Mass Spectral Studies of Alkaloids Related to Morphine[1]

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Abstract: The mass spectra of morphine and ten related alkaloids have been determined. Fragmentation pathways of these compounds are discussed. The extent and position of unsaturation in ring C plays a dominant role in determining the fragmentations.

We present a detailed description[1] of our studies on the mass spectra of the morphine alkaloids[3-7] I–XI (Figure 1). In all these compounds except sinomenine (IX) and isosinomenine (X) the molecular ion is the base peak.

Morphine (I) and Its Derivatives II–VI

Ions Common to Alkaloids I–VI. The spectrum of morphine (Figures 2 and 3) determined by the direct sample introduction technique shows clean fragmentation patterns,[8] containing eight fragment peaks above *m/e* 120 with intensity greater than 5% of that of the base peak (Table I).[9] Assignments of individual peaks were made with the help of shifts observed in spectra of derivatives containing the same degree and position of olefinic unsaturation (Table I), while individual fragmentation processes were documented by metastable ion peaks (Table II).

A priori, one might expect some localization of charge on nitrogen in the molecular ion of morphine, to be followed by cleavage at the three carbon–carbon bonds β to the nitrogen atom,[10,11] leading to radical ions a (Figure 4), b (Figure 5), and c (C-15, C-16 bond broken, not illustrated). The stability of ions a and b is enhanced by the allylic and benzylic radicals present, and the fragmentations to all the major peaks in I–VI can be ascribed to these two ions (*e.g.*, a-I, a-II, etc.). The possible fragmentations of ion a are illustrated (Figure 4) for morphine itself; hence the ions are designated a-I, etc. The loss of a hydroxyl radical from C-6 leading to ion d-I is established by the shift of the peak in the spectra of II–V. The peak at *m/e* 282 is very much larger in the spectra of III and IV, which form ion d by loss of the more stable methoxyl and acetoxyl radicals, respectively.

Ion f at *m/e* 215 (also derived from a) is the third most abundant peak in the spectrum of I. We propose ion f arises from transfer of the sterically available hydrogen atom at C-10 to the radical at C-14 to give the stable benzylic radical e, which undergoes a reverse Diels–Alder reaction to give the aromatic benzofuran f, a stabilizing feature of other fragments to be discussed later. That ion f includes ring A of morphine but not all the atoms of ring C is shown by its occurrence at

Table I. Corresponding Peaks in Mass Spectra of Morphine Alkaloids

Ions	I	II	III	IV	V	VI	VII	VIII	IX	X	XI
M, a, b, c	285	299	313	341	315	297	299	311	329	329	327
d	268	282	282	282	298	280[a]	282	280	298	...	296
M − 29	256	270	284	312	286	268	270	282	...	300	298
M − 43	242	256	270	298	272	254	258	268	286	286	284
n	228	242	256	284	258	240	242	254	272	272	270
f	215	229	229	229	...	229	...	...	...	...	...
g	200	214	214	214	...	214	...	...	...	...	...
h	174	188	188	188	204[b]	188	...	...	...	...	...
j	162	162	176	204	162	...	162	174	192	192	...
m	124	124	138	166	124	122	...	...	...	...	...

[a] Does not correspond to structure d, origin unknown. [b] Formed by different route, may not correspond to other peaks (h).

(1) Preliminary reports presented: (a) 149th National Meeting of the American Chemical Society, Detroit, Mich., April 1965 (*cf.* Abstracts, p 15P); (b) EUCHEM Conference on Mass Spectroscopy, Sarlat, France, Sept 1965.

(2) Visiting Lecturer, University of Illinois, summer, 1964.

(3) The mass spectra of the morphine alkaloids had not been reported at the time these studies were undertaken.[2] Shortly after our preliminary report had been submitted,[1a] preliminary papers appeared from three other laboratories[4-6] describing mass spectral fragmentations of a number of compounds related to morphine (including some studied by us).

(4) H. Audier, M. Fetizon, D. Ginsburg, A. Mandelbaum, and T. Rull, *Tetrahedron Letters*, 13 (1965).

(5) H. Nakata, Y. Hirata, A. Tatematsu, H. Tada, and Y. K. Sawar, *ibid.*, 829 (1965).

(6) A. Mandelbaum and D. Ginsburg, *ibid.*, 2479 (1965).

(7) For reviews see (a) K. W. Bentley, "The Chemistry of the Morphine Alkaloids," Oxford University Press, London, 1954; (b) G. Stork, "The Alkaloids," Vol. VI, R. H. Manske, Ed., Academic Press Inc., New York, N. Y., 1960, p 219; (c) H. G. Boit, "Ergebnisse der Alkaloid Chemie bis 1960," Akademie-Verlag, Berlin, 1961, pp 288–329.

(8) By contrast, the mass spectrum of morphine determined on a sample introduced by the earlier method involving a heated gas bulb was both unreproducible and uninterpretable in terms of the morphine structure, indicating considerable thermal rearrangement.

(9) We did not observe some peaks reported by Audier, *et al.*,[4] to be in the spectra of morphine and its derivatives. These include peaks at *m/e* 257 (M − 28) and 146 in the spectrum of morphine itself, and peaks at *m/e* 268 (M − 31) and 146 in the spectrum of codeine.

(10) R. S. Gohlke and F. W. McLafferty, *Anal. Chem.*, **34**, 1281 (1962).

(11) (a) K. Biemann, "Mass Spectrometry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962; (b) H. Budzikiewicz, D. Djerassi, and D. H. Williams, "Structure Elucidation of Natural Products by Mass Spectrometry. Vol. I. Alkaloids," Holden-Day, Inc., San Francisco, Calif., 1964.

