Table V

Fraction	Volume, ml.	Compd.	Amount, mg.
A	260	None	
B	168	Adenine	264
C	48	Adenine + IX	
D	40	IX	7
E	68	IX + XVIII	
F	112	XVIII	100
G	160	Impure XVIII	

tracted twice with 30% potassium iodide solution (400 ml.), then with water (1600 ml.), dried over anhydrous magnesium sulfate, treated with Norite, filtered, and evaporated to dryness *in vacuo*. The resulting dark brown syrup was dissolved in methanol (60 ml.) containing 1 *N* methanolic sodium methoxide (4 ml.), and the solution was refluxed for 0.5 hr. Water (20 ml.) was added to the cold solution, which was then treated batchwise with Rexyn RG50 resin (pyridinium form) until neutral. The neutral solution plus the water–methanol wash of the resin was evaporated to dryness and the residue was extracted three times with boiling water (100-ml. portions). The cold, aqueous solution was extracted several times with ether and the residual ether was removed by aspiration. The aqueous solution was then added to a suspension of 5% palladium on charcoal (2.8 g.) in 20 ml. of water. Hydrogenation was carried out at 50 p.s.i. and 80° for about 16 hr. The catalyst was removed by filtration before the solution was evaporated to dryness *in vacuo*. The residue was transferred to the top of a Whatman cellulose column (4 × 45 cm.) with 140 ml. of water-saturated butanol and the fractions obtained are reported in Table V.

Fraction F was evaporated to dryness *in vacuo* and, since the residue could not be induced to crystallize, it was dissolved in water and a saturated solution of picric acid added. The crystalline picrate that formed was removed by filtration and dissolved in water. Treatment of this solution with Dowex 1 (CO_3^{2-} form) regenerated the free nucleoside (XVIII), which crystallized on concentration of the aqueous solution: yield 21 mg.; m.p. 220–222°[37]; $[\alpha]^{25}D$ 0° (0.397 g./100 ml. of H_2O); τ (p.p.m.), 6.38 m (H-5′), 5.82 m (H-2′, H-3′, H-4′), 5.08 t (O-5′H), 4.78 and 4.38 (O-2′H and O-3′H), 3.66 (H-1′), 3.17 (NH_2), 1.81 (H-8), and 1.59 (H-2).

Anal. Calcd. for $C_{10}H_{13}N_4O_4$: C, 44.98; H, 4.93; N, 26.23. Found: C, 45.06; H, 5.13; N, 26.62.

A second reaction using 21.9 g. of VII gave a mixture that was chromatographed on a longer cellulose column (4 × 90 cm.), which gave a clean separation of the isomers. From this reaction there was obtained 236 mg. of the β-anomer (IX), 400 mg. of the α-anomer (XVIII), and 2.00 g. of adenine. These amounts indicate a 8% conversion of VII to the β-anomer and 14% conversion to the α-anomer.

Following the procedure of Khorana[25] both the α- and β-anomers were oxidized in aqueous solution with metaperiodate and the resulting dialdehydes reduced, without isolation, with sodium borohydride. The rotation ($[\alpha]^{21}D$) of the product from the α-anomer (XVIII) was −117.9 ± 0.2° (0.4330 g./100 ml. of original sample) and that of the product from the β-anomer (IX) was +118.1 ± 0.2° (0.4197 g./100 ml. of original sample).

Acknowledgment. The authors are indebted to Dr. W. J. Barrett and members of the analytical chemistry section of this institute who performed the spectral and analytical determinations reported herein and to Mrs. S. Clayton for technical assistance.

(37) The reported melting point of the nucleoside from pseudovitamin B_{12} is 218–222°.[5]

Thermal Methyl Transfer. The Mass Spectrum of Voacamine-d_3[1]

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Contribution from the Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts. *Received August 9, 1965*

The thermally induced intermolecular methyl transfer which can lead to the appearance of higher homologs in the mass spectrum of voacamine (I) and related compounds has been investigated using voacamine-d_3 (IV). The mass spectrum of IV demonstrates that the methyl group of the voacangine carbomethoxy group is transferred to the basic nitrogen of the vobasinol moiety. The structural requirements for this reaction, which could lead to a misassignment of a molecular weight, are shown to be the simultaneous presence of a methylating group (such as carbomethoxy) and an alkylatable group (such as a basic nitrogen) in a molecule of very low volatility. A method was developed for the preparation of trideuteriomethyl esters with high deuterium content.

