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The Structure of Consticitic Acid

In 1968 Asahina reported[1] the existence of constictic acid together with or without stictic acid in some kinds of lichens and pointed out nonidentity of the acid with protocetraric acid (I). With the generous gift of lichen (*Usnea aciculifera* Vain) from Professor Asahina, we have worked on the structure of constictic acid obtained by successive extraction of the lichen using benzene and acetone followed by preparative thin–layer chromatographic (TLC) separation and finally have reached a conclusion that the acid is expressed as V, which is the subject of the present communication.

Constictic acid (V), $C_{19}H_{14}O_{10} \cdot 3H_2O$[2] *m/e*: 402 ($M^+$), mp 195—200°, exhibits quite similar chemical property as stictic acid (II).[3] It afforded a pentaacetate (Va), $C_{29}H_{26}O_{16}$, *m/e*: 630 (M^+), mp 210°, with acetic anhydride and sulfuric acid.

The nuclear magnetic resonance (NMR) spectra of V and Va in comparison with those[4] of related depsidone derivatives such as stictic acid (II), norstictic acid (III), salazinic acid (IV), tetraacetyl-stictic acid (IIa), and hexaacetyl-salazinic acid (IVa) are given in Table I. As is evident from the data, the significant difference between constictic and stictic acids is that the former possesses one each of aromatic methyl (δ: 2.48, singlet) and hydroxymethyl (δ: 4.67, singlet) functions as is similarly observed in salazinic acid, while the latter carries two aromatic methyls (δ: 2.22 and 2.47) similarly as norstictic acid. The methyl signals appearing

Table I. NMR Spectra of Constictic Acid and Related Compounds
(in δ-Value from Tetramethylsilane)

	PhMe	MeCO	$PhCH_2$	OMe	PhH	CHO
Constitic acid (V)[a,b]	2.48		4.67	3.93	7.11	6.64 10.49
Norstictic acid (III)[4,b]	2.22 2.46				6.86	6.90 10.48
Stictic acid (II)[a,b]	2.22 2.47			3.92	7.07	6.66 10.49
Salazinic acid (IV)[4,b]	2.45		4.65		6.80	6.85 10.33
Pentaacetyl-constictic acid (Va)[a,b]	2.49	1.94 2.09 2.18 2.22 2.40	5.26[c]	3.94	7.14	7.82 7.94
Tetraacetyl-stictic acid (IIa)[4,d]	2.20 2.43	2.06 2.16 2.30 2.43		3.94	6.73	7.88 8.05
Hexaacetyl-salazinic acid (IVa)[4,d]	2.56	1.96 2.08 2.13 2.21 2.35 2.42	4.93 5.15 5.36 5.56		6.95	7.83 7.95

a) measured with a varian A-60 NMR spectrometer; *b*) measured in d_6-DMSO;
c) a quartet-like multiplet centered at δ: 5.26; *d*) measured in $CDCl_3$

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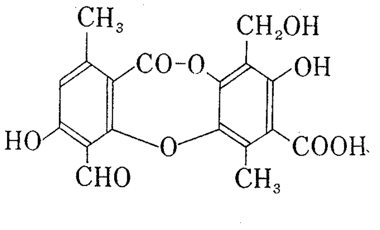
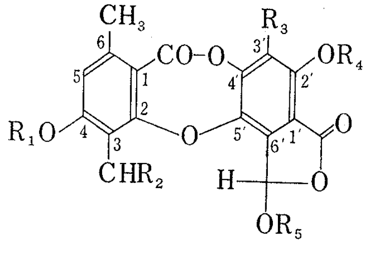
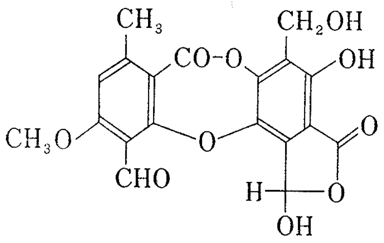
1) Y. Asahina, *Journ. Jap. Bot.*, **43**, 97 (1968).
2) Satisfactory analytical data were obtained for the compounds given with chemical formulae.
3) Y. Asahina and S. Shibata, "Chemistry of Lichen Substances," Japan Society for the Promotion of Science, Tokyo, Japan, 1954, p. 134.
4) S. Huneck and P. Linscheid, *Z. Naturforsh.*, **23b**, 717 (1968).

at δ: 2.22 of II and III are assigned to methyl protons at C-3′, whereas signals at δ: 2.47 of II and δ:2.46 of III are ascribed to C-6 methyl protons.[4] These observations have led us to assign a methyl function of constictic acid at C-6 and a hydroxymethyl grouping at C-3′. The splitting pattern due to methylene protons of acetoxymethyl functions in pentaacetyl-constictic acid (Va) and hexaacetyl-salazinic acid (IVa) also supports the assignment.



