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MASS SPECTRA OF HASUBANONINE, METAPHANINE AND THEIR DERIVATIVES

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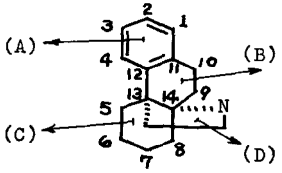
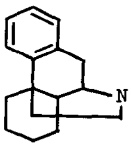
RECENTLY, the structure of hasubanonine[1](V), metaphanine[2](XXII) and prometaphanine[3] from Stephania japonica MIERS. have been reported. The skeleton (hasubanan) of these alkaloids are closely related to morphinan and the difference between two groups is that the ethanamine bridge of hasubanan forms five membered ring, whereas of morphinan forms six membered one. The mass spectra of hasubanan derivatives are of special interest with respect to diagnostic purpose of compound having hasubanan skeleton. In this paper the authors wish to report the mass spectra of hasubanan (I) derivatives and a few morphinan (II) derivatives.



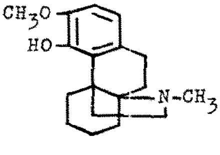
(I)



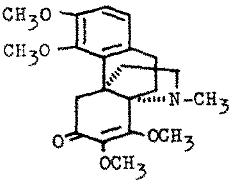
(II)

The mass spectra of twenty-four compounds were examined and may be divided into seven groups and the mass spectra of each group exhibit characteristic fragments as shown in TABLE 1.

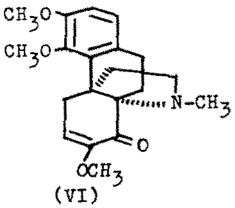
All mass spectra were measured with a Hitachi mass spectrometer model RMU 6C equipped with a heated inlet system: Ion accel. voltage m/e 600; Chamber voltage 80 V; Total emission 80μA; Target current 55 μA.



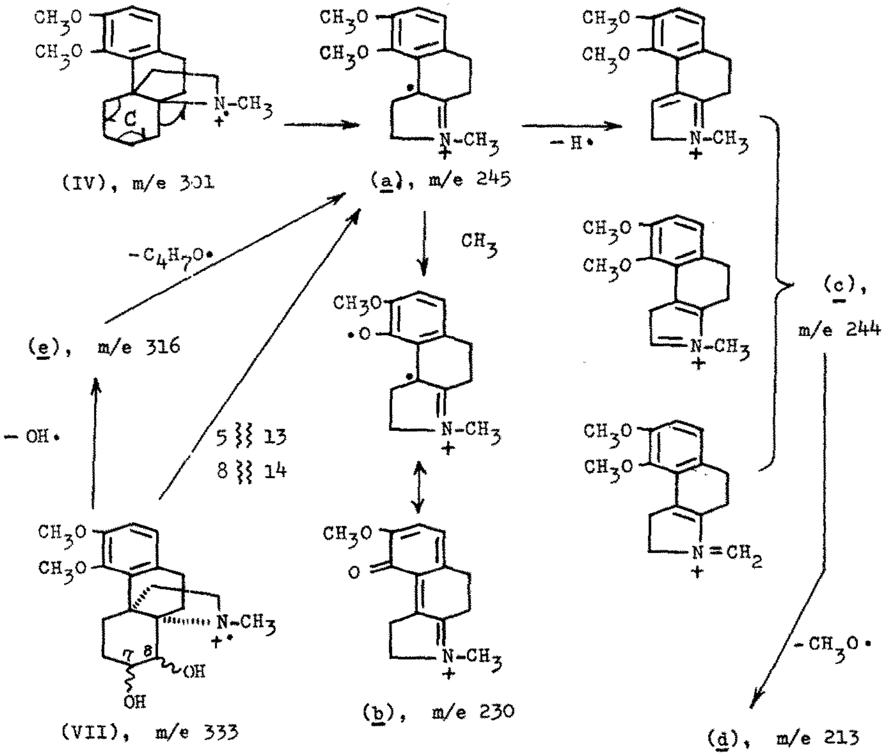
(III)

