added to MeOH solution of *dl*-α-[N-bis(β-chloroethyl)amino]propionamide (39 g.) and *d*-camphor-β-sulfonic acid (42.5 g.) and the mixture was kept in ice-box over night. The precipitated product (47 g.; m.p. 135~137°) was recrystallized from MeOH-acetone (80 cc. : 300 cc.) to plates, m.p. 150~151° (decomp.); $[\alpha]_D^{21}$ +3.3°(c=3.0, *l*=1, H_2O). *Anal.* Calcd. for $C_{17}H_{30}O_5N_2Cl_2S$: C, 45.84; H, 6.79. Found: C, 45.64; H, 6.73.

***l*-α-[N-Bis(β-chloroethyl)amino]propinamide (II)**—When a concentrated solution of (I) (9.3 g.) was added with a solution containing an equivalent amount of K_2CO_3, (II) separated as crystals (3.4 g.) melting at 70~72°; $[\alpha]_D^{16}$ −57° (c=3.0, *l*=1, EtOH). *Anal.* Calcd. for $C_7H_{14}ON_2Cl_2$: C, 39.45; H, 6.63; N, 13.15. Found : C, 39.43; H, 6.45; N, 13.00.

Hydrochloride (III) of (II)—Dry HCl was passed into a solution of (II) (3 g.) and the separated product was recrystallized from MeOH, m.p. 189~191°(decomp.). Yield : 3.0 g. $[\alpha]_D^{15}$ −17° (c=3.0, *l*=1, H_2O). *Anal.* Calcd. for $C_{17}H_{15}ON_2Cl_3$: C, 33.69; H, 6.05. Found : C, 33.68; H, 5.90.

***d*-α-[N-Bis(β-chloroethyl)amino]propionamide (IV)**—The whole filtrate, from which (I) was removed, was concentrated. The crude precipitate thus obtained was recrystallized 5 times from dehyd. EtOH. Plates, m.p. 151~152°(decomp.). Yield, 7.0 g. (IV) was obtained by treating this *d*-camphor-β-sulfonate with conc. KOH, as scales, m.p. 71~73°; $[\alpha]_D^{21}$ +40.5° (c=3.0, *l*=1, EtOH).

***dl*-N-Bis(β-chloroethyl)alanine α-Chloro-*d*-camphor-π-sulfonate**—*dl*-N-Bis(β-chloroethyl)alanine hydrochloride (5.0 g.) and ammonium α-chloro-*d*-camphor-π-sulfonate (2.8 g.) were dissolved in hot H_2O (24 cc.) and the solution was kept in a cool place over night. A crystalline salt precipitated which melted at 172~175°. $[\alpha]_D^{8}$ +33.3°(c=3.0, *l*=1, H_2O). Its specific rotation did not change after repeated recrystallization from H_2O, acetone-ether, or hydr. acetone. *Anal.* Calcd. for $C_{17}H_{28}O_6NCl_3S$: C, 42.46; H, 5.87. Found : C, 42.62; H, 6.10.

***l*-N-Bis(β-chloroethyl)alanine Hydrochloride**—(III) (5.2 g.) was added into conc. HCl (d=1.19) (31 cc.) and heated at 80° for 1 hr. After evaporation *in vacuo* to dryness, a crystalline residue was extracted with hot acetone. The cooled extract was added with ether and a crystalline precipitate was obtained. Yield, 3.4 g. of m.p. 86~87°. It was recrystallized from acetone, m.p. 90°. $[\alpha]_D^{25}$ −22° (c=3.0, *l*=1, H_2O), $[\alpha]_D^{25}$ −30° (c=1.5, *l*=1, H_2O+1*M* HCl). *Anal.* Calcd. for $C_7H_{14}O_2NCl_3$: C, 33.55; H, 5.63; N, 5.59. Found : C, 32.99; H, 6.31; N, 5.13.

Summary

Racemic α-[N-bis(β-chloroethyl)amino]propionamide was resolved into the optical isomers. There was however found no difference between the two isomers in toxicity or anticancer activity against the Yoshida sarcoma.