Mass spectrometry is generally considered the best method for the determination of molecular weights because if the molecular ion is sufficiently stable, it will be detected as the peak of highest mass in the spectrum (disregarding isotope peaks). However, two situations are known in which the peak of highest mass does not correspond to the molecular weight. When the molecular ion lacks sufficient stability to give rise to a detectable peak, the ion of highest mass will originate by

(1) Part XXXIII of the series "Application of Mass Spectrometry to Structure Problems." For part XXXII see H. Achenbach and K. Biemann, *J. Am. Chem. Soc.*, 87, 4944 (1965).

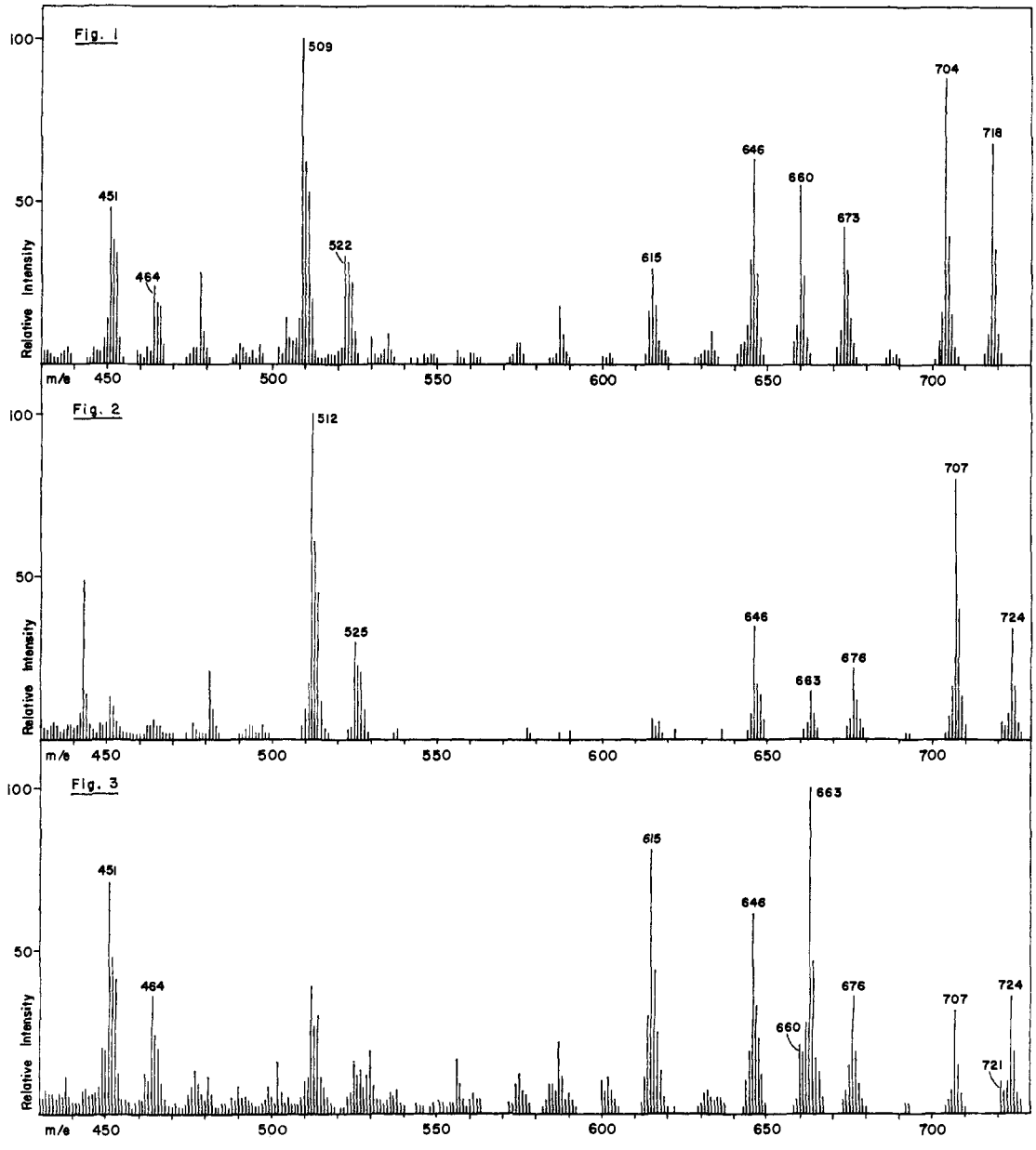


Figure 1. Mass spectrum of natural voacamine (I).
Figure 2. Mass spectrum of voacamine-d_3 (IV); vaporization temperature 200°.
Figure 3. Mass spectrum of voacamine-d_3 (IV); vaporization temperature 210°.