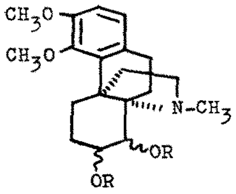


(V)



(VI)





(VIII): R = D

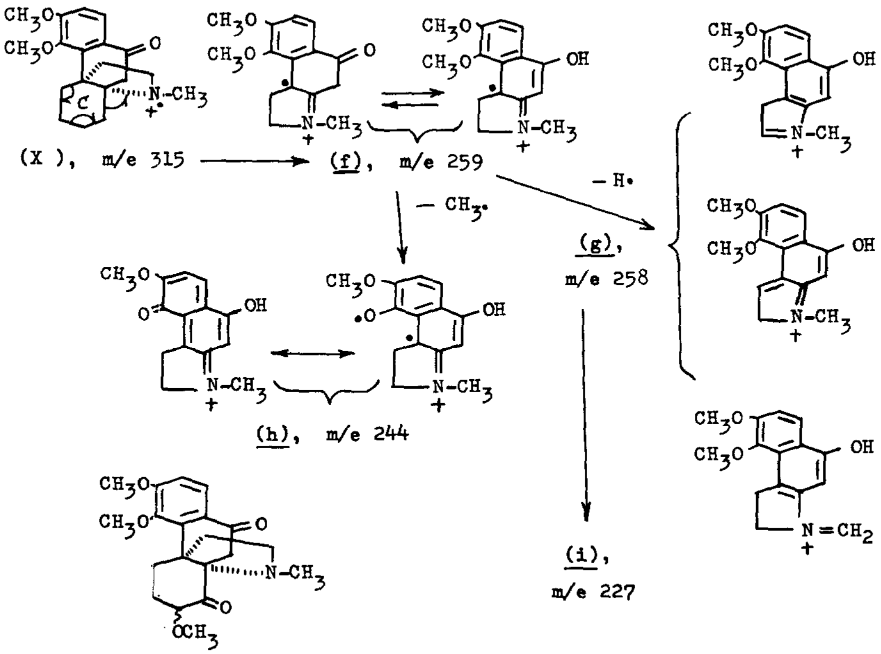
(IX) : R = Ac

Group A[1] (Compound (III), (IV), (VI) and Hasubanonine (V)): The base ion peak in the mass spectrum of compound (IV)(molecular ion at m/e 301) occurs at m/e 245 and is presumably due to the loss of C_4H_8 unit (presumably two mol. of ethylene) from ring C to form ion (a). The presence of a metastable ion at m/e 199.5 ($245^2/301 = 199.4$) seems to substatiate such a process. Ion (a) decomposes further through explusion of a methyl radical to ion (b)(m/e 230). The operation of this process is supported by the existence of a metastable ion at 215.9 ($230^2/245 = 215.9$). Loss of a hydrogen radical from ion (a) to form ion (c)(m/e 244), which further decomposes through explusion of methoxyl to ion (d) (m/e 213). The presence of a metastable ion at m/e 186.0 ($213^2/244 = 185.9$) seems to support such a fragmentation. The mass spectrum of hasubanonine (V) exhibit all of the characteristic fragments noted with compound (IV): M^+ (m/e 373), ion (a)(m/e 245), ion (b)(m/e 230), ion (c)(m/e 244) and ion (d)(m/e 213). The mass spectrum of compound (IV) is shown in Fig. 1.

Group B[2] (Compound (VII), (VIII) and (IX)): The mass spectrum of compound (VII)(Fig. 2) follows the fragmentation pattern of compound (IV), with the exception of a pronounced M-17 ion (e)(m/e 316), which presumably arises from loss of the C-7 or C-8 hydroxyl group. Elimination of C_4H_7O unit from ion (e) furnishes the ion (a)(substantiated by a metastable ion at m/e 190.0 ($245^2/316 = 189.9$)). The ion (a) is also formed from molecular ion (VII) which is substantiated, at least in part, by a metastable ion at m/e 180.1 ($245^2/333 = 180.2$). The fragmentation of this compound is supported by mass shift of compound (IX) and deuterium labelled compound (VIII). Further fragmentations of the ion (a) furnishes ion (b), ion (c) and ion (d), respectively. These fragmentations are substantiated by the presence of metastable ions.

