Mass Spectra of 5,11b-Methanomorphanthridine Alkaloids. The Structure of Pancracine[1]

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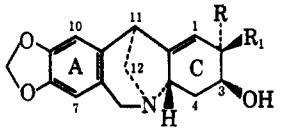
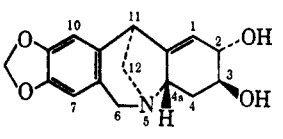
Abstract: Degradative and spectroscopic evidence is presented to show that pancracine, an alkaloid isolated from *Pancratium maritimum*, *Narcissus poeticus*, and *Rhodophiala bifida*, possesses the structure **2**. The mass spectral fragmentation patterns observed for montanine, pancracine, and other alkaloids containing the 5,11b-methanomorphanthridine nucleus are discussed in detail.

Montanine, coccinine, and manthine are the only alkaloids known to possess the 5,11b-methanomorphanthridine ring system.[2] These rare alkaloids occur mainly in *Haemanthus* spp. native to S. Africa. Recently, montanine (**1a**) has been found to be the major alkaloid of *Rhodophiala bifida*, a plant which is readily obtainable in the United States. Our investigation of the minor alkaloids of *R. bifida* has revealed the presence of a fourth alkaloid, pancracine, containing this basic ring system.

Pancracine ($C_{16}H_{17}NO_4$, mp 272–273°) also occurs in poeticus-type *Narcissi*[3] and in *Pancratium maritimum*.[4] A comparison of the physical and chemical properties of "alkaloid 6," isolated from *P. maritimum*[4] with pancracine, showed the two bases to be identical. Pancracine formed crystalline picrate and perchlorate salts as well as an O,O-diacetyl derivative. The latter derivative was particularly important for spectroscopic studies since pancracine was only very slightly soluble in common organic solvents. The ir and uv spectra were typical of many Amaryllidaceae alkaloids and showed the presence of a methylenedioxyphenyl group and one or more hydroxyl functions. No carbonyl absorption was present. The alkaloid was tentatively assigned the montanine-type nucleus when it was found that montanine (**1a**) could be hydrolyzed to pancracine with hydrobromic acid. This suggested that pancracine might be represented by structure **2**. To verify this



1a, R = OCH_3; R_1 = H
b, R = H; R_1 = OCH_3



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structure, other chemical conversions as well as detailed ir, nmr, and mass spectrometric studies were undertaken using pancracine and suitable montanine derivatives.

The insolubility of pancracine in deuteriochloroform prevented its use for a detailed nmr examination, even with the aid of spectral accumulation. The nmr spectrum of pancracine could be obtained in DMSO-d_6; however the nmr spectrum of O,O-diacetylpancracine is much more amenable to interpretation (Figure 1). The two singlets at 6.53 and 6.47 ppm correspond to the two aromatic protons. The two protons of the methylenedioxy group appear as a singlet at 5.88 ppm. The one-proton multiplet at 5.47 ppm represents the olefinic proton. The two multiplets at 5.02 and 5.12 ppm correspond to the C_3 and C_2 protons, respectively. The C_2 and C_3 protons were differentiated by double-resonance studies which showed that the olefinic proton was coupled to the multiplet at 5.12 ppm (C_2 proton) but was not coupled to the multiplet at 5.02 ppm (C_3 proton). A well-defined AB pattern centered at 4.05 ppm (J = 17 Hz) was found for the benzylic protons at C_6. These two protons give this pattern due to the rigid nature of the skeleton which holds them in different environments. Decoupling studies showed that the aromatic proton having the lower chemical shift (C_{10}) exhibited a small long-range coupling to the peak at 3.28 ppm which is assigned to the C_{11} proton. There is also a single proton multiplet at 3.28 ppm which is assigned to the C_{4a} proton. It appears as a multiplet due to splitting by the two C_4 protons and the lesser allylic splitting of the olefinic proton. The singlet at 3.02 ppm corresponds to the two protons at C_{12}. The two methyl groups of the O,O-diacetate occur at 2.0 and 2.05 ppm. The highest field protons in the spectrum are the C_4 protons which comprise a very broad multiplet of peaks between 1.4 and 2.4 ppm. Double-resonance experiments show that the C_4 protons were coupled to the C_3 proton, but not to the C_2 proton, an observation consistent with their assignment. Double-resonance experiments have been carried out with montanine, and the findings are in complete accord with the information cited above.[5]

Although these nmr data were consistent with our assignment of **2** to pancracine, more detailed information concerning the stereochemistry of the functional groups was desired. Partial hydrolysis of O,O-diacetylpancracine with 0.01 M sodium methoxide in methanol provided a mixture of the possible monoacetates (**3** and **4**). Compound **4** was not oxidized by manganese dioxide but afforded pancracine upon acid hydrolysis. 3-O-Acetylpancracine (**3**) was oxidized by this reagent to an α,β-unsaturated ketone, **5**, which was identical in all respects with the ketone obtained by the oxidation of **6**.[6] Since **3** and **6** were not identical, it

(1) This research was supported by Grant HE 7503 from the National Institutes of Health; taken in part from the Ph.D. dissertation of C. L. Brown, Iowa State University, 1968.

(2) Y. Inubushi, H. M. Fales, E. W. Warnhoff, and W. C. Wildman, *J. Org. Chem.*, **25**, 2153 (1960).

(3) M. Young, unpublished observations, Iowa State University, 1964.

(4) F. Sandberg and K.-H. Michel, *Lloydia*, **26**, 78 (1963).

(5) A. I. Feinstein, Ph.D. Thesis, Iowa State University, 1967.

