*Tetrahedron*. Vol. 25, pp. 4671 to 4680. Pergamon Press 1969. Printed in Great Britain

# MASS SPECTRA OF BAKKENOLIDES AND THEIR DERIVATIVES

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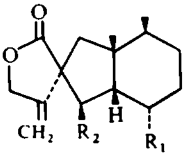
(*Received in Japan* 25 *April* 1969; *Received in the UK for publication* 16 *June* 1969)

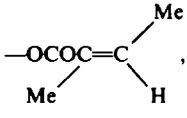
**Abstract**—Mass spectra (including high resolutions) of bakkenolides and their derivatives (I–X) were measured and the common fragmentation patterns discussed with the help of metastable ions. Fragmentation of B–A(I) is characterized by a McLafferty-type rearrangement, whereas oxygen functions at 1 and 9-positions of B–A take part in the fragmentation of bakkenolides-B, C, D and E.

DURING the structure elucidation of the bitter principles from *Petasites japonicus* subsp. *giganteus* Kitam., five sesquiterpene lactones named Bakkenolide-A, B, C, D, and E were isolated and their structures were determined on the basis of chemical and physical evidence particularly mass spectra[1]

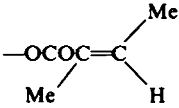
The fragmentation of bakkenolides on electron impact are of special interest since



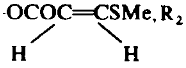
I: $R_1 = R_2 = H$ (B–A)
V: $R_1 = R_2 = OH$
VI: $R_1 = R_2 = OAc$

VII: $R_1 =$  , $R_2 =$ OAc (B–B)

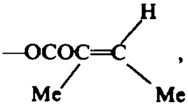
$-OCOC(Me){=}C(Me)H$

VIII: $R_1 =$  , $R_2 =$ OH (B–C)

$-OCOC(Me){=}C(Me)H$

IX: $R_1 =$  , $R_2 =$ OAc (B-D)

$-OCOC(H){=}C(H)SMe$

X: $R_1 =$  , $R_2 =$ OAc (B–E)

$-OCOC(Me){=}C(H)Me$

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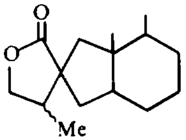
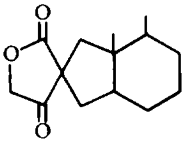
they belong to a new type of sesquiterpene and have a novel bakkane skeleton with spiro-γ-lactone grouping.

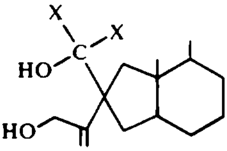
The mass spectra including high resolution mass spectrometry of the bakkenolides and their derivatives (I–X) were measured and the fragmentation patterns are discussed with the help of metastable ions.



II



III



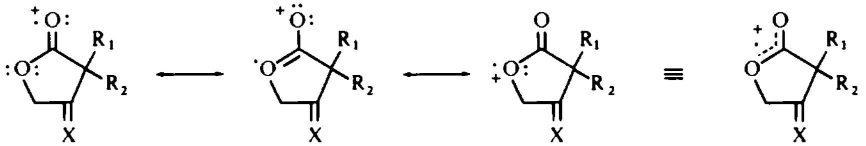
IV

a: X = H

b: X = D

1. *Bakkenolide-A* (I) *and its derivatives* (II, III)

Since the lactone group of B–A (I) and its derivatives (II, III) is most susceptible to electron impact, all the fragment ions in the spectra of I, II, and III are considered to arise from radical cation of the lactone group which is formed at the earliest stage of the electron impact. Species of the radical cations should exist as resonance hybrids as shown below.