fragmentation of the molecular ion, thus being smaller than the molecular weight. The second exception is the occurrence of peaks with masses higher than the molecular weight, due to ion–molecule collisions. (The most common are M + H ions, but M + CHO, M + CH_3CO, M + CH_3CN, and even an M + 25 ion of unknown origin have also been observed.[2]) Several techniques are available for the recognition of these exceptions and for the consequent determination of the correct molecular weight.[3]

Recently, it was found that the mass spectra of several dimeric indole alkaloids showed major peaks 14 and even 28 mass units greater than the expected molecular weights. Thus, voacamine (mol. wt. 704) gave a peak at *m/e* 718,[4-6] and the spectrum of vinblastine (mol. wt. 810) exhibited ions of 824 and 838 mass units.[7] The intensities of these peaks relative to the M^+ peak varied with vaporization temperature, but were not a function of the sample pressure and thus were not due to ion–molecule collisions.

In order to restore the confidence to be placed in the reliability of the mass spectrometric determination of molecular weights we found it necessary to elucidate the origin of these anomalous peaks and to delineate the experimental conditions and structural characteristics which may lead to their formation. For this purpose,

(2) (a) J. H. Beynon, G. R. Lester, R. A. Saunders, and A. E. Williams, "Advances in Mass Spectrometry," Vol. 2, R. M. Elliott, Ed., Pergamon Press Ltd., London, 1963, p. 337; (b) D. C. DeJongh and K. Biemann, *J. Am. Chem. Soc.*, 85, 2289 (1963); (c) F. W. McLafferty, *Anal. Chem.*, 28, 306 (1956).

(3) K. Biemann, "Mass Spectrometry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, Chapter 3.

(4) G. Büchi, R. E. Manning, and S. A. Monti, *J. Am. Chem. Soc.*, 85, 1893 (1963).

(5) G. Büchi, R. E. Manning, and S. A. Monti, *ibid.*, 86, 4631 (1964).

(6) H. Budzikiewicz, C. Djerassi, F. Pusieux, F. Percheron, and J. Poisson, *Bull. soc. chim. France*, 1899 (1963).

(7) P. Bommer, W. McMurray, and K. Biemann, *J. Am. Chem. Soc.*, 86, 1439 (1964).

we undertook a detailed investigation of the behavior of voacamine (I) in the mass spectrometer and the results are the subject of this paper.

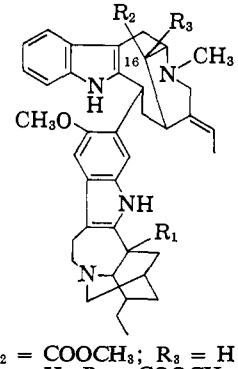
The possibility that the ion of mass 704 in the voacamine spectrum (Figure 1) is a fragment of a molecular ion at *m/e* 718 may be ruled out, since loss of 14 mass units (CH_2) is very unlikely and has never been observed. The remaining alternative is that *m/e* 704 is the molecular ion, and the peak at *m/e* 718 is either a ketonic impurity or a higher homolog.

Examination of a high-resolution mass spectrum of natural voacamine ($C_{43}H_{52}N_4O_5$) revealed a doublet at *m/e* 718. Thus an oxygenated impurity, $C_{43}H_{50}N_4O_6$ (found, 718.3733; calcd., 718.3730), was present. However, its contribution to the total M + 14 species was small; the major portion of the peak was due to a higher homolog, $C_{44}H_{54}N_4O_5$ (found, 718.4094; calcd., 718.4094).

A mass spectrum of voacamine obtained within a few minutes after sample introduction contained no peaks above mass 550 which were greater than 5% of the intensity of the molecular ion at *m/e* 704. Therefore, none of the peaks in this mass region, which appeared later and are already visible in the spectrum of Figure 1, are due to the fragmentation of voacamine; any electron-induced fragmentation gives a spectrum which remains constant, independent of time and sample temperature (at constant ion source temperature). Similarly, vinblastine had been shown to thermally produce higher homologs.[7]

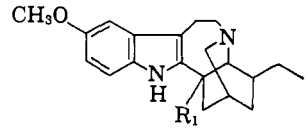
A sequence of thermal reactions, occurring in the mass spectrometer prior to ionization, has been suggested to account for the M + 14 peak, as well as the other major peaks of the upper mass region of the voacamine spectrum.[5] According to this hypothesis, an intermolecular methyl transfer occurs to produce two new species, each of which may undergo further thermal reactions, Hofmann elimination and decarboxylation, respectively.

