Tetrahedron Letters No.6, pp. 623-632, 1966. Pergamon Press Ltd.
Printed in Great Britain.

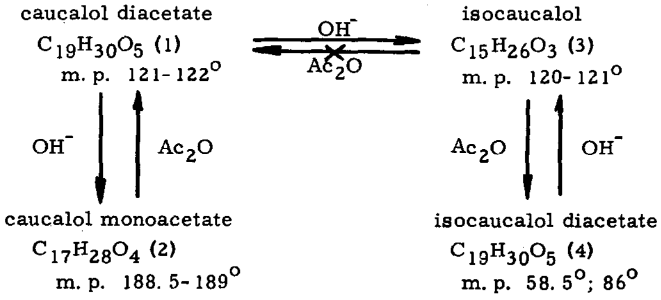
MASS SPECTRA OF CAUCALOL DIACETATE AND RELATED COMPOUNDS

S. Sasaki, Y. Itagaki, H. Moriyama, K. Nakanishi,
Department of Chemistry, Tohoku University, Sendai, Japan
E. Watanabe, T. Aoyama,
Japan Electron Optics Laboratory Co. Ltd. , Akishima, Tokyo, Japan.

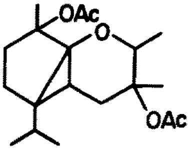
(Received 14 December 1965)

Structure 1a had been assigned[1] to caucalol diacetate (1), $C_{19}H_{30}O_5$, the sesquiterpene which is extracted with benzene from the fluffy seeds of Caucalis scabra Makino (oyabujirami), but this has been recently reinvestigated[2] because of its incompatibility with spectroscopic properties.

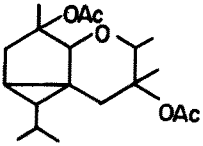
As indicated below, the original diacetate can be hydrolyzed with base to the monoacetate 2, but further hydrolysis is accompanied by a rearrangement leading to an isomer, isocaucalol (3), which in turn yields the straightforward diacetate 4.



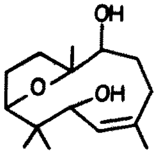
Since caucalol diacetate gave no crystalline derivatives other than the monoacetate, the structural studies, which depended heavily on spectroscopy because of the limited amount available, were concentrated on the rearranged isomer, isocaucalol. **These studies lead to the following five** possibilities for isocaucalol[2]:



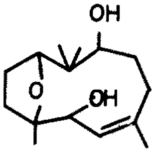
or



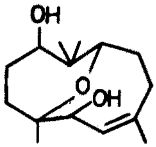
1a



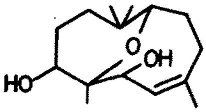
3



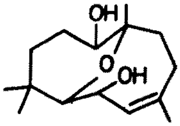
3a



3b

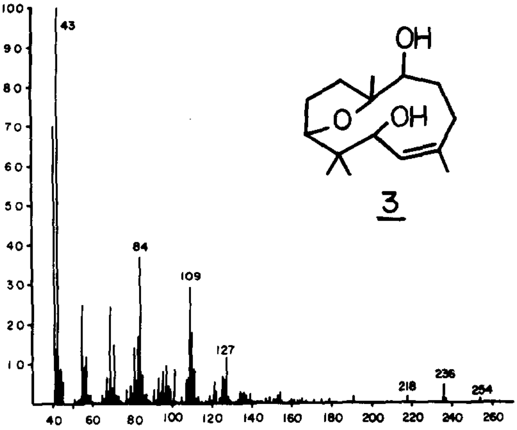


3c



3d

Mass spectroscopy data[3] described in this paper establish that the structure of isocaucalol, without stereochemical implications, should be 3. The mass spectrum of isocaucalol (Fig. 1) has a peak at m/e 127; when isocaucalol was treated with D_2O the intensity was greatly reduced as



3

Fig. 1 Isocaucalol (3)

	Before D₂O treatment	After D₂O treatment
m/e 127	83 %	35 %
m/e 128	11 %	53 %
m/e 129	6 %	12 %

Table 1 Change in intensities of m/e 127-129 peaks. Numerals in each column indicate relative % of the three peaks.