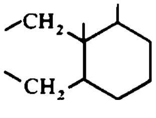


I: X = $CH_2$

II: X = H, Me

III: X = O

$R_1, R_2$ =



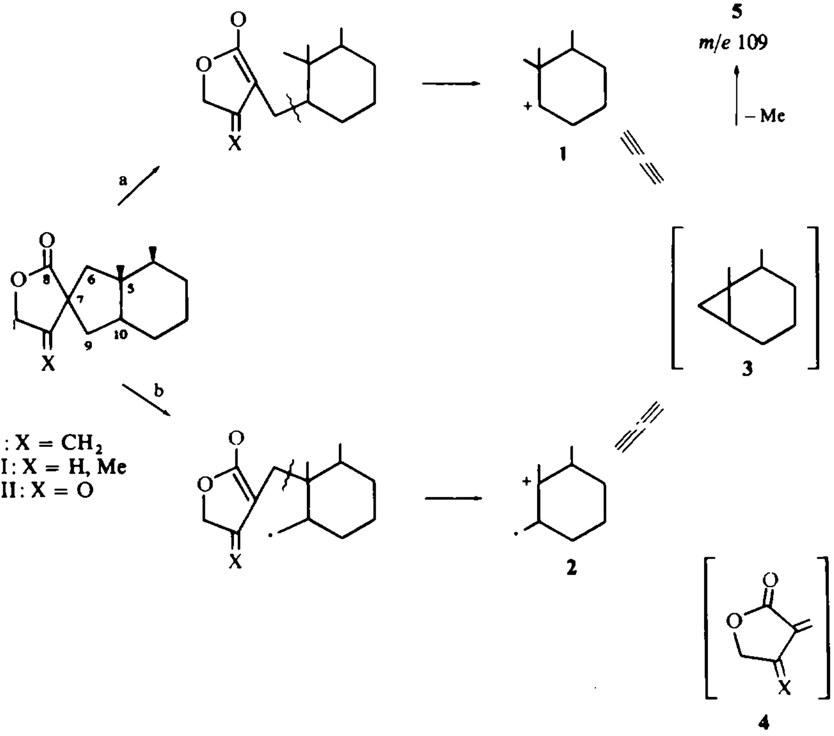
The mass spectrum of B–A (I) shows, in addition to the molecular ion at *m/e* 234, strong peaks at *m/e* 124, 111, and 109 (Fig. 1), whereas major peaks are observed at *m/e* 124, 113, and 109 in the spectrum of dihydro B–A (II) (Fig. 2).

Comparison of these spectra shows that the fragment ions at *m/e* 124 and 109 are common in both compounds, while the remainder of the intense peak at *m/e* 111 in I is shifted to 113 in the spectrum of II. These relationships indicate that the common fragment ions (*m/e* 124 and 109) result from the loss of C-ring (butenolide group) and the other peaks at *m/e* 111 in I and 113 in II are the fragment ions retaining the C-ring.

A similar phenomenon is observed in the spectrum of norketone (III) where the prominent fragment ion is shown at *m/e* 113 besides the common peaks at *m/e* 124 and 109 (Fig. 3).

The clear metastable ions at *m/e* 65·8 (I) and 65·1 (II) show that the common fragment ion at *m/e* 124 is directly derived from the corresponding molecular ion. The other peak at *m/e* 109 corresponds to loss of a Me radical from the *m/e* 124 fragment ion, which is supported by the metastable ion at 95·8 in each spectrum.

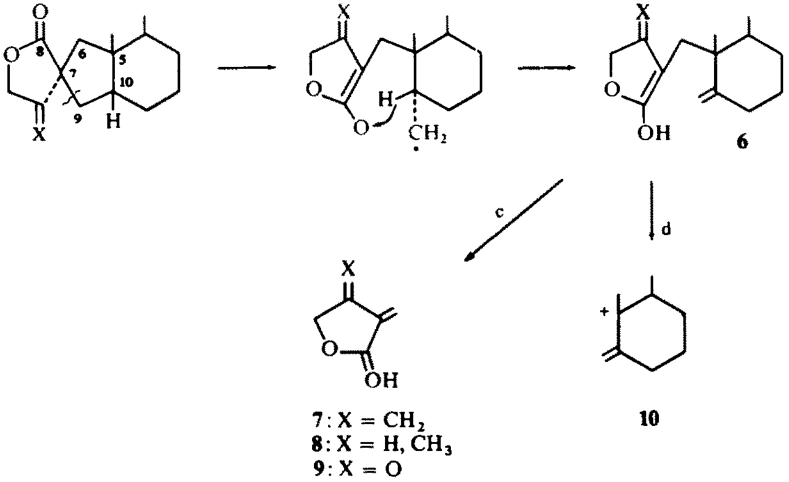
One of the possible paths for the fragmentation to *m/e* 124 could be the initial bond fission at $C_6$—$C_7$ (a), or $C_7$—$C_9$ (b) and subsequent cleavage at $C_9$—$C_{10}$ or $C_5$—$C_6$ with formation of the common *m/e* 124 fragment ion (**1** or **2**) and a neutral conjugated lactone fragment (**4**). Both **1** and **2** may be related to the ion radical of bicyclo[4.1.0]-cycloheptane derivative (**3**). Successive loss of a Me radical is a reasonable process to yield the allylic cation at *m/e* 109 (**5**).