Several observations suggested that the major source of the transferred methyl group might be the carbomethoxy group R_1 of voacamine (I). The mass spectrum of voacamine has a peak at *m/e* 646 which could

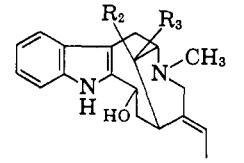


I, $R_1 = R_2 = COOCH_3$; $R_3 = H$
II, $R_1 = R_3 = H$; $R_2 = COOCH_3$
III, $R_1 = R_2 = H$; $R_3 = COOCH_3$
IV, $R_1 = COOCD_3$; $R_2 = COOCH_3$; $R_3 = H$

originate by decarboxylation of the species which donated the methyl group. That the carbomethoxy group lost is R_1 rather than R_2 is shown by an intense peak at *m/e* 149. Initially predominant is *m/e* 148, a major ion in the fragmentation of voacangine (V)[6] which is part of the voacamine molecule (I). However,



V, $R_1 = COOCH_3$
VI, $R_1 = H$
VII, $R_1 = COOH$
VIII, $R_1 = COOCD_3$



IX, $R_2 = COOCH_3$; $R_3 = H$

the related fragment from ibogaine (decarbomethoxyvoacangine, VI), *m/e* 149,[8] increases as pyrolysis proceeds. Another clue to the origin of the transferred methyl group was that the mass spectrum of decarbomethoxyvoacamine (II)[9] showed only a small M + 14, peak, even though its vaporization temperature was somewhat higher than that required for voacamine.

The proposed transmethylation process should be distinguishable from any other source for the *m/e* 718 ion (*e.g.*, contamination of the original sample with a higher homolog) if one or both of the carbomethoxy groups, R_1 and R_2, were labeled with deuterium. Two approaches were considered for effecting this labeling: (1) the incorporation of CD_3 groups into the dimer itself, or (2) the partial synthesis[5] of voacamine from vobasinol (IX) and labeled voacangine. Treatment of voacamine with base, followed by acid-catalyzed re-esterification leads to decarbomethoxyepivoacamine (III)[5] and can therefore not be used to produce labeled voacamine. Acid-catalyzed transmethylation, using CD_3OH, would avoid the problems of decarbomethoxylation and epimerization; however, preliminary experiments with voacangine (V) led to incorporation of CD_3 only at the aromatic methoxyl group, with no transesterification of the ester.

It was thus necessary to prepare labeled voacangine for use in the partial synthesis of voacamine. The potassium salt of voacangic acid (VII) was esterified with diazomethane in the presence of deuterium oxide and hydrochloric acid with the expectation to obtain a mixture of unlabeled and monodeuterated voacangine. Instead, the deuterium content varied from 0 to 3 deuterium atoms per molecule, all located at the carbomethoxy group. Partial exchange of diazomethane with either the acid or deuterium oxide must have occurred prior to esterification. After this work had been completed, a similar exchange was reported, including a method for the synthesis of up to 50% trideuterated esters[10] involving the slow addition of acid to diazomethane in dioxane–deuterium oxide as a solvent.

For the preparation of labeled voacamine, it was important to use highly deuterated material, because the object of this study was not merely to demonstrate the occurrence of pyrolytic intermolecular methyl transfer when heating voacamine into the ion source of the mass spectrometer, but to determine the specificity, if any, with respect to the two different carbomethoxy groups.

It seemed likely that the extent of deuteration of the method mentioned above could be increased by exchange of diazomethane before its addition to the or-

(8) K. Biemann and M. Friedmann-Spiteller, *J. Am. Chem. Soc.*, 83, 4805 (1961).

(9) Decarbomethoxyvoacamine (m.p. 223–228° dec.) was isolated in this laboratory from *Voacanga africana*, and its structure was confirmed by partial synthesis from ibogaine and vobasinol.

(10) K. J. Van Der Merwe, P. S. Steyn, and S. H. Eggers, *Tetrahedron Letters*, 3923 (1964).

ganic acid. A number of solvent systems were investigated for the exchange of diazomethane with deuterium oxide. In ether the exchange was very rapid, but its efficiency was reduced by the slow rate of equilibration of the deuterium oxide phase with the deuterium oxide dissolved in the ether phase. Attempts to increase this equilibration rate by stirring or shaking were unsatisfactory because they caused rapid decomposition of diazomethane.

