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Mass Spectrometry of Oxidation Products of Δ^1- and Δ^6-Tetrahydrocannabinols[1]

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The mass spectra of Δ^1- (Ia), Δ^6-tetrahydrocannabinol (Δ^6-THC) (IIa), 6α- (IIIa), 6β-hydroxy- (IVa), 7-hydroxy-Δ^1-THC (Va), 7-hydroxy- (VIa), 7-oxo-Δ^6-THC (VIIa), cannabinol (CBN, VIIIa), 6-hydroxy- (IXa), 7-hydroxy- (Xa), 7-oxo-CBN (XIa) and their acetyl derivatives were determined. Structure correlations and principal fragmentation pathways for these compounds were studied with the aid of the high resolution mass spectrometry and of d_3-acetyl derivatives. A typical fragmentation pattern was observed in both spectra of Δ^1- and Δ^6-THC series. The structure of the essential fragment ion for the compound mentioned above was well characterized by reasonable interpretation.

The mass spectrometry of the constituents (cannabinoids) of *Cannabis Sativa L* (hemp) has been studied by Budzikiewicz, *et al.*, Claussen, *et al.*, Vree, *et al.* and Terlouw, *et al.*[3] Several reports on the chemistry of hydroxytetrahydrocannabinols, which are the primary metabolites of the physiologically active principle, (—)-Δ^1-3,4-*trans*-tetrahydrocannabinol (Δ^1-THC, Ia), have appeared, whereas those mass spectrometries have not yet been argued in detail.[4] In view of our interest in the chemical and pharmacological properties of marihuana or hashish, the well-known resin of hemp, we have recently investigated several oxidation products of Δ^1- (Ia) and Δ^6-THC (IIa) using selenium dioxide.[5] The structural determination of these compounds has been facilitated by spectrometric aids, especially by interpretation of the mass fragmentation and characterization of the ion structures. The present paper concerns a discussion on the mass spectra and fragmentation behaviors of these compounds.

Experimental

Material——The compounds submitted to the measurements are Δ^1-THC (Ia), Δ^6-THC (IIa) and cannabinol (CBN, VIIIa) as well as oxidation products of Ia, that is, 6α- (IIIa), 6β-hydroxy- (IVa), 7-hydroxy-Δ^1-THC (Va), 6-hydroxy- (IXa), 7-hydroxy-(Xa), 7-oxo-CBN (XIa) and those of IIa, that is, 7-hydroxy- (VIa) and 7-oxo-Δ^6-THC (VIIa).[5] The purity of these compounds was estimated to be 94—98% by gas chromatography (GLC). Acetyl and d_3-acetyl derivatives were obtained by the usual manner of acetylation with acetic anhydride/pyridine, and hexadeutero acetic anhydride (Merck)/pyridine, respectively.

Apparatus——The mass spectrometry was performed on a Hitachi RMS-4 mass spectrometer with direct inlet system. The acceleration and ionizing potential were 3 kV and 35 eV, respectively. The temperature of the source was 120° for hydroxy derivatives (a) and 90° for acetyl analogues (b), and the temperature of the probe was adjusted at 230° for (a) and 170° for (b). The high resolution mass spectra were measured by JMS-01SG.

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1) Presented to the 94th Annual Meeting of Pharmceutical Society of Japan, Sendai, Apr., 1974; Abstracts II, p. 239.
2) Location: *Shinanomachi, 35, Shiniuku-ku, Tokyo.*
3) *a*) H. Budzikiewicz, R.T. Alpin, D.A. Lightner, C. Djerassi, R. Mechoulam, and Y. Gaoni, *Tetrahedron*, **21**, 1881 (1965); *b*) U. Claussen, H-W. Fehlhaber, and F. Korte, *ibid.*, **22**, 3535 (1966); *c*) T.B. Vree and N. M.M. Nibbering, *ibid.*, **29**, 3849 (1973); *d*) J.K. Terlouw, W.H eerma, P.C. Burgers, C. Dukstra, A. Boon, H.F. Kramer, and C.A. Salemink, *ibid.*, **30**, 4243 (1974).
4) F. Mikes, A. Hofmann, and P.G. Waser, *Biochem. Pharmacol.*, **20**, 2469 (1971), references *loc. cit.*
5) S. Inayama, A. Sawa, and E. Hosoya, *Chem. Pharm. Bull.* (Tokyo), **22**, 1519 (1974).

Results and Discussion

1) Δ^1-THC (Ia), Δ^6-THC (IIa), and Their Acetyl Derivatives (Ib, IIb)

The spectra of Δ^1- (Ia) and Δ^6-THC (IIa), which are consistent with those in Claussen's reports,[3b] are exhibited in Fig. 1 for a convenience of comparison with those of the oxidation products. One methyl radical separates easily from *gem*-dimethyl at C-8 (*m/e* 299) in both cases. The subsequent cleavage occurs between the benzyl carbon and its neighboring methylene in the amyl side chain to result in liberation of butylene (*m/e* 243). Both the peak heights of the fragment ion (a) (*m/e* 246) and (b) (*m/e* 231) in IIa are stronger than those in Ia. IIa produces ion (a) *via* a well-known retro Diels-Alder reaction with loss of 2-methylbutadiene.[3] Ion (a) is converted by expulsion of a methyl radical to the stable ion (b) to produce further ion (c) by a rupture of the side chain.

On the contrary, the isomerization of the double bond to the 1, 6 position followed by the subsequent retro Diels-Alder reaction must be essential for Ia to produce ion (b), but such a migration may hardly occur in Ia. Vree, *et al.* states that ion (b) is not produced by the retro Diels-Alder reaction, but preferentially by a phenolic proton transfer to 1, 2 double bond.[3c] The prominent fragment ion (f) (*m/e* 271) of Ia should be produced by elimination of isopropyl radical from the molecular ion.[3a] In general, the mass spectral feature of Δ^1-THC (Ia) exists in the liberation of isopropyl radical, and that of Δ^6-THC (IIa) is a retro Diels-Alder reaction.