Table II. Corresponding Metastable Ion Peaks in Mass Spectra of Morphine Alkaloids

Fragmentation process	I	II	III	IV	V	*m**, found (calcd) VI	VII	VIII	IX	X	XI
a → d	252.0 (252.0)	266.0 (266.0)	254.0 (254.0)	233.5 (233.5)	281.0 (282.0)	264.0 (263.8)	265.8 (266.0)	252.0 (251.8)	...	...	...
M → M − 15	256.0 (256.0)	...	...	...	286.0 (285.7)	268.0 (269.0)	270.0 (270.0)	281.5 (281.8)	299.7 (300.0)	300.0 (300.0)	298.0 (297.8)
M → M − 29											
M → M − 43											
a → n	182.5 (182.4)	196.0 (195.8)	209.7 (209.6)	236.5 (236.5)	211.3 (211.6)	...	196.0 (195.8)	207.3 (207.4)	...	...	219.0 (219.6)[a]
a → f	(162.1)[b]	175.5 (175.4)	167.5 (167.7)	154.0 (153.8)	...	176.5 (176.7)	...	...	...	...	...
f → g	186.2 (186.0)	200.2 (200.0)	199.8 (200.0)	200.2 (200.0)	...	200.2 (200.0)	...	...	...	...	...
f → h	141.0 (140.8)	...	...	154.0 (154.3)	[132.0 (132.1)][d]	154.5 (154.3)	...	...	...	...	...
b → j	92.4 (92.1)	87.8 (87.8)	99.1 (98.9)	122.0 (122.1)	83.7 (83.3)	...	...	...	112.1 (112.0)	112.1 (112.0)	...
b → m	...	...	61.0 (60.8)[c]	...	...	...	...	...	...	...	...
M → p	...	...	15.3 (15.7)	...	...						

[a] Corresponds to lo ss of 59 rather than 57 mass units. [b] Masked by the intense fragment ion at *m/e* 162. [c] Very low intensity. [d] M → *m/e* 204.

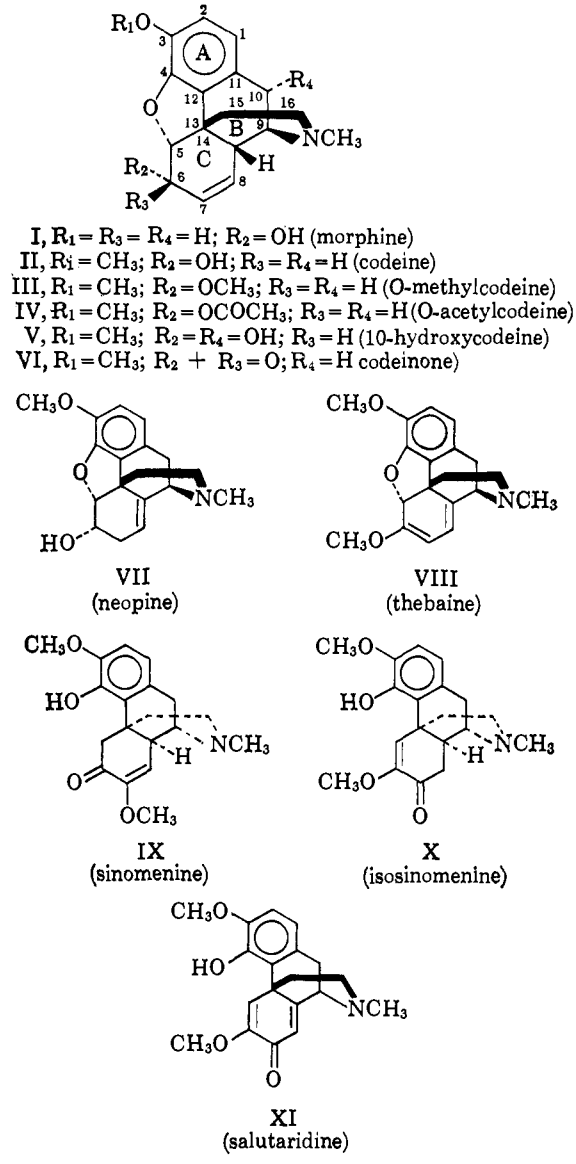


Figure 1. Alkaloids whose mass spectra are discussed in the present paper.

m/e 229 in the mass spectra of compounds II–IV and VI. Conversion of a to e requires transfer of the sterically available back-side proton at C-10, not present in V.[12] In accord with this proposal ion f is absent from the mass spectrum of 10-hydroxycodeine (V). Although the metastable ion peak for a → f in morphine itself (m_c* 162.1) is obscured by the large peak at *m/e* 162, metastable peaks in the spectra of II, III, IV, and VI (Table II) show the process a → f involves a one-step mass loss. The scheme proposed by Audier, *et al.*,[4] for the formation of f (to which they assign a different structure) does not account for the absence of f from 10-hydroxycodeine.

Ions g and h, at *m/e* 200 and 174 [$C_{11}H_{10}O_2$ by high-resolution mass spectrometry (hrms)][13] in the spectrum of morphine, are derived (Table II) from ion f (or an isomer).

(12) H. Rapoport and S. Masamune, *J. Am. Chem. Soc.*, 77, 4330 (1955).

(13) We are greatly indebted to Professor K. Biemann and Dr. S. Tsunakawa for data from their high-resolution spectra, determined on a CEC 21-110 mass spectrometer.

