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FIVE TETRAHYDROISOQUINOLINE-MONOTERPENE GLUCOSIDES AND A TETRAHYDRO-β-CARBOLINE-MONOTERPENE GLUCOSIDE FROM *ALANGIUM LAMARCKII*[1]

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ABSTRACT.—Reinvestigation of the fruits of *Alangium lamarckii* has led to the isolation and structural determination of five new tetrahydroisoquinoline-monoterpene glucosides, methylisoalangiside [**5**], isoalangiside [**6**], 3-*O*-demethyl-2-*O*-methylisoalangiside [**7**], demethylneoalangiside [**8**], and neoalangiside [**9**], as well as a novel tetrahydro-β-carboline-monoterpene glucoside, 10-hydroxyvincoside lactam [**10**]. Demethylalangiside, sweroside, and phenethyl alcohol xylopyranosyl (1→6) glucopyranoside were also isolated for the first time from this plant. The structures of the new compounds were elucidated by spectroscopic and chemical methods. The biogenesis of these glucosides is also discussed.

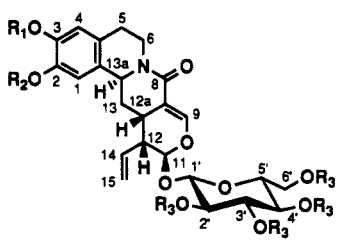
Alangium lamarckii Thwaites (Alangiaceae) is a deciduous shrub that is widely distributed throughout India and southeast Asia. The root bark of this plant finds extensive usage in folk medicine as an anthelmintic, purgative, emetic, and febrifuge, as well as in the treatment of leprosy and other skin diseases. Previous phytochemical studies on this plant focused mainly on its alkaloidal constituents, which include ipecac alkaloids, represented by emetine [**1**] and cephaeline [**2**] (2). The glucosidal constituents, by contrast, remained to be examined except for alangiside [**3**] and loganic acid (3), although the alkaloids were shown to be biosynthesized via a glucosidal intermediate. In the course of our phytochemical studies on nitrogenous glycosides (4), we have recently investigated the constituents of the fruits of *A. lamarckii* and isolated 3-*O*-demethyl-2-*O*-methylalangiside [**4**] (5). Re-examination of the plant material was undertaken, since a preliminary study showed the presence of various nitrogenous glycosides. In this paper we describe the isolation and characterization of five new unusual tetrahydroisoquinoline-monoterpene glucosides and a tetrahydro-β-carboline-monoterpene glucoside, and discuss the biogenesis of these compounds.

RESULTS AND DISCUSSION

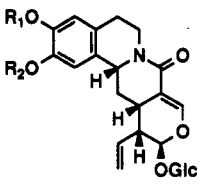
Dried and crushed fruits of *A. lamarckii* were extracted with hot MeOH. The MeOH extract was successively partitioned between H_2O and $CHCl_3$ and between H_2O and *n*-BuOH. The *n*-BuOH-soluble fraction was fractionated by open-column chromatography on Si gel and reversed-phase mplc and then purified by reversed-phase hplc and prep. tlc, affording five novel tetrahydroisoquinoline-monoterpene glucosides [**5–9**] and a tetrahydro-β-carboline monoterpene glucoside [**10**], along with the known glycosides alangiside [**3**], 3-*O*-demethyl-2-*O*-methylalangiside [**4**], demethylalangiside [**11**] (4), sweroside (6), and phenethyl alcohol xylopyranosyl (1→6) glucopyranoside (7). The latter three glycosides were isolated for the first time from this plant species.

Compound **5** was isolated as an amorphous powder, analyzed for $C_{26}H_{33}NO_{10}$ from its hrsims. It showed uv maxima at 235, 282, and 292 (sh) nm, and ir bands at 3406 (OH), 1657 (NCO), 1589 (Ar), and 1516 (Ar) cm^{-1}. Its ^1H-nmr spectrum (Table 1) indicated a structural similarity to methylalangiside [**12**] (5). However, when the ^1H-nmr data of the new compound **5** were compared with those of **12**, there were remarkable differences in the coupling constants between H_2-13 and H-13a (**5**: $J_{13\alpha,13a}$=5.5 Hz,

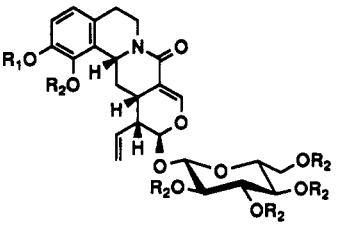
[1]A part of this work was reported in a preliminary communication (1).



