STRUCTURE OF CHLOROCHRYMORIN, A NOVEL SESQUITERPENE LACTONE

FROM CHRYSANTHEMUM MORIFOLIUM

Toshihiko Osawa, Akinori Suzuki and Saburo Tamura

Department of Agricultural Chemistry

The University of Tokyo, Bunkyo-ku, Tokyo, Japan

Yuji Ohashi and Yoshio Sasada

Laboratory of Chemistry for Natural Products,

Tokyo Institute of Technology, Ookayama, Meguro-ku, Tokyo, Japan

Recently, we have isolated a novel sesquiterpene lactone as a rooting promoter from juvenile plants of Chrysanthemum morifolium Ram. (cultivar "Otomezakura") through a bioassay using mung bean cuttings.[1] The yield was 8 mg from 100 kg of plants. In this paper we wish to report the structural elucidation of the active principle named chlorochrymorin ($\underline{1}$) by an X-ray crystallographic analysis.

$\underline{1}$ has the composition $C_{15}H_{19}O_5Cl$, $(\alpha)_D$ -18.3° (c 0.38, $CHCl_3$)* ν_{max}^{film} 3520 cm^{-1} (hydroxyl) and 1775 cm^{-1} (α-methylene-γ-lactone). The mass spectrum shows m/e 279(M^+-Cl) and 261(M^+-Cl-H_2O), but no molecular ion peak. The NMR spectrum (in D_6-benzene) exhibits a 3H singlet at δ 1.56 and a 3H doublet at δ 0.81 (J=6.5 Hz) due to C-methyl groups. The latter is coupled with -C$\underline{H}$-OH at δ 3.26 (1H, multiplet). A doublet of doublets at δ 3.67 (1H, J=11.0, 10.5 Hz) attributable to -C$\underline{H}$-O- of the lactone group is coupled with C-5 hydrogen at δ 2.24 (1H, doublet, J=11.0 Hz). A pair of doublets at δ 4.79 and 5.95 (1H each, J=3.0 Hz) are due to exocyclic methylene protons. Two singlets at δ 3.59 and 3.79 (1H each) are respectively attributable to the proton on an oxirane ring and the -C$\underline{H}$-Cl proton and vice versa.

Since deduction of molecular structure was extremely difficult from these

* M.p. was undetermined due to the scarcity of the sample.

spectroscopic data, an X-ray crystallographic analysis was attempted for $\underline{1}$.
Recrystallization from $\underline{n}$-hexane ethyl acetate yielded well formed crystals: Ortho-
rhombic, space group $p2_12_12_1$, a=11.34, b=17.16 and c=7.72 Å. The unit cell con-
tained four molecules. Intensity data were collected on a Rigaku automatic four
circle diffractometer with Cukα radiation. A total of 1686 independent reflec-
tions revealed non-zero intensities. Corrections were made for Lorenz and polari-
zation factors in the usual way, but not for absorption.

Due to the scarcity of the sample as well as the absence of molecular ion
peak in the mass spectrum, a chlorine atom was not detected at the earlier stage,
and, therefore, we adopted the symbolic addition method.[2] Tentative E values were
calculated assuming the formula as $C_{15}H_{18}O_5$ from mass spectrum (m/e 279). Three
origin-defining and one enantiomer-defining reflections were chosen as 0 12 5,
E=3.59; 0 9 1, E=3.00; 3 16 0, E=2.84; 1 5 0, E=2.26, which were assigned the
phases of 0°, 90°, 90° and 90°, respectively. In addition, the following four
symbols were given; 0 0 2 (A) E=3.27, 7 0 5 (B) E=2.82, 2 19 2 (C) E=2.42 and
4 15 0 (D) E=2.40. By use of the equation $\phi_h = <\phi_k + \phi_{h-k}>$, 69 phases (E>1.5) includ-
ing these symbols were obtained, and C was assumed to be 0 or 180°. Tangent re-
finement was made for each of possible sixteen combinations of symbol phases. An
E map was calculated using 315 reflections with the phases in the most consistent
set (R=0.375).[3] Eleven atoms attributable to an α-exomethylene-γ-lactone ring and
a six-membered ring were recognized in this map.

In order to find other atoms, the partial structure method[4] was applied
subsequently. Structure factors were calculated on the basis of the eleven atoms,
and the calculated phases were given to 132 reflections, in which $|F|_{calc} > 0.6|F|_{obs}$
and $|E|_{obs} > 1.5$ were satisfied. The tangent refinement was made starting with these
phases, and the resulting E map revealed twenty-one atoms. Assuming that all these
atoms would be carbons, refinement of the structure was undertaken by the block-
diagonal least-squares method. From the bond lengths and the temperature factors,
six of twenty-one atoms were supposed to be oxygens. After three cycles of refine-
ment, however, the temperature factor of the atom attatched to C-3 became unreason-
ably small, and the distance between the both atoms seemed to be somewhat longer
(1.80 Å) for C-O.

