(0.37 g.), filtered and passed through alumina. The eluate and the methylene chloride washings gave the crude acetoxy compound (392 mg.) which was crystallized from methanol–water; m.p. 200°, $[\alpha]_D$ −195°; λ_{max} 233 (4.43), 267 (3.16), shoulder 296 (3.89); pK_a' K 4.0.

Anal. Calcd. for $C_{35}H_{42}N_2O_{11}$: C, 63.06; H, 6.36. Found: C, 62.95; H, 6.42.

Isoreserpine Oxindole B.—(a) Acetoxyreserpine (0.5 g.) was refluxed for 1.5 hours in methanol (5 ml.), water (2 ml.) and acetic acid (7 drops). The product from methanol gave isoreserpine oxindole B (300 mg.), m.p. 253°, $[\alpha]_D$ −192°.

Anal. Calcd. for $C_{33}H_{40}N_2O_{10}$: C, 63.5; H, 6.46. Found: C, 63.63; H, 6.56.

(b) Methyl isoreserpate oxindole B (300 mg.) was mixed with 3,4,5-trimethoxybenzoyl chloride (192 mg., 1.2 molar equivalents) and freshly distilled dry pyridine (3 ml.) was added. The mixture stood at room temperature for 4 days. The pyridine was removed *in vacuo*, and the residue dissolved in methylene chloride and filtered through alumina, the eluate being discarded. Further elution by 1–2% methanol in methylene chloride yielded material which crystallized from ether (166 mg.); m.p. 245–246°, identical with that from preparation (a).

7-Methoxy 7H-Isoreserpine.—Lead tetraacetate (2.9 g., dried over KOH) was added to isoreserpine (4 g.) in methanol (500 ml.) and stirred for 5 minutes at 15°. The mixture was poured into ice and extracted into methylene chloride, dried ($MgSO_4$) and concentrated. The residue (4.30 g.) was chromatographed over alumina (200 g.). Elution with benzene yielded an oil (280 mg.), followed by a solid (527 mg.). Elution with methylene chloride furnished isoreserpine (1.03 g.), and finally a resin (1.4 g.). The solid eluted by benzene was recrystallized several times from cyclohexane; m.p. 120–130°, $[\alpha]_D$ −28°; ν_{max} 1716, 1704, 1590 cm.$^{-1}$; λ_{max} 230 (4.49), 266–269 (4.13), shoulder 239 (4.37). This compound was recovered unaltered after reflux in methanol containing a trace of acetic acid.

Anal. Calcd. for $C_{34}H_{42}N_2O_{10}$: C, 63.93; H, 6.63; N, 4.39. Found: C, 63.86; H, 6.74; N, 4.29.

7-Methoxy-7H-reserpine.—Reserpine (4 g.) oxidized in an analogous manner yielded after chromatography a solid (435 mg.) which could be recrystallized from ether–methylene chloride; m.p. 233–235°, $[\alpha]_D$ −190°; ν_{max} 1718, 1596 cm.$^{-1}$; λ_{max} 230 (4.47), 263–266 (4.18), shoulder 236 (4.41).

Anal. Calcd. for $C_{34}H_{42}N_2O_{10}$: C, 63.93; H, 6.63; N, 4.39. Found: C, 64.23; H, 6.56; N, 4.36.

Acknowledgments.—We are grateful to Dr. E. Schlittler for his constant interest and encouragement. We are indebted to Mr. L. Dorfman and his staff for the microanalytical and physical measurements and to Mr. B. Korzun and Mr. S. Brody for paper and thin-layer chromatograms.

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Mass Spectrometry in Structural and Stereochemical Problems. XX.[1] Carapanaubine, a New Alkaloid from *Aspidosperma carapanauba* and Some Observations on Mass Spectra of Oxindole Alkaloids[2]

BY B. GILBERT, J. AGUAYO BRISSOLESE, NEVILLE FINCH, W. I. TAYLOR, H. BUDZIKIEWICZ, J. M. WILSON AND CARL DJERASSI

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The mass spectra of a number of naturally occurring, as well as recently synthesized, oxindole alkaloids have been investigated. By the use of deuterium labeling, as well as variations in substitution in the aromatic and alicyclic portions of the molecule, the principal mass spectral fragmentation processes have been elucidated. Some of these processes are uniquely different from those observed with other indole alkaloids, and mass spectrometry can thus be used as an excellent criterion for establishing membership in this class of alkaloids. As an illustration, there is reported the first isolation of a new oxindole alkaloid, carapanaubine, from an *Aspidosperma* species—mass spectrometry pointing toward an oxindole structure, which was subsequently confirmed by synthesis.

Our studies[3] of the alkaloids of Brazilian Aspidosperma species have led to a remarkable variety of structural types ranging in complexity from hexacyclic N-acyldihydroindoles such as pyrifoline,[4] refractine[5] and aspidoalbine[6] to the relatively simple dihydrocorynantheol[7] and even harman-3-carboxylic acid.[8]

From the bark of another Amazonian species, *Aspidosperma carapanauba* M. Pichon, we have isolated a new base to which the empirical formula $C_{23}H_{28}N_2O_6$ could be attributed with certainty on the basis of elementary analysis and mass spectrometrically determined molecular weight. As noted in Table I, the n.m.r. spectrum of this new alkaloid, now named carapanaubine, showed remarkable similarities to that of isoreserpiline ($C_{23}H_{28}N_2O_5$) IIb originally isolated[9] from *Rauwolfia canescens* L. and recently encountered[10] in *Aspidosperma discolor* A. DC. The similarity of these spectra indicated that the main portion of the carapanaubine (Ic) structure might be identical with that of isoreserpiline (IIb).[9]

The non-indolic ultraviolet spectrum and the presence of an additional carbonyl band in the infrared spectrum of carapanaubine, coupled with the downfield shift of the N–H proton signal in the n.m.r. spectrum (Table I) and the presence of a sixth oxygen atom in the molecule, suggested the possibility of an oxindole structure. Since such alkaloids have hitherto not been encountered in this genus, it was decided to examine the mass spectra of known oxindoles, which have recently become readily available[11–13] by partial synthesis, in order to determine whether some correlation could be made between mass spectral fragmentation patterns and the structures of these alkaloids.

