To a solution of 0.03 mole of primary alkylamine hydrochloride in 30 ml of water, 3.0 g of 37% formalin and then a solution of 0.03 mole of amide in 30 ml of EtOH were added. The mixture was heated at 35—40° with occasional shaking. After 30 min the reaction solution was concentrated under reduced pressure and the resulting residue was solidified, if necessary, by washing with small amount of dry ether. By recrystallization from EtOH pure N-(alkylaminomethyl)amide hydrochloride was obtained. Yields of the products are shown in Table I and their physical, spectral and analytical data are listed in Table II.

N-(Alkylaminomethyl) benzamides——N-(Benzylaminomethyl) benzamide, N-(2-phenylethylaminomethyl)benzamide and N-(cyclohexylaminomethyl)benzamide were obtained by the following procedure.

To a solution of 4.5 g (0.045 mole) of potassium bicarbonate in 50 ml of water, finely powdered N-(alkylaminomethyl)benzamide hydrochloride was added and the mixture was stirred at room temperature. The suspending product was extracted with benzene. The benzene solution was dried over K_2CO_3. Removal of benzene and recrystallization of the solid residue gave N-(alkylaminomethyl)benzamide. Physical, spectral and analytical data of the products are shown in Table III.

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Synthesis of Arctigenin-4′-β-gentiobioside

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In the preceding papers[2] we reported the isolation and structual elucidation of arctigenin-4′-β-gentiobioside (I), which is a sole example of naturally occuring of lignan having glucosyl glucose moiety.

In this paper the synthesis of I has been achieved to confirm finally the structure.

Hepta-O-acetyl-α-gentiobiosyl bromide (III), mp 141—143° (lit.[3] mp 143—144.5°), was prepared according to the procedure described in literature[3] from octa-O-acetyl-β-gentiobiose. Sodium arctigenate (IV) was added to III in chloroform. After stirring the mixture for 12 hr at room temperature, the product was extracted with chloroform and the chloroform

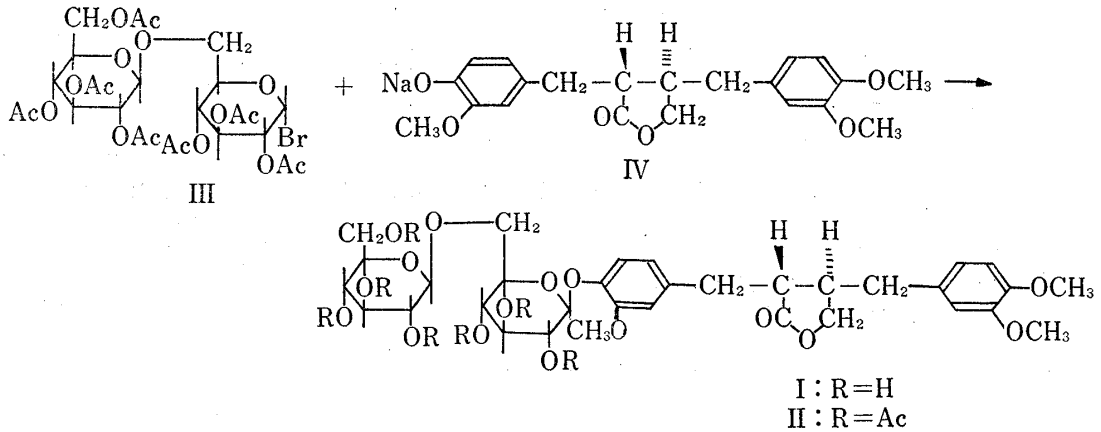

Chart 1

1) Location: *Tanabe-dori, Mizuho-ku, Nagoya, 467, Japan.*
2) S. Nishibe, S. Hisada, and I. Inagaki, *Experientia*, **29**, 17 (1973); *idem*, *Chem. Pharm. Bull.* (Tokyo), **21**, 639 (1973).
3) K. Takiura, S. Honda, T. Endo, and K. Kakehi, *Chem. Pharm. Bull.* (Tokyo), **20**, 438 (1972).

extracts were subjected to column chromatography on silica gel, eluting with chloroform–ethyl acetate (1:1) to give arctigenin-4′-β-gentiobioside heptaacetate (II), $C_{47}H_{58}O_{23}$, mp 186—186.5°, $[\alpha]_D^{17}$ −42.4° (chloroform). II was identical with the natural arctigenin-4′-β-gentiobioside heptaacetate in all respects.