The intense peak at *m/e* 111 in I or 113 in II corresponds to an addition of an H atom to the neutral fragment (**4**), while the prominent peak at *m/e* 123 in I and III has a mass number of the fragment ion (**3**) minus an H atom. These relations could be explained by assuming H-transfer from A-ring to C-ring since the fragment ion (**3**) and the neutral fragment (**4**) are the part of A- and C-ring respectively.

The possible mode of the H transfer would be a McLafferty-type rearrangement. As Djerassi *et al.* have reported in the mass spectra of steroids,[2] transfer of a γ-hydrogen which is more than 1·8 Å distant from a carbonyl function, the maximum bond length for the occurrance of conventional McLafferty rearrangement, is also operative when β-cleavage takes place first and the fixed γ-hydrogen becomes mobile.

Bakkenolide-A is rigidly fixed and the internal distance between $C_{10}$-hydrogen and the carbonyl function is about 3·1 Å by measurement with a Dreiding model. Although this distance is not close for the normal McLafferty rearrangement to be operative as in the case of pregnane-12-one, the geneses of the fragment ions at *m*/*e* 111 (I), 113 (II and III) and 123 would be proceeded by homolysis of the β-bond at $C_7$—$C_9$ and subsequent $C_{10}$-hydrogen migration to the carbonyl group to furnish the intermediate ion (**6**), which then undergoes homolytic (**c**) or heterolytic (**d**) fission of the $C_5$—$C_6$ bond to afford the fragment ions at *m*/*e* 111 (**7**) and 113 (**8** and **9**) or *m*/*e* 123 (**10**) respectively. Release of strain of B-ring would assist the β-bond fission.



This proposal is supported by the observation of metastable ions at 64·7 (I) and 64·2 (III) which correspond to the formation of the fragment ion (**10**) from the intermediate (**6**).

In contrast to I and II, the relative abundance of the peak at *m*/*e* 124 is small in the spectrum of III, which would be due to the predominant occurrence of the McLafferty-type rearrangement of III, in which the presence of two CO groups enhances the chance of the H-transfer.

It is interesting to note that the relative intensity of the peaks at 111, 113 and 123 depends on the character of 11-carbon. When 11-carbon consists of a $sp^2$-hybrid as in the cases of I and III, the fragment ion (**10**) is prominent and the intensity of **7** and **9** is weak, whereas the relative abundance of these peaks are reversed in II where the $C_{11}$-carbon exists as $sp^3$-hybrid.

## 2. *B–A diol*

B–A diol (IV) has two OH groups but no CO function in C-ring and hence its spectrum (Fig. 4) is different from those of I, II, and III.

The peak with the largest mass number in the spectrum of IV appears at *m*/*e* 220 due to loss of water from the molecular ion which is not detectable.

Introduction of two deuterium atoms at $C_8$-position of IV results only the fragment ion (**11a**) at *m*/*e* 220 being shifted to *m*/*e* 222 (**11b**), the remaining peaks are completely superimposable, indicating that all the peaks except that at *m*/*e* 220 contain no $C_8$-methylene unit. The abundant peak at *m*/*e* 190 represents loss of $C_8$-methylene, pre-

