[Chem. Pharm. Bull. 26(7)2266—2267(1978)]

UDC 547.918.02 : 581.192

Paniculosides-I—V, Diterpene-glucosides from *Stevia ovata* Lag.

Norito Kaneda,[1a] Hiroshi Kohda,[1a,c] Kazuo Yamasaki, Osamu Tanaka,[1a] and Kozaburo Nishi[1b]

Institute of Pharmaceutical Sciences, Hiroshima University School of Medicine[1a] and Kasukabe Experimental Station of Medicinal Plants, National Institute of Hygienic Sciences[1b]

(Received January 13, 1978)

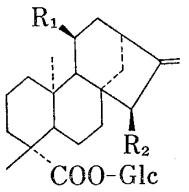
From leaves of *Stevia ovata* Lag. (Compositae), there were isolated five kinds of kaurane-type ester-glucosides, paniculosides-I, -II, -III, -IV, and -V, all of which had already been isolated from leaves of *S. paniculata* Lag.

Keywords——kaurane type diterpenes; *Stevia ovata* Lag.; Compositae; paniculosides-I—V; glucosides

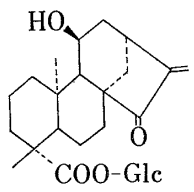
In continuation of our chemical studies on sweet diterpene-glycosides of *Stevia rebaudiana* Bertoni (Compositae),[2] the present authors have investigated constituents of related *Stevia* spp.; *S. serrata* Cav.[3] and *S. paniculata* Lag.[4] The present report deals with isolation and identification of glucosides of *S. ovata* Lag., cultivated at the Kasukabe Experimental Station of Medicinal plants.[1b]

A glycoside-fraction of the dried leaves was subjected to repeated column chromatography to give five crystalline compounds (**1**—**5**), all of which do not taste sweet unlike the glycosides of *S. rebaudiana*.[2] Comparison of thin-layer chromatograms (TLC), ^{13}C nuclear magnetic resonance (NMR) spectra as well as other physical constants led to identification of these compounds (**1**—**5**) to be paniculosides-I—V, respectively, all of which had already been isolated from leaves of *S. paniculata* and formulated as shown in Chart 1.[4]

The present result strongly suggests the close taxonomical relationship between *S. paniculata* and *S. ovata*.



	R_1	$_2R$
1:	H	OH
2:	OH	OH
5:	H	O-Glc



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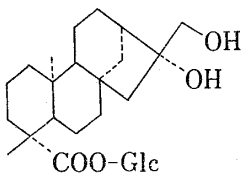

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Glc: β-Glucopyranosyl

Chart 1

1) Location: *a) 1-2-3 Kasumi, Hiroshima-shi, 734 Japan*; *b) Kasukabe, Kasukabe-shi, 344 Japan.* Correspondence should be addressed to O. Tanaka; *c)* Present address of H.K.: *National Institute of Hygienic Sciences, Kamiyoga 1-chome, Setagaya-ku, Tokyo, 158 Japan.*

2) H. Kohda, R. Kasai, K. Yamasaki, K. Murakami, and O. Tanaka, *Phytochemistry*, **15**, 981 (1976); I. Sakamoto, K. Yamasaki, and O. Tanaka, *Chem. Pharm. Bull.* (Tokyo), **25**, 844 and 3437 (1977).

3) H. Kohda, K. Yamasaki, O. Tanaka, and K. Nishi, *Phytochemistry*, **15**, 846 (1976).

4) K. Yamasaki, H. Kohda, T. Kobayashi, N. Kaneda, R. Kasai, O. Tanaka, and K. Nishi, *Chem. Pharm. Bull.* (Tokyo), **25**, 2895 (1977) (Preliminary communication: *idem*, *Tetrahedron Lett.*, **1976**, 1005).