Concerning the acetyl derivatives of Ia and IIa, the spectrum of 3'-acetyl-Δ^6-THC (IIb) is almost same as that of IIa in the mass region less than the fragment ion (*m/e* 314), which

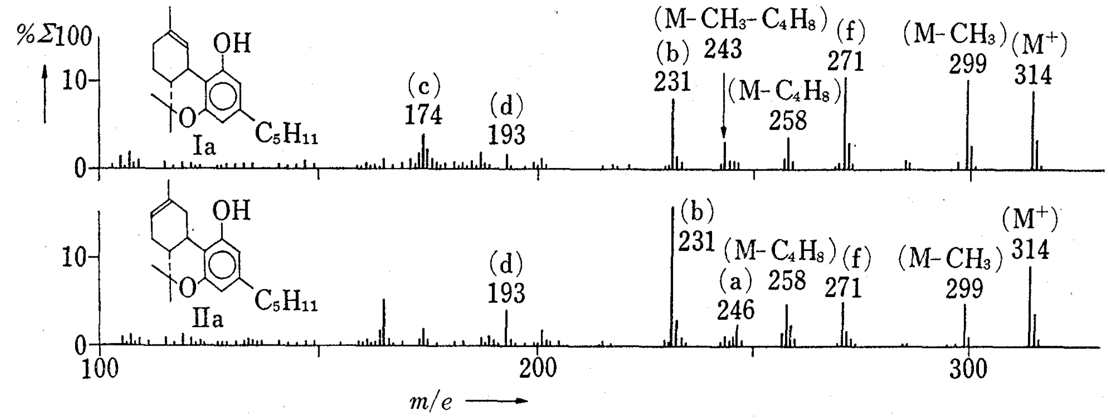


Fig. 1. Mass Spectra of Δ^1-(Ia) and Δ^6-THC (IIa)

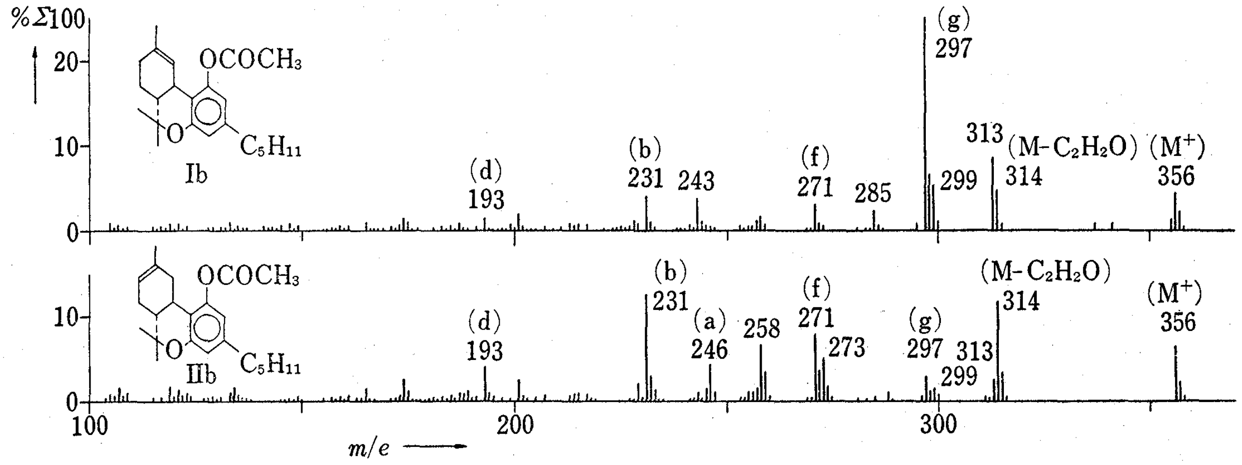
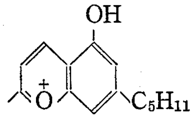
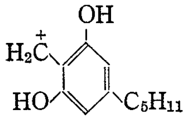


Fig. 2. Mass Spectra of Ib and IIb

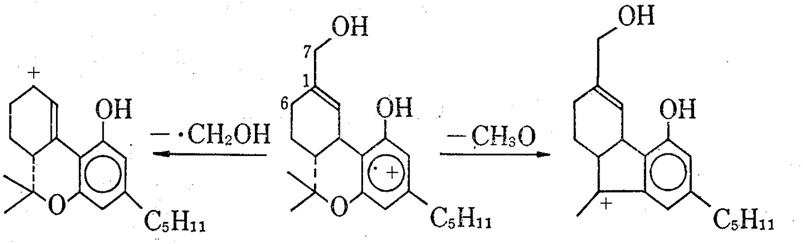
is produced by elimination of ketene from acetyl group in the molecular ion (Fig. 2). On the other hand, the fragment ion (g) (*m/e* 297, $M-CH_3COO$), which is not seen in Ia, is remarkable in the case of 3′-acetyl-Δ^1-THC (Ib). This elimination is also supported by the fact that the most abundant fragment ion peak appears at *m/e* 297 in the spectrum of the d_3-acetyl derivative of Ia (Table I). Such an elimination of acetoxy radical is rarely observed in phenyl acetates, since the elimination of ketene occurs commonly. The ratio of intensity of the two ion peaks (*m/e* 297: 314) is approximately 5: 1 in Ib, whereas it is 1: 4 in IIb inversely. The elimination of isopropyl radical from the molecular ion affords the fragment ion *m/e* 313. The intensity of this ion in Ib is more abundant than that in IIb similarly in the case of Ia and IIa. Thus, the characteristic difference of abundance observed between the fragment ion peaks at *m/e* 297 of acetyl derivatives (Ib and IIb) is remarkable, although there exists only a slight one between the spectra of Ia and IIa. Δ^1- and Δ^6-isomer can be therefore distinguished from each other by comparison of the mass spectra of the corresponding acetyl derivatives.