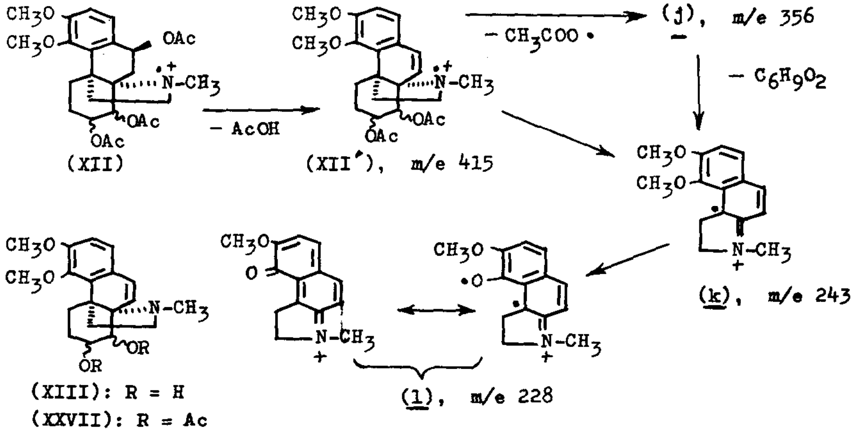
Group C (Dehydrodeoxometaphanine-B (X)$^{2)}$ and Compound (XI)$^{3)}$):

In the mass spectrum of (X)(molecular ion at m/e 315)(Fig. 3) the base ion peak (f) appears at m/e 259 which was presumably formed by loss of C_4H_8 unit (presumably $CH_2{=}CH_2 \times 2$) from ring C. The presence of a metastable ion at m/e 213.0 ($259^2/315 = 212.9$) seems to support such a fragmentation. The ion (f) may undergo further loss of methyl group (substantiated by a metastable ion at m/e 229.9 ($244^2/259 = 229.8$)) to ion (h)(m/e 244). Ion (g)(m/e 258) would at least in part arise from ion (f) by loss of a hydrogen. The ion (g) can also lose methoxyl group to provide ion (i)(m/e 227). The mass spectrum of compound (XI) exhibit all of the characteristic fragments noted with compound (X): M^+(m/e 359), ion (f)(m/e 259), ion (h)(m/e 244), ion (g)(m/e 258) and ion (i)(m/e 227).

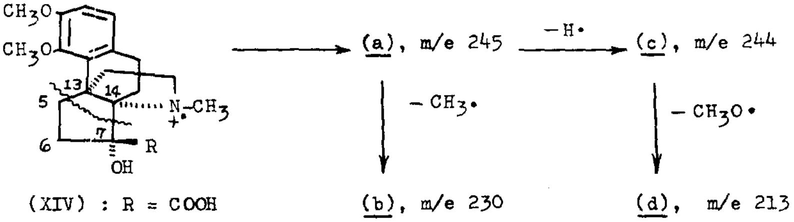


(XI)

Group D2)(Compound (XII) and (XIII)): In the mass spectrum of compound (XII) the molecular ion (m/e 475) is very weak, though detectable. Presumably, loss of an acetic acid in the evaporating system of mass spectrometer leads to ion (XII′). Indeed, distillation of compound (XII) under reduced pressure afforded compound (XXVII)4). Explusion of CH_3COO radical from fragment (XII′)(m/e 415) decomposes further to ion (j)(m/e 356). Existence of a metastable ion at 305.3 ($356^2/415$ = 305.2) seems to substantiate this fragmentation. An ion at m/e 243 (ion (k)) may perhaps ascribed to a loss of $C_6H_9O_2$ unit from ion (j). The operation of this step is supported by the existence of a metastable ion at m/e 166.1 ($243^2/356$ = 165.8). Ion (k) may conceivably also arise from ion (XII′) by loss of a $C_8H_{12}O_4$ (presumably loss of a ethylene and CH(OAc)=CH(OAc)). The presence of a metastable ion at m/e 142.5 ($243^2/415$ = 142.3) seems to substantiate such a process. Loss of methyl radical from ion (k) leads to ion (l)(m/e 228), which is supported by the existence of a metastable ion at m/e 213.4 ($228^2/243$ = 213.1). The mass spectrum of compound (XIII) exhibit all of the characteristic fragments noted with compound (XII): M^+ (m/e 331), ion (k)(m/e 243) and ion (l)(m/e 228), respectively. The mass spectrum of compound (XII) is shown in Fig. 4.