Dioxane had the advantage that it is completely miscible with water, but the rate of exchange in this solvent was slow relative to the rate in ether. Up to 20% deuteration of diazomethane could easily be obtained. Longer reaction times led to higher deuterium incorporation, but this was accompanied by significant decomposition and consequent low yield of diazomethane.

The best solvent system was found to be a mixture of ether and tetrahydrofuran, in such proportions that the desired amount of deuterium oxide is completely soluble. The advantage of this solvent is the slow rate of decomposition of diazomethane, allowing the deuterium exchange to go to completion.

Since the exchange reaction is acid catalyzed, the most efficient catalyst should be acidic enough to result in a high rate of exchange, yet sufficiently weak that only little becomes methylated. Phenol seemed to be the best choice, giving up to 90% deuterium in the carbomethoxy group upon esterification of benzoic acid-O-*d*, a result indicating almost complete exchange of the diazomethane with the solvent system.

To obtain a higher yield, more than one exchange appeared necessary. We had previously discovered that preparation of partially deuterated diazomethane (67% D total) was accomplished very easily, with essentially no decomposition, by generating the compound from potassium hydroxide-*d*. This method, followed by the phenol-catalyzed deuterium oxide exchange, gave methyl esters containing 96% deuterium when used in the esterification of benzoic acid-O-*d*. The maximum deuterium content which could be expected in the absence of traces of water is 97%, due to hydrogen from unexchanged diazomethane and phenol. An even better yield could be expected if deuterated phenol were used. The yield of ester (methyl benzoate) in this method, determined using nondeuterated reagents, was 44%, based on the weight of nitrosomethylurea. This is considerably better than yields obtained with any other variation of the technique investigated, all of which were accompanied by extensive decomposition.

Having developed the method of incorporating deuterium into diazomethane, there remained the problem of using the product to esterify voacangic acid (VII) under conditions which excluded all exchangeable hydrogen. Since voacangic acid decarboxylates very readily to give ibogaine,[11] it could not be isolated prior to its esterification. Thus it was necessary to acidify the potassium salt of the acid either after or immediately before the addition of diazomethane. It was required that the compound used for this acidification be easily deuterated, soluble in a nonprotic organic solvent, and sufficiently acidic to react with the potassium salt. After unsuccessful attempts to use *p*-toluenesulfonic acid-O-*d*, benzoic acid-O-*d* was found to give good results.

For the preparation of voacangine-d_3 (VIII), partially deuterated diazomethane was generated and distilled from ether–potassium hydroxide-*d*. Tetrahydrofuran, deuterium oxide, and phenol-O-*d* were added to complete the exchange. The potassium salt of voacangic acid was added to the mixture, followed by 2 equiv. of benzoic acid-O-*d*. The product was separated into basic and neutral fractions. The basic fraction was crystallized to give labeled voacangine (33% yield), identified by its mass spectrum, and the neutral fraction consisted of a mixture of methyl benzoate-d_3 and anisole-d_3. The mass spectrum of VIII is in agreement with previously proposed fragmentation processes of voacangine.[6]

Table I lists the deuterium content of the labeled voacangine, corrected for the molecular ion distribution of natural voacangine. The observed 97% total deuterium content of the carbomethoxy group compares favorably with the theoretical yield of 98%, which is based on the hydrogen of residual unexchanged diazomethane and the unexchanged indole N–H of the voacangic acid potassium salt.

Table I. Deuterium Content of Voacangine-d_3 (VIII)

m/e		Rel. abundance, %	D, %
368	M − d_0	0	0
369	M − d_1	0	0
370	M − d_2	8.3	5.5
371	M − d_3	91.7	91.7
		Total	97.2

The methyl benzoate-d_3 isolated from the reaction mixture also contains 97% deuterium in the methyl group (92.5% d_3, 6.3% d_2, 0.5% d_1, 0% d_0), which confirms the calculations for voacangine-d_3.

Voacamine-d_3 (IV) was synthesized by condensation of voacangine-d_3 (VIII) and vobasinol (IX) in 2% methanolic hydrochloric acid, under conditions similar to those used by Büchi, *et al.*[5] The reaction product after chromatography gave a 48% yield of crystalline voacamine-d_3. Its infrared spectrum resembled that of natural voacamine except for minor changes due to the deuterium content. The mass spectra at various degrees of pyrolysis (Figures 2 and 3) are similar to the spectrum of unlabeled voacamine (Figure 1) with appropriate shifts of peaks. Figure 4 outlines both pyrolysis reactions and electron-induced fragmentations of voacamine-d_3 to account for all major peaks in the mass region above *m/e* 450.