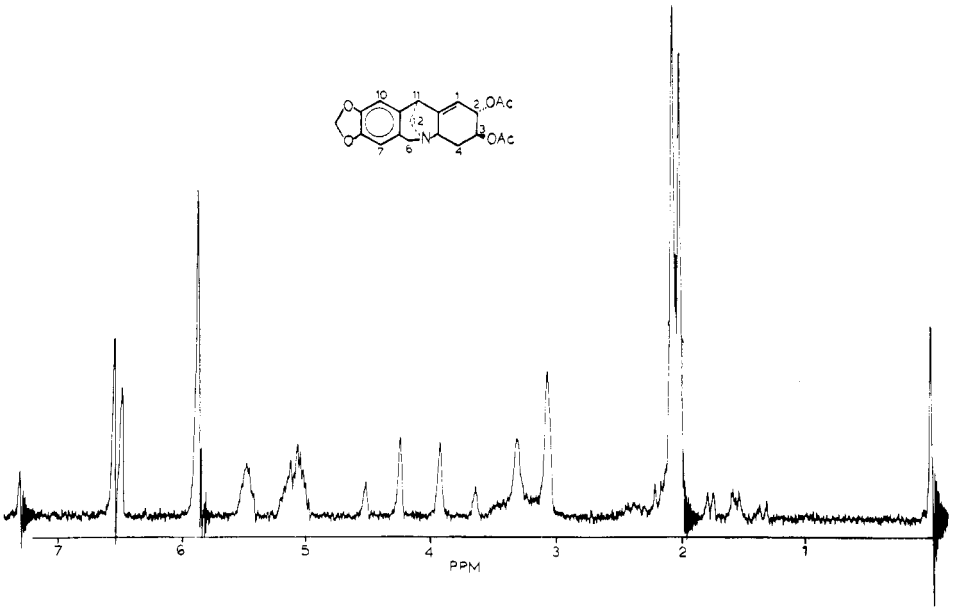
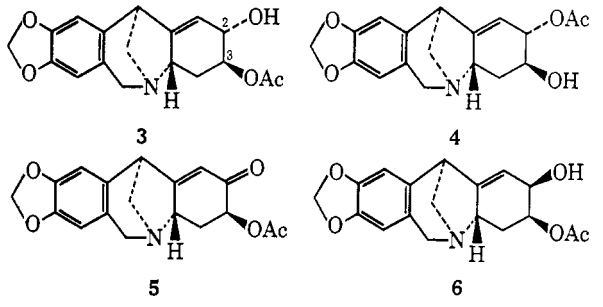


Figure 1. Nmr spectrum of O,O-diacetylpancracine.

may be assumed that these isomers differ only in the configuration of the C_2 hydroxyl group. Possible epimerization of the acetoxyl group at C_3 in either **3** or **6** seems unlikely since the crude oxidation products had identical ir spectra and formed identical hydrochlorides. The products were not subjected to any alkaline conditions.



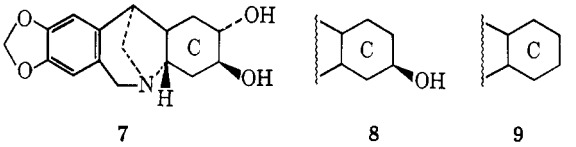
3 **4**

5 **6**

The configuration of the C_2-hydroxyl groups in **3** and **6** was determined by infrared hydrogen bonding studies. Because of the conformational mobility of both ring C and the C_3-acetoxyl groups both **3** and **6** showed OH–carbonyl bonding (3603 and 3592 cm^{-1}, respectively). These data are far less definitive than that found in the analogous methyl ether series.[2] Pancracine and the diol (**6**, OH instead of OAc) provided a better basis for stereochemical assignments. The latter was strongly intramolecularly bonded (3586 cm^{-1}). The lack of intramolecular hydrogen bonding in **2** was suggested by its insolubility in chloroform. Comparable chloroform insolubility has been noted for lycorine, which also has vicinal *trans* axial–pseudoaxial hydroxyl groups.

O,O-Diacetylpancracine (**3**, OAc instead of OH) gives a mixture of three products when hydrogenated with palladium–charcoal in glacial acetic acid. Acid hydrolysis of this mixture and separation by tlc gave dihydropancracine (**7**) (mp 271–272°), desoxydihydropancracine (**8**) (mp 222–224°), and a small amount of **9** (an oil).

The two hydrogenolysis products were assigned structures **8** and **9** mainly on the basis of their mass spectra which are consistent with the mode of fragmentation of the dihydro derivatives in this ring system which are discussed later. The stereochemistry of the B/C ring in dihydropancracine (**7**) and the two hydrogenolysis products (**8** and **9**) is not known.[7]



7 **8** **9**

The Mass Spectra of Montanine-Type Alkaloids

The mass spectra of montanine and coccinine have been reported.[8] The spectrum of pancracine (Figure 2) contained several ions of considerable abundance (*m/e* 185, 199, 214) which were not observed for montanine and coccinine. Montanine (**1a**), coccinine (**1b**), manthine (**11**), and pancracine differ in the stereochemistry of the two substituents (OH or OCH_3) at C_2 and C_3. The nature of the substituents and their particular configuration have a very significant effect on the electron-induced fragmentation of these molecules. A number of compounds containing the montanine nucleus (**10**, **12a**, **12b**, **12c**, and **13**) were available which differed only in the stereochemistry and nature of substituents at C_2 and C_3. The differences in fragmentation of these molecules would then necessarily be attributable to stereochemical differences in the substituents at C_2 and C_3, and a correlation of fragmentation patterns with these structural variables is possible.

(6) W. C. Wildman and K.-H. Michel, Abstracts of the Fourth International Symposium on National Products, Stockholm, Sweden, 1966.

(7) The particular catalyst used has an effect on the relative amount of each isomer obtained. In the hydrogenation of pancracine (**2**) palladium–charcoal in acetic acid gives mainly one dihydropancracine, whereas platinum in ethanol gives two isomers in equal amounts. The hydrogenolysis products are observed only with the O,O-diacetate.

(8) A. M. Duffield, R. T. Aplin, H. Budzikiewicz, C. Djerassi, C. F. Murphy, and W. C. Wildman, *J. Amer. Chem. Soc.*, 87, 4902 (1965).

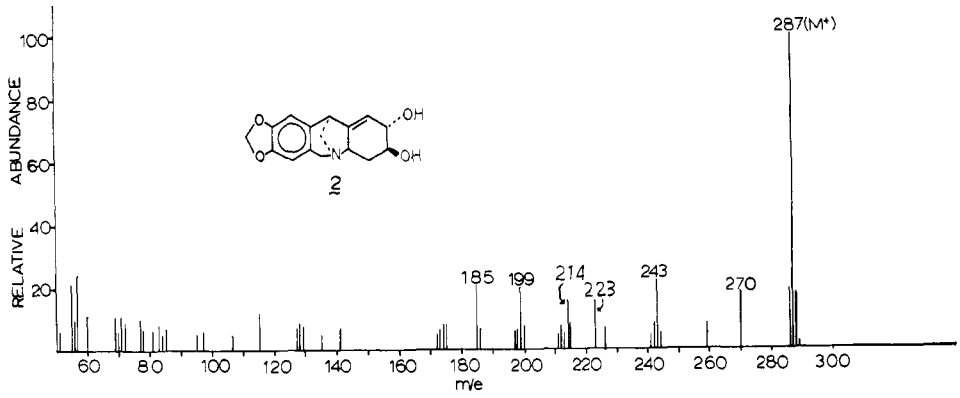


Figure 2. Mass spectrum of pancracine.