(1) For paper XIX see H. Budzikiewicz, J. M. Wilson, C. Djerassi, J. Levy, J. Le Men and M.-M. Janot, *Tetrahedron*, in press.

(2) (a) This work represents part of a joint program, supported by the Rockefeller Foundation, between the Instituto de Quimica Agricola and Stanford University on the chemistry of Brazilian plant products. Additional financial support was provided by the National Institutes of Health of the United States Public Health Service through Grants No. A-4257 and 29-682. (b) First presented at the second I.U.P.A.C. International Symposium on the Chemistry of Natural Products, Prague, August, 1962.

(3) For the first paper see B. Gilbert, L. D. Antonaccio, A. A. P. G. Archer and C. Djerassi, *Experientia*, **16**, 61 (1960). The most recent article is by B. Gilbert, J. A. Brissolese, J. M. Wilson, H. Budzikiewicz, L. J. Durham and C. Djerassi, *Chem. Ind.* (London), 1949 (1962).

(4) B. Gilbert, J. M. Ferreira, R. J. Owellen, C. E. Swanholm, H. Budzikiewicz, L. J. Durham and C. Djerassi, *Tetrahedron Letters*, 59 (1962).

(5) C. Djerassi, T. George, N. Finch, H. F. Lodish, H. Budzikiewicz and B. Gilbert, *J. Am. Chem. Soc.*, **84**, 1499 (1962).

(6) C. Djerassi, L. D. Antonaccio, H. Budzikiewicz, J. M. Wilson and B. Gilbert, *Tetrahedron Letters*, 1001 (1962).

(7) B. Gilbert, L. D. Antonaccio and C. Djerassi, *J. Org. Chem.*, **27**, 4702 (1962).

(8) L. D. Antonaccio and H. Budzikiewicz, *Monatsh.*, **93**, 962 (1962).

(9) A. Stoll, A. Hofmann and R. Brunner, *Helv. Chim. Acta*, **38**, 270 (1955).

(10) Unpublished observation of Dr. R. J. Owellen, Stanford University.

(11) N. Finch and W. I. Taylor, *J. Am. Chem. Soc.*, **84**, 1318, 3871 (1962).

(12) J. Shavel and H. Zinnes, *ibid.*, **84**, 1320 (1962).

(13) N. Finch, C. W. Gemenden, I. H. Hsu and W. I. Taylor, *ibid.*, **85**, 1520 (1963).

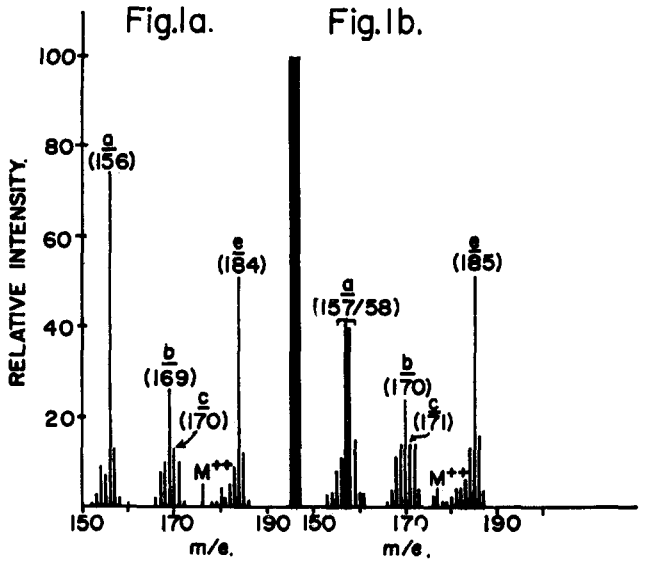


Fig. 1.—Portion of mass spectrum of ajmalicine (IIA) (Fig. 1a) and of 1:1 mixture of 3-d_1- (Va) and 3,14-d_2- (Vb) ajmalicine (Fig. 1b).

The first alkaloid to be investigated was mitraphylline (Ia)[14] which has recently been synthesized[11,12] from ajmalicine (IIa). Since 3,5,6-trideuterioajmalicine (III) can be prepared readily[15] from serpentine by reduction with sodium borodeuteride, the way was open to 3,5,6-d_3-mitraphylline (IVc). A second, and for our

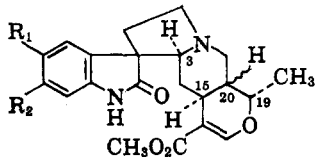
TABLE I

CHARACTERISTIC N.M.R. SIGNALS[a] OF CARAPANAUBINE (Ic) AND ISORESERPILINE (IIb)

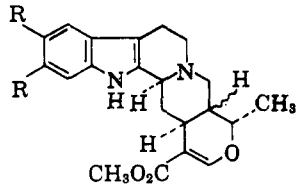
Group	No. of protons	Nature of signal	Carapanaubine	Isoreserpiline
CH_3CHO	3	Doublet	1.40 (J = 6)	1.37 (J = 6)
CH_3CHO	1	Octet	4.56 ($J_{Me\|H}$ = 6[b])	4.44
$-CO_2CH_3$	3	Singlet	3.61 ($J_{H\|H}$ = 5.7)	3.72
CH_3O	6	Singlets	3.90, 3.92	3.83, 3.87
Allylic H	1	Quartet	4.2–4.7	4.2–4.7
Aromatic H	2	Singlets	6.55, 6.74	6.77, 6.90
Olefinic H	1	Singlet	7.44	7.57
N_aH	1	Singlet	8.73	7.95

[a] The n.m.r. spectra were measured in $CDCl_3$ solution (tetramethylsilane added as an internal standard) with Varian A-60 (courtesy of Dr. Lois J. Durham, Stanford University) and H-100 (courtesy of Mr. N. S. Bhacca, Varian Associates) spectrometers. All signals are reported in δ values (T.M.S. = 0.0 p.p.m.). [b] Shown by decoupling to be due to a single hydrogen about 315 c.p.s. downfield at 100 Mc.