The molecular ion of the labeled voacamine appears as a singlet at *m/e* 707, indicating the expected trideuterated compound of very high purity. *The former M + 14 peak appears now at m/e 724 (M + 17), requiring intermolecular thermal transmethylation involving the specific transfer of the methyl group of the voacangine carbomethoxy group* (R_1 *in I*). There is a small but significant peak at *m/e* 721 (M + 14) due to transfer of an unlabeled methyl group, probably from the vobasinol carbomethoxy group R_2. This *m/e*

(11) F. Percheron, *Ann. Chim.*, 4, 303 (1959).

721 peak increases slightly with respect to *m/e* 724 as pyrolysis proceeds, but it never exceeds about 20% of the total transmethylation product.

The data also indicate that the transmethylation proceeds by transfer of a methyl group to the vobasinol moiety. The peak at *m/e* 676 in the spectrum of IV (Figures 2 and 3) points to the alicyclic nitrogen as the methyl acceptor, based on the following argument. In unlabeled voacamine, the corresponding peak at *m/e* 673 might at first be thought to have originated by loss of OCH_3 from the molecular ion at *m/e* 704, as suggested by Budzikiewicz, *et al.*[6] This is, however, in contradiction to the observation that *m/e* 673 is a pyrolysis product which increases in intensity with sample temperature. The elemental composition of $C_{42}H_{47}N_3O_5$ (found, 673.3506; calcd., 673.3516), determined by high-resolution mass spectrometry, corresponds to loss of $(CH_3)_2NH$ from the M + 14 transmethylation product. Since the peak at *m/e* 673 is completely shifted to *m/e* 676 (rather than becoming a doublet at *m/e* 673/676 resembling the M + 14 doublet at *m/e* 721/724), the group $N(CH_3)(CD_3)$ must be present in the transmethylation product. The nitrogen of the piperidine moiety of vobasinol is the only site for such a group, which could originate by the transmethylation and Hofmann elimination indicated in Figure 4.

The molecules which act as methyl donors may subsequently become decarboxylated. Thus voacamine itself forms decarbomethoxyvoacamine (II), mass 646. This pyrolytic species still appears at *m/e* 646 in the spectrum (Figures 2 and 3) of trideuterated voacamine (IV), since the labeled group R_1 is lost rather than the second carbomethoxy group R_2. The compound of mass 660 may originate in a similar manner by the decarbomethoxylation of an M + 14 molecule, or it may be a methylated form of the species of mass 646. The characteristic doublet at *m/e* 660/663 in the labeled compound proves that the CD_3 group of this ion was derived by transmethylation, rather than occurring as the original carbomethoxy group R_1.

The peak at *m/e* 615 may originate from the mass 660 compound in the same manner as *m/e* 673 was derived from *m/e* 718 (a second methylation followed by elimination of trimethylamine), or it may result by the decarbomethoxylation of *m/e* 673. Either route leads to the same structure, containing no labeled methyl groups.

Peaks at *m/e* 509 and 522 arise by loss from voacamine of fragments of the vobasinol moiety. Consequently the voacangine carbomethoxy group R_1 is present, and these peaks are each shifted three mass units to *m/e* 512 and 525 in voacamine-d_3. The pyrolysis product of mass 646 no longer contains the labeled group, and the corresponding peaks appear at *m/e* 451 and 464 in both natural and labeled voacamine.

The results of this study of the mass spectrum of voacamine may be generally applicable to mass spectra of other alkaloids of very low volatility and thus requiring heating to relatively high temperatures to effect vaporization. It appears that similar pyrolytic reactions may occur whenever a carbomethoxy group is present which may serve as a methyl donor, and a basic nitrogen is available to accept the transferred methyl group. Thus the following alkaloids all give M + 14 peaks: voacamine, decarbomethoxyvoacamine,