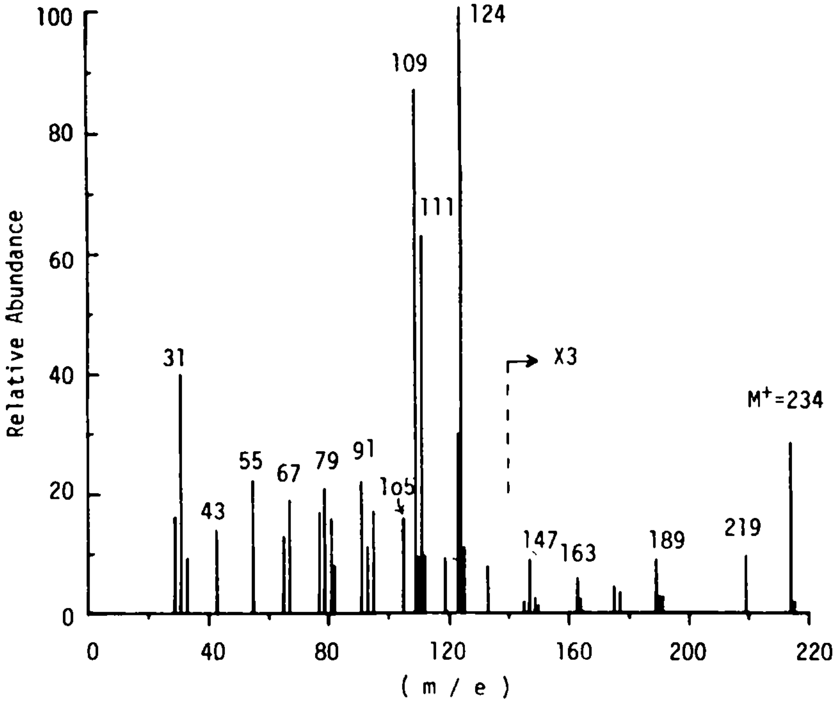


FIG. 1 Mass Spectrum of Bakkenolide-A (I)

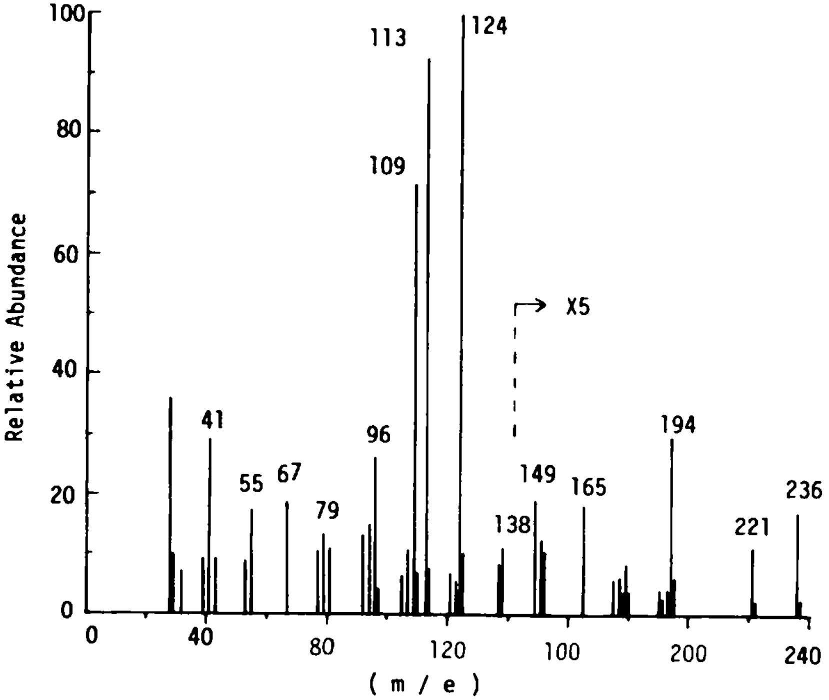


FIG. 2 Mass Spectrum of Dihydro derivative (II)