TABLE I. Mass Number of Ion from Compounds Ib and VIb

Assignment	Ib			VIb		
	m/e obsd. (calcd.)	Component	*m/e* [d_3-Ac]	*m/e* obsd. (calcd.)	Component	*m/e* [d_3-Ac]
M	356.2309 (356.2351)	$C_{23}H_{32}O_3$	359	414.2379 (414.2406)	$C_{25}H_{34}O_5$	420
$M-C_2H_2O$	314.2205 (314.2245)	$C_{21}H_{30}O_2$	315, 314	372.2297 (372.2300)	$C_{23}H_{32}O_4$	376, 375
$M-CH_3CO_2H$				354.2195 (354.2195)	$C_{23}H_{30}O_3$	357
$M-C_2H_2O-CH_3$	299.1999 (299.2011)	$C_{20}H_{27}O_2$	300, 299			
$M-CH_3CO_2H-CH_3$				339.1966 (339.1960)	$C_{22}H_{27}O_3$	342
$M-CH_3CO_2H-C_2H_2O$				312.2078 (312.2089)	$C_{21}H_{28}O_2$	313, 312
$M-CH_3CO_2H-C_2H_2O-CH_3$				297.1863 (0.1854)	$C_{20}H_{25}O_2$	298, 297
$M-CH_3CO_2$	297.2198 (297.2218)	$C_{21}H_{29}O$	297			
$M-CH_3CO_2H-CH_3CO_2$				295.2080 (295.2061)	$C_{21}H_{27}O$	295
$M-CH(CH_3)_2$	313.1806 (313.1803)	$C_{20}H_{25}O_3$				
$M-C_2H_2O-CH(CH_3)_2$	271.1680 (271.1698)	$C_{18}H_{23}O_2$	272, 271			
$M-C_2H_2O-CH_3CO_2H-CH(CH_3)_2$				269.1534 (269.1541)	$C_{18}H_{21}O_2$	270, 269
$M-C_2H_2O-C_4H_8$	258.1616 (258.1619)	$C_{17}H_{22}O_2$	259, 258			
$M-C_2H_2O-CH_3CO_2H-C_4H_8$				256.1449 (256.1463)	$C_{17}H_{20}O_2$	256
$M-C_2H_2O-C_4H_8-CH_3$	243	$C_{16}H_{19}O_2$	244, 243			
	231	$C_{15}H_{19}O_2$	232, 231	231.1388 (231.1385)	$C_{15}H_{19}O_2$	232, 231
	193	$C_{12}H_{17}O_2$	194, 193	193.1221 (193.1228)	$C_{12}H_{17}O_2$	194, 193
$231-C_4H_9$	174	$C_{11}H_{10}O_2$	175, 174	174.0692 (174.0680)	$C_{11}H_{10}O_2$	175, 174
$193-C_3H_8$	149	$C_9H_9O_2$	149	149.0596 (149.0602)	$C_9H_9O_2$	149

2) Oxidation Products of Δ^1-THC (Ia), Δ^6-THC (IIa), and Their Acetyl Derivatives

The stereoisomers, 6α- (IIIa) and 6β-hydroxy-Δ^1-THC (IVa) gave almost the same fragmentation (Fig. 3). The configuration of the hydroxy group at C-6 in IIIa and IVa has been mainly established by proton magnetic resonance spectrometry to be equatorial and axial, respectively,[5] and found to reflect the respective abundance of the dehydrated fragment ion (*m/e* 312) in each spectrum. Since the equatorial hydroxyl group in IIIa is more readily eliminated than the axial one in IVa, the dehydration may proceed *via* the process represented in term of a thermal *cis* elimination of the hydroxy group at C-6 and a proton at C-5.[6] The other major fragmentation is observed in the course of elimination of a methyl radical from the molecular ion (*m/e* 315), subsequent dehydration (*m/e* 297) and of elimination of an isopropyl radical (*m/e* 287, $M-C_3H_7$). There exist in addition minor fragment ions produced by elimination of isopropyl radical or butylene accompanying dehydration (*m/e* 269 or 256). The most abundant fragment ion peak (h) (*m/e* 271), base peak, is derived by liberation of the isopropoxy radical from the molecular ion. The elemental composition of the ion (h) ($C_{18}H_{23}O_2$) has been confirmed by the high resolution mass spectrum (Table II). It can be seen that the butyl radical is further eliminated from the side chain of the ion (h) to yield the fragment ion *m/e* 214. The ion (b), (c), (d) and (e) are the same fragment ions as those mentioned in Ia and IIa. There is no significant difference between the spectra of IIIa and IVa except that the dehydrated ion peak (*m/e* 312) of IVa is relatively less abundant than that of IIIa.