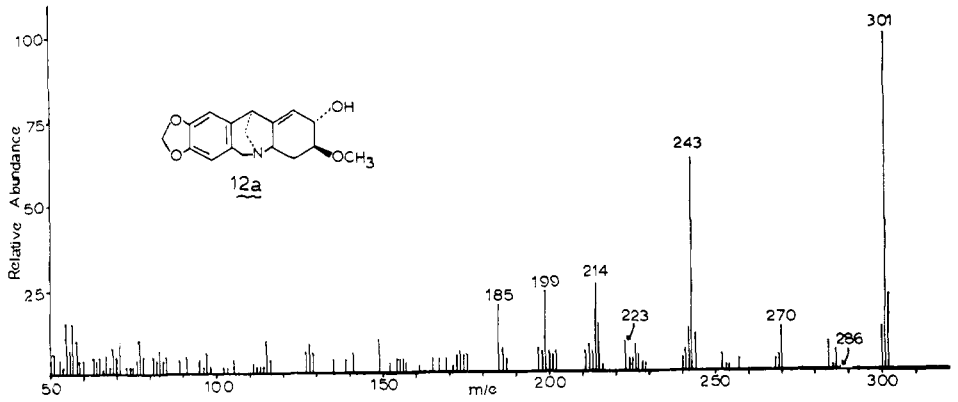
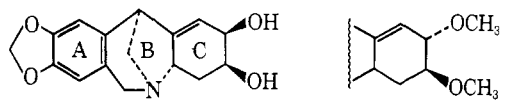


Figure 3. Mass spectrum of isohaemanthamine.



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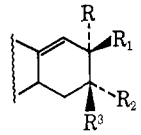
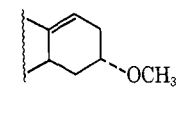


12a, R = OH; $R_1 = R_2 = H$; $R_3 = OCH_3$
b, R = R_3 = H; R_1 = OH; $R_2 = OCH_3$
c, R = OH; $R_1 = R_3 = H$; $R_2 = OCH_3$



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Direct Cleavage of the C_2 and C_3 Substituents. As in the reported spectra of montanine and coccinine,[8] the mass spectra of isohaemanthamine (**12a**, Figure 3), α-isocrinamine (**12b**, Figure 4), and β-isocrinamine (**12c**, Figure 5) show an M − 15 peak at *m/e* 286 due to the loss of the O-methyl group. In addition, **12a**, **12b**, and **12c** exhibit weak M − OH peaks at *m/e* 284 which correspond to the cleavage of the C_2-hydroxyl group. The spectrum of manthine (**11**, Figure 6) exhibits an analogous M − 15 peak at *m/e* 300. Pancracine (**2**) and **10** exhibit the loss of an hydroxyl group to give peaks at *m/e* 270 in their spectra.

All the compounds which possess a methoxyl group give rise to an M − 31 ion. A comparison of the relative abundance of the *m/e* 270 ion in the spectra of **1a**, **1b**, **12a**, **12b**, and **12c** showed that the intensity of this ion is independent of the stereochemistry of the methoxyl group. However, a comparison of the spectra of **1a** and **1b** with **12a**, **12b**, and **12c** shows that the C_2-methoxyl (whether α or β) is cleaved in an abundance three to four times greater than the C_3-methoxyl group. This enhanced cleavage is probably due to the allylic C_2 methoxyl group. The *m/e* 269 ion corresponds to the loss of methanol in the spectra of **12a**, **12b**, and **12c**. In the spectra of manthine (**11**, Figure 6) and desoxyisocrinamine (**13**) peaks at *m/e* 283 and 253, respectively, represent the loss of methanol from the parent ion. The loss of methanol (M − 32) is greater than the loss of the methoxyl group (M − 31) only in the spectra of **12c** (Figure 5) and **13**. At lower electron voltages the ratio of the relative abundance of the (M − 32)/(M − 31) increased in the compounds **12a**, **12b**, and **12c** and also in **11**. At 15 eV, the M − 32 ion observed with **12c** is four times greater than the M − 31 ion.

Elimination of the C_3–C_4 Atoms of Ring C. An ion corresponding to the direct loss of the C_3 and C_4 carbon atoms including any substituent at C_3 was present in the spectra of every compound investigated in the montanine series. This particular type of fragmentation gives the most abundant fragment ion (*m/e* 243) in the spectra of both isohaemanthamine (Figure 3) and β-isocrinamine (Figure 5). Its origin is analogous to the retro-Diels–Alder formation[9] of the *m/e* 257 ion in the spectra of montanine and coccinine[8] as shown in the fragmentation of **14** to **a** and **b**. In the spectra of pancracine (Figure 2) the retro-Diels–Alder cleavage gives an ion at *m/e* 243. In manthine (**11**) and **13** the analogous ion occurs at *m/e* 257 and 227, respectively. The configuration of the C_2 substituent has a con-

(9) H. Budzikiewicz, J. I. Brauman, and C. Djerassi, *Tetrahedron*, **21**, 1855 (1965).

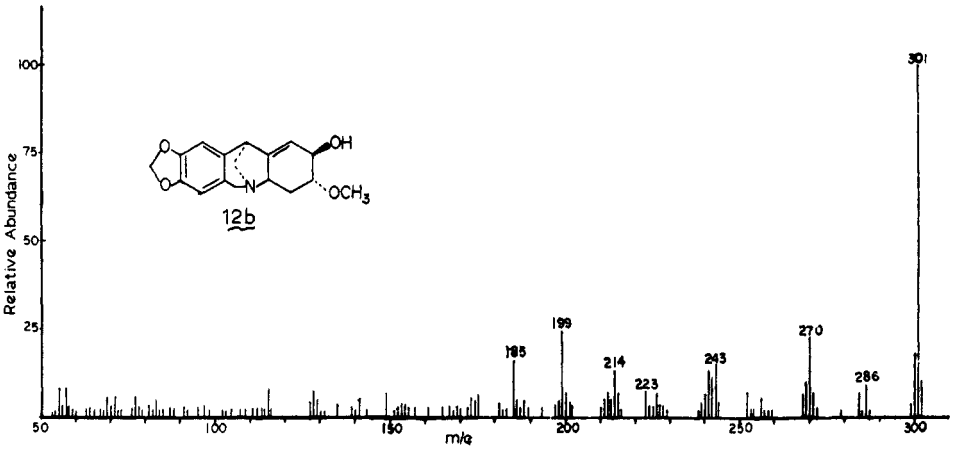


Figure 4. Mass spectrum of α-isocrinamine.