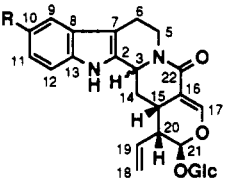
5 $R_1=R_2=Me, R_3=H$
6 $R_1=Me, R_2=R_3=H$
7 $R_1=R_3=H, R_2=Me$
14 $R_1=R_2=Me, R_3=Ac$
15 $R_1=R_2=R_3=H$
16 $R_1=R_2=R_3=Ac$
17 $R_1=Me, R_2=R_3=Ac$
18 $R_1=R_3=Ac, R_2=Me$



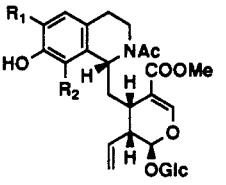
3 $R_1=Me, R_2=H$
4 $R_1=H, R_2=Me$
11 $R_1=R_2=H$
12 $R_1=R_2=Me$



8 $R_1=R_2=H$
9 $R_1=Me, R_2=H$
19 $R_1=R_2=Ac$



10 R=OH, H-3β
21 R=OH, H-3α
22 R=H, H-3β
23 R=H, H-3α



20 $R_1=H, R_2=OH$
26 $R_1=OH, R_2=H$

TABLE 1. ^{1}H-Nmr Spectral Data of Compounds **3–9**, **11**, **12**, and **15** in CD_3OD (500 MHz).