ia *m/e* 299 Va *m/e* 330 ib *m/e* 299

Chart 1

In the spectrum of 7-hydroxy-Δ^1-THC (IVa), there exists a characteristic predominant fragment ion (i) (*m/e* 299), whose elemental composition is deduced to be $C_{20}H_{27}O_2=M-CH_3O$ by means of a high resolution mass spectrometry (Fig. 3, Table II). The probable structure of the ion (i) is estimated to be (ia) being produced by expulsion of hydroxymethyl radical at C-7 on the basis of labeled experiment with the deuterated derivative of Va. The alternative ion structure (ib) should be possibly produced by elimination of one of the *gem*-dimethyl together with the etheral oxygen adjacent to C-8, whereas the corresponding fragment ion peak can not be observed indeed in the spectra of other THC derivatives (Ia, IIa, IIIa, IVa, VIa and VIIa). Thus, the former (ia) may be considered reasonable and more favorable than the latter (ib) (Chart 1). Other fragment ion peaks are similar to those of IIIa and IVa. The elimination of methyl radical, water and the both from the molecular ion produces the fragment ion *m/e* 315 ($M-CH_3$), *m/e* 312 ($M-H_2O$) and *m/e* 297 ($M-CH_3-H_2O$), respectively. The fragment ion at *m/e* 256 should be produced by elimination of water and butylene from the side chain of Va, and *vice versa.* The elimination of water and isopropyl radical and isopropoxy radical from the molecular ion should lead to the fragment ions *m/e* 269 ($M-H_2O-C_3H_7$) and *m/e* 271 ($M-C_3H_7O$), respectively, the latter of which corresponds to the prominent ion (h)

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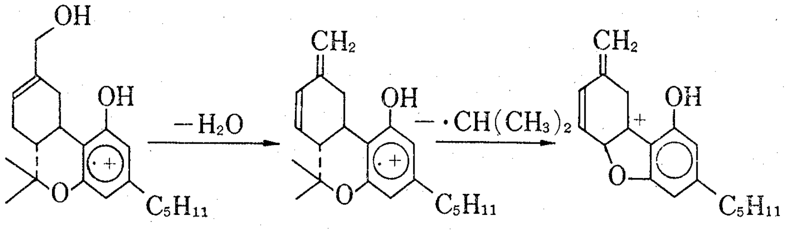
6) H. Budzikiewicz, C. Djerassi, and D.H. Williams, "Mass Spectrometry of Organic Compounds," Holden-day, Inc., San Francisco, 1967, p. 111.

in IIIa and IVa. Further fragment ion at *m/e* 243, (b) *m/e* 231, (d) *m/e* 193 and (e) *m/e* 149 are also observed in the lower mass range of the same spectrum mentioned as above.

On the other hand, in the spectrum of 7-hydroxy-Δ^6-THC (VIa), the ion peak at *m/e* 299, which corresponds to the prominet ion (i) being characteristic of Va, is neglegible (Fig. 3). The molecular ion (*m/e* 330) and chromenyl ion (b, *m/e* 231) are, instead, in abundance with similarity to Δ^6-THC (IIa). The demethylated ion peak from the molecular ion (*m/e* 315) appears very weak, but the dehydrated ion (*m/e* 312) and the same one followed by demethylation (*m/e* 297) are all abundant as in Va. Instead of the deisopropoxy ion from the molecular ion (*m/e* 271), the deisopropylated ion with dehydration (*m/e* 269) is relatively strong when



VIa *m/e* 330   *m/e* 312   *m/e* 269

Chart 2

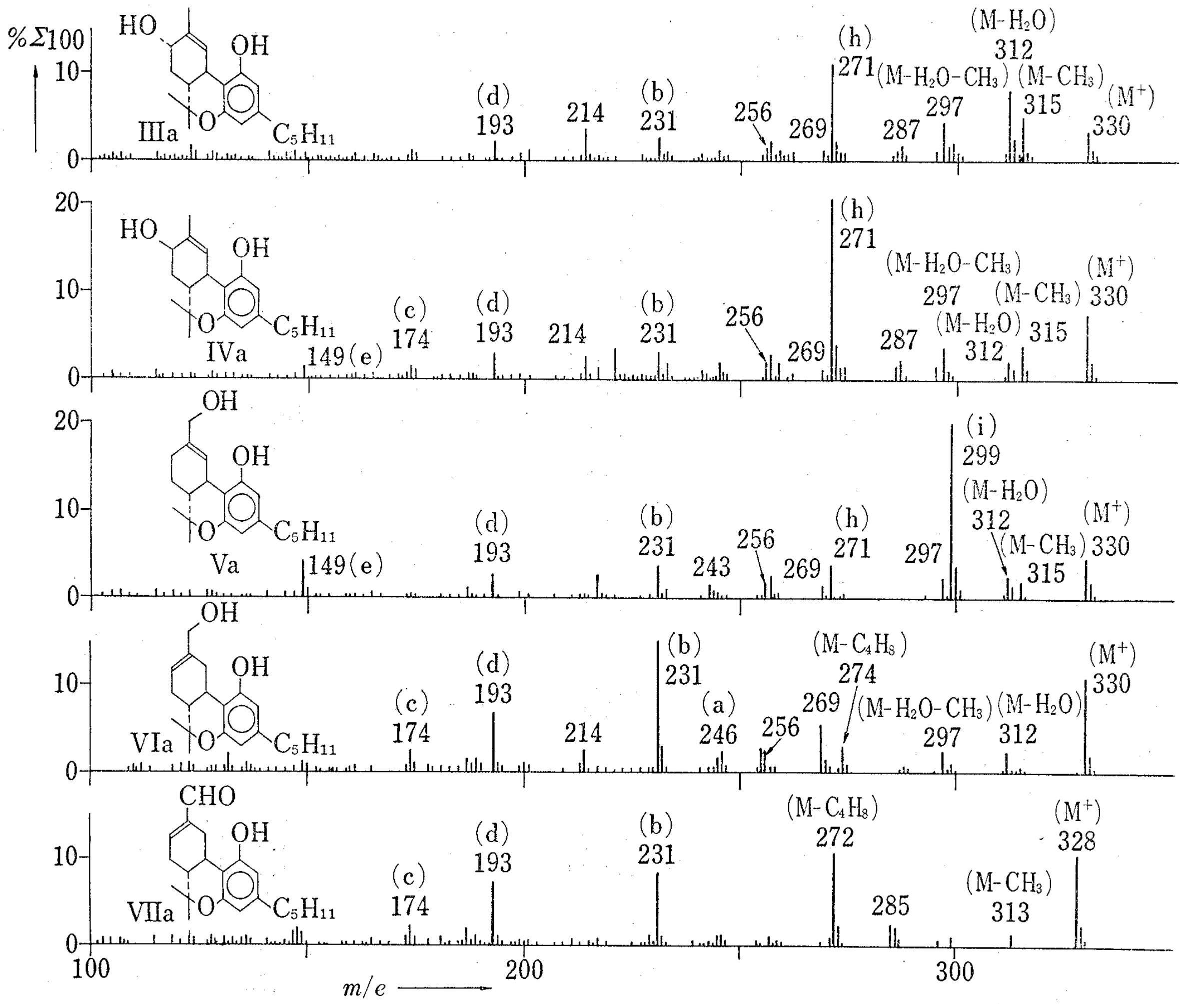
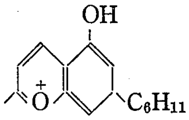
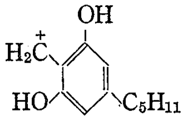


