Tetrahedron Letters No. 12, pp. 527-532, 1962. Pergamon Press Ltd. Printed in Great Britain.

APPLICATION OF MASS SPECTROMETRY TO STRUCTURE PROBLEMS:[1] CONDYLOCARPINE.

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(Received 23 April 1962)

Recently, a number of alkaloids were isolated[2] by one of us (D.S.) from Diplorrhynchus condylocarpon (Muell. Arg.). Among them were yohimbine, β-yohimbine, tombozine and stemmadenine, all indole alkaloids, and condylocarpine, norfluorocurarine, and mossambine. The last three are α-methyleneindolenines as judged from their typical ultraviolet spectra.

Condylocarpine ($C_{20}H_{22}O_2N_2$, m.p. 159-162°) showed UV (λ_{max} 228, 295, 328; log. ε 4.04, 4.01, 4.17) and IR spectra very similar to akuammicine, which also has the same elemental composition. Part structure I was therefore suggested for that alkaloid.[2]

On the basis of mass spectrometric evidence we have found condylocarpine to have structure II.

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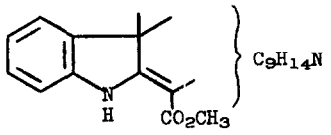
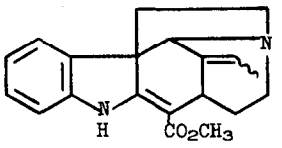
[1] Part VII. For part VI see K. Biemann and J. A. McCloskey, J. Am. Chem. Soc. 84, in press.

[2] D. Stauffacher, Helv. Chim. Acta 44, 2006 (1961).



I



II

Under the conditions of a Clemmensen reduction followed by re-esterification with HCl/CH_3OH condylocarpine gave a crystalline product (m.p. 145-147°) the mass spectrum of which is shown in Fig. 1. The mol. wt., 326, indicates an increase of 4 mass units over the starting material and therefore the reduction of two double bonds as the over-all change during this conversion. In addition to peaks at m/e 130 and 144, typical for a (dihydro)indole grouping with one and two CH_2-groups, respectively, attached to the beta-position,[3] the most intense peak is found, at m/e 196. This corresponds to the loss of 130 m.u. which seems to represent the indole moiety and requires that the carbomethoxy group is still present in the fragment of mass 196. Subtracting the contribution of this group vs. hydrogen (=58 m.u.) leads to mass 138 which thus would be expected for a decarbomethoxy analogue of the Clemmensen product. Such a fragment has been found[3] earlier to be characteristic both of the carbon skeleton of dihydro-aspidospermatine (III, R_1=H, R_2 = CH_3CO, R_3=CH_3O), and of tetrahydrodecarbomethoxyakuammicine (IV, R_1=H). Both are believed to cleave on electron impact to form an ion of type V, which then fragments at a. The spectrum thus suggested either structure IIIa or IVa for the reduction product. As in the earlier case of the elucidation of the structure of aspidospermatine and its derivatives[3] the fragment due to cleavage of ion V at b was used to differentiate between the two possibilities. There is a

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[3] K. Biemann, M. Friedmann-Spiteller and G. Spiteller, Tetrahedron Letters No. 14, 485 (1961).