Experimental

All melting points were measured on a micro hot-stage and uncorrected. Conditions of TLC and ^{13}C NMR spectra determination are referred to the previous paper.[4]

Extraction and Identification of Glucosides——The dried leaves (145 g) harvested in September (1977), were extracted with hot MeOH. After concentration of the solution, the MeOH-extract was digested with H_2O and the suspension was washed with ether and then extracted with *n*-BuOH (saturated with H_2O). The BuOH-extract (10.0 g) was chromatographed on silica gel by eluting with $CHCl_3$: MeOH: H_2O (200: 30: 1) affording three fractions (A, B, and C).

The less polar fraction-A was subjected to re-chromatography on silica gel by eluting with AcOEt: MeOH: H_2O (800: 35: 10), yielding three colorless crystalline glucosides, **1**, **2**, and **3** which were proved to be identical with paniculosides-I, -II, and -III, respectively by comparison of TLC, ^{13}C NMR spectra, melting points, and optical rotations; **1**: mp 135—139° (from MeOH–H_2O), $[\alpha]_D^{10}$ −63.0° (c=0.07, MeOH), yield 0.028%; **2**: mp 230—234° (from MeOH–H_2O), $[\alpha]_D^{20}$ −60.0° (c=0.1, MeOH), yield 1.1%; **3**: mp 153—157° (from MeOH–H_2O), $[\alpha]_D^{20}$ −118.0° (c=0.1, MeOH), yield 0.8%.

The more polar fraction-B was re-chromatographed on silica gel by eluting with $CHCl_3$: MeOH (5: 1), to give colorless prisms, mp 155—157° (from MeOH–H_2O), $[\alpha]_D^{10}$ −63.8° (c=0.08, MeOH), yield 0.12%, which were proved to be identical with paniculoside-IV by comparison of TLC, ^{13}C NMR spectra, and other physical constants. The optical rotation of paniculoside IV in our previous paper[4] (+65.6°) was mis-typewritten and should be corrected as above.

The most polar fraction-C was re-chromatographed on silica gel by eluting with AcOEt: MeOH: H_2O (420: 40: 35) to give colorless prisms, mp 173—175° (from MeOH–H_2O), $[\alpha]_D^{10}$ +59.0° (c=0.15, MeOH), yield 0.22%, which were identified with paniculoside-V by comparison of TLC, ^{13}C NMR spectra, and other physical constants.

Acknowledgement This work was supported in part by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture which is gratefully acknowledged.

[Chem. Pharm. Bull. 26(7)2267—2269(1978)]

UDC 547.831.8.04 : 542.943.6.04

Oxidation of Procaterol to 5-Formyl-8-hydroxycarbostyril

Shiro Yoshizaki, Shigeharu Tamada, and Eiyu Yo

Laboratories of Medicinal Chemistry, Tokushima Factory, Otsuka Pharmaceutical Co., Ltd.[1]

(Received January 17, 1978)

5-Formyl-8-hydroxycarbostyril (**5**), one of the major metabolites of procaterol (**1**), was synthesized by oxidation of **1** and 8-benzyloxy procaterol (**2**).

Keywords——procaterol; 5-formyl-8-hydroxycarbostyril; oxidation; sodium metaperiodate; *m*-chloroperoxybenzoic acid

Recently we reported on procaterol, 5-(1-hydroxy-2-isopropylaminobutyl)-8-hydroxycarbostyril (**1**), which is a potent and selective β-adrenoceptor stimulating agent.[2] Shimizu, *et al.*[3] investigated the metabolic fate of **1** in the rat and found that one of the major metabolites of **1** was 5-formyl-8-hydroxycarbostyril (**5**). To obtain an authentic sample of **5**, we investigated the oxidation reaction of **1**.

1) Location: *Kagasuno, Kawauchi-cho, Tokushima.*
2) *a*) S. Yoshizaki, K. Tanimura, S. Tamada, Y. Yabuuchi, and K. Nakagawa, *J. Med. Chem.*, **19**, 1138 (1976); *b*) S. Yoshizaki, Y. Manabe, S. Tamada, K. Nakagawa, and S. Tei, *ibid.*, **20**, 1103 (1977).
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