Fig. 3. Mass Spectra of 6α-(IIIa), 6β-(IVa), 7-Hydroxy-Δ^1-THC(Va), 7-Hydroxy-(VIa) and 7-Oxo-Δ^6-THC (VIIa)

compared to those in IIIa, IVa and Va. The elimination of butylene (*m/e* 274) from the side chain of the molecular ion appears somewhat prominent in VIa, whereas the corresponding ion peak is much less abundant in the case of IIIa through Va. As another feature in fragmentations of IIIa through VIa, the elimination of both isopropyl radical and water (*m/e* 269) in VIa occurs predominantly, while the expulsion of isopropoxy radical (*m/e* 271) is characteristic of IIIa, IVa and Va (Chart 2). Thus, the introduction of the hydroxy group at C-7 position of Δ^1- (Ia) and Δ^6-THC (IIa) causes a characteristic difference between the mass spectra of the respective 7-hydroxy derivatives (Va and VIa), in which the elimination of C-7 hydroxy methylene predominates in the former (Va) (Va/VIa=222/1, Fig. 3). The above mentioned fact may be rationalized by assuming that the cation at C-1 in the fragment ion (ia, *m/e* 299) produced from Va could be stabilized by a way of conjugation through the migrated double bond (Δ^2) with the aromatic nucleus.

In the spectrum of 7-oxo-Δ^6-THC (VIIa), which is prepared by the oxidation of the primary alcohol (VIa),⁵⁾ the fragment ion (b) (*m/e* 231) and (d) (*m/e* 193) are abundant similarly in other Δ^6-THC derivatives. The molecular ion (*m/e* 328) and the ion left after elimination of butylene from the side chain (*m/e* 272) are more abundant than those of VIa (Fig. 3). The demethylated ion (*m/e* 313) and deisopropylated ion (*m/e* 285) from the molecular ion are also involved in the spectrum.

Table II. Mass Number of Ion from Compounds IIIa, Va and VIIa

Assignment	IIIa	Va		VIIa	
	m/e obsd.	*m/e* obsd. (calcd.)	Component	*m/e* obsd. (calcd.)	Component
M	330.2191	330.2193 (330.2195)	$C_{21}H_{30}O_3$	328.1961 (328.2038)	$C_{21}H_{28}O_3$
$M-CH_3$	315.1975	315.1959 (315.1960)	$C_{20}H_{27}O_3$	313.1804 (313.1803)	$C_{20}H_{25}O_3$
$M-H_2O$	312.2086	312.2129 (312.2089)	$C_{21}H_{28}O_2$		
$M-CH_2OH$		299.2021 (299.2011)	$C_{20}H_{27}O_2$		
$M-CH_3-H_2O$	297.1865	297.1861 (297.1854)	$C_{20}H_{25}O_2$		
$M-CH(CH_3)_2$	287.1677	(287.1647)	$C_{18}H_{23}O_3$	285.1532 (285.1490)	$C_{18}H_{21}O_3$
$M-OCH(CH_3)_2$	271.1699	271.1681 (271.1698)	$C_{18}H_{23}O_2$		
$M-H_2O-CH(CH_3)_2$	269.1536	269.1562 (269.1541)	$C_{18}H_{21}O_2$		
$M-CH_2OH-CH(CH_3)_2$ or $M-H_2O-C_4H_8$	256.1471	256.1483 (256.1463)	$C_{17}H_{20}O_2$		
$M-C_4H_8$				272.1427 (272.1412)	$C_{17}H_{20}O_3$
$M-CH_2OH-C_4H_8$		243.1400 (243.1385)	$C_{16}H_{19}O_2$		
$M-OCH(CH_3)_2-C_4H_9$	214.1000	(214.0993)	$C_{14}H_{14}O_2$		
	231.1403	231.1395 (231.1385)	$C_{15}H_{19}O_2$	231.1414 (231.1385)	$C_{15}H_{19}O_2$
	193	193	$C_{12}H_{17}O_2$	193.1240 (193.1228)	$C_{12}H_{17}O_2$
$231-C_4H_9$				174.0686 (174.0680)	$C_{11}H_{10}O_2$

3′-Acetyl-6α- (IIIb) and 3′-acetyl-6β-acetoxy-Δ^1-THC (IVb) show almost the same mass spectra (Fig. 4). Both the molecular ion peaks (*m/e* 414) appear to be very weak, whereas the fragment ion formed by elimination of acetic acid from the molecular ion (*m/e* 354) and that derived by further elimination of ketene (*m/e* 312) are much abundant. Facile cleavage of 6-acetoxy group in IIIb and IVb may be considered to proceed through the McLafferty rearrangement. In the spectra of the d_3-acetyl compounds, the most abundant ion peaks (*m/e* 357 and 313) corresponding to *m/e* 354 and 312 in the normal compounds are observed. The metastable ion appeared at *m/e* 275 means the ion *m/e* 354 affording the ion *m/e* 312 under the expulsion of ketene. The other fragment ions of *m/e* 339 and *m/e* 297 are produced by elimination of methyl radical from the ion *m/e* 354 and *m/e* 312, respectively. The somewhat prominent ion peak at *m/e* 295 in IVb seems to be produced like in Ib by elimination of the acetoxy radical from the phenylacetate.