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Shoji Shibata : On the Structure of Strepsilin. II.[1]

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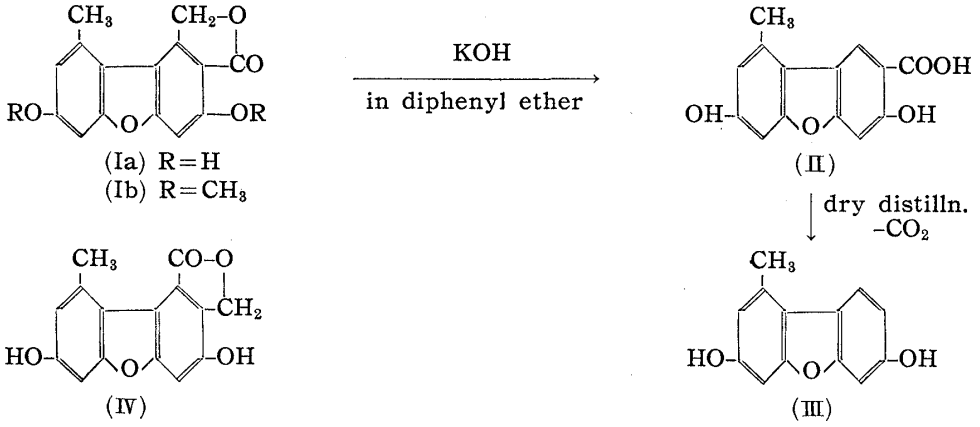
Previously I proposed that strepsilin, $C_{15}H_{10}O_5$, m.p. 324°, a lichen substance isolated from *Cladonia strepsilis* (ACH.) WAIN., is a dibenzofuran derivative, which should be represented by the formula (Ia). Evidence for the structure (Ia) was provided chiefly by the conversion of strepsilin by alkaline degradation into 1-methyl-3,7-dihydroxydibenzofuran (III), m.p. 212°, which was synthetically obtained. For an acidic intermediate product of the alkaline degradation, $C_{14}H_{10}O_5$, m.p. 308°, the structure (II) was adopted mainly by its blue coloration with ferric chloride.

The compound (III) might be formed by the reactions which involved oxidation of the phthalide ring followed by decarboxylation at the 9-position.

* Hongo, Tokyo (柴田承二).

1) S. Shibata : Acta Phytochim., **14**, 177(1944) (C. A., **45**, 5677(1951)).



(Ia) R=H
(Ib) R=CH_3

(II)

(IV)

(III)

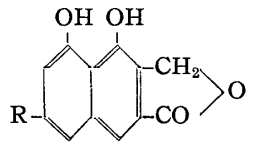
However, the above evidences could not entirely exclude a possible alternative structure (IV) for strepsilin, though the blue coloration with ferric chloride would favor the structure (Ia).

Recently infrared spectral analysis of phthalides[2] has usefully been employed for the studies of natural products having phthalide ring in their structures.

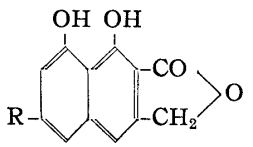
According to Duncanson, Grove, and Zeally[2] 4- and 7-hydroxyphthalides are distinguished by their infrared spectra in dilute solution, wherein the 7-hydroxyl derivative shows a marked lowering of the C=O stretching frequencies (1738 cm^{-1} (in $CHCl_3$), 1754 cm^{-1} (in dioxane), 1749 cm^{-1} (in CCl_4)) in comparison with the 4-hydroxyl derivative (1760 cm^{-1} (in $CHCl_3$), 1772 cm^{-1} (in dioxane)).

Methylation of the hydrogen-bonded hydroxyl of 7-hydroxyphthalide raises the C=O frequencies (1764 cm^{-1}, $\Delta\nu$ 26 (in $CHCl_3$), 1772 cm^{-1}, $\Delta\nu$ 18 (in dioxane), 1782 cm^{-1}, $\Delta\nu$ 33 (in CCl_4)), whereas the 4-methoxyphthalide shows no shift of the C=O band.

Referring the above result, Haber, Nikuni, Schmid, and Yagi[3] amended the formerly proposed structures of α- and β-sorigenins (Va and Vb), the aglycones of α- and β-sorinins isolated from the bark of *Rhamnus japonica* MAXIM., to the formulae (VIa) and (VIb), respectively, as the correct structures.



(Va) R=OCH_3
(Vb) R=H



(VIa) R=OCH_3
(VIb) R=H

α- and β-Sorigenins were found to show their C=O stretching frequencies at 1725 and 1730 cm^{-1} (in $CHCl_3$), respectively.

