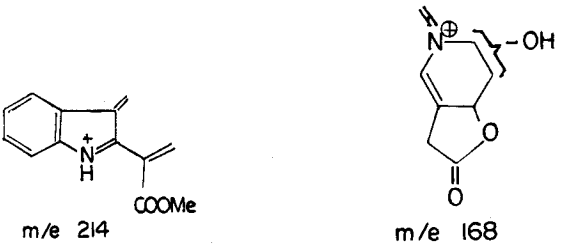


Fig. 1. Peaks at 214 and 168 corresponding to the normal cleavage in apodinine.

In spite of the fact that we could also see the loss of CO_2 in the mass spectrum of decarbometoxyapodine[5].

All these data allowed postulation of the structure for apodine shown in Fig. 2.

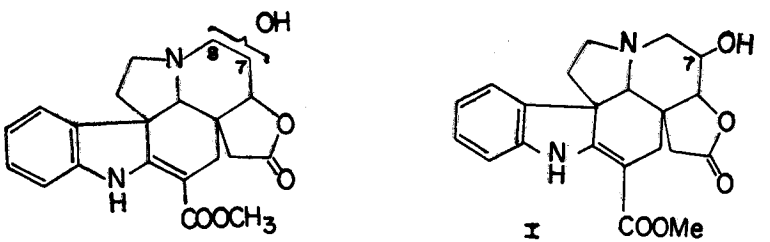


Fig. 2a. Apodinine proposed structure.

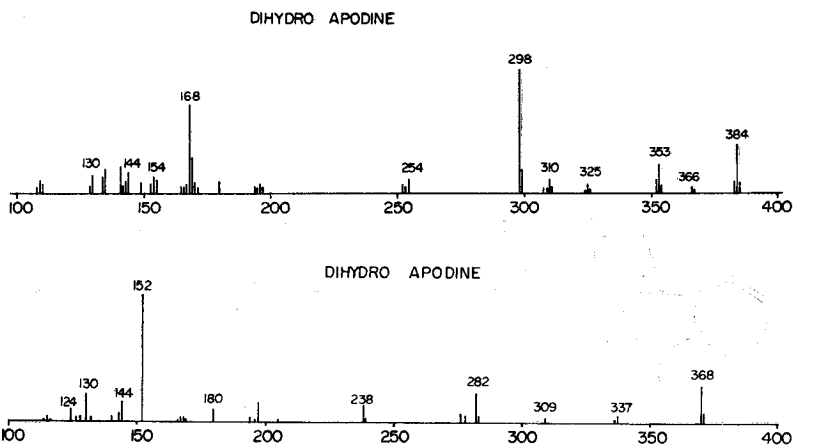
Fig. 2b. Apodinine real structure.

Position 7 and 8 are available from the OH. But the high stability of the molecule an a probable biosynthetic pathway for the formation of the OH[6] through the latone cyclization and the ring opening of a cyclic other, indicated that the OH is at the 7, position as in (2b). Further more, apodinine doesn't reduce an amoniacal silver nitrate solution as ajmaline does[7] and this is another proof in favor of the 7 position from the OH.

The reduction of apodinine with Zn in acid media produces three products that confirms the proposed structure. Two products were isomers as was demonstrated by their U.V. and Mass Spectra (They are alike and correspond to two dihydroapodinine).

The U.V. spectra of these compounds show maxima at 218, 246 and 298 nm as do all the dihydrocompounds of apodine and desoxoapodine[1,2,5].

The mass spectra (Fig. 3a) as we expected, show the molecular peak at 384 mass units and when these were compared with that of dihydroapodine (Fig. 3b) peaks at m/e 152, 180, 258, 282, 337, 368 present in the mass spectrum of dihydroapodine appeared shifted 16 mass units in the mass spectrum of dihydroapodinine. So the peaks at m/e 366, 353 and 325 correspond to $M^{+\cdot} - H_2O$,$M^{+\cdot}$ — OMe and $M^{+\cdot}$ — COOMe groups, respectively. The rest can be explained with the following mechanism. (Fig. 4).



Figs. 3a and 3b. Mass spectra of dihydro apodinine and dihydroapodine.

A metastable peak at 94.6 mass units shows that m/e 298 produces m/e 168 and confirm the OH presence in the allycyclic moiety.

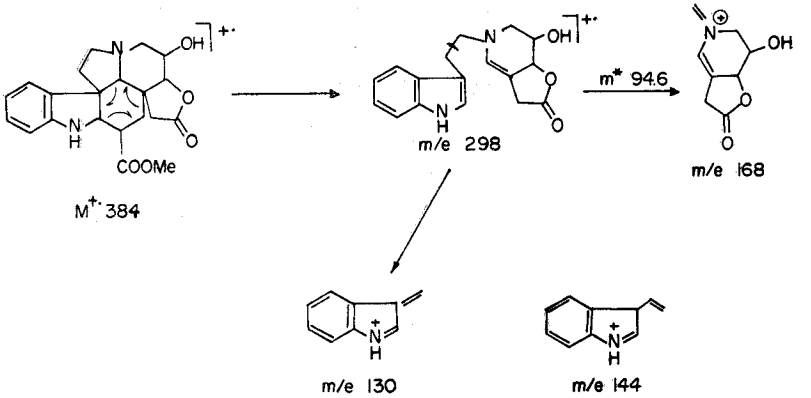


Fig. 4. Dihydroapodinine normal fragmentation mechanism.

The third compound was characterized as our well known alkaloid dihydroapodine[1]. All its spectral properties were identical to an original sample obtained synthetically in our laboratory.

CONCLUSIONS

A new alkaloid has been isolated from the leaves of T. Apoda and characterized by its spectral and chemical properties.

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