The mass spectrum of the diacetyl derivative (Vb) of 7-hydroxy-Δ^1-THC (Va) is almost the same as those of IIIb and IVb (Fig. 4). The acetoxy group at C-7 can be easily expeled as an acetic acid from the molecular ion. The resulting fragment ions (*m/e* 354 or 312) are considered stable because the linear conjugated diene in each molecule is further in conjugation with the aromatic ring. A metastable ion is observed at *m/e* 375 in the spectrum like in IIIb and IVb. The ion peak at *m/e* 269 in Vb is somewhat abundant when compared to the corresponding one in IIIb or IVb. This fragment ion must be produced by elimination of the isopropyl radical from the ion *m/e* 312.

In the mass spectrum of the diacetyl derivative (VIb) of 7-hydroxy-Δ^6-THC (VIa), the molecular ion *m/e* 414 appears clearly, and the fragment ion *m/e* 372 is more abundant than *m/e* 354 differing from the case of IIIb through Vb (Fig. 4, Table I). The above mentioned fact suggests that the elimination of ketene from the phenyl acetate in the former occurs more easily than that of acetic acid from acetoxy group at C-7 in the latter, and is further

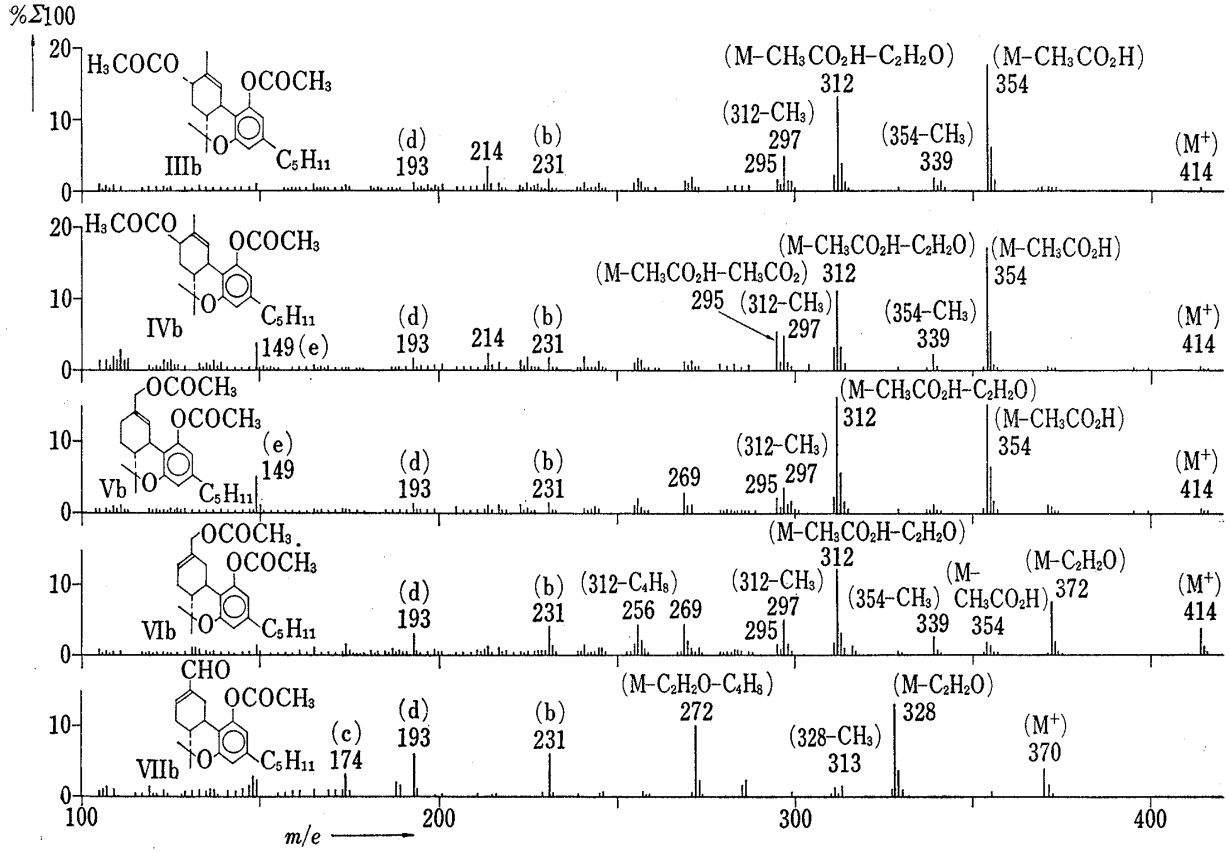


Fig. 4. Mass Spectra of IIIb, IVb, Vb, VIb, and VIIb

supported by the metastable ion (m*) appeared at *m/e* 335 (Calcd. $372^2/414$) in the former. It can be assumed to ascribe to the following reason: The acetoxy carbonyl at C-7 would be so hard of access to the hydrogen at C-2 due to the steric hindrance of 3′-acetoxy group that no elimination of acetic acid could occur. In fact, once the fragment ion *m/e* 372 is produced by elimination of ketene from the molecular ion, it expels easily acetic acid to result in formation of the ion *m/e* 312 ($m^*=262=312^2/372$). The fragmentation in the lower mass range is same as that of VIa.