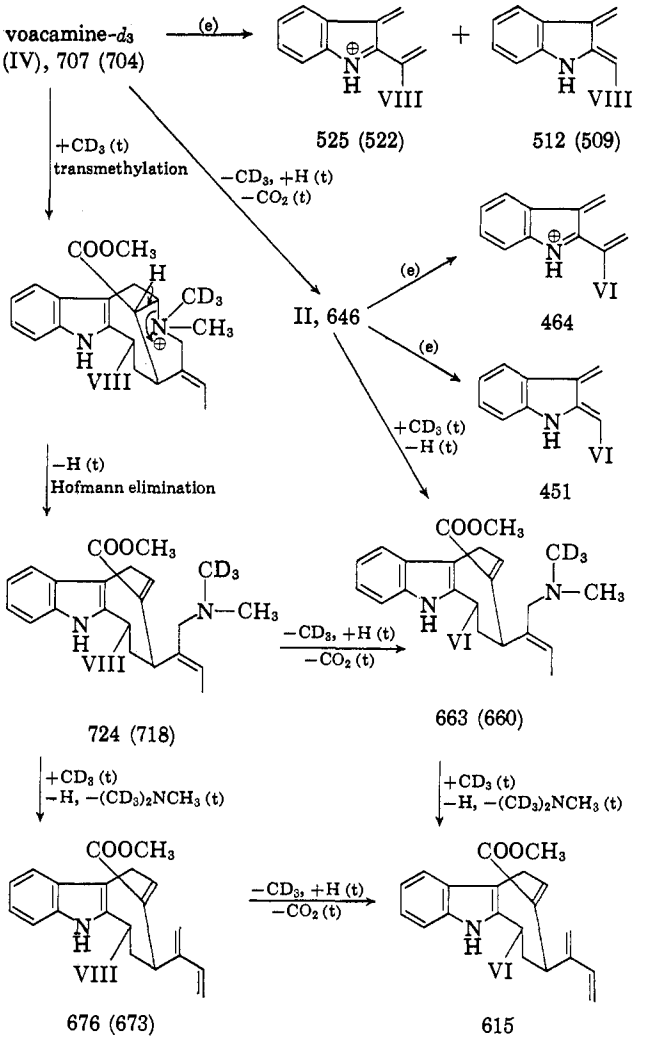


Figure 4. Mass spectral pyrolysis and fragmentation of voacamine-d_3. Masses in parentheses occur in the spectrum of natural voacamine. (t) indicates a pyrolysis reaction. and (e) an electron-induced fragmentation.

and the C-16 epimers of each, and vinblastine. Voacamine derivatives which lack carbomethoxy groups do not give rise to any transmethylation products.[5]

The closely related voacorine[5] (20-hydroxyvoacamine) behaves in a manner similar to that of voacamine. Dehydration occurs extremely readily, so the spectrum is essentially that of a dehydrovoacorine (mol. wt. 702) with its transmethylation product at *m/e* 716. All other peaks in the upper portion of the spectrum are also two mass units lower than the corresponding peaks in the spectrum of voacamine, and must be of similar origin.

Experimental Section[12]

Potassium Salt of Voacangic Acid (VII). Voacangine (V, 500 mg.) was refluxed for 22 hr. in 2 *N* methanolic potassium hydroxide (25 ml.). After evaporation nearly to dryness, 50 ml. of water was added and unreacted voacangine was removed by extracting twice

(12) Conventional mass spectra were determined with a CEC 21-103C mass spectrometer, equipped with an inlet system for the vaporization of samples directly into the ion source. Ionizing potential was 70 e.v. High-resolution mass spectra were determined with a CEC 21-110 mass spectrometer.

with 25 ml. of ether. Potassium hydroxide (5 g.) was added to the aqueous phase which was then extracted with three 25-ml. portions of chloroform. The chloroform extracts were combined, dried, and evaporated to give 475 mg. of the potassium salt of voacangic acid. The product was crystallized from tetrahydrofuran and dried under vacuum, m.p. 204–208°, $\nu_{max}^{CHCl_3}$ 1580 cm.$^{-1}$.

Benzoic Acid-O-d. Benzoyl chloride (2 ml.) was added to 0.5 ml. (excess) of deuterium oxide. After 2 days at room temperature, the crystalline benzoic acid-O-*d* was filtered, rinsed with deuterium oxide, and dried under vacuum.

Phenol-O-d. Phenol (5 g.) was dissolved in 10 ml. of hot deuterium oxide. The solution was cooled to room temperature and centrifuged. The upper phase was removed and distilled to give crystalline phenol-O-*d* on cooling.

Potassium Hydroxide-d. Potassium *t*-butoxide (5 g.) was dissolved in 3.1 ml. of deuterium oxide. The aqueous phase was removed and warmed to 80° under slight vacuum for about 1 hr. to remove any *t*-butyl alcohol, leaving a solution of approximately 50% potassium hydroxide-*d* in deuterium oxide.

