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Studies on Monoterpene Glucosides and Related Natural Products. XXXIII.[1] Structure of Bakankosin

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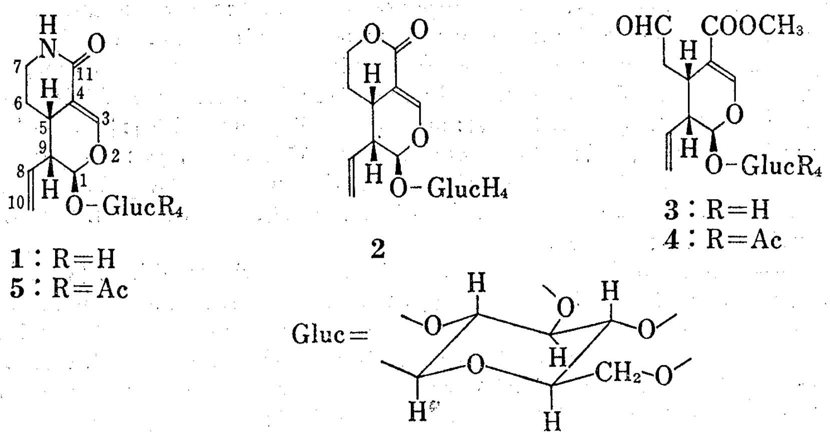
Chemical conversion of secologanin (**3**) into bakankosin established the absolute structure of the latter to be represented as **1**.

Bakankosin (**1**) is a nitrogen–containing glucoside first isolated by Bourquelot and Hérissey[3] from the seed of *Strychnos vacacoua* Baillon in 1907. Later in 1952 Prelog, *et al.*[4] reported on this glucoside without giving the entire picture of the structure. In 1960, Büchi and Manning[5] referred to bakankosin in their report on the structure of verbenalin as a structurally related substance presumably on the basis of Prelog's experimental data and proposed structure **1** for it, without giving any stereochemical consideration.

Although this substance has the same carbon skeleton as that of sweroside (**2**),[6] it is unique in having a lactam ring. The plants of the genus *Strychnos* from which bakankosin (**1**) was isolated have been well known for containing several indole alkaloids such as strychnine. Formation of bakankosin (**1**) in a plant is therefore reasonably explained by supposing the reductive condensation of secologanin (**3**),[7] a common precursor of these alkaloids, with ammonia or its equivalent instead of tryptamine followed by lactamization.



1 : R=H
5 : R=Ac

2

3 : R=H
4 : R=Ac

Chart 1

Thus, we intended to verify the structure of bakankosin (**1**) through conversion of secologanin (**3**) into it by reductive amination.

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1) Part XXXII: Y. Takeda, H. Nishimura, and H. Inouye, *Chem. Pharm. Bull.* (Tokyo), **24**, 1216 (1976).
2) Location: *Yoshida-Shimoadachi-cho, Sakyo-ku, Kyoto.*
3) E. Bourquelot and H. Hérissey, *C. R. Acad. Sci. Paris*, **144**, 575 (1907); *idem*, *J. Pharm. Chim.*, **25**, 417 (1907); *idem*, *Arch. Pharmacie*, **247**, 56 (1907).
4) K. Balenović, H.U. Däniker, R. Goutarel, M.M. Janot, and V. Prelog, *Helv. Chim. Acta*, **35**, 2519 (1952).
5) G. Büchi and R.E. Manning, *Tetrahedron Letters*, **1960**, 5; *idem*, *Tetrahedron*, **18**, 1049 (1962).
6) H. Inouye, T. Yoshida, Y. Nakamura, and S. Tobita, *Chem. Pharm. Bull.* (Tokyo), **18**, 1889 (1970).
7) A.R. Battersby, A.R. Burnett, and P.G. Durst, *J. Chem. Soc.* (*C*), **1969**, 1187.

Namely, secologanin tetraacetate (**4**) was left standing with ammonium acetate in anhydrous methanol in the presence of sodium cyanohydridoborate[8] at room temperature and the product was hydrolysed with diluted alkali. Preparative thin layer chromatography (TLC) followed by the acetylation of the product yielded colorless needles, mp 213—215°, which were identical with the tetraacetate (**5**) prepared from bakankosin (**1**) in all respects. This fact corroborates the structure of bakankosin proposed by Büchi and Manning and also established its absolute structure to be represented as **1**.