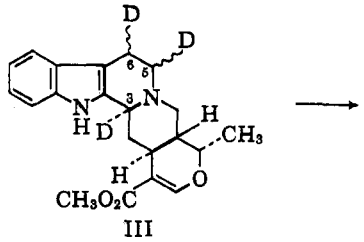
purposes even more important, labeled compound became available through the observation that sodium borodeuteride reduction of 3-dehydroajmalicine chloride leads to a 1:1 mixture[16] of mono- and dideuterio species. The singly deuterated substance is clearly the expected 3-deuterioajmalicine derived from $\Delta^{3(4)}$-dehydroajmalicine. The doubly deuterated compound must be 3,14-d_2-ajmalicine arising either by reduction of the other double bond tautomer, $\Delta^{3(14)}$-dehydroajmalicine, or exchange of C_{14}-proton by operation of the enamine–imino tautomerism, on 3-dehydroajmalicine chloride, in the presence of deuteriomethanol, prior to reduction. Application of the standard[11] indole to oxindole conversion method to Va and Vb thus provided a 1:1 mixture of 3-mono-(IVa) and 3,14-di-(IVb) deuteriomitraphyllines, which represented very important labels for analysis of the mass spectral fragmentation processes. The fact that the 3,14-d_2-ajmalicine (IVb) was accompanied by an equal proportion of the d_1-species IVa presented no serious problem, since the contribution of the deuterium atom attached to C_3 could usually be detected by comparison with the spectrum of the 3,5,6-d_3-analog IVc.



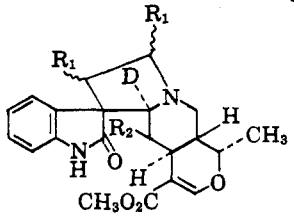
Ia, 20-Hβ; $R_1 = R_2 = H$
b, 20-Hα; $R_1 = OCH_3$, $R_2 = H$
c, 20-Hα; $R_1 = R_2 = OCH_3$



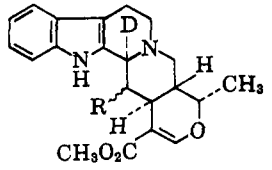
IIa, 20-Hβ; R = H
b, 20-Hα; R = OCH_3



III



IVa, $R_1 = R_2 = H$
b, $R_1 = H$, $R_2 = D$
c, $R_1 = D$, $R_2 = H$



Va, R = H
b, R = D

The mass spectrum of the mixture of 3-d-(Va) and 3,14-d_2-(Vb) ajmalicine permits a confirmation of the earlier[15] assignments of the main fragments in the ajmalicine spectrum. In Fig. 1 there are reproduced parts of the mass spectrum of ajmalicine (IIa, Fig. 1a) and of the deuterated species Va and Vb (Fig. 1b). On the basis of a comparison of the mass spectra of ajmalicine (IIa) and its 3,5,6-d_3-analog III, we had proposed[15] that the important m/e 156 ion (Fig. 1a) should be represented by structure a, which should contain the original hydrogens attached at C_3 and C_{14}. Consequently, in the spectrum of the 3-d_1-(Va) and 3,14-d_2-(Vb) mixture, this peak should be split in a 1:1 ratio between m/e 157 and 158, which is precisely what is observed (Fig. 1b). Similarly, the m/e 169 and 170 peaks in the ajmalicine spectrum (Fig. 1a) were attributed[15] to structures b and c, both retaining only the C_3, but not the C_{14} deuterium. In accordance with this assignment, it will be noted in Fig. 1b that this group of peaks is shifted by one mass unit only. Of particular pertinence is the important m/e 184 peak (Fig. 1a) for which two alternative representations (d and e) had been proposed,[15] the information then available not being sufficient to differentiate between them. The ion d contains the β-carboline moiety together with C_{14} (hydrogen migration from C_3 to C_{14} was assumed[15]), and if correct, the m/e 184 peak in Fig. 1a should be distributed evenly between m/e 185 and 186 in Fig. 1b. On the other hand, the ion e contains only the hydrogen (respectively deuterium) attached to C_3, but lacks C_{14}. Consequently, the m/e 184 peak should move only to m/e 185 in the spectrum of the deuterated mixture (Va and Vb);

(14) J. C. Seaton, R. Tondeur and L. Marion, *Can. J. Chem.*, **36**, 1031 (1958); T. Nozoye, *Chem. Pharm. Bull.* (Japan), **6**, 306 (1958).

(15) L. D. Antonaccio, N. A. Pereira, B. Gilbert, H. Vorbrueggen, H. Budzikiewicz, J. M. Wilson, L. J. Durham and C. Djerassi, *J. Am. Chem. Soc.*, **84**, 2161 (1962).

(16) The exact composition was 15% d_0, 42% d_1, 43% d_2 species as determined by low voltage mass spectrometry. In Fig. 1b no correction has been made for the 15% of non-deuterated ajmalicine.

