Kosuge, *et al.*[2] had studied on the oxidation of quinoline derivatives with hydrogen peroxide in glacial acetic acid, and reported that quinolines, carbostyril, and quinoline oxide were oxidized to corresponding nitro benzoic acids.

Those findings described above suggest that the oxidation of I to III will proceed through II as an intermediate product, as shown in Chart 1.

Recently, Toyoshima, *et al.*[3] reported that they were able to isolate II.

In this study, other oxidation products were also obtained, but the chemical structures of those are not clarified yet. Further investigations of those oxidation products of I will be reported in the near future.

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2) T. Kosuge, S. Miyashita : Pharm. Bull. (Japan), **2**, 397 (1954).
3) S. Toyoshima, H. Hamano : Abst. of the 83rd Annual Meeting of the Pharmaceutical Society of Japan (Nov., 1963 in Tokyo), p. 74 (1963).

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Structure of Mokko Lactone and Dehydrocostus Lactone

From the chinese crude drug "Sen-mokko" has newly been isolated a sesquiterpenoid lactone for which the name mokko lactone is proposed.

Dehydrocostus lactone was first isolated by Ukita[1] from costus root and subsequently investigated by Crabalona,[2] Naves,[3] and Romaňuk, *et al.*[4] Although structure (IX) was proposed by Romaňuk, *et al.*,[4] no unambiguous evidence was presented concerning the attachment of the lactonic oxygen at C-6.

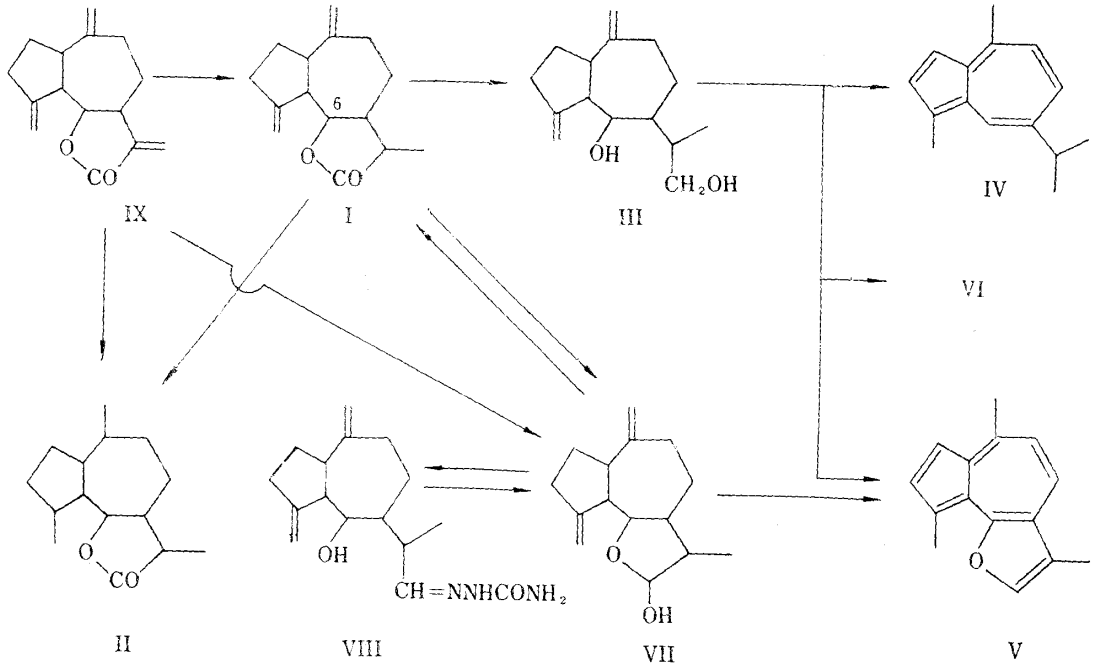
In this communication, the authors wish to report that mokko lactone is expressed by formula (I) and that dehydrocostus lactone is firmly established as shown in the proposed formula (IX) on the basis of the following evidence.