I : protocetraric acid





V : constictic acid

		R_1	R_2	R_3	R_4	R_5
II	: stictic acid	CH_3,	O,	CH_3,	H,	H
IIa	: tetraacetyl-(II)	CH_3,	$(OAc)_2$,	CH_3,	Ac,	Ac
III	: norstictic acid	H,	O,	CH_3,	H,	H
IIIa	: pentaacetyl-(III)	Ac,	$(OAc)_2$,	CH_3,	Ac,	Ac
IV	: salazinic acid	H,	O,	CH_2OH,	H,	H
IVa	: hexaacetyl-(IV)	Ac,	$(OAc)_2$,	CH_2OAc,	Ac,	Ac
Va	: pentaacetyl-(V)	CH_3,	$(OAc)_2$,	CH_2OAc,	Ac,	Ac

Chart 1

The noticeable common feature in the NMR spectra of constictic and stictic acids is the existence of one methoxyl function, which is found at δ: 3.93 or 3.92 and assignable to methoxyl protons at C-4. The remaining signals of constictic acid and its pentaacetate are assigned as for II, III, IV, and IIa, IVa. It follows that constictic acid possesses three hydroxyl and one aldehyde functions. The Mass spectrum of constictic acid giving fragment ions (*m/e*) at 402 (M^+), 384 (M^+-H_2O), 356 (M^+-H_2O-CO) is reminiscent of that of stictic acid, which gave ions at 386, 368, and 340.[5] Furthermore, nonlactonized rings of both constictic and stictic acids give same fragment ions at 193 and 191 describable as (a) and (b).[5]

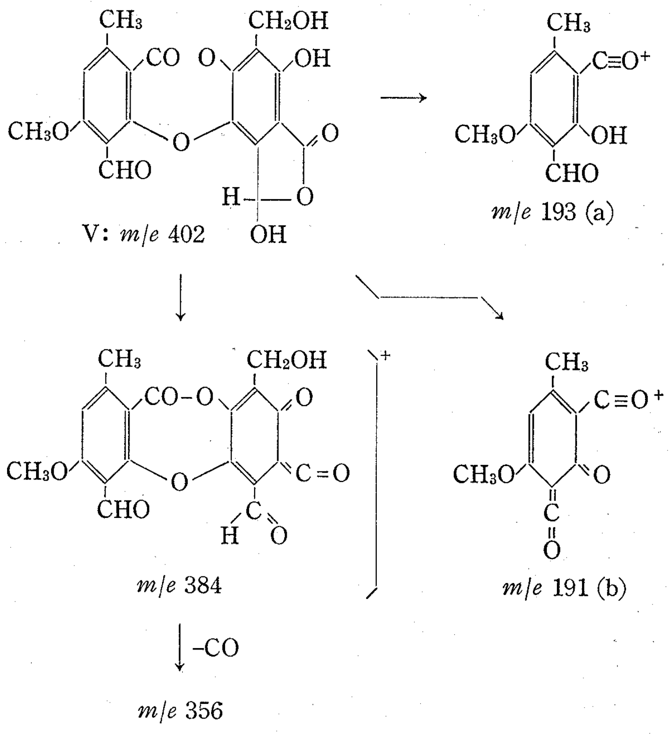


Chart 2. Fragmentation of Constictic Acid

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[5] S. Huneck, C. Djerassi, D. Becher, M. Barber, M. Von Ardenne, K. Steinfelder and R. Tümmler, *Tetrahedron*, 24, 2707 (1968).

The combined evidence given above has enabled us to assign the structure V to constictic acid. Although the structure V is identical with the structure of salazinic acid β-methyl ether proposed by Asahina and Tsukamoto in 1935,[6] we were able to identify both samples only by TLC comparison. In agreement with Professor Asahina, we wish to keep the name constictic acid for the compound possessing the structure V.

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[6] Y. Asahina and C. Tsukamoto, *Yakugaku Zasshi*, **55**, 1107 (1935).

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Behaviour of Plasma Sugars after Oral Administration of Lactose

Disaccharide tolerance tests have been performed in order to find the deficiency of digestive capacity of the small intestine. Judgement of the tests has been done only by examining the degree of blood glucose rise. However, if the concentration of disaccharides in blood is known, it will be resulted in obtaining more detailed information about their metabolism which must be useful for clinical biochemistry. As disaccharides in blood after oral administration have never been determined owing to their low concentration, we have realized this to get the following results.

Volunteers aged from 23 to 33 years and generally in good health were fasted for 12 hr except for one subject D (4 months old, 6 hr starvation). Oral tolerance tests were performed by administering them either 50 g disaccharide (lactose, maltose or sucrose) in 160—290 ml of water or 2 g lactose per kg body weight in 250 ml of water.

Blood was drawn from arm vein at 30 min intervals for 2.5 hr. Urine was collected at 30 min intervals for 3 hr and at 1 hr intervals for additional 1—7 hr. Blood plasma was prepared by adding NaF to the blood (10 mg per ml). The deproteinization was carried out at 75% ethanol concentration. Urine was incubated with urease for 30 min at 45° to decompose urea. The deproteinized plasma or the urea-free urine was deionized by passing through columns of Amberlite CG-120 (H^+) and Amberlite CG-4B (CH_3COO^-).

Gas chromatographic analysis of monosaccharides was carried out after Imanari, *et al.*[1] with a modification in which N,N-dimethylformamide was used as a solvent instead of ethyl acetate. Disaccharides were analyzed by the previous method.[2]

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[1] T. Imanari, Y. Arakawa and Z. Tamura, *Chem. Pharm.Bull.* (Tokyo), **17**, 1967 (1969).
[2] H. Nakamura and Z. Tamura, *Chem. Pharm. Bull.* (Tokyo), **18**, 2314 (1970).