Group E[2] (Amino acid (XIV), Amino acid methyl ester (XV), Compound (XVI) and (XVII)): Although not possessing an intact hasubanan (I) skeleton, compounds belong to Group E are included in this report because of their close structural relation to hasubanan (I). Fission C-5 ∿ C-13 bond and C-7 ∿ C-14 bond of group E furnish base ion peak at m/e 245 (ion (a)). The presence of metastable ions at m/e 166.5 ($245^2/361$ = 166.3) of amino acid methyl ester (XV), m/e 180.5 ($245^2/333$ = 180.7) of compound (XVI) and m/e 189.4 ($245^2/317$ = 189.3) of compound (XVII) would support such fragmentations. Further fragmentations of ion (a) gave ion (b)(m/e 230), ion (c)(m/e 244) and ion (d)(m/e 213), respectively. The presence of metastable ions seems to support such fragmentation processes. The mass spectrum of amino acid methyl ester (XV) is shown in Fig. 5.



(XIV) : R = COOH

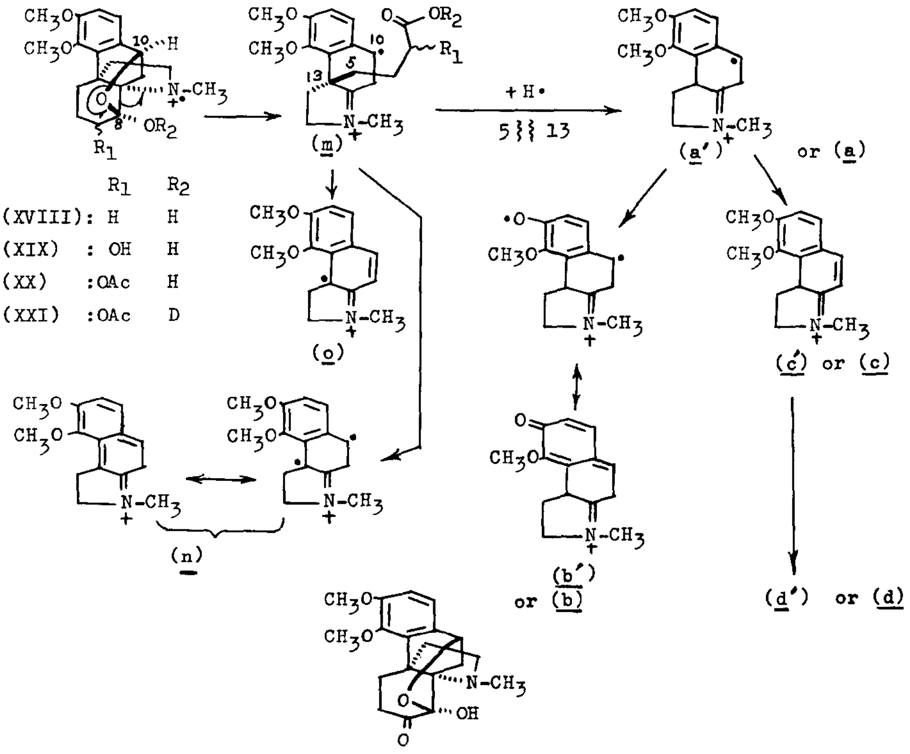
(XV) : R = $COOCH_3$

(XVI) : R = CH_2OH

(XVII): R = CH_3

Group F[2] (Deoxometaphanine-D (XVIII), Dihydrometaphanine (XIX), Monoacetyldihydrometaphanine (XX), Monoacetyldihydrometaphanine-d (XXI) and metaphanine (XXII)): It is surprising that in the mass spectra of compounds possessing a hemiketal ether bridge between C-8 and C-10 showed base ion peak at m/e 245 (ion (a) or (a′)). Ion (a)(or (a′)) would arise by a hydrogen rearrangement to C-10 (or C-13) and by a loss of a $C_4H_3O_2R_1R_2$ unit from intermediate ion (m)(molecular ion).