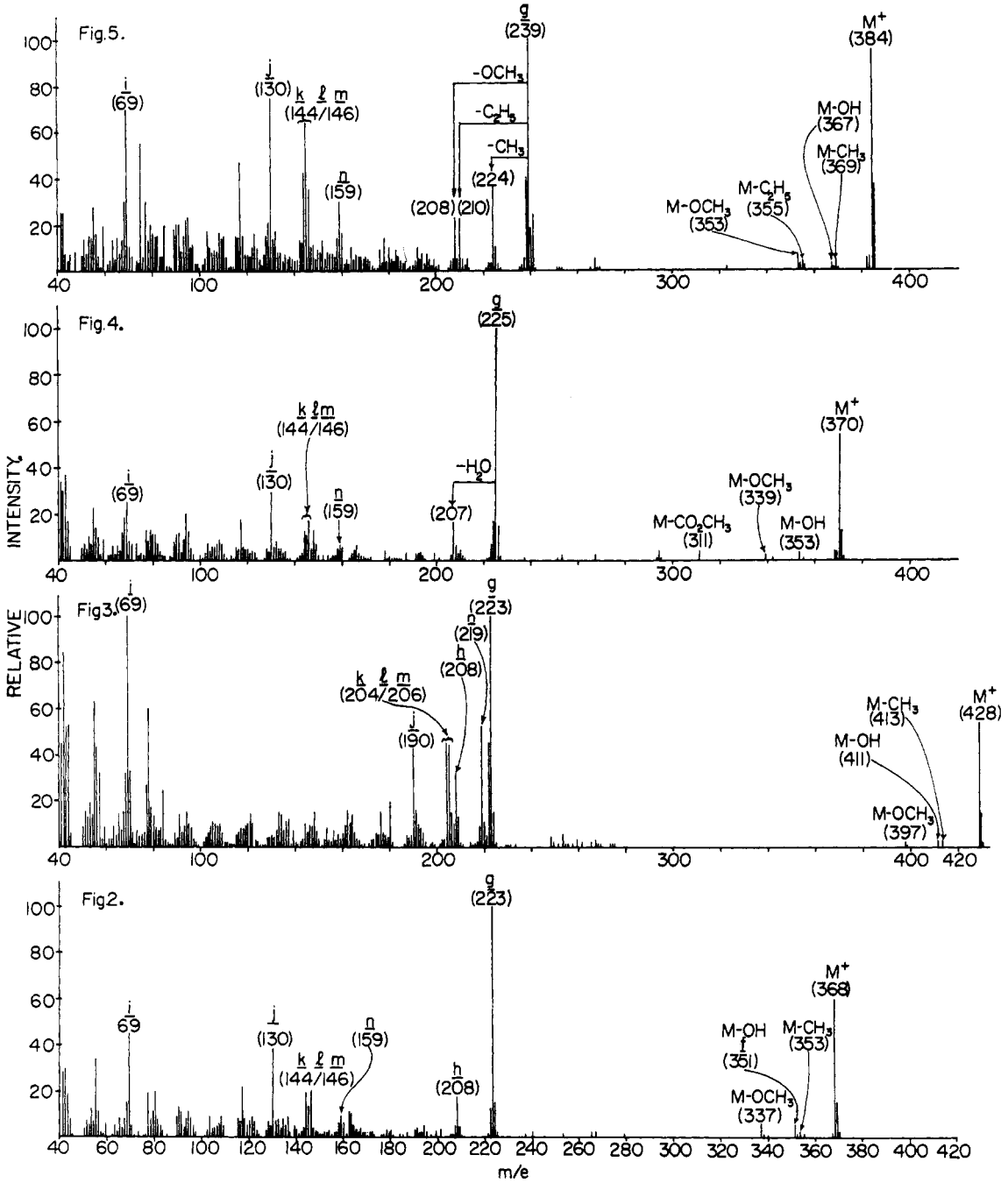
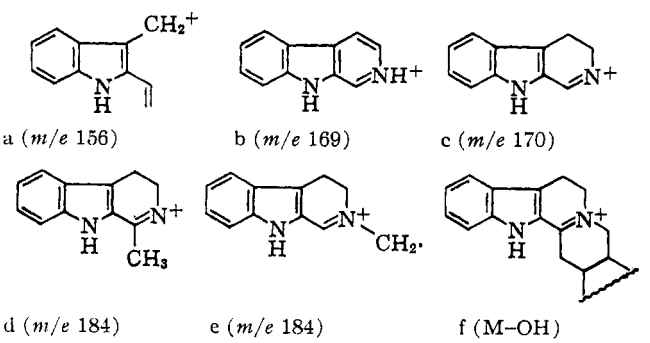


Fig. 2.—Mass spectrum of mitraphylline (Ia).
Fig. 3.—Mass spectrum of carapanaubine (= isoreserpiline oxindole) (Ic).
Fig. 4.—Mass spectrum of yohimbine oxindole B (VI).
Fig. 5.—Mass spectrum of rhyncophylline (VII).

since this is actually observed (Fig. 1b), expression e, rather than d, is the correct one for the *m/e* 184 ion fragment.



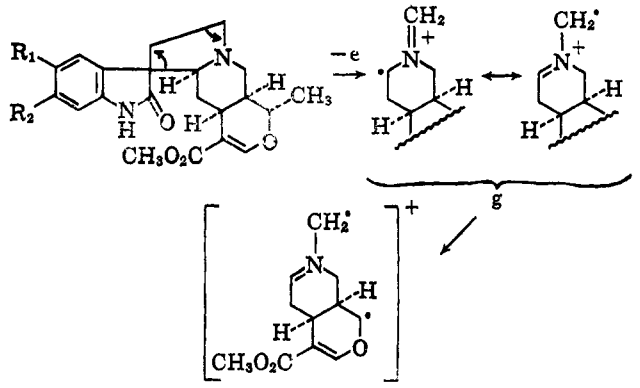
a (*m/e* 156) b (*m/e* 169) c (*m/e* 170)

d (*m/e* 184) e (*m/e* 184) f (M–OH)

We can now turn to a consideration of the mass spectrum (Fig. 2) of mitraphylline (Ia) and its deuterated analogs (IVa, b, c), and we note immediately that its fragmentation behavior is completely different from that[15] of tetrahydro-β-carboline alkaloids such as ajmalicine (IIa). Thus, the characteristic M-1 peak of the latter group is essentially absent, since formation of an ammonium ion in conjugation with the indole system is impossible in oxindoles. On the other hand, the mass spectra of all oxindole alkaloids investigated by us exhibit a small but recognizable M-17 peak (*m/e* 351 in Fig. 2), which must be due to the loss of OH. Since this fragment occurs in substances which contain no hydroxyl function (*e.g.*, Ia, VII), its formation must involve the loss of the lactam oxygen together with one hydrogen atom. In the spectra of the deuterated mitra-

phyllines (IVa, b, c), this peak is shifted to M-18, and since the C_3-deuterium is the only one common to these three deuterated analogs, it must be the one that is lost during this fragmentation. Possibly, the energy gained by forming species f is the driving force for the rearrangment involved in this fragmentation, although no obvious mechanism can be proposed with the information presently in hand.