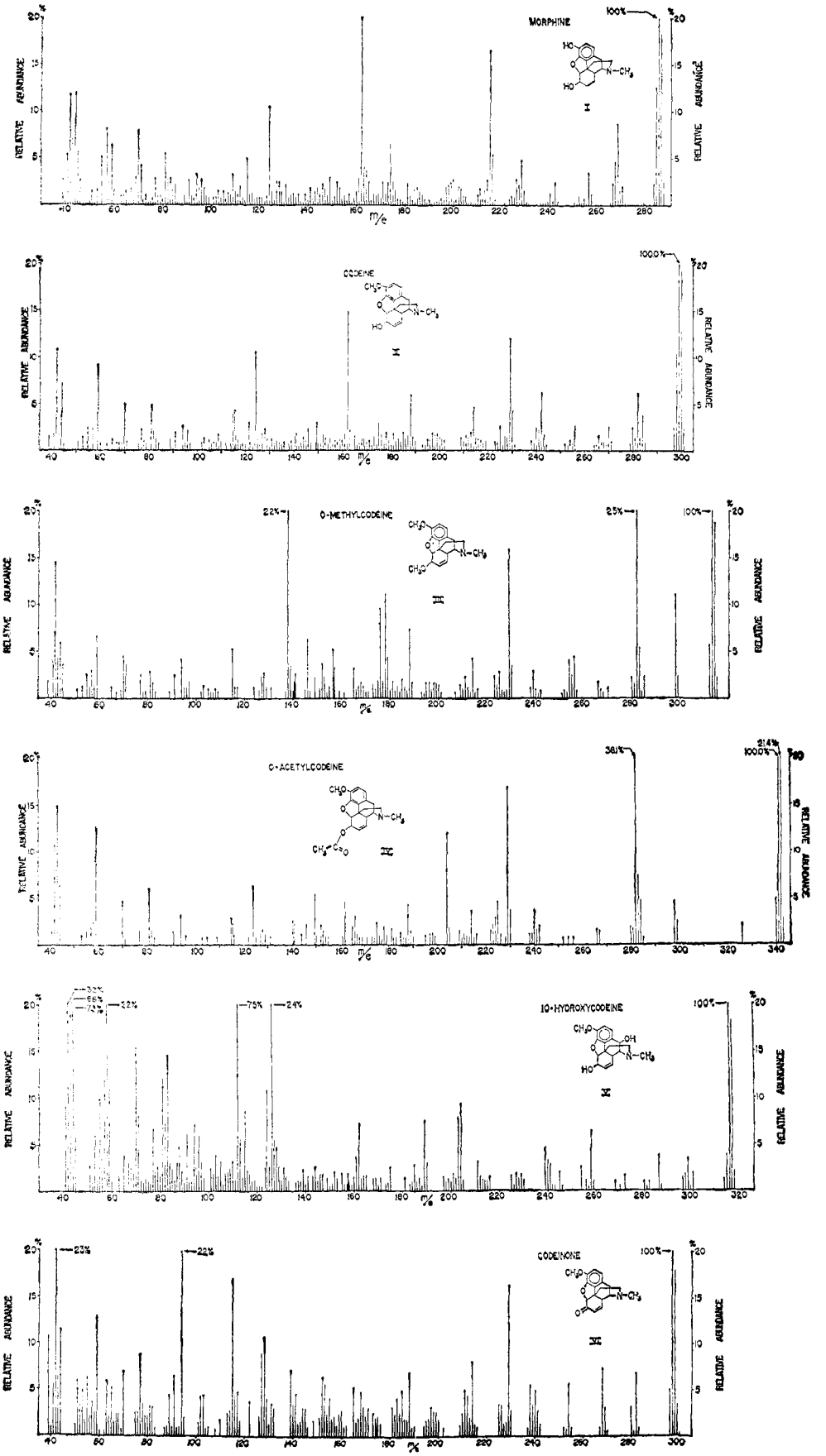


Figure 2. Mass spectra of alkaloids I–VI related to morphine.

Shifts in the mass values (Table I) indicate they do not involve ring A elisions; possible structures are shown in Figure 4. The spectrum of 10-hydroxycodeine does not contain a peak for ion g-V since ion