Mokko lactone (I), $C_{15}H_{20}O_2$, m.p. 35~37°, $[\alpha]_D$ +18.2°,*1 has an infrared band at 1770 cm^{-1}, attributed to a γ-lactonic grouping. In the nuclear magnetic resonance spectrum, a doublet at 8.83 τ (J=6.2 c.p.s.) suggests the presence of a secondary methyl group adjacent to the lactonic carbonyl. Two sets of peaks at 5.28 and 5.20 τ and 5.02 and 4.84 τ are assigned to two terminal methylene groups; infrared bands at 3110, 1642, and 889 cm^{-1} are in good accord with this assignment. Catalytic hydrogenation of I over

*1 All analytical values are in good accord with the molecular formulae shown. $[\alpha]_D$s refer to $CHCl_3$ solutions and IR spectra to KBr disks unless otherwise indicated. NMR spectra were measured at 60 Mc. in CCl_4 solutions *vs.* Me_4Si as internal reference.

1) C. Ukita : Yakugaku Zasshi, **59**, 80 (1939).
2) L. Crabalona : Bull. soc. chim. France, **15**, 357 (1948).
3) Y. R. Naves : Helv. Chim. Acta, **31**, 1172 (1948).
4) M. Romaňuk, V. Herout, F. Šorm : Coll. Czechoslov. Chem. Comm., **21**, 894 (1956).

Adams' catalyst in acetic acid took up two moles of hydrogen to furnish the tetrahydro-derivative (II), $C_{15}H_{24}O_2$, n_D^{25} 1.498, $[\alpha]_D$ +15.1°, infrared band (liquid) at 1767 cm^{-1} (γ-lactone), which, by means of gas chromatography, was detected to consist of more than three components, considered to be stereoisomers. Reduction of I with lithium aluminum hydride gave the diol (III), $C_{15}H_{24}O_2$, m.p. 56.5~58°, $[\alpha]_D$ +37.1°, infrared band at 3356 cm^{-1} (hydroxyl), which on dehydrogenation with selenium yielded a mixture of S-guaiazulene (IV), artemazulene (V), and an unidentified violet azulene (VI). On reduction with sodium borohydride at room temperature over night, I afforded the lactol (VII), $C_{15}H_{22}O_2$, m.p. 110~111°, $[\alpha]_D$ −40.0°, infrared bands at 3448 (hydroxyl), 3106, 1637, 890 cm^{-1} (vinylidene), which reverted on chromic acid oxidation to I. VII gave the semicarbazone (VIII), $C_{16}H_{25}O_2N_3$, m.p. 170°, which was easily hydrolyzed to regenerate VII. By dehydrogenation with selenium, VII afforded exclusively artemazulene (V).



Mokko lactone might correspond to costus lactone of Semmler and Feldstein[5] which, however, is an indefinite substance.

Dehydrocostus lactone (IX), $C_{15}H_{18}O_2$, m.p. 61~61.5°, $[\alpha]_D$ −19.8°, possesses the infrared spectrum which exhibits a band at 1764 cm^{-1}, associated with γ-lactone, and bands at 3125, 1639, and 893 cm,$^{-1}$ related to a vinylidene group. In good agreement with the proposed structure (IX), the nuclear magnetic resonance spectrum shows a triplet at 6.16 τ (H–C≤O–CO–), two sets of peaks at 5.20 and 5.16 τ and 5.03 and 4.78 τ (CH_2=C<), and two peaks at 4.65 and 3.94 τ (CH_2=C(–)–CO–O–). On catalytic hydrogenation with Adams' catalyst in acetic acid, IX consumed three moles of hydrogen to give hexahydrodehydrocostus lactone, $C_{15}H_{24}O_2$, n_D^{25} 1.505, $[\alpha]_D$ +27.1°. Gas chromatography of this saturated product gave four peaks among which the main three peaks had the same retention times as those observed in the case of tetrahydromokko lactone (II). The infrared spectrum (liquid) of hexahydrodehydrocostus lactone was almost identical with that of tetrahydromokko lactone (II) but, despite the statement of Romañuk, *et al.*,[4] apparently different from that of deoxodihydrocarpesia lactone,[6] although some common