The origin of a rearranged hydrogen and a mechanism for this complex process are not apparent. Ion (a)(or (a')) decomposes further to ion (b) (or (b'))(m/e 230), ion (c)(or (c'))(m/e 244) and ion (d)(or (d'))(m/e 213). The operation of this process are supported by the existence of metastable ions. An ion m/e 244 would also arise by C-5~C-13 bond fission from ion (m) to afford ion (n)(m/e 244). An ion (o)(m/e 243) would arise by loss of a hydrogen and C-5~C-13 bond fission from molecular ion (m) which is more abundant than in the mass spectra of Group A, B and E. The mass spectrum of metaphanine (XXII)(Fig. 6) shows qualitatively similar characteristic fragmentation ions: ion (a)(or (a')) (m/e 245), ion (b)(or (b'))(m/e 230), ion (c)(or (c'), (n))(m/e 244), ion (e)(m/e 213) and ion (o)(m/e 243).



	R1	R2
(XVIII):	H	H
(XIX) :	OH	H
(XX)	:OAc	H
(XXI)	:OAc	D

(XXII)

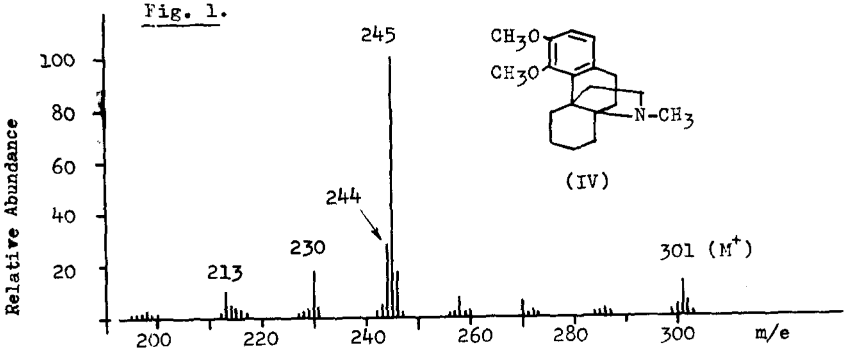


Fig. 1.

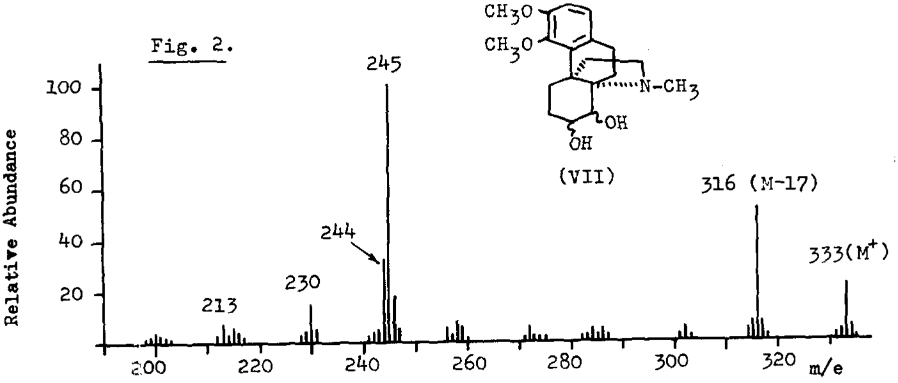


Fig. 2.

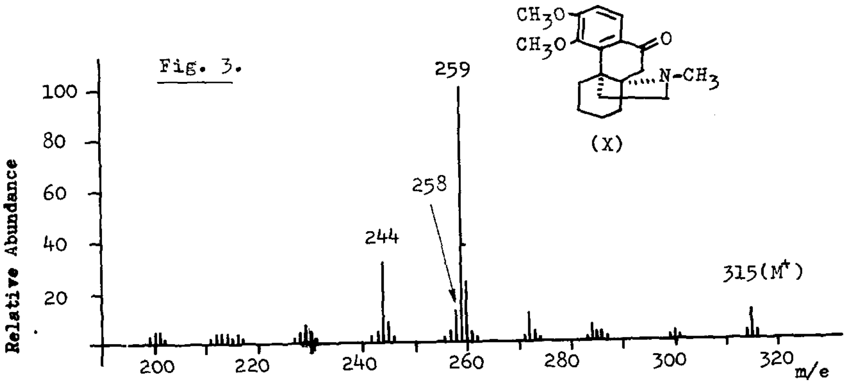


Fig. 3.