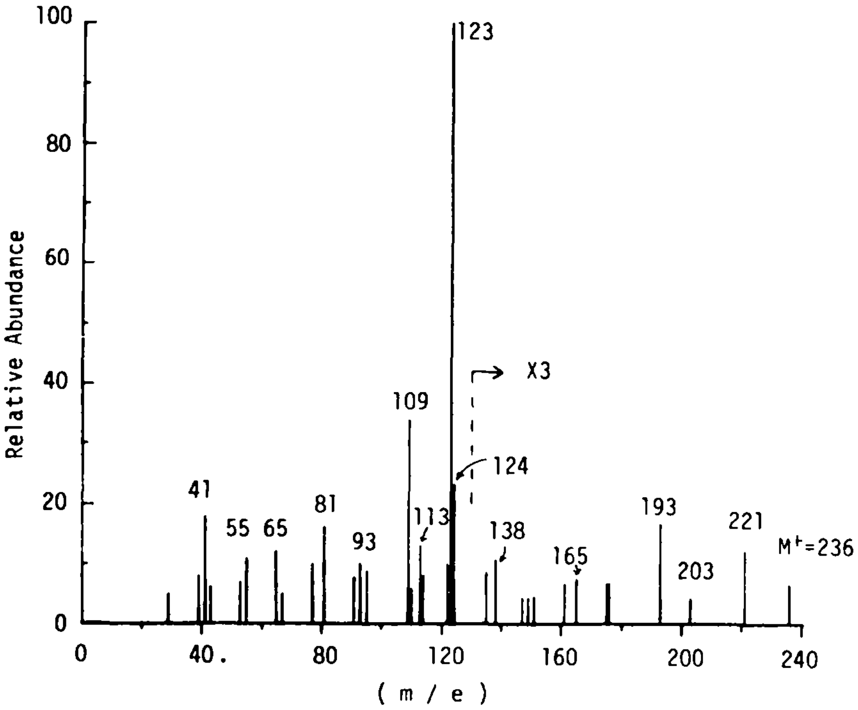
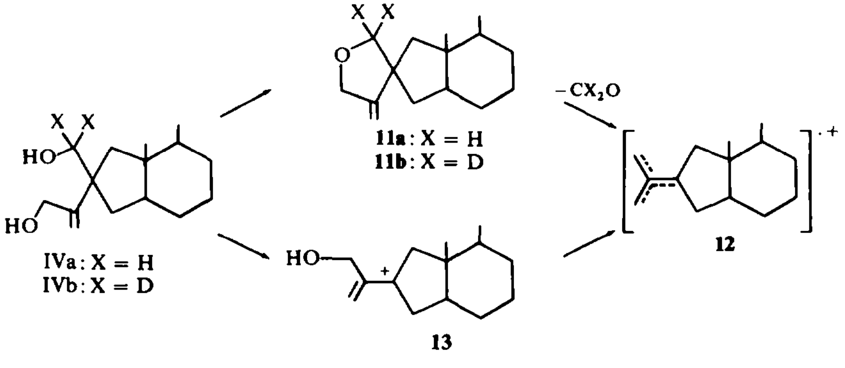


Fig. 3 Mass Spectrum of Norketone (III)

sumably as formaldehyde, to give a fragment ion (12), the composition ($C_{14}H_{22}$) of which was ascertained by high resolution mass spectrometry.

A fragment ion at *m/e* 207 which appears in both IVa and IVb corresponds to loss of a hydroxymethylene unit ($-CX_2OH$) from the molecular ion and may proceed by rupture of the $C_7-C_8$ bond to yield allylic cation (13). Removal of the OH group from the fragment ion (13) would lead to the formation of the ion radical (12), which is supported by the observation of the corresponding metastable ion at 174·1. The formation of ion radical (12) by two different routes would be responsible for its tending to stabilize as an allylic cation (or radical).



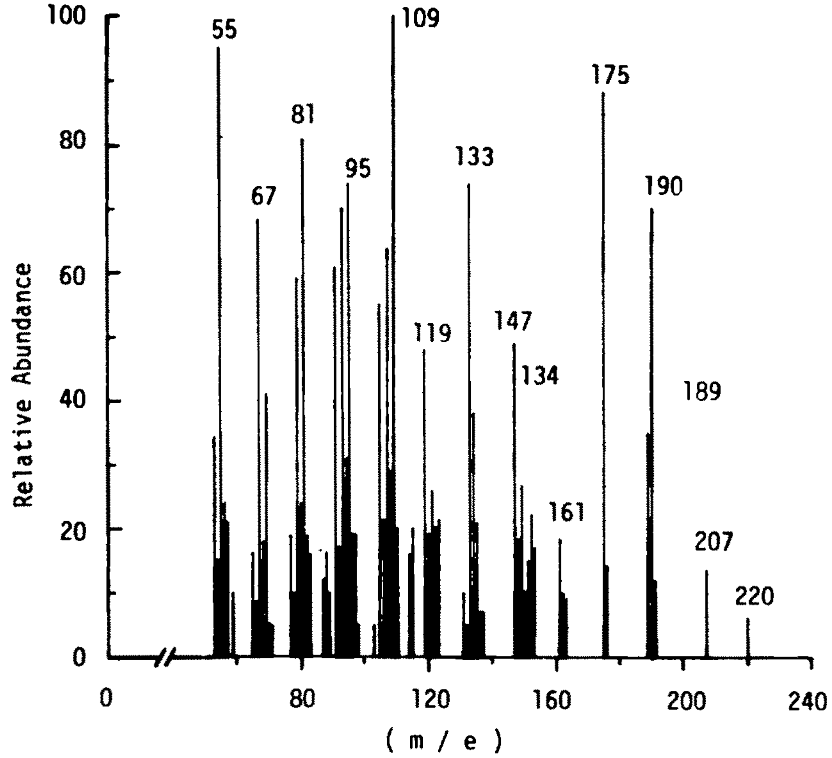


Fig. 4 Mass Spectrum of B-A diol (IVa)