Proton	Compound				
	3	**4**	**5**	**6**	**7**
H-1	6.690[a] s	6.78 s	6.83 s	6.72 s	6.80 s
H-3	—	—	—	—	—
H-4	6.693[a] s	6.57 s	6.74 s	6.71 s	6.59 s
H-5	2.66 dt (15.5, 3.0)	2.60 dt (15.5, 3.0)	2.70 m	2.68 ddd (16.0, 4.5, 2.0)	2.62 ddd (16.0, 4.5, 2.0)
H-5	2.76 ddd (15.5, 11.5, 4.0)	2.71 ddd (15.5, 12.5, 4.5)	2.99 ddd (15.5, 11.5, 5.5)	2.96 ddd (16.0, 11.0, 6.0)	2.92 ddd (16.0, 12.0, 6.0)
H-6	2.88 td (11.5, 3.0)	2.84 td (12.5, 3.0)	3.05 m	3.06 ddd (12.5, 11.0, 4.5)	3.04 td (12.0, 4.5)
H-6	4.71 ddd (11.5, 4.0, 3.0)	4.73 ddd (12.5, 4.5, 3.0)	4.68 ddd (12.0, 5.5, 2.0)	4.64 ddd (12.5, 6.0, 2.0)	4.65 ddd (12.0, 6.0, 2.0)
H-9	7.41 d (2.5)	7.41 d (2.5)	7.33 d (2.5)	7.32 d (2.5)	7.33 d (2.5)
H-11 ...	5.49 d (1.5)	5.49 d (1.5)	5.42 d (1.5)	5.41 d (1.5)	5.42 d (1.5)
H-12 ...	2.70 ddd (10.0, 5.5, 1.5)	2.71 ddd (10.0, 5.5, 1.5)	2.70 m	2.67 ddd (10.5, 5.5, 1.5)	2.70 ddd (10.0, 5.5, 1.5)
H-12a ..	3.19 dddd (13.0, 5.5, 3.5, 2.5)	3.21 dddd (13.0, 5.5, 3.5, 2.5)	2.85 dddd (12.5, 5.5, 4.5, 2.5)	2.87 dddd (13.0, 5.5, 4.5, 2.5)	2.87 dddd (12.5, 5.5, 4.5, 2.5)
H-13 ...	1.35 td (13.0, 11.0)	1.36 td (13.0, 11.5)	2.00 ddd (14.0, 12.5, 5.5)	1.96 ddd (14.0, 13.0, 5.5)	1.99 ddd (14.0, 12.5, 5.0)
H-13 ...	2.30 dt (13.0, 3.5)	2.37 dt (13.0, 3.5)	2.46 ddd (14.0, 4.5, 3.0)	2.35 ddd (14.0, 4.5, 3.0)	2.45 ddd (14.0, 4.5, 3.0)
H-13a ..	4.72 dd (11.0, 3.5)	4.76 dd (11.5, 3.5)	4.78 br t (4.5)	4.72 br t (4.5)	4.76 br t (4.0)
H-14 ...	5.52 dt (17.0, 10.0)	5.53 dt (17.0, 10.0)	5.67 dt (17.0, 10.0)	5.66 dt (17.0, 10.5)	5.67 dt (17.0, 10.0)
H-15 ...	5.19 dd (10.0, 2.0)	5.19 dd (10.0, 2.0)	5.32 dd (10.0, 2.0)	5.31 dd (10.5, 2.0)	5.32 dd (10.0, 2.0)
H-15 ...	5.28 dd (17.0, 2.0)	5.28 dd (17.0, 2.0)	5.39 dd (17.0, 2.0)	5.38 dd (17.0, 2.0)	5.39 dd (17.0, 2.0)
H-1′ ...	4.69 d (8.0)	4.69 d (8.0)	4.61 d (8.0)	4.61 d (8.0)	4.62 d (8.0)
H-2′ ...	3.20 dd (9.0, 8.0)	3.19 dd (9.0, 8.0)	3.06 dd (9.0, 8.0)	3.06 dd (9.0, 8.0)	3.06 dd (9.0, 8.0)
H-3′ ...	3.38 t (9.0)	3.38 t (9.0)	3.30 t (9.0)	3.30 t (9.0)	3.29 t (9.0)
H-4′ ...	3.29 dd (9.5, 9.0)	3.28 dd (9.5, 9.0)	3.23 t (9.0)	3.23 t (9.0)	3.23 dd (9.5, 9.0)
H-5′ ...	3.32 ddd (9.5, 5.5, 2.0)	3.33 ddd (9.5, 5.5, 2.0)	3.28 ddd (9.0, 6.0, 2.0)	3.28 ddd (9.0, 5.5, 2.0)	3.28 ddd (9.5, 5.5, 2.0)
H-6′ ...	3.68 dd (12.0, 5.5)	3.67 dd (12.0, 5.5)	3.64 dd (12.0, 6.0)	3.65 dd (12.0, 5.5)	3.65 dd (12.0, 5.5)
H-6′ ...	3.90 dd (12.0, 2.0)	3.89 dd (12.0, 2.0)	3.87 dd (12.0, 2.0)	3.87 dd (12.0, 2.0)	3.87 dd (12.0, 2.0)
OMe ...	3.83 s	3.82 s	3.80 s	3.82 s	3.85 s
OMe ...	—	—	3.83 s	—	—

TABLE 1. Continued.