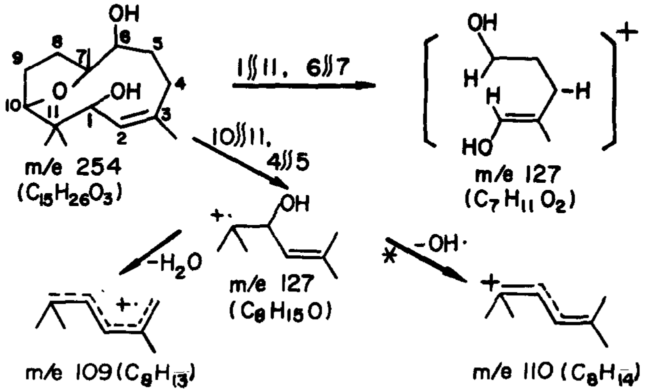


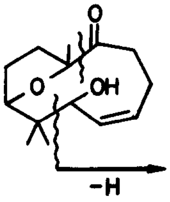
CHART 1.

shown in Table 1, and the m/e 128 and 129 peaks became stronger. High resolution measurement of the m/e 127 peak indicated that actually it was composed of a low mass fragment, $C_7H_{11}O_2$, and a high mass fragment, $C_8H_{15}O$. On the other hand, the compositions of cations m/e 109 and 110 were found to be C_8H_{13} and C_8H_{14}, respectively, and moreover, the C_8H_{13} ion is derived from the $C_8H_{15}O$ ion as evidenced by a metastable peak at m/e 93.5.

$$\begin{tikzcd}
 & \text{m/e 127 } (C_7H_{11}O_2) & \\
\text{isocaucalol} \arrow[ru] \arrow[r] & \text{m/e 127 } (C_8H_{15}O) \arrow[ld, "-H_2O"'] \arrow[rd, "-OH\cdot"] & \\
\text{m/e 109 } (C_8H_{13}) & & \text{m/e 110 } (C_8H_{14})
\end{tikzcd}$$

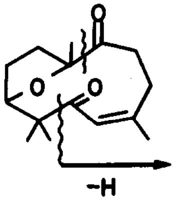
Production of the $C_7H_{11}O_2$ fragment (m/e 127) can be rationalized on the basis of structures 3 and 3a by ruptures of bonds C_1-C_{11} and C_6-C_7. However, if this fragment had originated from structures 3b, 3c or 3d, three bonds including the ethereal C-O bond would have to be cleaved simultaneously; this is most improbable and allows one to eliminate these three possibilities, thus leaving 3 and 3a. Of the two alternatives, structure 3 can account satisfactorily for the $C_8H_{15}O$ (m/e 127) fragment and its further decomposition to the C_8H_{13} and C_8H_{14} fragments as indicated in Chart 1. However, formation of these three C_8- fragments cannot be rationalized by structure 3a, and consequently isocaucalol should be represented by 3.

Oxidation of isocaucalol 3 with CrO_3/pyridine afforded a monoketone 5 and a diketone 6.



m/e 125 (14%)
base peak: m/e 43

5



m/e 123 (15%)
base peak: m/e 43

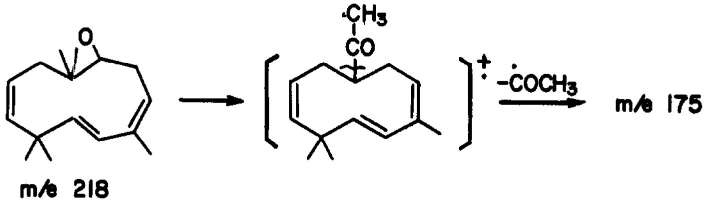
6

In these two ketones, the m/e 127 ($C_7H_{11}O_2$) peak of isocaucalol is shifted to m/e 125 (in 5) and m/e 123 (in 6), respectively, in accordance with the increase in oxo functions, and the productions of these cations can also be rationalized in a straightforward manner from structures 5 and 6.

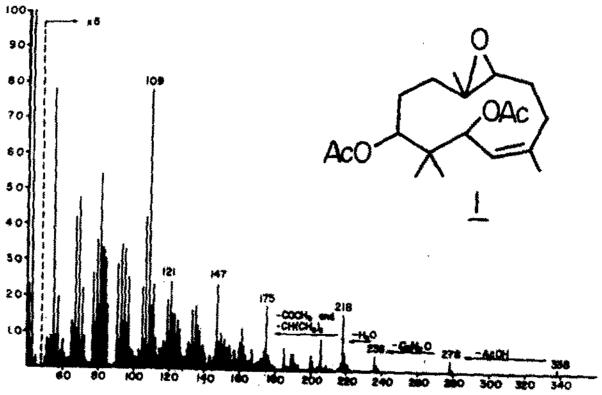
Structure 1 (Fig. 2) for caucalol diacetate is based on mechanistic considerations, i. e., base hydrolysis leading eventually to isocaucalol 3, and on the fact that in its NMR spectrum the C_6 methine hydrogen of the methyl oxirane moiety appears at 2. 99 ppm[4)] (quartet, J 10. 2, 3. 6 cps). The mass spectrum of this compound (Fig. 2) provided additional support for the structure and also revealed an interesting fragmentation. Thus investigation of the spectrum under high resolution indicated that the main peaks had the following compositions:

m/e	338	$C_{19}H_{30}O_5$	M^+
m/e	278	$C_{17}H_{26}O_3$	M-AcOH
m/e	236	$C_{15}H_{24}O_2$	M-AcOH-CH_2CO
m/e	218	$C_{15}H_{22}O$	M-AcOH-2AcOH
m/e	175	$C_{12}H_{15}O$	M-2AcOH-C_3H_7
		$C_{13}H_{19}$	M-2AcOH-CH_3CO

The fragmentation can be rationalized by assuming the C-10 acetoxyl group to be expelled as acetic acid (m/e 278) and the allylic acetoxyl group as ketene (m/e 236). The m/e 218 cation is produced by the expulsion of 2 moles of acetic acid. As indicated in Chart 2 the genesis of the $C_{12}H_{15}O$ fragment with m/e 175 can be accounted for by loss of an isopropyl radical, which in turn can arise from the gem-dimethyl grouping. On the other hand, the elimination of $COCH_3$ from m/e 218 leading to the $C_{13}H_{19}$ hydrocarbon fragment (m/e 175) suggested a rearrangement leading to a methyl ketone followed by α-cleavage[5):]



That this indeed was the case was confirmed by studying the fragmentations of several models containing the alkyl oxirane grouping[6)]. Namely, in the spectra of 1-methyl-1,2-epoxycyclohexane (Fig. 3a) and 1,2-epoxymenthane (Fig. 3b), a conspicuous peak occurs at M-43 (intensity relative to base peak: 37% and 100%, respectively), while in 3,4-epoxymenthane (Fig. 3c) the corresponding peak occurs at M-71 which is due to expulsion of an isobutyryl radical[7)]. This fragmentation of an alkyloxirane moiety involving rearrangement to an alkyl ketone can be of diagnostic value, especially for the detection of such oxirane groups in natural products. Appearance of the $C_{13}H_{19}$ peak (m/e 175) thus provides additional support for structure 1.



1

Fig. 2 Caucalol diacetate

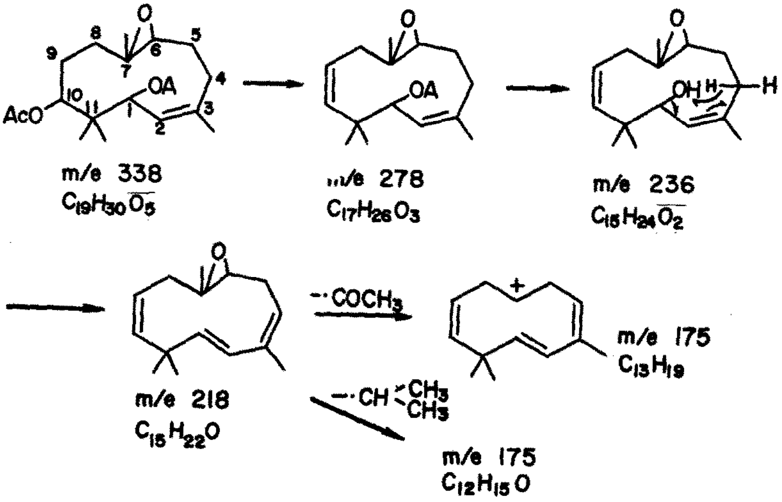


CHART 2. Fragmentations of Caucalol diacetate based on high resolution mass measurements.

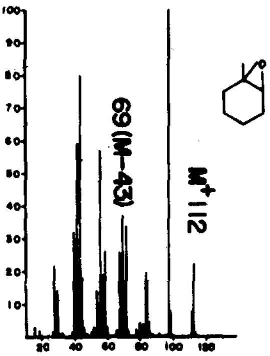


Fig. 3a 1-methyl 1, 2-epoxy cyclohexane.