### 3. 1,9-*Dihydroxy bakkenolide-A and its ester derivatives*

Since two oxygen functions are attached to 1 and 9-positions of bakkenolide-A, the mass spectra of V and its ester derivatives (VI–X) are quite different from that of B–A.

As expected from the stability of the fragment ion, the conjugated acylium ions ($R_1'CO^+$) appear as the strongest peak in the spectra of VII, IX and X where both acetate and the conjugated ester (angerate, tiglate or β-methylthioacrylate) are present.

Spectra of these compounds show many common fragment ions (Fig. 5 and Table 1) and some of the compositions were evaluated by high resolution mass spectrometry. A detailed inspection of the metastable ions indicates the following possible fragmentation pathways.

Elimination of a ketene fragment from the molecular ion is observed in all the compounds possessing the acetate group at $C_9$. Successive removal of $R_1H$ from (M-42) ion affords the intense peak at *m/e* 248, from which the common peaks at *m/e* 220, 137 and 111 would be derived by $C_5$—$C_6$ and $C_7$—$C_9$ bond fissions. It is reasonable to postulate a sequence involving McLafferty rearrangement of **14a** or **15a** to give **14b** or **15b** respectively.

Elimination of water and then carbon dioxide affords the fragment ion at *m/e* 186 ($C_{14}H_{18}$), the composition of which was determined by high resolution mass spectro-

TABLE 1*.

| m/e | composition | V | VI | VII | VIII | IX |
|---|---|---|---|---|---|---|
| 408 | $C_{21}H_{28}O_6S$† | – | – | – | – | M |
| 390 | $C_{22}H_{30}O_6$ | – | – | M | – | – |
| 366 | $C_{19}H_{26}O_5S$† | – | – | – | – | M |
| 350 | $C_{19}H_{26}O_6$ | – | W | – | – | – |
| 348 | $C_{20}H_{28}O_5$† | – | – | M | S | S |
| 330 | $C_{20}H_{26}O_4$ | – | – | W | W | – |
| 308 | $C_{17}H_{24}O_5$† | – | M | – | – | – |
| 291 | | – | W | S | – | W |
| 290 | | – | W | W | – | W |
| 266 | $C_{15}H_{22}O_4$ | M | W | – | – | – |
| 248 | $C_{15}H_{20}O_3$† | M | S | S | S | S |
| 231 | $C_{15}H_{19}O_2$† | W | W | S | M | M |
| 230 | $C_{15}H_{18}O_2$† | W | M | S | W | S |
| 220 | $C_{14}H_{20}O_2$† | W | M | M | M | M |
| 187 | $C_{14}H_{19}$† | W | M | W | M | M |
| 186 | $C_{14}H_{18}$† | M | M | S | M | S |
| 138 | $C_9H_{14}O$† | S | S | S | S | S |
| 137 | $C_9H_{13}O$† | M | S | M | S | S |
| 111 | $C_6H_7O_2$† | W | S | W | W | W |
| 109 | $C_8H_{13}$† | M | S | S | S | S |

Common Fragment ions of V–IX

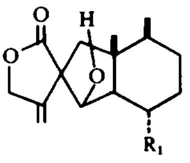
* Measured with JMS-OISG on photo plates and the relative abundances could not be determined.

† Determined by high resolution mass spectrometry.

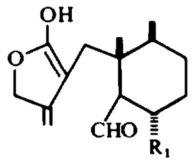
$$\begin{tikzcd}
 & & & m/e\ 111 & m/e\ 137 \\
M \arrow[r, "CH_2CO"] & (M\text{–}42)^+ \arrow[r, "-R_1H"] & m/e\ 248 \arrow[ur] \arrow[urr] \arrow[r] \arrow[dd] & m/e\ 220 \arrow[r, "17"] & m/e\ 109 \\
 & 14 & 15 & 16 & 18 \\
M \arrow[r] & (M\text{–}R_1H) \arrow[r, "-R_2H"] & m/e\ 230 \arrow[r, "-CO_2"] & m/e\ 186 & \\
 & & 19 & 20 &
\end{tikzcd}$$

metry. The fragment ion at m/e 230 is also derived by the successive elimination of $R_1H$ and $R_2H$ from the molecular ions.