Voacangine-d_3 (VIII). Nitrosomethylurea (0.6 g., dried at room temperature under vacuum) was added to 10 ml. of ether over 2 ml. of 50% potassium hydroxide-*d*. The partially deuterated (67% D) diazomethane was immediately distilled and added to 30 ml. of dry tetrahydrofuran which contained 2 ml. of deuterium oxide and 200 mg. of phenol-O-*d*. (All glassware and pipets were oven dried and cooled in a desiccator prior to use.) After 1 hr. at room temperature in darkness, 200 mg. of voacangic acid potassium salt was added. Benzoic acid-O-*d* (120 mg. in 0.5 ml. of tetrahydrofuran) was added gradually over 2 min. with gentle stirring. After 15 min. of continued stirring, the mixture was reduced to 5 ml. by evaporation under vacuum. Water (50 ml.) was added and the solution was extracted twice with 50 ml. of ether. Bases were isolated by extraction of the ether solution with two 25-ml. portions of 1 *N* hydrochloric acid. The acidic solution was made basic with potassium hydroxide and extracted with ether to give 94 mg. of basic material after drying and evaporation. The ether phase of the acid partition was rinsed with 5% potassium hydroxide, dried, and evaporated to give 95 mg. of neutral compounds. The base fraction was crystallized twice from methanol to give 51 mg. of voacangine-d_3 (VIII), m.p. 136–137°. The mother liquors gave an additional 11 mg. of crystalline voacangine-d_3 after chromatography on alumina. The neutral fraction was analyzed by mass spectrometry which indicated a mixture of methylbenzoate-d_3 and anisole-d_3.

Voacamine-d_3 (IV). Vobasinol (IX, 50 mg.) and 30 mg. of voacangine-d_3 (VIII) were refluxed for 9 hr. in 4 ml. of 2% methanolic hydrochloric acid (from concentrated aqueous HCl). Water (5 ml.) was added and most of the methanol was removed under vacuum. After neutralization with sodium carbonate, the product was extracted twice with 10 ml. of chloroform. The combined extracts were rinsed with 5 ml. of water, then dried over sodium sulfate, and evaporated to give 74 mg. of crude product. Crystallization from methanol gave 19 mg. of voacamine-d_3 (IV), m.p. 215–220° dec. An additional 8 mg. of crystals was obtained by chromatography of the mother liquor on alumina.

Acknowledgment. This investigation was supported in part by Public Health Service Fellowship 5-Fl-GM-21, 624-02 from the National Institute of General Medical Sciences (to D. W. T.) and a research grant from the National Science Foundation (GP-3734).

Rimocidin. I. Carbon Skeleton, Partial Structure, and Absolute Configuration at C-27[1]

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The carbon skeleton of rimocidin has been established by conversion to the "parent" hydrocarbon, 3-methyluntriacontane, and by the result of oxidative degradation. The aglycone is C_{32} and contains no free carboxyl group. The carbohydrate component has been identified as a glycoside of D-*mycosamine (3-amino-3,6-dideoxy-D-mannopyranose). The location of the conjugated tetraene system has been determined. The terminus of the macrocyclic lactone is shown to be at C-27 and the absolute configuration at that center is R.*

The isolation of rimocidin, an antifungal antibiotic from *Streptomyces rimosus* cultures, was briefly reported in 1951.[2] Its ultraviolet spectrum ($\lambda_{max}^{ethanol}$ 279, 291, 304, 318 mμ; $E_{1\,cm}^{1\%}$ 306, 622, 965, 890) was characteristic of a conjugated tetraene.[3] Preliminary structural investigations were conducted at the Chas. Pfizer Laboratories[4] and at Harvard University.[5]

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(2) J. W. Davisson, F. W. Tanner, Jr., A. C. Finlay, and I. A. Solomons, *Antibiot. Chemotherapy*, **1**, 289 (1951).

(3) Reported (R. Kunn and C. Grundmann, *Ber.*, **71**, 442 (1938)) for the simplest case, 2,4,6,8-decatetraene, is λ_{max}^{hexane} 272, 283, 297, and 320 mμ. A much closer analogy is that of pimaricin (O. Ceder, *Acta Chem. Scand.* **18**, 77 (1964)), $\lambda_{max}^{ethanol}$ 279, 290, 303, and 318 mμ.

(4) W. M. McLamore and I. A. Solomons, unpublished report.