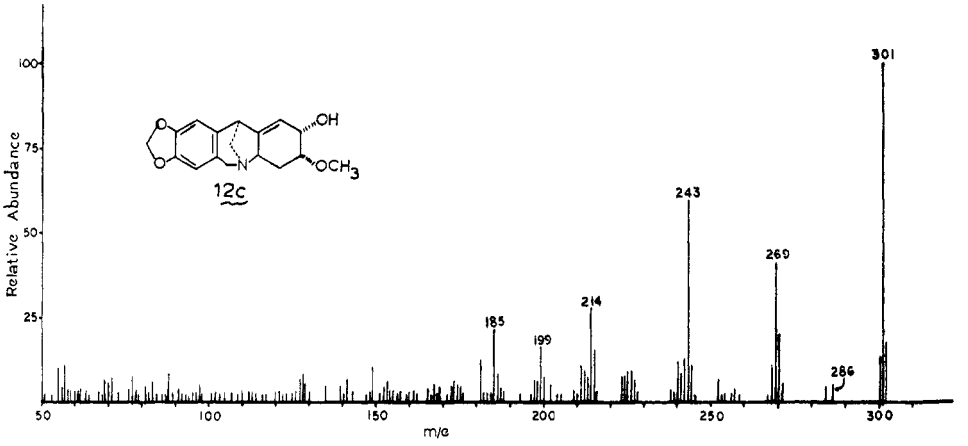


Figure 5. Mass spectrum of β-isocrinamine.

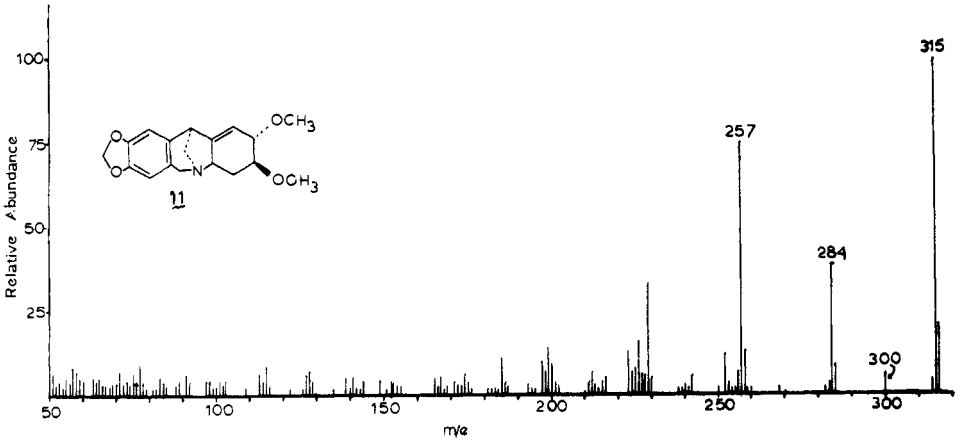
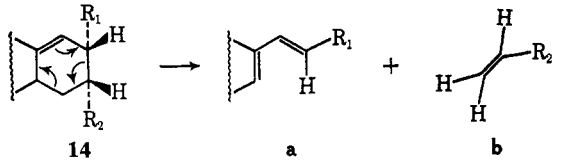


Figure 6. Mass spectrum of manthine.

siderable effect on the extent to which the retro-Diels–Alder fragmentation ion is observed. There is a



14 a b

definite enhancement of this fragmentation when the C_2 substituent has an α configuration (see Table I). This is shown by a comparison of the relative abundance of the *m/e* 243 ion in α-isocrinamine (Figure 4) and β-isocrinamine (Figure 5) (15 and 64%, respectively). This is substantiated by the relative intensity of the analogous ion in isohaemanthine (62%) and manthine (66%). In both cases the C_2-hydroxyl group has the α configuration. Another factor affecting this fragmentation is the composition of the cleaved fragment. In the compounds **1a**, **1b**, **2**, and **10**, where the cleaved fragment is $CH_2{=}CHOH$, the relative abundance of this ion is less than in fragmentations where $CH_2{=}CHOCH_3$ is lost. In the latter case, there is a distinct preference for this cleavage to occur when the C_2

Table I. The Relative Abundance of the Retro-Diels–Alder Ion

α-C_2 substituted	% base peak	m^*_c	m^*_f	β-C_2 substituted	% base peak
Montanine (**1a**)	25	196.5	197.0	Coccinine (**1b**)	8
Pancracine (**2**)	25	205.9	206.0	Iso-11-hydroxy-vittatine (**10**)	25
β-Isocrinamine (**12c**)	64	196.5	196.5	α-Isocrinamine (**12b**)	15
Isohaemanthamine (**12a**)	62	196.5	196.3		
Manthine (**11**)	66	209.7	210.0		

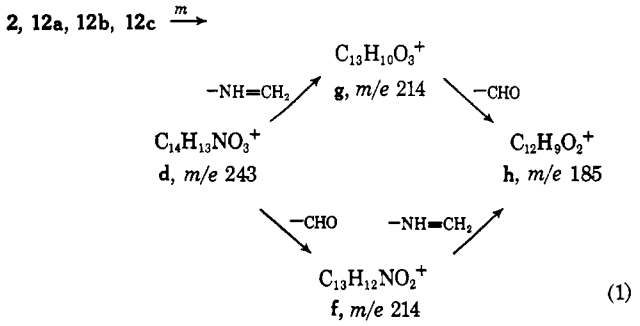
substituent is α, as shown in Table I. Attempts to explain these results on the basis of steric arguments were ambiguous, and we were frustrated in our attempts to apply Woodward–Hoffmann orbital symmetry arguments, since we cannot be certain of the electronic state of the ionized molecule. It should be noted that the low-energy spectra (20 and 15 eV) of the compounds that undergo the retro-Diels–Alder fragmentation show a very large increase in the relative abundance of this ion when compared to the other fragment ions.