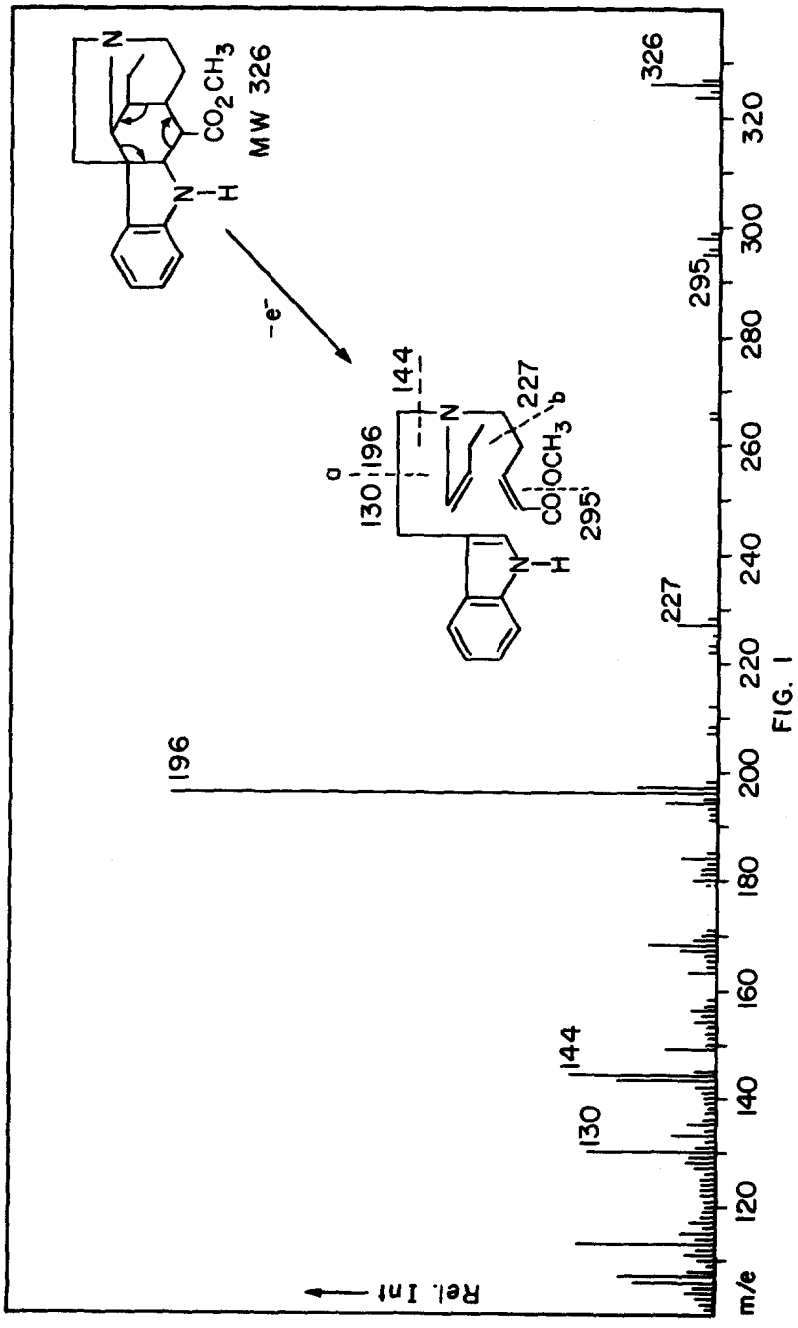
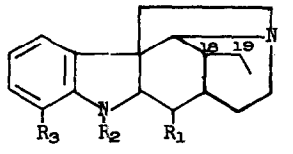
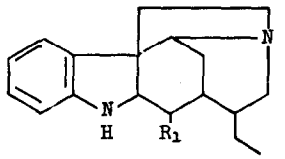

N
CO_2CH_3
MW 326
N–H
-e⁻
144
227
196
130
295
a
b
CO_2CH_3
N–H
326
295
227
196
144
130
Rel. Int
m/e
120
140
160
180
200
220
240
260
280
300
320

FIG. 1



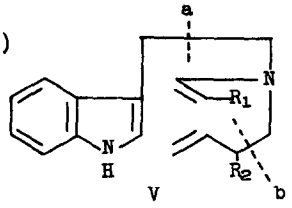
III

IIIa (R_2=R_3=H, R_1=CO_2CH_3)



IV

IVa (R_1=CO_2CH_3)



V

199 (R_1=H, R_2=C_2H_5)
227 (R_1=C_2H_5, R_2=H)

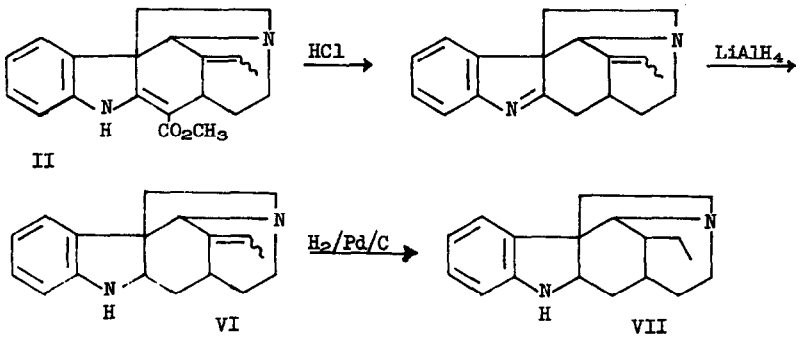
peak at m/e 227 but none at m/e 199 in the spectrum (Fig. 1) of the reduction product of condylocarpine which is thus best represented by IIIa.