The most intense ion in the spectrum (Fig. 2) of mitraphylline (Ia) occurs at *m/e* 223 and must be derived from the alicyclic portion of the molecule, since the same strong peak is also noted in the mass spectra (*e.g.*, Fig. 3) of aricine oxindole (Ib) and carapanaubine (*i.e.*, isoreserpiline oxindole) (Ic), which possess one and two methoxyl groups in the aromatic ring, respectively. The most plausible representation is the following, the *m/e* 223 fragment being represented by the ion g.

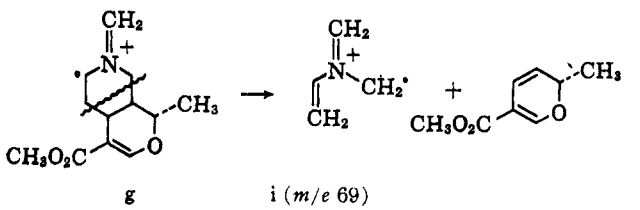


h (*m/e* 208)

This supposition is fully confirmed by the mass spectra of the deuterated analogs. Thus, the spectrum of the 3,5,6-d_3-mitraphylline (IVc) shows a two-mass unit shift to *m/e* 225 in accordance with formulation g in which carbon atoms 3 and 5, but not 6, are retained. Similarly, the *m/e* 223 peak is split between *m/e* 224 and *m/e* 225 in the mass spectrum of the 3-d_1-(IVa) and 3,14-d_2-(IVb) mixture, both deuterium atoms being retained in this instance.

The intense *m/e* 223 fragment is accompanied by a less abundant one, fifteen mass units lower (*m/e* 208) which, just like the g fragment, is shifted to *m/e* 210 in the 3,5,6-d_3-mitraphylline (IVc) spectrum and to *m/e* 209 and 210 in the 3-d_1-(IVa) and 3,14-d_2-(IVb) mixture. The most obvious candidate for this further loss of a methyl group (no metastable peak corresponding to this transition could be observed) is the substituent at C_{19}, the resulting fragment h being stabilized by the electrons of the ether oxygen.

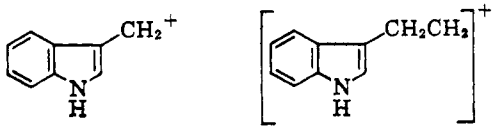
A second intense fragment, evidently formed by further decomposition of g, is one at *m/e* 69, for which structure i can be proposed unambiguously. This formulation follows from its shift to *m/e* 71 in the 3,5,6-d_3-mitraphylline (IVc) spectrum and its distribution between *m/e* 70 and 71 in the mass spectrum of the 3-d_1-(IVa) and 3,14-d_2-(IVb) mixture, thus showing that carbon atoms 3, 5 and 14, but not 6, are contained in it. The formation of i is easily visualized by cleavage (wavy line in g) of the 14–15 and 20–21 bonds with simultaneous generation of a neutral diene.



g i (*m/e* 69)

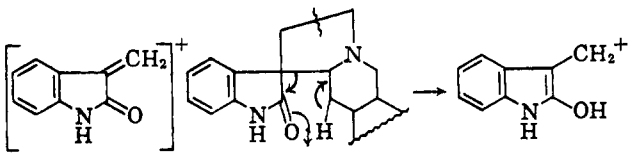
Fragments containing the indole moiety are found (Fig. 2) at *m/e* 130, 144–146 and at *m/e* 159. These assignments are unequivocal because of an observed shift of 30 mass units in the aricine oxindole (Ib) spectrum and of 60 mass units in that (Fig. 3; *m/e* 190, 204–206, 219) of carapanaubine (= isoreserpiline oxindole) (Ic) due to the additional methoxyl functions in the aromatic ring. A fragment of mass 130 is found commonly[1,17] in the mass spectra of indole and dihydroindole alkaloids and can be represented by species j. This *m/e* 130 peak is split between *m/e* 131 and 132 in the 3,5,6-d_3-mitraphylline (IVc) spectrum, while in the spectrum of the 3-d_1-(IVa) and 3,14-d_2-(IVb) mixture, it is largely retained at *m/e* 130 with only a partial shift to *m/e* 131. This suggests retention in fragment j of the C_6-deuterium atom, while the rearranged one (C_2 in j) is apparently transferred from different carbon atoms, a situation reminiscent of the occurrence of nonspecific hydrogen transfers among α-decalones.[18]

The *m/e* 130 indole peak in indole or dihydroindole alkaloids (unsubstituted in the aromatic ring) is usually accompanied[1,17] by one at *m/e* 144, which generally may be represented by species k. This *m/e* 144 peak is also found (Fig. 2) in the mitraphylline (Ia) spectrum, remains unchanged upon deuterium labeling at C_3 (IVa) and C_{14} (IVb), but is shifted partially[19] to *m/e* 145 in the 3,5,6-d_3-mitraphylline (IVc) spectrum. Since the formation of an ion such as k from mitraphylline (Ia) requires extensive rearrangement, it is a moot point whether the spectra of the deuterated analogs can be considered to offer any support for structure k. Especially puzzling is the observation that introduction of three deuterium atoms (IVc) still leaves recognizable a *m/e* 144 peak, the structure and formation of which is difficult to visualize.



j (*m/e* 130) k (*m/e* 144)

Plausible representations for the *m/e* 145 and 146 peaks are l and m, the former being produced in the manner indicated above for g, and the latter by the following path. The extensive spread of this series of peaks over the range *m/e* 144–147 in the spectra of the deuterated species makes it impossible to provide proof or disproof for these postulates.