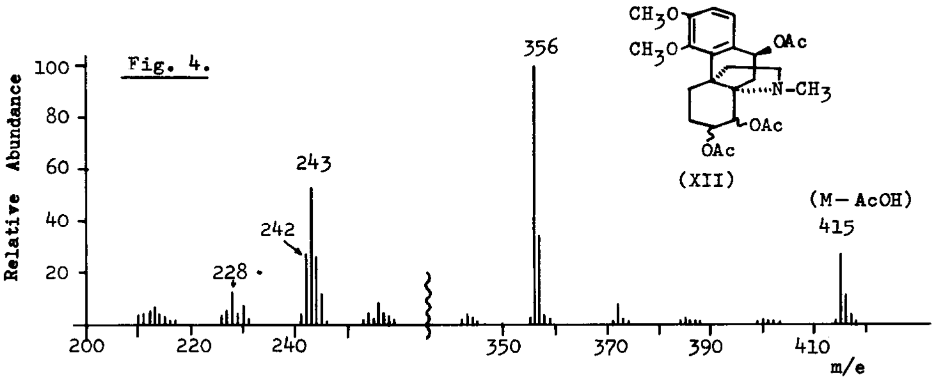


Fig. 4.

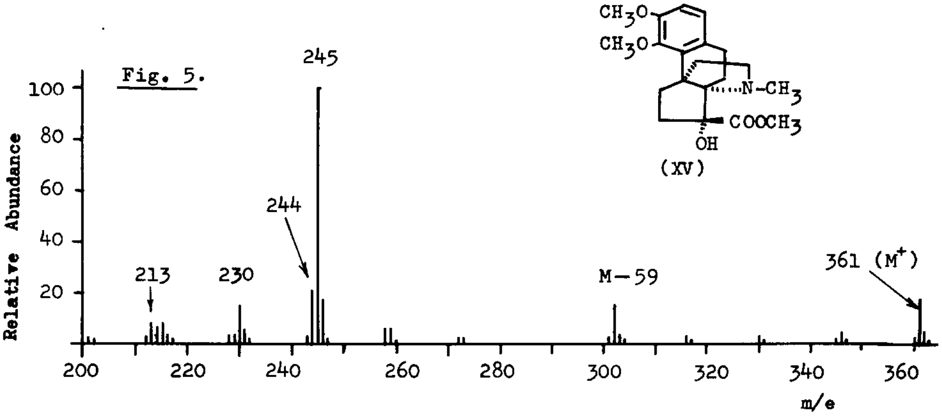


Fig. 5.

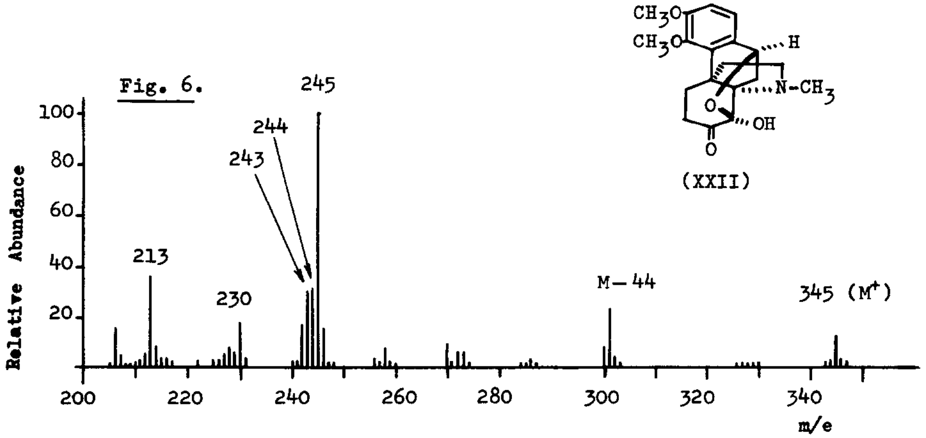


Fig. 6.