The mass spectrum of the acetyl derivative (VIIb) of 7-oxo-Δ^6-THC (VIIa) exhibits nearly the same fragmentation as that of VIIa in the mass range less than *m/e* 328 produced by elimination of ketene from the molecular ion, and the molecular ion shows the same abundance as that of VIb (Fig. 4).

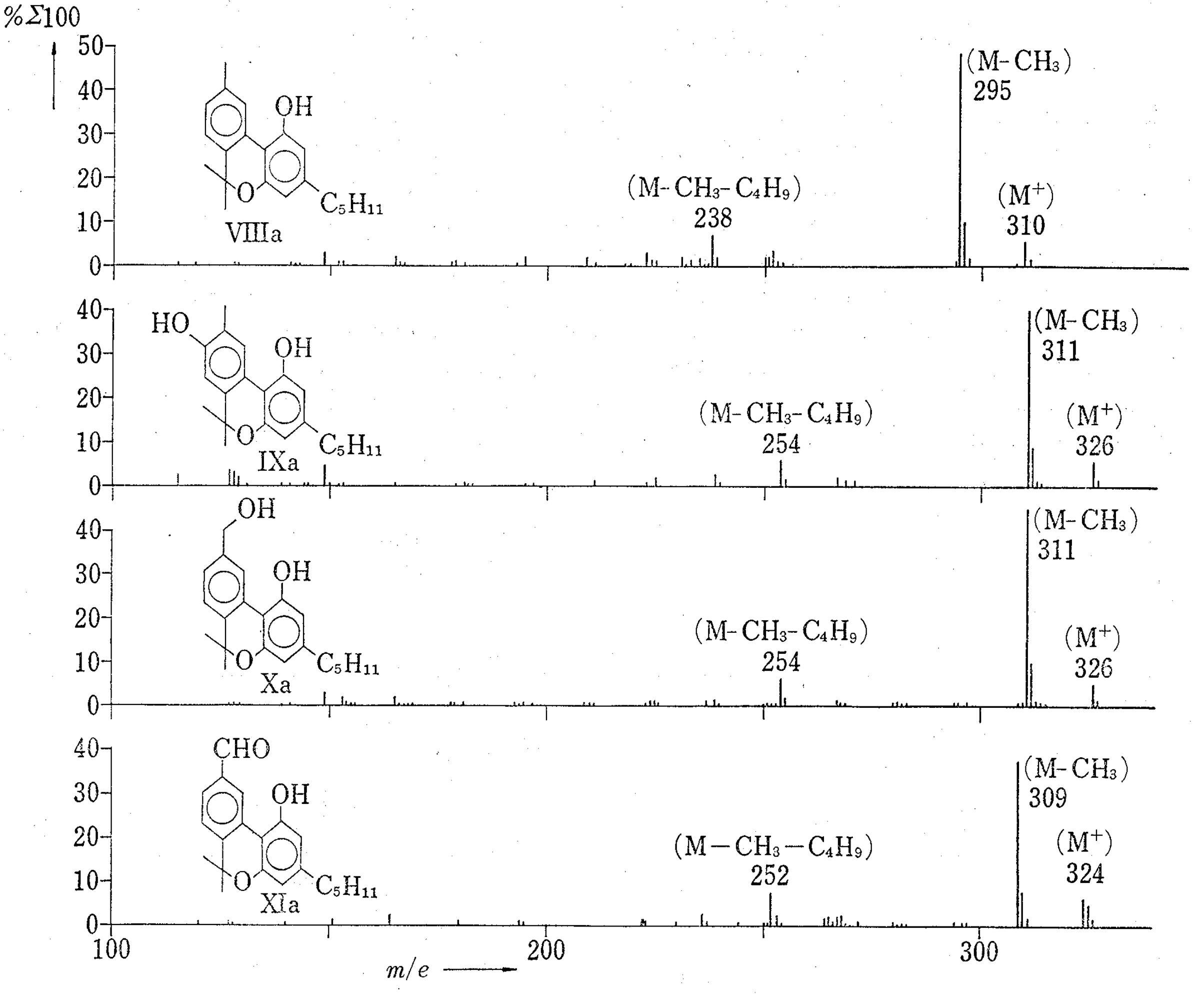


Fig. 5. Mass Spectra of CBN (VIIIa), 6-Hydroxy- (IXa), 7-Hydroxy- (Xa) and 7-Oxo-CBN (XIa)

Table III. Mass Number of Ion from Compounds IXa and XIa

Assignment	IXa			XIa		
	m/e obsd.	(calcd.)	Component	*m/e* obsd.	(calcd.)	Component
M	326.1817	(326.1882)	$C_{21}H_{26}O_3$	324.1684	(324.1725)	$C_{21}H_{24}O_3$
$M-CH_3$	311.1639	(311.1647)	$C_{20}H_{32}O_3$	309.1479	(309.1490)	$C_{20}H_{21}O_3$
$M-CH_3-C_4H_9$	254.0957	(254.0942)	$C_{16}H_{14}O_3$	252.0790	(252.0786)	$C_{16}H_{12}O_3$

3) CBN (VIIIa), Oxidation Products of CBN, and Their Acetyl Derivatives

In the mass spectra of the compounds having the skeleton of cannabinol (CBN, VIIIa) that contains the benzene ring instead of the cyclohexene ring in THC, it is remarkable that the prominent fragment ion formed by eliminating a methyl radical from the *gem*-dimethyl group ($M-CH_3$) is very stable due to its aromatic plannar ring system. Hence, the simple mass spectrum of VIIIa shows only three major fragments, which consist of the molecular ion (*m/e* 310), the most abundant ion (*m/e* 295) formed by expulsion of a methyl radical and the fragment ion (*m/e* 238) formed with further loss of a butyl radical from the side chain (Fig. 5). In the mass spectra of CBN derivatives such as a phenol, 6-hydroxy-CBN (IXa, Table III), an alcohol, 7-hydroxy-CBN (Xa) and an aldehyde, 7-oxo-CBN (XIa, Table III), those show all the same fragmentation as CBN, except for the shift of mass number due to each different molecular weight. It is of interest to add here that $M+1$ ion in XIa and its acetate (XIb) mentioned below appears somewhat abundant when compared to those of other CBN derivatives (Fig. 5).