Reexamination of the high resolution mass spectrum revealed the presence of
an ion peak of HCl (m/e 35.9735(-3.1)) as well as of several fragments involving
chlorine (C_3H_2OCl m/e 88.9824(3.0) and $C_{13}H_{14}O_3Cl$ m/e 253.0614(-1.6)) etc.).
Least-squares refinement was performed assuming that the atom in question would
be chlorine. In this case, neither bond length nor temperature factor was unusual,
and the R factor decreased to 0.109. After three cycles of refinements using
anisotropic temperature factors, all the hydrogen atoms were located on a differ-
ence map. The final R factor was 0.054. The absolute configuration of the struc-
ture was established by the anomalous dispersion method using FeKα radiation.
The three-dimensional structure is shown in Fig. 1. and the bond lengths in Fig. 2.
Thus the formula of chlorochrymorin has been established as 1.

1
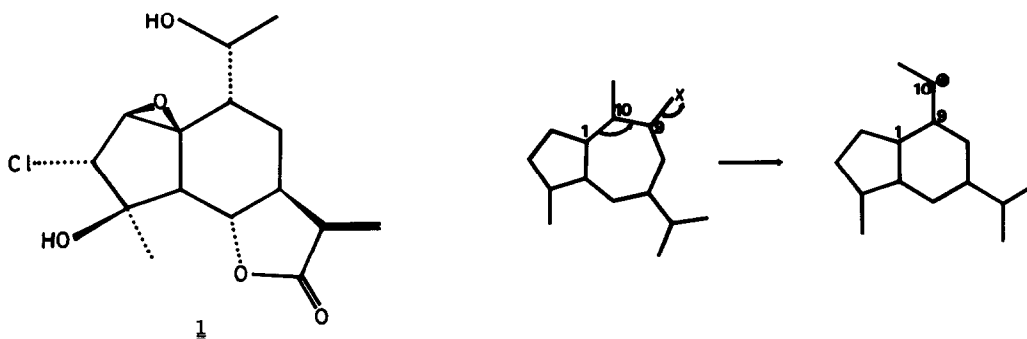
1 is the first natural sesquiterpene lactone with 4-methyl-7-isopropyl-9-ethyl
perhydroindene skeleton. This compound seems to be derived from a guaianolide by
the attack of C-1~C-10 bond against C-9 carbon through the 1,2-shift mechanism.
Similar chemical reaction has been known for sesquiterpenes and steroids.[5] Other
than 1, eupachloroxin and chlorohyssopifolin have been isolated as natural chlori-
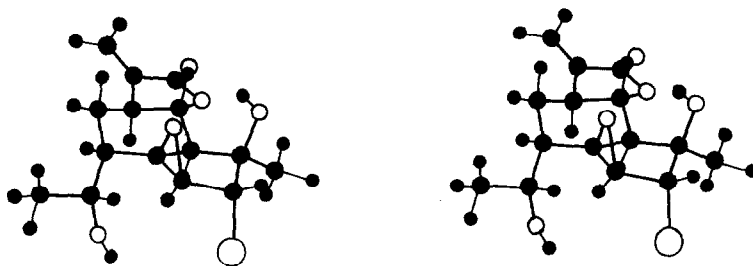nated sesquiterpene lactones.

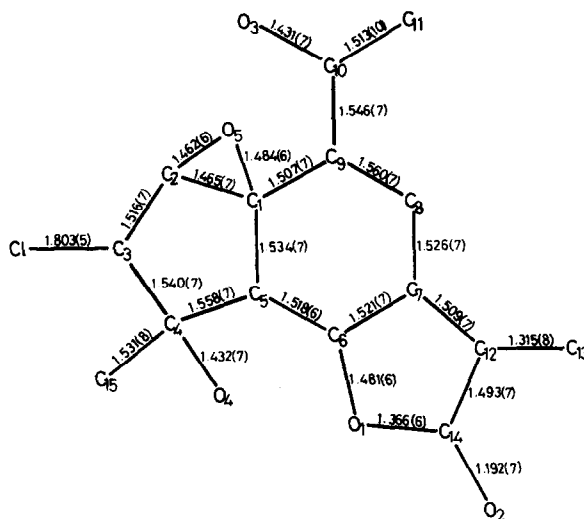Fig. 1.   Stereoscopic view of chlorochrymorin.

Fig. 2.   Bond lengths (Å) in chlorochrymorin

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