TABLE I (A)

Abundance of characteristic fragments of hasubanan derivatives
(The most intense peak (base peak) is taken as 100%).

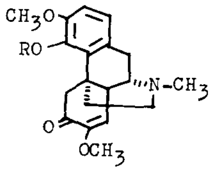
No.	M^+(%)	M-15(%)	$^m/_e$ (%)	$^m/_e$ (%)	$^m/_e$ (%)	$^m/_e$ (%)
(III)	287(24)	272 (3)	231(100)	230(30)		
(IV)	301(14)	286 (3)	245(100)	244(28)	230(19)	213(10)
(V)	373(47)	358(11)	245(100)	244(33)	230(26)	213(17)
(VI)	343(36)	328(21)	245 (73)	244(23)	230(28)	213(17)
(VII)	333(22)	318(2)	245(100)	244(32)	230(16)	213 (7)
(VIII)	335(9)	320(1)	245(100)	244(33)	230(20)	213(9)
(IX)	417(32)	402(2)	245(99)	244(26)	230(42)	213(7)
(X)	315(11)	300(3)	259(100)	258(13)	244(32)	227(2)
(XI)	359(30)	344(42)	259(57)	258(47)	244(31)	227(17)
(XII)	475(-)	360(-)	243(52)	242(27)	228(10)	211(4)
(XIII)	331(61)	316(7)	243(100)	242(88)	228(27)	211(17)
(XIV)	347(8)	332(2)	245(100)	244(72)	230(34)	213(12)
(XV)	361(18)	346(5)	245(100)	244(21)	230(15)	213(7)
(XVI)	333(6)	318(2)	245(100)	244(44)	230(18)	213(11)
(XVII)	317(17)	302(3)	245(100)	244(48)	230(16)	213(12)
(XVIII)	331(34)	316(4)	245(100)	244(53)	230(14)	213(48)
(XIX)	347(3)	332(1)	245(100)	244(61)	230(27)	213(73)
(XX)	389(10)	374(1)	245(100)	244(46)	230(22)	213(49)
(XXI)	390(5)	385(1)	245(100)	244(53)	230(19)	213(43)
(XXII)	345(12)	330(2)	245(100)	244(32)	230(19)	213(36)

TABLE I (B)

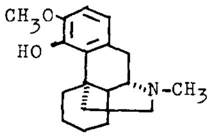
Abundance of fragments of morphinan derivatives in comparison with hasubanan derivatives.
(The most intense peak (base peak) is taken as 100%).

No.	M^+(%)	M-15(%)	$^m/_e$(%)	$^m/_e$(%)	$^m/_e$(%)	$^m/_e$(%)
(XXIII)	329(59)	314(80)	231(2)	230(5)		
(XXIV)	343(100)	328(92)	245(1)	244(4)	230(1)	213(3)
(XXV)	287(71)	272(7)	231(5)	230(14)		
(XXVI)	299(100)	284(14)	245(3)	244(3)	230(2)	213(2)

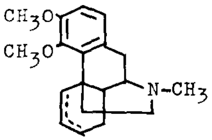
Group G (Sinomenine (XXIII), Methylsinomenine (XXIV)[5], Demethoxydeoxodihydrosinomenine (XXV)[6] and $\Delta^{5(\text{or } 6)}$– Tetrahydrodeoxycodeine methyl ether (XXVI)[7]): The outstanding feature of the mass spectra of this group is the appearance of intense molecular ion peaks and the ions corresponding to m/e 245 were below 5% of base ion peaks, though a few numbers of the compounds were examined. This should be important in diagnostic purpose to differentiate hasubanan (I) derivative from morphinan (II) derivative (— those of not having C-4 ∼ C-5 ether bridge —).



(XXIII): R = H
(XXIV) : R = CH_3



(XXV)



(XXVI)

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