In the 3′-acetyl-CBN (VIIIb), the easier elimination of one of the *gem*-dimethyl (*m/e* 337, $m^*=322.5=337^2/352$) predominates that of ketene from phenyl acetate (*m/e* 310) (Fig. 6). Further elimination of a ketene (*m/e* 295, $m^*=258=295^2/337$) from the above demethylated fragment followed by loss of a butyl radical in the side chain resulted in formation of the ion *m/e* 238 ($M-CH_3-C_2H_2O-C_4H_9$). It is also observed that the elimination of one of the *gem*-dimethyl in the diacetyl derivative (IXb) of IXa (*m/e* 395, $m^*=381=395^2/410$) occurs easier rather than that of ketene from two phenyl acetates (Fig. 6). The elimination of one or two ketenes (*m/e* 353, $m^*=316=353^2/395$; *m/e* 311, $m^*=274=311^2/353$) occurs in the demethylated ion (*m/e* 395) similarly in VIIIb. The spectrum of the diacetyl derivative (Xb) of Xa is entirely same as that of IXb, in which the molecular ion (*m/e* 410), the demethylated ion (*m/e* 395, $m^*=381=395^2/410$), the fragment ion derived by loss of ketene (*m/e* 368) and the ion produced by expeling both methyl radical and ketene from the molecular ion (*m/e* 353, $m^*=315=353^2/395$) are observed (Fig. 6). The elimination of an acetic acid in Xb can

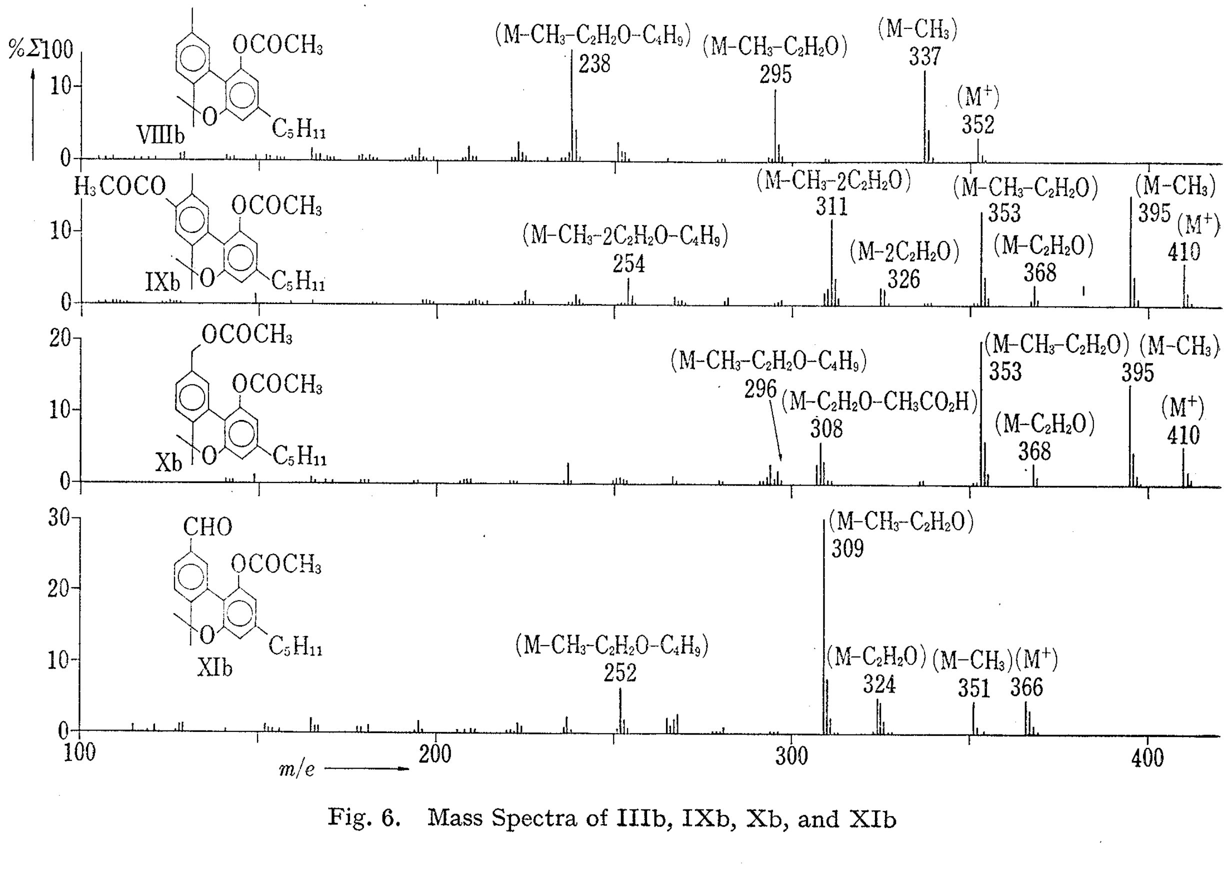


Fig. 6. Mass Spectra of IIIb, IXb, Xb, and XIb

hardly occur due to difficulty of expulsion of C-7 acetyl group, which differs from the case of Vb and VIb, resulting in formation of much less fragment ion at *m/e* 308. The spectrum of the acetyl derivative (XIb) of XIa is same as that of XIa except for the elimination of ketene (Fig. 6).

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