Fragmentations Involving the Loss of the Nitrogen Atom. The results of high-resolution measurements on several ions of considerable abundance in the mass spectrum of pancracine are shown in Table II. These

Table II. High-Resolution Data for Ions from Pancracine

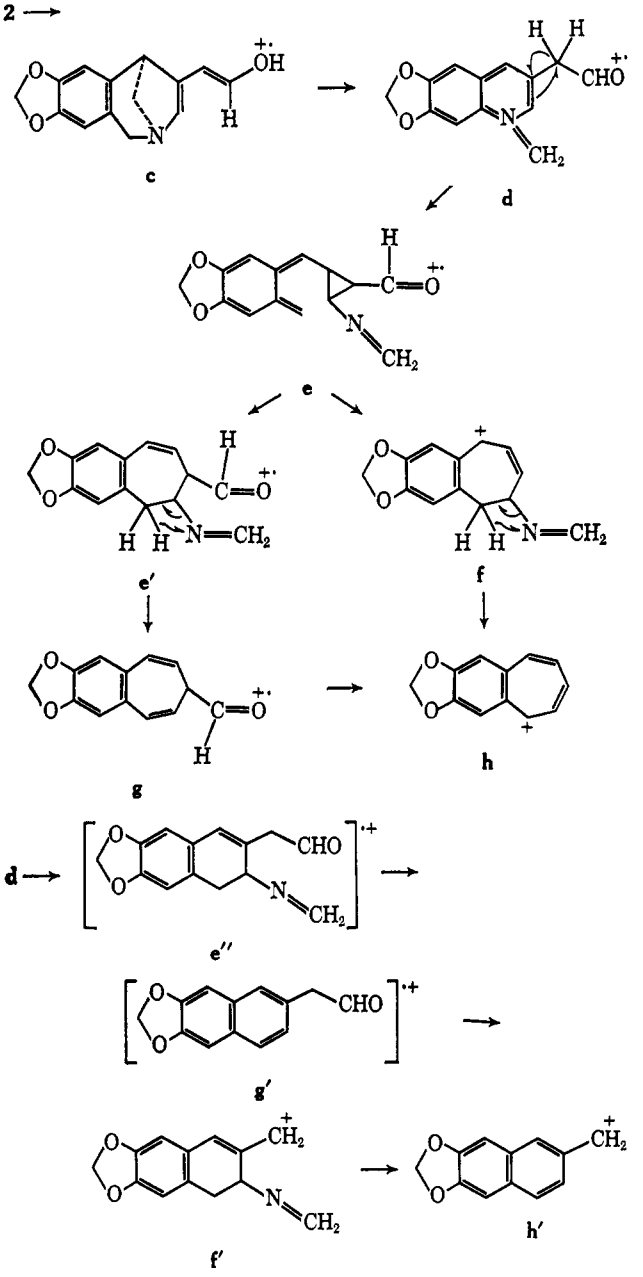
m/e	Compn	Calcd	Obsd
223	$C_{15}H_{11}O_2$	223.0758	223.0762
214a (60%)	$C_{13}H_{12}NO_2$	214.0867	214.0825
214b (40%)	$C_{13}H_{10}O_3$	214.0629	214.0620
199	$C_{13}H_{11}O_2$	199.0759	199.0766
185	$C_{12}H_9O_2$	185.0602	185.0620

ions (*m/e* 223, 214, 199, and 185) are also present in the spectra of isohaemanthamine, α- and β-isocrinamine, and in varying relative abundance in most of the other compounds investigated in this series. The most obvious observation concerning these ions is that, except for half of the doublet at *m/e* 214, none of the ions contains a nitrogen atom. A comparison of these data and the correlation of several metastable ions can be used to postulate possible mechanisms of formation for the nitrogen-free ions. In the spectrum of pancracine a metastable ion at *m/e* 188.5 (m^*_c = 188.5) showed that there is a one-step loss of 29 mass units ($NH{=}CH_2$) from the *m/e* 243 ion to give an ion, *m/e* 214 ($C_{13}H_{10}O_3^+$). The other ion of the doublet [at *m/e* 214 ($C_{13}H_{12}NO_2^+$)] shows a direct loss of 29 mass units (m^*_c = 160.1, m^*_f = 160.8) to give an ion at *m/e* 185 ($C_{12}H_9O_2^+$) as shown in eq 1. A proposed mechanism



(1)

Scheme I



for the above sequence is shown in Scheme I. The retro-Diels–Alder ion (**d**) may rearrange to form ion **e′** which loses $NH{=}CH_2$ to give **g**. From the same intermediate ion (**e**), the formyl radical can be lost to form **f** and subsequently lose $NH{=}CH_2$ to give the *m/e* 185 ion **h**. A loss of the formyl radical from **g** could give the same *m/e* 185 ion (**h**). Alternatively, the retro-Diels–Alder ion (**d**) could reclose to form **e″** which would give **f′** and **g′** for the two *m/e* 214 ions. A loss of the formyl radical and $NH{=}CH_2$ from **g′** and **f′**, respectively, could give **h′**. Isohaemanthamine (**12a**), β-isocrinamine (**12c**), and α-isocrinamine (**12b**) give the same *m/e* 243 peak as pancracine. There are metastable peaks in the spectra of each of these compounds at *m/e* 188.5 ($214^2/243$ = 188.5) and 160.0 ($185^2/214$ = 160.1) which provide evidence that these three compounds undergo the same fragmentations as depicted for pancracine in Scheme I.

In the mass spectra of montanine, coccinine, and manthine the analogous fragmentations from the

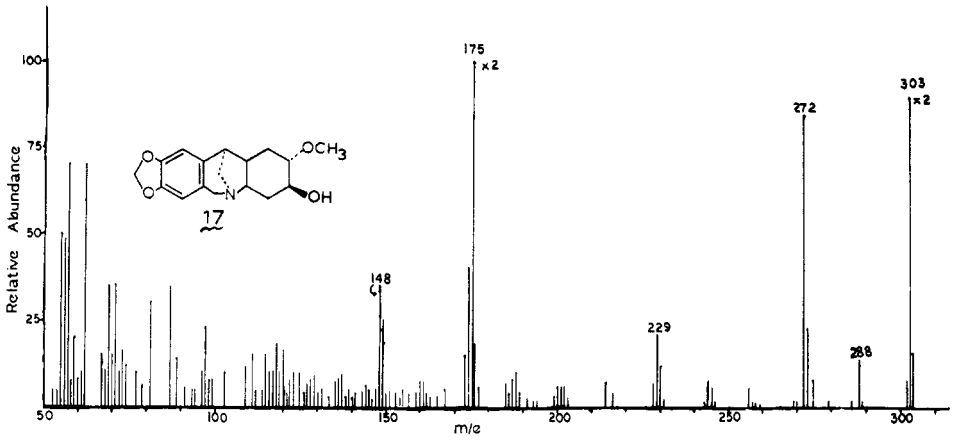


Figure 7. Mass spectrum of dihydromontanine.