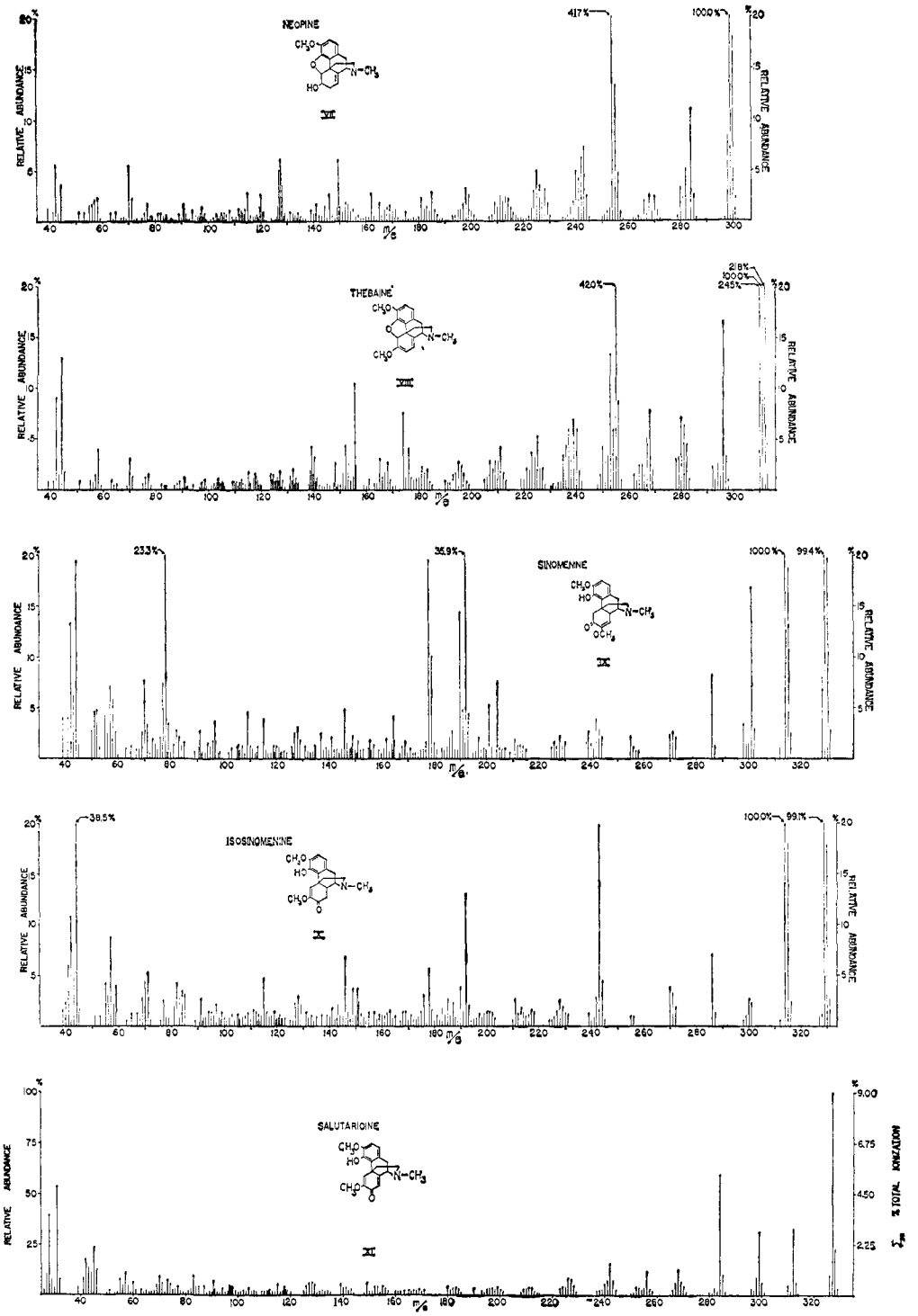


Figure 3. Mass spectra of alkaloids VII–XI related to morphine.

f-V, its progenitor, is missing. A peak does appear at *m/e* 204, which corresponds formally to that expected for h, but it arises directly from the molecular ion (see Table II).

The intense ion at *m/e* 162 (ion j-I), the most abundant in the spectrum of morphine after the molecular ion, is also prominent in all the other spectra in which it appears. Shifts in the position of j (Table I) indicate the origin of its carbon atoms, while the data in Table II show that mass is lost only in the final step. A scheme conforming to these requirements is shown in Figure 5. Ion j is not found in the mass spectrum of codeinone (VI), since in that compound the hydrogen atom at C-6 is lacking, nor in that of 14-hydroxycodeine,[4] which lacks a C-14 hydrogen. Audier, *et al.*,[4] proposed the same loss of atoms to form ion j, and confirmed its composition by hrms on morphine and codeine.

Ion b is also suggested as the precursor of the abundant ion m (found in the morphine spectrum at *m/e* 124), as shown in Figure 5. The position of m, like that of j, shifts with substitution in ring C (III, IV, and VI), but not with substitution in ring A (II) or with hy-

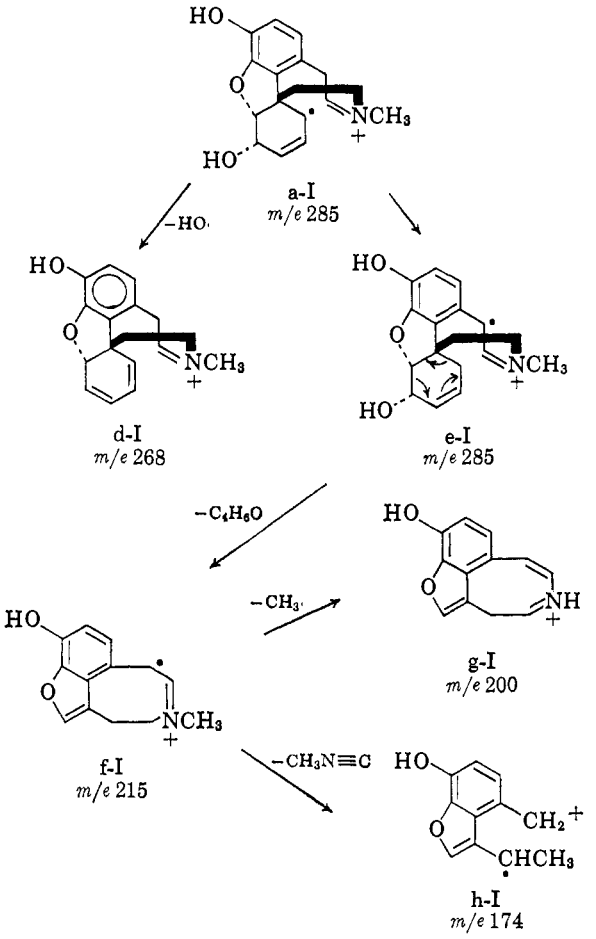
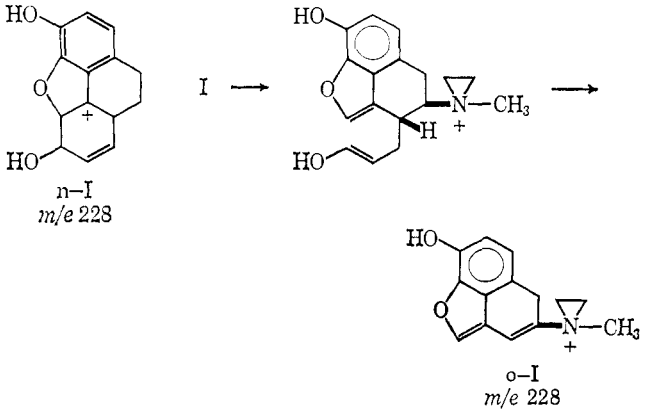


Figure 4. Ions derived from ion a-I.

droxylation at C-10 (V). Its composition ($C_7H_{10}NO$) has been confirmed by hrms of morphine and codeine.[4,14]

The position of ion n (M − 57, at *m/e* 228 in the spectrum of morphine) shifts in all derivatives of morphine (II–VI), indicating that the neutral fragment lost is C_3H_7N, from the bridge.[15] This ion is accompanied by others (usually less intense) at M − 58 and M − 59 and is derived in one step from the molecular ion or its isomer (Table II).