5) F. W. Semmler, J. Feldstein : Ber., **47**, 2433 (1914).
6) S. Naito : Yakugaku Zasshi, **75**, 93 (1955).

features were present. Reduction of Ⅸ with sodium borohydride at a room temperature for 1.5 hours or with aluminum amalgam in ether–water afforded dihydrodehydrocostus lactone, $C_{15}H_{20}O_2$, m.p. 35~36°, $[\alpha]_D$ +17.7°, which was identified as mokko lactone (Ⅰ). On prolonged reduction with sodium borohydride, Ⅸ gave the lactol (Ⅶ), $C_{15}H_{22}O_2$, m.p. 111°, $[\alpha]_D$ −40.0°.

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Über die Konstitution und Konfiguration des Anhydrotetrodotoxins*1

In einer früheren Mitteilung[1] ist bereits beschrieben worden, daß man auf Grund der Analysen- und Titrationsresultate dem Tetrodotoxin (Ⅰ) eine Bruttoformel von $C_{12}H_{19}O_9N_3$ geben kann, wenn man es als eine monoacidische Base ansieht. Aber, Ⅰ zeigt keinen Schmelzpunkt und ist eine Substanz, die sich schwer durch Umkristallisierung reinigen läßt. Deshalb wurde diesmal Ⅰ in 6,11-Diacetyl-(Ⅱ) bzw. 11-Monoformylanhydrotetrodotoxin (Ⅲ) übergeführt und dann durch Behandlung mit 5%-iger Salzsäure in den ursprünglichen Zustand zurückversetzt; das auf diese Weise gereinigte Ⅰ*2 zeigte die der Bruttoformel von $(C_{11}H_{17}O_8N_3)_n$ (n=1 oder 2) entsprechenden Analysenwerte*3,2) (Ber. : C, 41.38; H, 5.33; O, 40.12; N, 13.17. Gef. : C, 41.14, 41.16, 40.88; H, 5.46, 5.52, 5.57; O, 39.85, 39.59; N, 13.16, 13.02, 13.23).

In der vorliegenden Kurzmitteilung schreiben wir zuerst über die verschiedenen Derivate, die bis jetzt von uns gewonnen worden sind, und dann befassen wir uns mit der Struktur von Anhydrotetrodotoxin bzw. Tetrodotoxin in der Beziehung einerseits zu Tetrodonsäurebromohydrat (Ⅳa) anderseits zu Bromoanhydrotetrodonsäurelactonbromohydrat; denn das erstgenannte ist von uns[3] und das letzte von Nitta, *et al.*[4] die Struktur betreffend ohne Frage durch Röntgenuntersuchungen aufgeklärt worden. Außerdem möchten wir über unsere letzte Röntgenanalyse von Anhydrotetrodotoxindiacetat-Jodhydrat berichten, was der Struktur von Anhydrotetrodotoxin bzw. Tetrodotoxin betreffend wichtige Rolle spielt.

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*1 Sie wird bei der Jahresversammlung der 84st Japanischen Pharmazeutischen Gesellschaft in Tokio, am 7, April 1964 sowie dem IUPAC Symposium für Naturstoffchemie in Kyoto, am 13. April 1964 vorgetragen.

*2 Dessen Tierversuche mit Mäusen zeigen den LD_{50}-Wert von 9.5 γ/1 Kg.

*3 Goto, *et al.* haben dem Tetrodotoxin die Formel $C_{11}H_{17}O_8N_3$ gegeben (Siehe Fußnote 2); aber wir geben dem Tetrodotoxin die Bruttoformel $C_{22}H_{32}O_{15}N_6 \cdot H_2O$, die sich aus unserer nachfolgenden Kurzmitteilung erklärt.

1) K. Tsuda, K. Kawamura : dieses Bulletin, 8, 257 (1960).
2) T. Goto, Y. Kishi, S. Takahashi, Y. Hirata : Tetrahedron Letters, No. **30**, 2105 (1963).