Experimental[9]

Conversion of Secologanin Tetraacetate (4) to Bakankosin Tetraacetate (5)——$NaBH_3CN$ (400 mg) was added to a solution of secologanin tetraacetate (**4**)[10] (470 mg) and ammonium acetate (660 mg) in anhyd. MeOH (11 ml) and the mixture was stirred at room temperature for 46 hr. The yellow reaction solution was concentrated *in vacuo* and the resulting residue was extracted with $CHCl_3$. After washing with water, the $CHCl_3$ extract was dried over anhyd. $MgSO_4$ and the solvent was removed. To a solution of the resulting oily residue (366 mg) in MeOH (15 ml) was added 15% aq. Na_2CO_3 (2 ml) while stirring. After stirring for 30 more min, the reaction mixture was concentrated *in vacuo* to give a residue, which was dissolved in water (5 ml), mixed with another 3 ml of 15% aq. Na_2CO_3 and stirred at room temperature for 3 hr. After dilution with water, the reaction mixture was neutralized with Amberlite IR-120B. The resin was filtered off and the filtrate was concentrated *in vacuo*. A small amount of EtOH was added to the resulting residue and the insoluble material was filtered off. The residue (154 mg) obtained by concentrating the filtrate under reduced pressure was subjected to preparative TLC (0.5 mm, 20 × 20 cm) with $CHCl_3$–MeOH (7 : 3) as a developing solvent. The band around *Rf* 0.2—0.3 was scrapped and extracted with MeOH and the MeOH extract was concentrated *in vacuo*. After mixing with 4 ml each of Ac_2O and pyridine, the resulting residue was left standing at room temperature for 1 hr and the mixture was concentrated *in vacuo* to give an oily residue. A $CHCl_3$ solution of the residue was washed successively with 5% HCl, water, 5% Na_2CO_3 and water, dried over anhyd. $MgSO_4$ and concentrated to give an oily residue (38 mg), which was recrystallized from EtOH yielding colorless needles, mp 213—215°. Yield 9.5 mg. $[\alpha]_D^{25}$ $-119.6°$ ($c=0.90$, $CHCl_3$). UV λ_{max}^{MeOH} (log ε): 236 (4.20). IR ν_{max}^{KBr} cm^{-1}: 1740, 1670, 1620. NMR δ: 1.97—2.08 ($4\times OCOCH_3$), 1.67 (m, H_2–6), 2.50—2.92 (m, H–5, H–9), 3.17—3.58 (m, H_2–7), 3.58—3.97 (m, H–5′), 4.13—4.32 (m, H_2–6′). 4.83—5.78 (H–1, H–8, H_2–10, H–1′—4′), 6.73 (NH, disappeared on the addition of D_2O), 7.38 (d, $J=2$ Hz, H–3). *Anal.* Calcd. for $C_{24}H_{31}O_{12}N$: C, 54.85; H, 5.95; N, 2.67. Found: C, 54.91; H, 6.07; N, 2.54. This substance did not show depression on admixture with the tetraacetate derived from an authentic sample of bakankosin. Several properties described above were also identical with those of the tetraacetate of the natural glucoside.

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[8] R.F. Borch, M.D. Bernstein, and H.D. Durst, *J. Am. Chem. Soc.*, **93**, 2897 (1971).

[9] Melting points were measured on a Yanagimoto micromelting point apparatus and are uncorrected. Silica gel G acc. to Stahl (E. Merck) was used for TLC and spots were detected by exposing in iodine vapour or by spraying the anisaldehyde–H_2SO_4 reagent followed by heating. Nuclear magnetic resonance (NMR) spectra were taken on a Varian A 60 spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard.

[10] Secologanin (**3**) used in this experiment was isolated from *Lonicera morrowii* A. Gray. *cf.* I. Souzu and H. Mitsuhashi, *Tetrahedron Letters*, **1970**, 191.