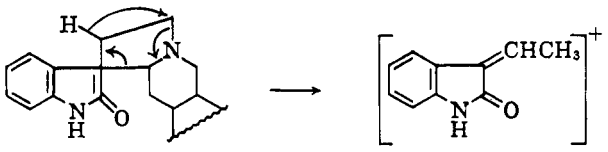
l (*m/e* 145) m (*m/e* 146)

The remaining peak for which the presence of an oxindole moiety was demonstrated (see peak n in Fig. 2 and 3) occurs at *m/e* 159. Here the situation is much clearer since a shift to *m/e* 161 is observed in the 3,5,6-d_3-analog IVc while no shift is noted upon deuteration at C_3 (IVa) or C_{14} (IVb). It follows, therefore, that the tryptamine bridge is retained and a reasonable representation for this fragment n and its genesis is

(17) See, for instance, K. Biemann, "Mass Spectrometry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, Chapter 8.

(18) E. Lund, H. Budzikiewicz, J. M. Wilson and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 941 (1963).

(19) Only qualitative statements are possible in this instance, because the presence of three relevant peaks (*m/e* 144, 145, 146) in the parent spectrum (Fig. 2) makes it impossible to follow exactly the shifts incident to deuteration.

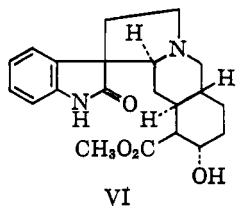


n (*m/e* 159)

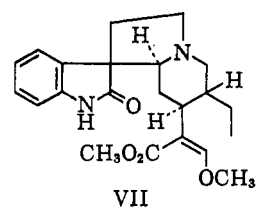
From a diagnostic standpoint, cleavage of the spiran ring to generate fragment g is by far the most characteristic feature of the oxindole alkaloids and other fragmentations in the high mass range occur to only a small extent. Aside from the above-mentioned small M–OH peak, there can also be noted (see Fig. 2 and 3) M–CH_3 and M–OCH_3 peaks in the mass spectra of the oxindoles Ia, Ib and Ic.

Yohimbine oxindole B (VI)[11] and rhyncophylline (VII)[20] represent interesting examples of oxindoles differing from mitraphylline (Ia) in the nature of the E ring rather than the aromatic portion. Their mass spectra are reproduced in Fig. 4 and 5, and again it may be noted that the most characteristic peak (g) is due to the cleavage of the spiran ring, thus demonstrating that this type of fragmentation can be employed for purposes of recognizing a variety of differently substituted oxindole alkaloids. The indole fragments j, k, l, m and n occur at the same positions (*m/e* 130, 144–146, 159) as had already been noted in the mass spectrum (Fig. 2) of mitraphylline, but the latter's intense *m/e* 69 (i) fragment is much weaker in the yohimbine oxindole spectrum (Fig. 4). This is reasonable, since rupture of the 14–15 bond is not favored by allylic activation, a feature which is again possible in rhyncophilline (VII) and thus leads again (Fig. 5) to a more intense *m/e* 69 ion.

In the yohimbine oxindole spectrum (Fig. 4), there is present a moderately intense peak at *m/e* 207, which is best explained by dehydration of the C_{17}-hydroxyl group in fragment g, although no metastable peak could be observed for this transition. The h peak (*m/e* 208 in Fig. 2) of mitraphylline (Ia), due to the loss of the methyl group from fragment g, is absent in accordance with expectation. The high mass range of the spectrum (Fig. 4) shows, in addition to the M–OH and M–OCH_3 peak, a weak fragment (*m/e* 311) corresponding to the loss of the carbomethoxy group, this type of cleavage being inhibited in mitraphylline (Ia) by the presence of the additional double bond.



VI



VII

The only other noteworthy features in the rhyncophylline spectrum (Fig. 5) are the loss of the elements of methyl (*m/e* 224), ethyl (*m/e* 210) and methoxyl (*m/e* 208) from the principal ion g (*m/e* 239), as well as from the molecular ion.

The above discussion of the mass spectra of oxindole alkaloids demonstrates that the mass spectrum offers a simple and highly characteristic criterion for membership among the oxindole class of alkaloids. Since the mass spectrum (Fig. 3) of the new Aspidosperma alkaloid carapanaubine exhibited all of the characteristic features of such oxindole alkaloids and since the n.m.r. spectrum (Table I) indicated close resemblance to isoreserpiline (IIb), it was reasonable to assign structure Ib to the alkaloid. This conclusion was verified completely by partial synthesis from isoreserpiline (IIb) as is described in the accompanying article.[13]

(20) J. C. Seaton and L. Marion, *Can. J. Chem.*, **35**, 1102 (1957).

Experimental[21]

Isolation of Carapanaubine (Ic).—The dried ground bark (14.2 kg.) of *Aspidosperma carapanauba* M. Pichon[22] was extracted exhaustively with boiling ethanol, and the solvent removed *in vacuo*. The resulting resin was dissolved in 2.5 l. of 10% acetic acid and extracted successively with petroleum ether (1.25 l.), benzene (1 l.) and chloroform (1.5 l.). The chloroform solution was concentrated at 30° and the resulting resinous residue (14.7 g.) was chromatographed on 138 g. of silica gel, carapanaubine (Ic) (0.49 g., m.p. 215–220°) being eluted with chloroform. Recrystallization from ethyl acetate–hexane and aqueous ethanol provided the analytical specimen, m.p. 221–223°, $[\alpha]^{30}D$ −101° (*c* 1.0, chloroform); λ_{max}^{Nujol} 3.09, 5.90, 5.99 and 6.15 μ. The ultraviolet absorption spectrum showed λ_{max}^{EtOH} 215 and 244 mμ (log ε 4.57, 4.23); λ_{infl}^{EtOH} 278, 300 mμ (3.80, 3.66); λ_{min}^{EtOH} 238 mμ (4.21); $\lambda_{max}^{EtOH-HCl}$ 222 and 278 mμ (4.56, 3.79); $\lambda_{infl}^{EtOH-HCl}$ 246 and 300 mμ (4.15, 3.61); and $\lambda_{min}^{EtOH-HCl}$ 263 mμ (3.72).