(14) The absence of a peak at *m/e* 125 and the presence of a metastable ion for the formation of m-IV (313 → 138; *m** 61.0) favors the scheme in Figure 5 over an earlier proposal.[4]

(15) Audier, *et al.*,[4] have confirmed by hrms that C_3H_7N is lost; they and Nakata, *et al.*,[5] have shown that an analogous ion appears at M − 43 in spectra of compounds lacking the N-methyl group.

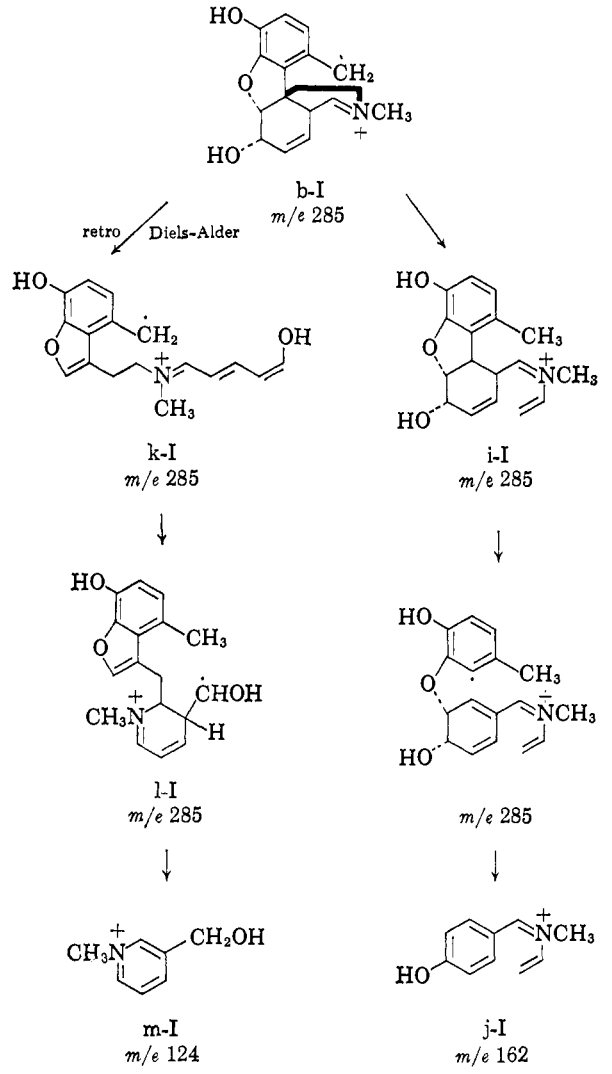


Figure 5. Ions derived from ion b-I.

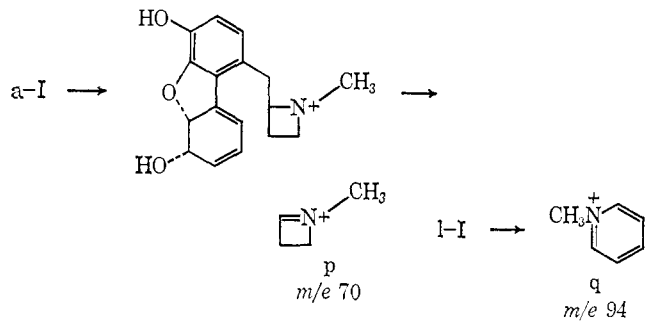
The high-resolution spectrum of morphine shows the ions at *m/e* 228 and 226 to be doublets and the 57 and 59 mass units lost to be due to C_3H_5O and C_3H_7O as well as to C_3H_7N and C_3H_9N.[13,16] Very different pathways are required for formation of ions at M − C_3H_5O and M − C_3H_7O. A possibility (o-I) is shown above for that at M − C_3H_5O. It receives some support from spectra of morphine derivatives III and IV, which contain small peaks at *m/e* 242.

Other ions due to loss of small fragments are found in the spectra of nearly all compounds investigated, at M − 29 and M − 43 (*m/e* 256 and 242 in the spectrum of morphine). That at *m/e* 256 is a doublet whose major component is $C_{16}H_{18}NO_2$ (M − CHO) and whose minor component is $C_{15}H_{14}NO_3$ (M − C_2H_5);[13] that at *m/e* 242 is also a doublet with components of approximately equal intensity, $C_{15}H_{16}NO_2$ (M − C_2H_3O) and $C_{15}H_{14}O_3$ (M − C_2H_5N).[13]

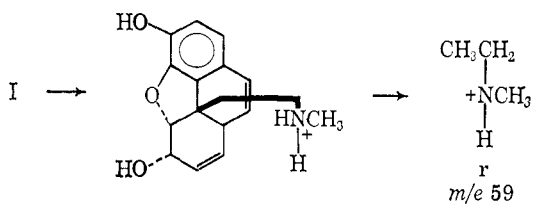
Ions of Masses below 120. Six peaks, at *m/e* 115, 94, 70, 59, 44, and 42, are distinguished not so much by their intensity as by their ubiquity. Reasonable structures have been suggested previously[4] for the ions at *m/e* 115, 70, and 94 (C_6H_8N).[13] We propose that the C_4H_8N ion (perhaps the azacyclobutenium ion

(16) The peak at *m/e* 227 (M − 58) is due to loss of C_3H_8N only.[13]

p) is formed from ion a as shown below and ion q from I (see Figure 5).