initially formed retro-Diels–Alder ion (*m/e* 257) as shown in Scheme I are not observed. A metastable peak at *m/e* 204.4 ($229^2/257 = 204.0$) in montanine and manthine indicates that a one-step loss of 28 mass units from the retro-Diels–Alder ion affords the ion at *m/e* 229. The retro-Diels–Alder ion (*m/e* 257) in montanine and manthine also gives rise to a one-step loss of 31 mass units (257 → 226, $m^*_f = 199.0$, $m^*_c = 198.8$) providing a peak at *m/e* 226. These two fragmentations from the retro-Diels–Alder ion in the C_2-OCH_3 compounds may successfully compete with, or inhibit, the cleavages shown in Scheme I for the C_2-hydroxy compounds. There is no evidence for the loss of $NH{=}CH_2$ from the retro-Diels–Alder ion in the C_2-methoxyl compounds. The loss of $NH{=}CH_2$ was postulated as a process for the formation of the *m/e* 223 ion from an ion at *m/e* 252 in the fragmentation of montanine and coccinine.[8] The *m/e* 252 ion was shown to arise from a direct loss of water from an ion at *m/e* 270 ($m^*_f = 235.5$).[8] There is some evidence for the occurrence of analogous fragmentations in pancracine which contains a relatively abundant ion at *m/e* 223 ($C_{15}H_{11}O_2^+$). The *m/e* 252 ion in the spectrum of pancracine is less than 3% of the base peak (not shown in Figure 2); however, there is a metastable peak at *m/e* 235.0 which substantiates the fact that the *m/e* 252 ion is formed directly from the *m/e* 270 ion (270 (−18) → 252, $m^*_c = 235.3$). The only other common ion of considerable abundance in the spectra of these compounds is at *m/e* 199 ($C_{13}H_{11}O_2^+$). This ion is unusually large (50%) in the spectrum of **13**. There are also peaks in the spectrum of **13** corresponding to M − CH_3, M − CH_3OH, M − OCH_3 at *m/e* 270, 253, and 254, respectively. The *m/e* 252, 223, and 185 ions are relatively abundant. The consecutive eliminations in **13** of CH_3OH and $NH{=}CH_2$ from the *m/e* 284 ion (M − 1) in a process analogous to the 270 → 252 → 223 pathway discussed for pancracine would give the same ions at *m/e* 252 and 223. The formation of the *m/e* 185 ion (**h** in Scheme I) in the spectrum of **13** is probably due mainly to the stability of this ion which allows its formation by a somewhat different route than proposed in Scheme I. The *m/e* 227 ion which is present in the spectrum of **13** represents the retro-Diels–Alder loss of the C_3–C_4 carbon atoms (**14** → **a** and **b**; $R_1 = H$, $R_2 = OCH_3$).

Mass Spectra of the Dihydro Derivatives

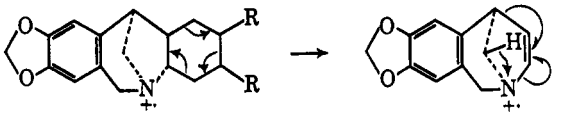
The removal of the double bond in the alkaloids and derivatives of the montanine ring system changes the fragmentation pattern drastically (see Figure 7). The major ions in the spectra of dihydrococcinine, dihydropancracine (**7**), and two hydrogenolysis products from pancracine (**8** and **9**) are shown in Table III. The retro-Diels–Alder loss of the C_3 and C_4 carbon atoms does not occur in the dihydro derivatives. The ubiquitous ions in the unsaturated compounds at *m/e* 214, 223, and 199 are absent in the spectra of the dihydro compounds. There is no evidence for the loss of $NH{=}CH_2$ from any ion in the spectra of the dihydro derivatives. Disappearance of the major ions of the montanine alkaloids in the dihydro derivatives demonstrates that the double bond plays a major role in the formation of these ions as our previous mechanistic proposals illustrate.

Table III. Dihydro Derivatives

Dihydrococcinine		7		8		9	
Ion	% base peak	Ion	% base peak	Ion	% base peak	Ion	% base peak
303	100	289	90	273	44	257	80
288	10	272	17	256	13	214	12
272	26	230	7	230	12	229	6
230	9	229	6	229	4	228	9
229	21	228	3	228	5	188	8
228	9	214	4	177	9	176	17
214	5	175	100	175	100	175	100
200	7	174	38	174	39	174	27
185	10	149	20	173	20	173	18
175	53	148	25	149	13	149	36
174	38	115	20	148	36	148	27
149	23					115	17.4
148	19						

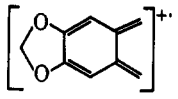
Diagnostic Fragmentation. Heretofore, there has been no simple spectral method to assign a given Amaryllidaceae alkaloid to the montanine ring system. However, as shown in the mass spectrum of dihydromontanine (Figure 7) and in Table III, there is a substantial ion at *m/e* 175. This ion has a molecular composition of $C_{10}H_9NO_2$. A proposed mechanism for the

formation of this ion is shown below. In this fragmentation, ring C is cleaved in its entirety (**15** → **i** → **k**).

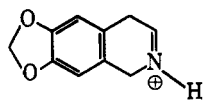


15

i

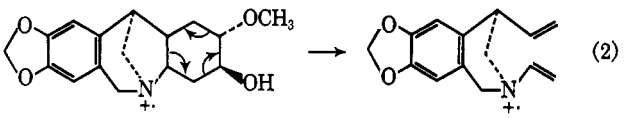


16, *m/e* 148



k, *m/e* 175

The presence of this *m/e* 175 ion in the spectra of dihydro compounds serves as a good diagnostic test for the presence of the montanine ring system. It is present in the spectra of all dihydro derivatives investigated and usually is the base peak. The nature of the substituents and their stereochemistry have no effect on the presence of this ion. This ion (*m/e* 175) is not present in any significant abundance in the mass spectra of the dihydro derivatives of the other ring systems of the Amaryllidaceae.[8,10] A somewhat less abundant ion (*m/e* 148) is present in all the dihydro derivatives and could be formed from the *m/e* 175 ion. It has an empirical formula of $C_9H_8O_2$. A possible structure is **16**. Two other ions that are characteristic of the dihydromontanine nucleus are observed at *m/e* 229 ($C_{14}H_{15}NO_2^+$) and 230 ($C_{13}H_{12}NO_3^+$). The *m/e* 229 ion observed in dihydromontanine (**17**, Figure 7) is formed in a one-step process from the parent ion (m^*_c = 173.2; m^*_f = 173.2) by elimination of the C_2–C_3 carbon and substituents attached from the parent ion. A proposed mechanism (**17** → **1**) is shown in eq 2.