It seemed, therefore, that the infrared spectral analysis would be most useful for the establishment of the structure of strepsilin. The infrared spectra of strepsilin and its methyl ether measured both in solid state and in solution in dioxane are shown in Table I.

TABLE I.

State / Compd.	Solid (in Nujol)	Solution (in dioxane)
Strepsilin (Ia)	1726 cm^{-1}	1745 cm^{-1}
Dimethyl ether (Ib)	1772	1770
Shift of band by methylation		$\Delta\nu$ 25

2) L. A. Duncanson, J. F. Grove, J. Zealley : J. Chem. Soc., **1953**, 1331.
3) R. G. Haber, Z. Nikuni, H. Schmid, K. Yagi : Helv. Chim. Acta, **39**, 1645(1956), where the earlier literatures (Z. Nikuni) are cited.

The C=O stretching frequencies in strepsilin which showed quite a good agreement with that of 7-hydroxyphthalide were markedly increased by methylation of the hydroxyls.

Accordingly strepsilin should possess a hydrogen-bonded carbonyl grouping of the phthalide ring and the correctness of the structure (Ia) has fully been established.

The intermediate product of the alkaline degradation of strepsilin was examined by infrared spectra and its C=O absorption band of the carboxyl grouping is given in Table II in comparison with some dibenzofuran-carboxylic acid derivatives.

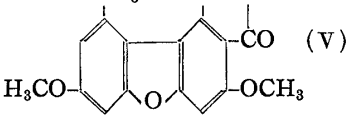
Table II.

	(in dioxane)
Phenolic acid (II), m.p. 212°	1680 cm^{-1}
Didymic acid monomethyl ether[4]	1735
1-Methyl-3,7-dimethoxydibenzofuran-9-carboxylic acid[4]	1735

A distinguished lowering of the C=O frequencies was shown in the phenolic acid derived from strepsilin, which would be caused by chelation between carbonyl and phenolic hydroxyl. Therefore, the intermediate product has been confirmed to possess the strcuture (II).

A yellow crystalline product, $C_{17}H_{12}O_6$, m.p. 247°, obtained by the oxidation of strepsilin dimethyl ether was assumed to be derived by the conversion of phthalide into dicarboxylic anhydride (V). The oxidation product gave two divided absorption bands of C=O as have characteristically been shown in some dicarboxylic anhydrides.[5]

Table III.

State / Compd.	Solid (in Nujol)	Solution (in dioxane)
	cm^{-1}	cm^{-1}
 (V)	1777 (s)* 1814 (m) 1839 (w)	1773 (s)* 1823 (m)
Phthalic anhydride[5]	1759 (s) 1787 (sh) 1847 (m)	1778 (s) 1830 (m)
3-Hydroxy-5-methoxy-4-methylphthalic anhydride	1753 (s) 1823 (m)	— —
3,5-Dimethoxy-4-methylphthalic anhydride	1766 (s) 1841 (m)	— —
γ-Coccinic acid anhydride methyl ether	1775 (s) 1833 (m)	— —
3,5-Dimethoxy-4-methylphthalic acid	1690 (s) 1703 (sh)	— —
Phthalic acid	1685 (s)	

* s : strong; m : medium; w : weak; sh : shoulder

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4) S. Shibata : Acta Phytochim., **14**, 9(1944) (C. A., **45**, 7100(1951)).

5) H. M. Randall, *et al.* : "Infrared Determination of Organic Structures," Van Nostrand, (1949); L. J. Bellamy : "The Infrared Spectra of Complex Molecules," 111(1954); R. G. Cooke : Chemistry & Industry, **1955**, 142.

Experimental

The infrared spectra were obtained with Perkin-Elmer Model 21, and Hilger, H-800, recording spectrophotometers, using NaCl prism. The solution in dioxane was measured in the concentration of 0.05~0.08*M*, using a cell of 0.125 mm. in thickness.

Summary

The structure of strepsilin was examined by infrared spectra. The C=O stretching frequencies of strepsilin at 1745 cm^{-1} (in dioxane) and its shift to 1770 cm^{-1} by the methylation of hydroxyls indicated that strepsilin possesses a hydrogen-bonded carbonyl of phthalide ring, which accounts for the structural formula (Ia) of strepsilin.

The structures of phenolic acid, m.p. 308°, and the yellow crystalline compound, m.p. 247°, which were derived from strepsilin, were discussed from their infrared spectra.

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