The ion at *m/e* 59 is a doublet whose major component is C_3H_9N.[13] The scheme below for its formation (r) accords with the observation[6] that the C-14 hydrogen atom is required for its formation. Similar amine fragmentation mechanisms account for the ions at *m/e* 44 (C_2H_6N)[13] and 42 (C_2H_4N).[13]



Mass Spectra at Reduced Electron Energies. Low-energy mass spectra of the morphine derivatives indicate the relative ease of formation of the various fragments discussed. Although not all compounds were studied, the following general pattern was observed. At 22 ev ions g and q and those at *m/e* 115, 44, and 42 were already much less intense or missing and ions h, m, and p were very much diminished or absent. By 17 ev ions j and r were decreasing in intensity and by 16 ev essentially all peaks except the molecular ion had disappeared. Nearly all of the last ions to disappear were formed directly from the molecular ion or its isomer by loss of a small fragment (H, CH_3, OH, C_3H_7N), while ion r (C_3H_9N) can be postulated to come from the same intermediate which gives ion n (M − C_3H_7). The persistence of ion j at low ionizing potential is perhaps more surprising since it must arise by a series of several steps.

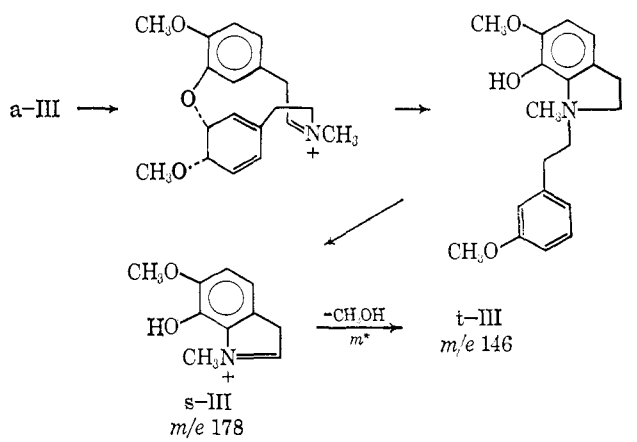
Ions Restricted to Specific Derivatives (II–VI) of Morphine. O-Methylcodeine (III). The spectrum of III shows one fragmentation pathway not observed for the closely related alkaloids I, II, and IV–VI; intense ions appear at *m/e* 178 (s-III) and 146 (t-III), connected with one another by a metastable ion (Table III). The composition of the ion is shown to be $C_{10}H_{12}NO_2$ by hrms,[17] and the following fragmentation pathway can be written. It is not clear why this fragmentation is less important for the other alkaloids.

O-Acetylcodeine (IV). The spectrum of O-acetylcodeine contains a peak at *m/e* 240 due to loss of acetyl and C_3H_6N and a peak at *m/e* 225 due to loss of acetoxyl and C_3H_7N, together with peaks at *m/e* 162 and 124 for loss of ketene from ions j-IV and m-IV or their precursors (to give ions j-I and m-I, respectively). The ketene losses are indicated by metastable ions (Table III).

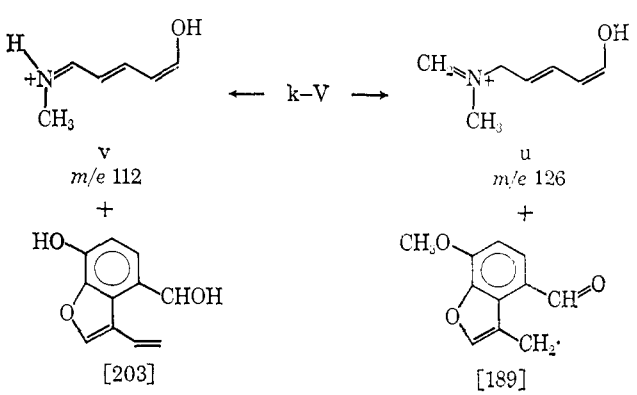
(17) Determined on a CEC 21-110 spectrometer (Professor F. W. McLafferty and Dr. R. D. Board) and on a Varian M-66 spectrometer (Dr. L. H. Smithson).

Table III. Additional Metastable Ion Peaks for Individual Alkaloids

Compd	Fragmentation process	*m**, found (calcd)
I	M → 267	250.0 (250.2)
III	178 → 146	119.8 (119.8)
IV	204 → 162	128.5 (128.7)
	166 → 124	92.5 (92.7)
VII	M → 254	216.0 (215.7)
	M → 255	217.5 (217.5)
	255 → 254	253.2 (253.0)
VIII	M → 254	207.0 (207.4)
	M → 255	209.0 (209.0)
	M → 250	200.8 (200.8)
	M → 227	165.5 (165.8)
	M → 176	100.0 (99.7)
IX	M → 314	300.1 (300.0)
	M → 301	275.5 (275.5)
	178 → 146	119.8 (119.7)
X	M → 314	300.1 (300.0)
	M → 301	276.0 (275.5)
	M → 243	180.0 (179.6)
	178 → 146	119.5 (119.7)
XI	327 → 299	274.0 (273.5)
	327 → 268	219.0 (219.6)
	299 → 242	196.0 (195.8)