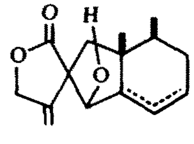
Some of the possible structures of these fragment ions are shown below.

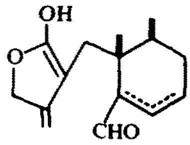


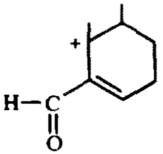
**14a**

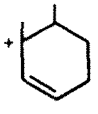


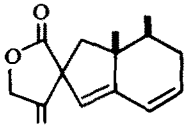
**14b**

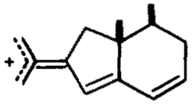

**15a**


**15b**


**17**


**18**


**19**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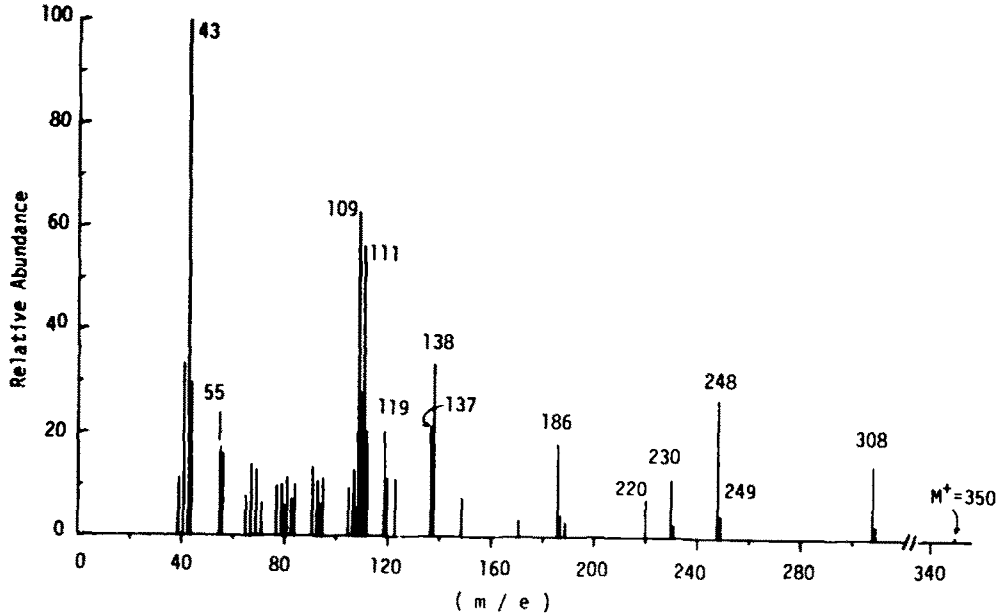

FIG. 5 Mass Spectrum of B-B diacetate (VI)

## EXPERIMENTAL

The mass spectra were measured with HITACHI-RMU 6D mass spectrometer by the following conditions: chamber voltage, 70 eV; Total Emission, 80 μA; Ion chamber temperature, 250°; Evaporation temp, 100–200°; Sample press, 3·0 × $10^{-7}$ mm Hg.

High resolution mass spectra were measured with JMS-01SG mass spectrometer on photo plates.

*Acknowledgement*—A part of this work was financially supported by Kurata Foundation, to which the authors express their deep acknowledgement.

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[1] K. Shirahata, T. Kato, Y. Kitahara and N. Abe, *Tetrahedron* **25**, 3179 (1969); see also, *Tetrahedron Letters* 369, 1993 (1968).

[2] [a] H. Budzikiewicz, C. Djerassi and D. H. Williams, *Structure Elucidation of Natural Products by Mass Spectrometry* Vol 2; chap 20. Holden-Day, San Francisco (1964);

[b] C. Djerassi, G. von Mutzenbercher, J. Fajkoo, D. H. Williams and H. Budzikiewicz, *J. Am. Chem. Soc.* **87**, 817 (1965);

[c] L. Tõkes, R. T. LaLonde and C. Djerassi, *J. Org. Chem.* **32**, 1020 (1967).