Anal. Calcd. for $C_{23}H_{28}N_2O_6$: C, 64.47; H, 6.59; N, 6.54; 3OCH_3, 21.73; C–CH_3, 3.51; mol. wt., 428.5. Found: C, 64.04; H, 6.76; N, 6.35; OCH_3, 21.24; C–CH_3, 3.89; mol. wt., 428 (mass spec.).

3-Dehydroajmalicine Hydrochloride.—Serpentine (500 mg.) was dissolved in methanol (10 ml.), and the solution cooled in ice. Sodium borohydride was added portionwise with shaking until the color faded to pale yellow. Completion of reaction was checked by qualitative ultraviolet. The reaction was diluted with water and extracted (methylene chloride). Removal of the solvent gave a foam (480 mg.) which was redissolved in methylene chloride (50 ml.). Triethylamine (0.2 ml.) and *t*-butyl hypochlorite (5.2 ml. of 0.265 *M* soln. in CCl_4) were added to the cooled (ice) solution. After stirring for ten minutes, the reaction mixture was washed with water and taken to dryness. The resulting foam was dissolved in methanolic HCl (10 ml. of 1 *N*) and warmed on a water bath for 5 min. Qualitative ultraviolet analysis showed complete conversion (λ_{max} 284 → λ_{max} 354 mμ). Ether was added to the hot solution until a cloudiness persisted; on cooling, yellow crystals separated (300 mg.), m.p. 270–274° dec.; λ_{max}^{EtOH} 236–239 mμ (18,870), 354–358 mμ (21,490); ν_{max}^{Nujol} 1710, 1648 $cm.^{-1}$.

Anal. Calcd. for $C_{21}H_{23}N_2O_3Cl$: C, 65.19; H, 5.99; N, 7.24. Found: C, 64.88; H, 6.21; N, 7.23.

3-Deuterio- (Va) and 3,14-Dideuterio- (Vb) ajmalicine.—3-Dehydroajmalicine hydrochloride (472 mg.) was dried (2 hr., 100°, 0.1 mm.) and dissolved by warming in deuteriomethanol (7 ml.). A slurry of sodium borodeuteride[15] in dry tetrahydrofuran was added dropwise with shaking until the color was discharged (10–15 minutes). Completion of the reaction was checked by qualitative ultraviolet (λ_{max} 354 → 290 mμ). The mixture diluted with water and extracted. The resulting foam (414 mg.) was recrystallized from methanol to yield 290 mg., m.p. 250–253°.

Since the mass spectrum[15] of ajmalicine exhibits a strong M-1 peak, which is not completely shifted to M-2 in the deuterated analogs, the actual composition of this material had to be determined by measuring low voltage spectra and was found to consist of 15% d_0, 42% d_1 and 43% d_2 species.

Deuterated Mitraphyllines (IVa, b, c).—The above-described mixture of 3-d_1 (Va) and 3,14-d_2- (Vb) ajmalicine or 3,5,6-d_3-ajmalicine (III)[15] was subjected to the chlorination and base treatment procedure exactly as described earlier[11] for ajmalicine itself. The resulting labeled mitraphylline specimens were recrystallized from methanol to m.p. 272–274° and were found by mass spectrometry to contain the same amount of deuterium as the ajmalicine precursors (III and Va + Vb).

Aricine Oxindole (Ib).—Aricine (1 g.) was oxidized by lead tetraacetate in the usual manner.[13] By chromatography on alumina and recrystallization from methanol, the acetoxyindolenine (321 mg.) was obtained, m.p. 185–187°, $[\alpha]^{26}D$ +140° (*c* 0.8, chloroform); $\nu_{max}^{CHCl_3}$ 1745, 1700, 1626 $cm.^{-1}$; λ_{max}^{EtOH} 227–230 mμ (4.35), 291 mμ (3.83).

Anal. Calcd. for $C_{24}H_{28}N_2O_5 \cdot CH_3OH$: C, 65.77; H, 7.07; N, 6.14. Found: C, 65.42; H, 6.68; N, 6.45.

A portion (210 mg.) was rearranged in the usual manner.[13] The material eluted by 1% methanol in methylene chloride from neutral III alumina (111 mg.) was separated by preparative thin-layer chromatography. The principal band (45 mg.) was recrystallized from aqueous methanol to give aricine oxindole,

(21) Melting points were determined on a Kofler block and in a Thomas "Hoover" capillary melting point apparatus. They are uncorrected. The microanalyses were obtained in part by Messrs. E. Meier and J. Consulo (Stanford University), Dr. A. Bernhardt (Mulheim), and Mr. L. Dorfman and his staff (CIBA Pharmaceutical Co.).

(22) We are indebted to Dr. William Rodriques (Instituto National de Pesquisas da Amazonia) near Manaus, Brazil, for the collection of this material.

m.p. 155–157°, $\nu_{max}^{CHCl_3}$ 1710, 1635 cm.$^{-1}$; λ_{max}^{EtOH} 248 mμ (4.22), 303 mμ (3.34).

Anal. Calcd. for $C_{22}H_{26}N_2O_5$: C, 66.31; H, 6.58. Found: C, 66.05; H, 6.71.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STANFORD UNIVERSITY, STANFORD, CALIF.]

Mass Spectrometry in Structural and Stereochemical Problems. XXI.[1] Fragmentation and Hydrogen Transfer Reactions after Electron Impact on β-Decalones[2]

BY E. LUND,[3] H. BUDZIKIEWICZ, J. M. WILSON AND CARL DJERASSI

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The mass spectra of a variety of *trans*- and *cis*-β-decalones together with their deuterated analogs have been measured in order to determine the principal fragmentation modes as well as to examine the occurrence of hydrogen transfer reactions. A comparison of the present results with those of the earlier recorded[4] α-decalone mass spectra show very distinct differences, which are of diagnostic value and which are discussed in detail. In contrast to α-decalones, where the stereochemistry of the ring juncture played an important role, both *trans*- and *cis*-β-decalones exhibit very similar mass spectral fragmentation patterns.