10-Hydroxycodeine (V). Most of the major peaks in the spectrum of 10-hydroxycodeine do not correspond to any in the spectra I–IV and are at *m/e* 126 (22.1% of base peak), 112 (40.1%), 239, 204, 203, and 189. The ion at *m/e* 239 (confirmed as $C_{15}H_{11}O_3$)[13] and ions at *m/e* 238 and 237 are probably formed by losses of C_3H_9N, C_3H_6N, and C_3H_7N, respectively, from ion d. The ions at *m/e* 204, 203, 189, 126, and 112 are formed by preferential cleavage of the C-9–C-10 bond. As



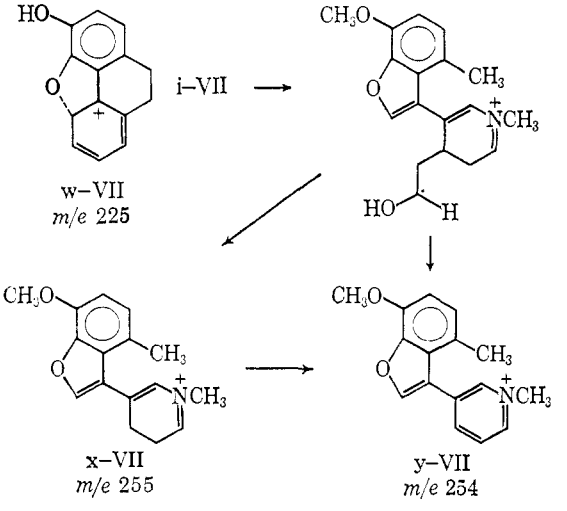
seen below, charge remains preferentially with the nitrogenous fragment (ions u and v at *m/e* 126 and 112) but can also remain with the nonnitrogenous residue (ions at *m/e* 204, 203, and 189). The compositions of the major components of the peaks are confirmed as $C_7H_{12}NO$, $C_6H_{10}NO$, $C_{12}H_{12}O_3$ (plus $C_{12}H_{14}NO_2$), $C_{12}H_{11}O_3$, and $C_{11}H_9O_3$ (*m/e* 126, 112, 204, 203, and 189, respectively).[13]

Neopine and Thebaine

The spectra of neopine (VII) and thebaine (VIII) are similar to one another but bear little resemblance to those previously treated nor to those of sinomenine, isosinomenine, and salutaridine (IX–XI). The differences are due to the following molecular features in VII and VIII: cleavage of the bond between C-9 and C-14 (to give a) would produce an unstable vinyl radical; there is no hydrogen at C-14 available for transfer in ion i (Figure 5); and the position of the C-8–C-14 double bond in ring C is not conducive to the retro Diels–Alder reaction of ion b.

Five cleavages are still found, however, corresponding to those in codeine or morphine, giving ions at M − 15 (loss of methyl), M − 29, M − 43, and M − 57, 58, 59 (ions like n) in both neopine and thebaine and at M − 17 (loss of hydroxyl, d) in neopine. Cleavage between C-13 and C-15 is now favored since the radical at C-13 will be both benzylic and allylic. The ion n-VII (*m/e* 242) is further stabilized by loss of a hydroxyl group to give the highly conjugated ion w-VII at *m/e* 225. Ions corresponding in mass to ion j are also found in the spectra of VII and VIII, at *m/e* 162 and 174 ($C_{11}H_{12}NO$),[13] respectively.

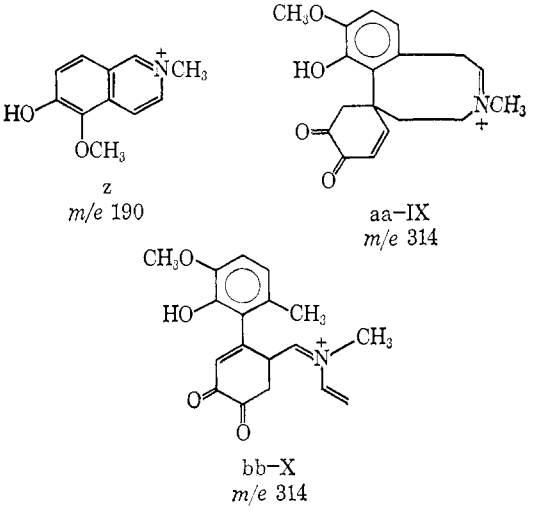
The scheme shown below is suggested to explain the two intense fragment ions in the spectrum of VII at *m/e* 254 (y) and *m/e* 255 (x). The latter, less intense, peak is $C_{16}H_{17}NO_2$, identified by hrms.[4] Ions x and y are both formed directly from the molecular ion of neopine (see Table III) though a weak metastable ion at *m/e* 253 suggests a step involving loss of a hydrogen atom (from x to y) probably also occurs.



The *m/e* 250–260 region is superficially similar in the thebaine (VIII) spectrum. However, much the largest peak here is at *m/e* 255, accompanied by smaller peaks at *m/e* 253 and 254. The ions at *m/e* 254 and 255 are formed directly from the molecular ion (Table III). The ion of mass 255 is $C_{16}H_{15}O_3$ (M − C_3H_6N),[13] arising from loss of the N-methyl unit with C-15 and C-16, presumably by a mechanism close to that leading to ion n. The much smaller peak at *m/e* 254 in the spectrum of VIII is a doublet;[13] the more intense ion is $C_{16}H_{14}O_3$, corresponding to ion n-VIII; the less intense is $C_{16}H_{16}NO_2$, corresponding to ion y-VIII. The peak at *m/e* 253 is presumably principally due to loss of C_3H_8N. Of some interest, too, in the spectrum of thebaine is the peak at *m/e* 268, $C_{17}H_{18}NO_2$ (M − C_2H_3O).[13] This corresponds to loss of the same elements leading to the ion at *m/e* 254 in the spectrum of neopine (VII) and suggests a possible multiple origin of that peak. Of the usual ions at low masses, that at *m/e* 59 is replaced by an ion at *m/e* 58. The latter shift is in accord with the lack of a hydrogen at C-14 required for the mechanism of formation of r as shown above.