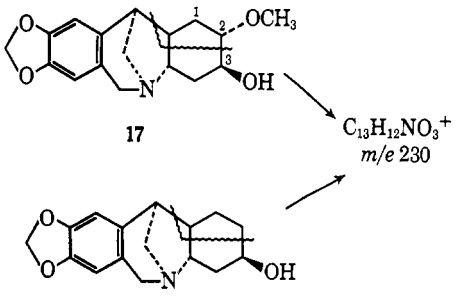


(2)

17

1, *m/e* 229

High-resolution mass spectroscopic examination of the *m/e* 230 ions in dihydromontanine and desoxydihydropancracine (**8**) showed that both had the composition of $C_{13}H_{12}NO_3$. This *m/e* 230 ion represents the loss of C_4H_7O and C_3H_5 from dihydromontanine and **8**, respectively. The composition of the *m/e* 230 ion showed that the C_3 carbon including the hydroxyl group in **8** is retained. This suggests that the loss of C_3H_5 from **8** may occur as shown below. Cleavage of dihydromontanine in a similar manner would give the same *m/e* 230 ion.



17

$C_{13}H_{12}NO_3^+$
m/e 230

8

(10) T. H. Kinstle, W. C. Wildman, and C. L. Brown, *Tetrahedron Letters*, 4659 (1966).

Experimental Section[11]

Isolation of Alkaloids from *Rhodophiala bifida* Herb. The *Rhodophiala bifida* bulbs (11.5 kg) were ground in ethanol with a Waring Blendor. Approximately 12 gal of ethanol was added, and the mixture was stirred for 2 days at room temperature. The mixture was filtered through cheesecloth, and the residue was extracted with 8 gal of ethanol. This process was repeated a third time and all filtrates were combined. Upon standing, a dark precipitate separated from the combined filtrates and was treated separately. The combined filtrates were concentrated to a volume of 2 l. under reduced pressure, acidified with 2 *N* hydrochloric acid and filtered. The filtrate was made basic with ammonium hydroxide and diluted to twice its volume with water. The basic solution was extracted eight times with chloroform and twice with a 3:2 chloroform–ethanol solution. This procedure yielded 47.06 g of crude material upon removal of the solvent. The neutral substances were separated by standard extraction procedures and 27.4 g of crude alkaloid mixture was obtained.

The dark precipitate isolated in the initial extraction procedure was triturated several times with ethanol. The ethanolic solutions provided 9.136 g of additional crude basic material. This was combined with the 27.4 g of crude bases.

The aqueous basic solutions that remained after these separations contained alkaloids and were combined and saturated with sodium chloride. Dilute sodium hydroxide was added to adjust the pH to 12. The resulting solution was extracted 20–25 times with warm ethanol–chloroform (1:3). This process provided an additional 7.46 g of crude basic material (fraction A).

The major alkaloid extract (36.34 g) was dissolved in chloroform and chromatographed on 700 g of basic alumina. Elution with chloroform and chloroform–ethanol (97:3) provided 23.9 g of the less polar alkaloids (fraction B). The more polar alkaloids remaining on the column were eluted with chloroform–ethanol (1:1) and ethanol to provide 4.7 g of basic material. This fraction was found to contain the same components as fraction A and these were combined. Trituration of the combined mixture with warm chloroform provided crude pancracine which was recrystallized from methanol, 960 mg, mp 272–273°. An additional 200 mg of pancracine was recovered from the filtrates. The chloroform-soluble alkaloids remaining were found to consist of 11-hydroxyvittatine, haemanthidine, tazettine, coranicine, and lycorine.[12] Chromatography of fraction B on 517 g of alumina provided, in addition to some nonbasic substances, 3.14 g of haemanthamine (mp 197–200°), 11.85 g of montanine (perchlorate salt, mp 248–251°), and 506 mg of vittatine (mp 210–211°).

Pancracine. The alkaloid, mp 272–273°, crystallized from methanol as elongated prisms, $[\alpha]^{25}D$ −74° (*c* 0.02, methanol); λ_{max}^{EtOH} 292 and 241 mμ (log ε 3.72 and 3.64, respectively).

Anal. Calcd for $C_{16}H_{17}NO_4$: C, 66.88; H, 5.96; N, 4.88. Found: C, 66.71; H, 6.12; N, 4.73.

Pancracine formed crystalline picrate (mp 249–252°) and perchlorate (mp 163–166°) salts.

O,O-Diacetylpancracine. A solution of 200 mg of pancracine in 25 ml of dry pyridine was treated with 1.5 ml of acetic anhydride for 2 min at 100° and then allowed to stand at room temperature for 28 hr. The reaction mixture was treated with aqueous potas-

(11) The proton nuclear magnetic resonance spectra were obtained in deuteriochloroform solution using either a Varian HR-60 or A-60 spectrometer. All low-resolution mass spectra were determined with an Atlas CH-4 mass spectrometer using the TO-4 ion source. The spectra were run at 70 eV except where stated otherwise. The high-resolution data were obtained on a A.E.I. M.S.-9 spectrometer. Melting points were observed on a Köfler microscope hot stage and are corrected. Optical rotations were determined in methanol with a Jasco Model ORD/UV 5 recording spectropolarimeter. Ultraviolet spectra were obtained in methanol solution using either a Beckman DK-2 ultraviolet-visible or Cary Model 14 spectrophotometer. Infrared spectra were obtained with a Beckman Model IR-12 spectrophotometer. Thin layer chromatography was carried out on silica gel PF 254 and 366 (Merck) using ultraviolet light of the appropriate wavelengths. The proof of identity of any two compounds was determined by a comparison of melting points, mixture melting points, infrared spectra, and thin-layer and gas phase chromatographic data.

(12) W. C. Wildman and K.-H. Michel, unpublished data, 1966.

sium carbonate and extracted with chloroform to give 220 mg of product, mp 163–165° after recrystallization from benzene–petroleum ether (bp 30–60°).

Anal. Calcd for $C_{20}H_{21}NO_6$: C, 64.68; H, 5.70; N, 3.77. Found: C, 64.48; H, 5.98; N, 3.67.