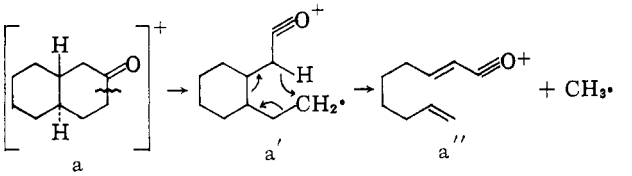
In an earlier paper[4] there was discussed in detail the synthesis and mass spectral fragmentation behavior of a substantial number of deuterated analogs of *trans*- and *cis*-α-decalone, this information being desired as a model for the evaluation of the fragmentation processes observed in polycyclic ketones such as steroids.[5] For this same purpose, it will also be necessary to know the intimate details of the mass spectral fragmentation patterns of β-decalones and of hydrindanones and the present article is concerned with the former group of compounds.

The mass spectra of only two members of this class—*trans*-(I) and *cis*-β-decalone—have been reported in the literature.[6] These measurements were performed with a double-focusing instrument and while no interpretation in terms of fragmentation processes was attempted, the results are nevertheless of considerable importance as the high resolution of the instrument permitted an unequivocal decision regarding the empirical formula of contributing species to a given peak (*e.g.*, *m/e* 55 being made up of $C_4H_7^+$ and $C_3H_3O^+$, while *m/e* 79 consisted only of $C_6H_7^+$ and no $C_5H_3O^+$). As shown below, this information together with observations about the presence or absence of peak shifts upon introduction of labels such as deuterium or methyl offered valuable information about the principal fragmentation modes and hydrogen transfer reactions.

Angularly Unsubstituted β-Decalones

The mass spectra of *trans*- and *cis*-β-decalone are very similar,[6] only slight intensity differences being observed, and our discussion will be limited, therefore, to the spectrum (Fig. 1) of the *trans* isomer I, which will be contrasted with that (Fig. 2) of its 1,1,3,3-d_4-analog II.[7]

Peak M-15 (*m/e* **137 in Fig. 1**).—This fragment is considerably more abundant than in α-decalone[4] and is due to the loss of methyl. In the spectrum (Fig. 2) of the d_4-analog II, this peak shifts to M-18, demonstrating that the CD_3 radical is lost. This observation is readily accommodated by the following mechanism, which involves first the usual[8] cleavage (a) of the C—C=O bond (wavy line) followed by loss of methyl in a six-membered transition state (a′) to pro-



vide the conjugated ion a″. It is interesting to note that this M-15 peak becomes much less pronounced in the mass spectra (Fig. 3 and 4) of the 3-methyl (III) and 1-methyl (V) homologs, and is not shifted to any appreciable extent in the deuterated analogs IV and VI. It cannot be stated unambiguously that instead there is occurring a loss of an ethyl radical, since the unsubstituted β-decalone (I) itself exhibits a significant M-29 peak (Fig. 1).

Peak M-18 (*m/e* **134 in Fig. 1**).—In the α-decalone series, this loss of water has been shown[4] to involve hydrogen atoms from all parts of the molecule. The same statement seems to apply to *trans*-β-decalone (I), where a partial shift to M-19 is noted in the spectrum (Fig. 2) of the d_4-derivative II. Such partial movements to M-19 were also observed in the mass spectra of d_3-3-methyl-(IV) and d_3-1-methyl-(VI) *trans*-decalone-2.

Peak M-29 (*m/e* **123 in Fig. 1**) **and M-28** (*m/e* **138 in Fig. 3 and 4**).—The double-focusing spectrum[6] demonstrates that the M-29 peak is made up of two species, the predominant one being M–C_2H_5 and the remainder (rather insignificant in the *cis* isomer) representing M–CHO. Since this M-29 fragment remains largely M-29 in the spectrum (Fig. 2) of the d_4-analog, the M-29 moiety must be derived from the non-oxygenated ring, an observation which has already been established earlier[4] in the α-decalone series by deuterium labeling in that ring.

An accompanying M-28 peak is relatively small in the β-decalone spectrum (*m/e* 124 in Fig. 1), but this becomes much more important in the spectra (*m/e*

(1) Paper XX, B. Gilbert, J. A. Brissolese, N. Finch, W. I. Taylor, H. Budzikiewicz, J. M. Wilson and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 1523 (1963).

(2) Acknowledgment is made to the National Institutes of Health of the U. S. Public Health Service for financial support (grants No. CRTY-5061 and A-4257).

(3) Taken from part II of the Ph.D. dissertation of E. Lund, Stanford University, 1963. The mass spectra of the various deuterated analogs (*e.g.*, Table I) are reproduced in the thesis.

(4) E. Lund, H. Budzikiewicz, J. M. Wilson and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 441 (1963).

(5) (a) H. Budzikiewicz and C. Djerassi, *ibid.*, **84**, 1430 (1962); (b) C. Djerassi, J. M. Wilson, H. Budzikiewicz and J. W. Chamberlin, *ibid.*, **84**, 4544 (1962); (c) H. Budzikiewicz, J. M. Wilson and C. Djerassi, *Monatsh.*, **93**, 1033 (1962).

(6) J. H. Beynon, R. A. Saunders and A. E. Williams, *Appl. Spectry.*, **14**, 95 (1960).

(7) For reasons which are outlined in our earlier paper (ref. 4), such comparisons with polydeuterated labeled derivatives will often afford only qualitative information. This is of no particular disadvantage, since in our present studies we are only concerned with a discussion of the principal fragmentation processes. Another problem to be considered in quantitative studies is the fact that deuterium in equilibratable positions may partially exchange with the water vapor in the inlet system. Thus when the mass spectrum of α-decalone was measured in an inlet system, which had first been exposed to deuterium oxide vapor, there was observed over 10% of an M + 1 species.

(8) A. G. Sharkey, J. L. Shultz and R. A. Friedel, *Anal. Chem.*, **28**, 934 (1956).