Two problems remained to be solved to complete the structure of condylocarpine itself. First, whether the double bond not present in the chromophore I is between C-18 and C-19, as in aspidospermatine,[3] or elsewhere. Secondly, whether the carbon skeleton of the Clemmensen product was the same as the one of the original alkaloid or whether a rearrangement had occurred. Both questions could be answered by conversion of condylocarpine into alkaloid 266B[4] (from Aspidosperma quebracho blanco) which has structure VI.[3]

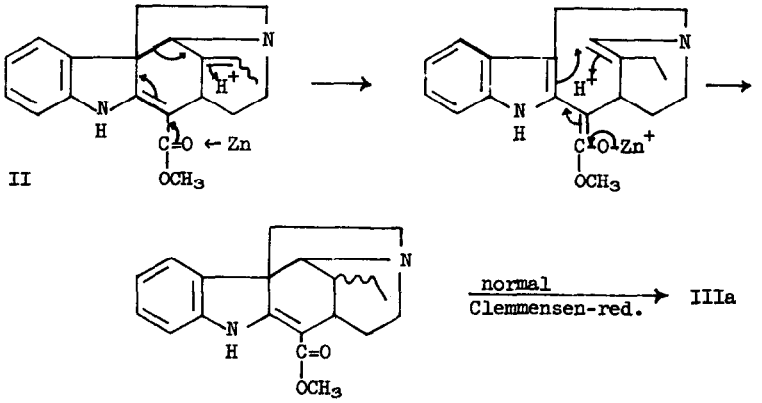
Heating condylocarpine with 20% HCl (115°, 2 hrs) followed by reduction of the product with $LiAlH_4$, reactions used in the degradation of akuammicine,[5] gave indeed a product whose mass spectrum was identical with the one of VI, but melted at 149-152° (m.p. of aspidospermatidine:[3] 184-6°). Our degradation product must therefore be an isomer at C-19, reflecting either such a difference between condylocarpine and aspidospermatidine or isomerization during the treatment with acid. Hydrogenation of

[4] We have chosen the name aspidospermatidine for this alkaloid because it represents the parent structure of a whole group of compounds (ref. 3).
[5] G. F. Smith and J. T. Wrobel, J. Chem. Soc. 1960, 792.

the degradation product led to a dihydro derivative whose mass spectrum was also identical with the one of dihydro-aspidospermatidine (VII). This conversion demands structure II for condylocarpine:

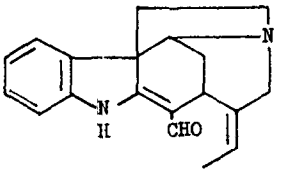


The formation of IIIa from II under Clemmensen conditions is somewhat surprising but can be rationalized by the following sequence:

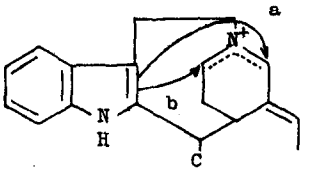


Two biogenetic aspects of the structure of condylocarpine are worthy of mention. First, the co-occurrence[2] of II with norfluorocurarine (VIII) implies the ability of a precursor of type IX to undergo ring closure either via a (to carbon skeleton III) or b (to carbon skeleton IV). Secondly, structure II contains a carbon atom at the position required for

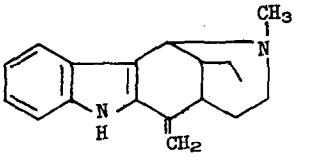
the methylene group in uleine, X,[6] which is thus even more closely related to II than to VI.



VIII



IX



X

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[6] G. Büchi and E. Warnhoff, J. Am. Chem. Soc. 81, 4433 (1959).