2-O-Acetylpancracine (4) and 3-O-Acetylpancracine (3). O,O-Diacetylpancracine (190 mg) was dissolved in 25 ml of methanol. Sodium methoxide (0.3 ml/0.01 *M*) was added. The solution was stirred 40 min, then an additional 0.3 ml of sodium methoxide solution was added. The solution was stirred for 35 min. The reaction mixture was acidified with a few drops of acetic acid and evaporated to dryness on a rotary evaporator. The residue was dissolved in 2 ml of chloroform. The chloroform solution was spread on two silica gel plates (20 × 20 cm, 1 mm thick) and eluted with chloroform, ethanol, and ammonia (15:2:0.1). The plates showed three bands. Elution of the band at R_f 0.9 gave O,O-diacetylpancracine (84 mg). The middle band (R_f 0.6) contained a mixture of both 2- and 3-O-acetylpancracines (35 mg). The recovered O,O-diacetylpancracine was subjected to the same separation. The mixture of the two monoacetates (R_f 0.6) was combined and triturated with methanol. 3-O-Acetylpancracine, mp 213–216° (30 mg), crystallized from the mixture. The ultraviolet spectrum showed absorption maxima at 293 mμ (log ε 4.71) and 241 mμ (log ε 4.64). The nmr ($CDCl_3$) showed peaks at (δ values) 6.60 (1 H, singlet), 6.52 (1 H, singlet), 5.90 (2 H, singlet), 5.57 (1 H, multiplet), 5.0 (1 H, multiplet), 4.0 (J_{AB} = 17 Hz), 4.03 (1 H, singlet, OH), 3.33 (2 H, multiplet), 3.08 (2 H, singlet), 2.03 (3 H, singlet), 1.4–2.1 (2 H, multiplet).

Anal. Calcd for $C_{18}H_{19}NO_5$: C, 65.64; H, 5.81, N, 4.25. Found: C, 65.70; H, 5.94; N, 4.37.

2-O-Acetylpancracine (17 mg) was obtained from the filtrates of 3-O-acetylpancracine. All attempts to crystallize 2-O-acetylpancracine were unsuccessful. 2-O-Acetylpancracine was left unchanged after stirring with 30 ml of chloroform and manganese dioxide (100 mg) for 2.5 hr. A sample of 2-O-acetylpancracine for an elemental analysis was obtained by evaporatively distilling under a reduced pressure (150°). The uv spectrum of 2-O-acetylpancracine showed absorption maxima at 293 mμ (log ε 4.71) and 241 mμ (log ε 4.66). The nmr spectrum is essentially the same as reported for 3-O-acetylpancracine.

Anal. Calcd for $C_{18}H_{19}O_5$: C, 65.64; H, 5.81; N, 4.25. Found: C, 65.46; H, 5.97; N, 4.21.

The R_f 0.1 band from the plate was pancracine (28 mg).

2-Oxo-3-O-acetylpancracine (5). A solution of 41 mg of 3-O-acetylpancracine in 7 ml of chloroform was mixed with 200 mg of manganese dioxide. The mixture was stirred 4 hr and filtered and the chloroform evaporated to yield a residue of 35 mg. The infrared spectrum ($CHCl_3$) of this residue was identical with an authentic sample of 2-oxo-3-O-acetyliso-11-hydroxyvittatine.[5]

2-Oxo-3-O-acetylpancracine Hydrochloride. A few drops of methanol, saturated with gaseous HCl, was added to 3 mg of 2-oxo-3-O-acetylpancracine. Trituration with acetone afforded white needles, mp 189–194°. A mixture melting point determination of this material and an authentic sample of 2-oxo-3-O-acetyliso-11-hydroxyvittatine hydrochloride[6] was not depressed (mp 188–192°).

Pancracine (2) from Montanine (1). Montanine (1.95 g, the acetone solvate) was refluxed with 25% HBr (25 ml) for 1.5 hr. The solution was cooled and diluted with 150 ml of water. The aqueous acidic solution was made basic (pH 8) with ammonium hydroxide and extracted several times with chloroform. The aqueous basic solution was extracted further with 25% ethanol in chloroform. The aqueous solution was adjusted to pH 12 with 20% NaOH and extracted with 25% ethanol in chloroform. All chloroform and ethanol extracts were combined and evaporated. Trituration with ethanol–acetone gave 300 mg of pancracine, mp 272–273°. Evaporation of the filtrate and further trituration with ethanol–acetone gave an additional 22 mg of pancracine. Unreacted montanine (922 mg) was also recovered.

Hydrogenation of O,O-Diacetylpancracine. O,O-Diacetylpancracine (150 mg) in glacial acetic acid (1.5 ml) was added to a prereduced mixture of 10% palladium on charcoal (200 mg) in 15 ml of acetic acid. The mixture was stirred under a hydrogen atmosphere for 4 hr. The material absorbed 1.2 equiv of hydrogen. The catalyst was removed by filtration. The filtrate was poured into 100 ml of water, and dilute sodium hydroxide was added to adjust the pH to 10. The basic solution was allowed to stand overnight, then extracted several times with chloroform and 20% ethanol in chloroform. This solution was evaporated to dryness under a reduced pressure to give a brown residue (126 mg). The residue was dissolved in a small volume of ethanol, and this solution was spread on a silica gel plate (20 × 20 cm, 1 mm thick) and eluted in chloroform–ethanol–ammonium hydroxide (70:30:5). There were three bands (approximate R_f 0.8, 0.4, 0.2). The middle band (R_f 0.4) was removed, and the residue obtained was crystallized twice from acetone to give 19 mg of 2-desoxydihydropancracine (**8**) (mp 222–224°); λ_{max}^{MeOH} 293 and 236 mμ (log ε 4.72 and 3.53, respectively).

Anal. Calcd for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.13. Found: C, 70.22; H, 7.10; N, 4.95.

The lower band (R_f 0.2) was removed, and the material obtained was recrystallized from methanol to give 45 mg of dihydropancracine (mp 271°), λ_{max}^{MeOH} 293 and 235 mμ (log ε 3.71 and 3.54, respectively).

Anal. Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.60; H, 6.45; N, 4.83.

The top band (R_f 0.8) gave 10 mg of **9** (an oil). Attempts to crystallize this material were unsuccessful. The mass spectrum of this material is summarized in Table III. The ir showed no hydroxy absorption, and the uv is essentially the same as that reported for 2-desoxydihydropancracine.

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