II was deacetylated with 2% sodium methoxide as the usual way. The solution was neutralized with acetic acid and evaporated to dryness. The residue was subjected to column chromatography on silica gel, eluting with chloroform–ethanol (3:2) to give I, $C_{33}H_{44}O_{16}\cdot H_2O$, mp 179—180°, $[\alpha]_D^{19}$ −52.0° (water). I was identical with the natural arctigenin-4′-β-gentiobioside in all respects.

Experimental

All melting points were not corrected. The following equipment was used: Infrared (IR) spectra, Infrared Spectrophotometer IRA-2 (JASCO); Ultraviolet (UV) spectra, Hitachi Recording Spectrophotometer Model EPS-3T; Nuclear magnetic resonance (NMR) spectra, JNM-MH-60 (JEOL) with tetramethylsilane ($\delta=0$) as internal standard; Optical rotation values, Direct Reading Polarimeter Model OR-10 (Yanagimoto).

The thin-layer chromatography (TLC) values were obtained with Kieselgur G nach Stahl (Merck) as adsorbent; the spots were detected by spraying with 10% H_2SO_4 and heating. For column chromatography silica gel (100 mesh, Mallinckrodt) was used.

The abbreviation used are as follows: s, singlet; d, doublet; m, multiplet; br, broad; br. s, broad singlet.

Reaction of Sodium Arctigenate (IV) with Hepta-O-acetyl-α-gentiobiosyl Bromide (III)——IV, which was prepared from arctigenin (150 mg) was added dropwise to III (400 mg) in $CHCl_3$ (30 ml). After stirring the mixture for 12 hr at room temperature, H_2O was added to the mixture and the product was extracted with $CHCl_3$. The $CHCl_3$ solution was washed with H_2O, dried over Na_2SO_4 and evaporated to dryness. The residue was chromatographed over a column of silica gel (60 g), eluting with $CHCl_3$–AcOEt (1:1). Fractions (25 ml each) were monitored by TLC using $CHCl_3$–AcOEt (1:1) as a developer. The fractions showing a spot at *Rf* value of the natural arctigenin-4′-β-gentiobioside heptaacetate were evaporated to dryness. The residue was crystallized from MeOH to yield II (53 mg) as colorless needles, mp 186—186.5°, $[\alpha]_D^{17}$ −42.4° ($c=1.0$ in $CHCl_3$). UV λ_{max}^{EtOH} nm (log ε): 228.5 (4.18), 280 (3.77). IR ν_{max}^{KBr} cm^{-1}: 1740 (γ-lactone and acetyl C=O), 1605, 1590, 1515 (arom. C=C). *Anal.* Calcd. for $C_{47}H_{58}O_{23}$: C, 56.97; H, 5.90. Found: C, 56.68; H, 6.20. NMR (in $CDCl_3$) δ: 6.35—7.20 (6H, m, aromatic), 4.75—5.35 (6H, m), 4.50 (1H, d, $J=6$ Hz, anometic), 4.15 (2H, br. s), 3.30—4.10 (7H, m), 3.83, 3.80, and 3.77 (9H, each s, methoxyl), 2.75—3.15 (2H, br, C-8, 8′), 2.57 (4H, br. s, C-7, 7′), 1.90, 2.00, and 2.05 (21 H, each s, acetyl).

II was identical with the natural arctigenin-4′-β-gentiobioside heptaacetate in all respects.

Deacetylation of Arctigenin-4′-β-gentiobioside Heptaacetate (II)——II (45 mg) dissolved in MeOH (5 ml) was added to 2% sodium methoxide (20 ml) and the mixture was warmed at 40° for 10 min. The solution was neutralized with acetic acid and evaporated to dryness. The residue was chromatographed over a column of silica gel (30 g), eluting with $CHCl_3$–EtOH (3:2). Fractions (25 ml each) were monitored by TLC using $CHCl_3$–EtOH (3:1) as a developer. The fractions showing a spot at *Rf* value of the natural arctigenin-4′-β-gentiobioside were evaporated to dryness. The residue was crystallized from MeOH to give I as colorless needles, mp 179—180°, $[\alpha]_D^{19}$ −52.0° ($c=0.4$ in H_2O). UV λ_{max}^{EtOH} nm (log ε): 230 (4.22), 280 (3.75). IR ν_{max}^{KBr} cm^{-1}: 3560—3200 br. (OH), 1765 (γ-lactone C=O), 1605, 1590, 1510 (arom. C=C). *Anal.* Calcd. for $C_{33}H_{44}O_{16}\cdot H_2O$: C, 55.46; H, 6.49. Found: C, 55.68; H, 6.56.

I was identical with the natural arctigenin-4′-β-gentiobioside in all respects.

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