Sinomenine, Isosinomenine, and Salutaridine

Striking differences were observed between the spectra of these three compounds (IX, X, and XI) and the others (I–VIII), probably resulting from the absence of the oxide ring. In the spectra of IX, X, and XI most ions of the morphine spectrum are lacking. Fragmentation *via* an ion corresponding to a is not observed, possibly because the driving force provided by the formation of a stable benzofuran ion (f) is lacking, and also the facile loss of methyl, discussed below, stabilizes the radical. Similarly, the allylic hydroxyl whose loss leads to d is missing, though an M − 31 ion is found in the spectrum of IX. Fragmentation of the benzylic ion corresponding to b accounts for the peak j-IX at *m/e* 192,[18] which is intense in both sinomenine (35.9% of base peak, major ion confirmed[13] as $C_{11}H_{14}NO_2$) and isosinomenine (13.1%). The difference in intensity probably arises because a doubly allylic C-14 hydrogen atom is transferred during this fragmentation in sinomenine, while a less labile hydrogen must be transferred in the corresponding fragmentation of isosinomenine. In salutaridine, which lacks a C-14 hydrogen, the peak j is missing. In the spectrum of sinomenine a related ion is found at *m/e* 190 ($C_{11}H_{12}NO_2$),[13] perhaps the fully aromatic z.



Other ions of the morphine spectrum found in the spectra of sinomenine, isosinomenine, and salutaridine

(18) Audier, *et al.*,[4] ascribe a similar structure to this ion.

are those at low masses, *m/e* 42 and 44, 59 (though *m/e* 57 is higher), 70, and 115.

The peak at M − 15 is very intense in the spectra of IX, X, and XI, being the base peak in the former two spectra. Since loss of methyl is not a dominant feature of codeine derivatives the methyl lost must be that of the ring C methoxyl group. Initial cleavage at an allylic or benzylic bond followed by loss of methyl would give the conjugated even-electron ions aa-IX (*via* a-IX), bb-X (*via* b-X and i-X), and bb-XI (*via* b-XI and i-XI).

Another strong peak common to the spectra of sinomenine, isosinomenine and salutaridine is found at M − 43 (*m/e* 286 or 284). This is stronger than the usual M − 43 peak and is probably due mainly to loss of carbon monoxide and methyl; the ion from IX has the expected composition $C_{17}H_{10}NO_3$ (M − C_2H_3O).[13] Although elision of carbon monoxide is a reasonable fragmentation of an α-diketone, only a weak, broad metastable ion peak links the peak at M − 15 in the spectrum of XI with that at M − 43. The alternative, loss of carbon monoxide, followed by methyl, would be difficult to support for isosinomenine, which lacks the peak at M − 28.

Strong peaks appear at *m/e* 178 ($C_{10}H_{12}NO_2$)[13] and 146 (C_9H_8NO)[13] in the spectra of IX and X (where that at *m/e* 178 is weaker) but not XI. These ions are presumably the same as those (s-III and t-III) from O-methylcodeine. Audier, *et al.*,[4] first proposed the structure of ion s after studying derivatives lacking the ether bridge. Presumably the C-8–C-14 double bond of salutaridine prevents the formation of ion s-XI by preventing formation of a-XI.

There are many differences between the spectra of IX and X. The reason for the pronounced loss of carbon monoxide from the molecular ion of sinomenine but only minor loss from that of isosinomenine is not obvious, but may involve unsaturation at C-8, a structural feature common to IX and salutaridine (XI), which also shows loss of carbon monoxide. Other peaks above *m/e* 100 in the spectrum of IX not found or much weaker in that of X are those at *m/e* 204 and 201. One large peak (at *m/e* 243) found in the spectrum of isosinomenine, but not that of IX, probably arises from loss of C-6, C-7, C-8, their substituents, and one additional hydrogen. It is formed directly from the molecular ion (Table III).

The spectrum of salutaridine contains, in addition to the peaks at *m/e* 312, 299, and 284 already discussed, only peaks of rather low intensity. The peak at *m/e* 268 (M − 59) is formed directly from the molecular ion and is accompanied by the usual peaks for ions n (M − 57) and M − 58. The peak at *m/e* 242 is similarly formed from that at *m/e* 299. Its loss of methyl gives that at *m/e* 227. The peak at *m/e* 256 is formed by loss of carbon monoxide from the peak at *m/e* 284.

The spectra of sinomenine and salutaridine were determined at reduced ionizing voltage. In the spectrum of IX only the peaks at *m/e* 314 and 301 remain at 15 and 14 ev. The loss of methyl is apparently a higher energy process than the loss of carbon monoxide, as the M − 15 peak diminishes in intensity much faster than that of M − 28.

Low-energy spectra of XI demonstrate that at 15 ev only the ions at *m/e* 327, 312, 299, 284, and 268 remain, that at 13 ev the loss of carbon monoxide is the only fragmentation observed, and at about 12 ev only the molecular ion remains.

Experimental Section

Mass spectra were determined, without heating, by the direct sample introduction technique on an Atlas CH_4 mass spectrometer equipped with vacuum lock, TO4 ion source, and secondary electron multiplier. The accelerating potential was 3000 v. The ionizing potential was maintained at 70 ev except as noted in the text. The ionizing current varied between 1 and 30 A.

Alkaloids. Morphine, codeine, and thebaine were commercial samples. O-Methylcodeine[19] and codeinone[20] were prepared by standard procedures. Purity of all samples employed was established by melting point, spectra, or thin layer chromatography. Purification, necessary for 10-hydroxycodeine and O-methylcodeine, was effected by thick layer chromatography on silica gel G (Brinkmann).

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