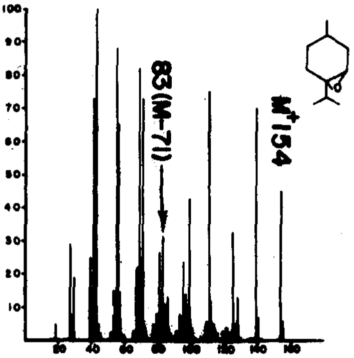


Fig. 3b 3, 4-epoxy menthane.

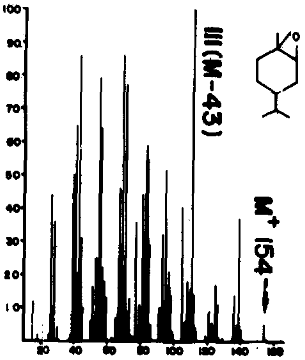
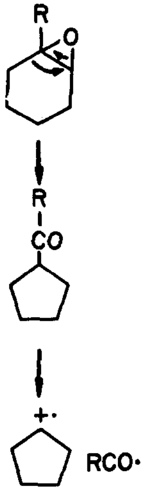
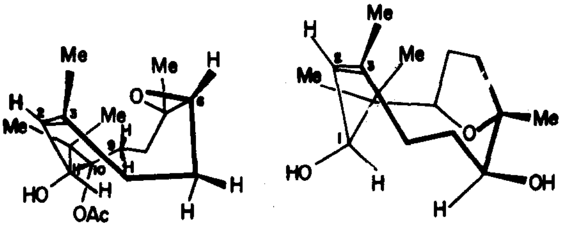


Fig. 3c 1, 2-epoxy menthane



The interpretation of spectroscopic and optical data of caucalol diacetate and derivatives based on the planar expression 1 has allowed us to extend this to the full stereochemical structure 7, which will be published in detail shortly.



Caucalol Monoacetate

Isocaucalol

7

TABLE 2. Exact Masses and Compositions of Ions.

Isocaucalol

m/e observed	m/e calculated	composition
127.111	127.112	$C_8H_{15}O$
127.076	127.076	$C_7H_{11}O_2$
110.110	110.110	C_8H_{14}
109.102	109.102	C_8H_{13}

Caucalol Diacetate

m/e observed	m/e calculated	composition
338.205	338.209	$C_{19}H_{30}O_5$
278.185	278.188	$C_{17}H_{26}O_3$
236.176	236.178	$C_{15}H_{24}O_2$
218.165	218.167	$C_{15}H_{22}O$
175.148	175.149	$C_{13}H_{19}$
175.110	175.112	$C_{12}H_{15}O$

Acknowledgements. The authors (K. N. and S. S.) are grateful to the Toyo Rayon Company for the grant to purchase the RMU-6D mass spectrometer.

REFERENCES

1) S. Mitsui, Scientific Papers of the Institute of Physical and Chemical Research (Tokyo, Japan), 20 708 (1941).

2) S. Sasaki, H. Moriyama, K. Shoji, T. Kobayashi, S. Fujise, K. Nakanishi, Abstracts of the International Symposium on the Chemistry of Natural Products, Kyoto, Japan, p. 19, (1964).

3) a) Mass spectra were determined with a Hitachi RMU-6D (Niei-Johnson type), equipped with an all glass heated inlet system (120-140°). Ionizing voltage 70 eV, ionizing current 80 μA, mult. sens. 100 x 1.2 KV, ion accel. volt. m/e_{max} 600.

b) High resolution mass spectra were measured with a JEOL-OIU (Mattauch-Herzog type). Temp. of ion source 130-150°, ionizing voltage 25-40 eV, ion accel. volt. 7.5 KV, and exposure 3×10^{-11} coulomb.

4) Chemical shift relative to internal tetramethylsilane.

5) A similar fragmentation has been noted in the sesquiterpene, alexandrofuran (H. Budzikiewicz, C. Djerassi, D. H. Williams, Structure Elucidation of Natural Products by Mass Spectrometry, Vol. 2, p. 151 (1964). Holden-Day, San Francisco, Calif. Several mechanisms are conceivable for the expulsion of the acetyl radical; the mechanism indicated here is only one possibility.

6) S. Sasaki, Y. Itagaki, T. Kurokawa, Y. Watanabe, Chem. and Ind. 1654 (1965).

7) The full fragmentation of these alkyl oxiranes will be reported shortly.