Proton	Compound				
	8	9	11	12	15
H-1	—	—	6.65[b] s	6.82[c] s	6.68 s
H-3	6.65 d (8.0)	6.81 d (8.0)	—	—	—
H-4	6.48 d (8.0)	6.61 d (8.0)	6.55[b] s	6.73[c] s	6.55 s
H-5	2.58–2.71 m	2.61–2.73 m	2.58 dt (15.5, 3.0)	2.68 dt (15.0, 2.5)	2.61 ddd (16.0, 5.0, 2.5)
H-5	2.58–2.71 m	2.61–2.73 m	2.70 m	2.77 ddd (15.0, 11.5, 3.5)	2.86–2.94 m
H-6	2.58–2.71 m	2.61–2.73 m	2.89 td (12.5, 3.0)	2.84 td (11.5, 2.5)	3.05 ddd (13.0, 11.5, 5.0)
H-6	n.d.[d]	n.d.[d]	4.64 dt (12.5, 3.5)	n.d.[d]	4.61 ddd (13.0, 6.5, 2.5)
H-9	7.45 d (2.5)	7.45 d (2.5)	7.41 d (2.5)	7.42 d (2.5)	7.32 d (2.5)
H-11 ...	5.50 d (1.5)	5.50 d (2.0)	5.49 d (1.5)	5.50 d (2.0)	5.41 d (1.5)
H-12 ...	2.58–2.71 m	2.61–2.73 m	2.70 ddd (10.0, 5.5, 1.5)	2.72 ddd (10.0, 5.5, 2.0)	2.66 ddd (10.0, 5.5, 1.5)
H-12a ..	3.24 *m*	3.24 *m*	3.19 *m*	3.22 dddd (13.0, 5.5, 3.5, 2.5)	2.86–2.94 m
H-13 ...	1.14 td (13.0, 11.0)	1.14 td (13.0, 11.0)	1.36 td (13.0, 11.5)	1.36 td (13.0, 11.5)	1.95 ddd (14.0, 12.5, 5.5)
H-13 ...	2.77 ddd (13.0, 3.5, 2.0)	2.76 ddd (13.0, 4.0, 2.5)	2.29 dt (13.0, 3.5)	2.39 dt (13.0, 3.5)	2.34 ddd (14.0, 4.5, 3.0)
H-13a ..	4.98 dd (11.0, 2.0)	4.99 dd (11.0, 2.5)	4.70 dd (11.5, 3.5)	n.d.[d]	4.70 br t (4.5)
H-14 ...	5.50 dt (17.0, 10.5)	5.50 dt (17.0, 10.0)	5.52 dt (17.0, 10.0)	5.53 dt (18.0, 10.0)	5.66 dt (17.0, 10.0)
H-15 ...	5.15 dd (10.5, 1.5)	5.15 dd (10.0, 2.0)	5.19 dd (10.0, 2.0)	5.19 dd (10.0, 2.0)	5.31 dd (10.0, 2.0)
H-15 ...	5.22 dd (17.0, 1.5)	5.22 dd (17.0, 2.0)	5.28 dd (17.0, 2.0)	5.29 dd (18.0, 2.0)	5.37 dd (17.0, 2.0)
H-1′ ...	4.71 d (7.5)	4.70 d (8.0)	4.69 d (8.0)	4.70 d (8.0)	4.61 d (8.0)
H-2′ ...	3.23 dd (9.0, 7.5)	3.22 dd (9.0, 8.0)	3.20 dd (9.0, 8.0)	3.20 dd (9.0, 8.0)	3.06 dd (9.0, 8.0)
H-3′ ...	3.39 t (9.0)	3.38 t (9.0)	3.39 t (9.0)	3.38 t (9.0)	n.d.
H-4′ ...	n.d.[d]	n.d.[d]	n.d.[d]	3.29 dd (9.5, 9.0)	n.d.[d]
H-5′ ...	n.d.[d]	n.d.[d]	n.d.[d]	3.33 ddd (9.5, 5.5, 2.0)	n.d.[d]
H-6′ ...	3.69 dd (12.0, 5.5)	3.68 dd (12.0, 5.5)	3.68 dd (12.0, 5.5)	3.68 dd (12.0, 5.5)	3.65 dd (12.0, 5.5)
H-6′ ...	3.90 dd (12.0, 1.5)	3.90 dd (12.0, 2.0)	3.90 dd (12.0, 2.0)	3.90 dd (12.0, 2.0)	3.87 dd (12.0, 2.0)
OMe ...	—	3.84 s	—	3.81 s	—
OMe ...	—	—	—	3.81 s	—

[b,c]Values with the same superscript are interchangeable.
[d]Not determined.

$J_{13\beta,13a}$=3.0 Hz; **12**:$J_{13\alpha,13a}$=11.5 Hz,$J_{13\beta,13a}$=3.5 Hz), whereas$J_{11,12}$ (**5**: 1.5 Hz; **12**: 2.0 Hz) and$J_{12,12a}$ (5.5 Hz) were nearly identical in both cases. Careful inspection of the coupling constants of all protons suggested that compound **5** is methylisoalangiside, with an *S*- configuration at C-13a, which has previously been prepared from secologanin [**13**] and 3-hydroxy-4-methoxyphenethylamine (3). The α- orientation of H-13a in **5** was also supported by NOESY experiments with **5** and its acetate **14**, where nOe interactions were observed between H-1 and H-13β and between H-1 and H-12a, but not between H-12a and H-13a in contrast to alangiside [**3**] which has an *R*- configuration at C-13a. Further evidence for the stereochemistry was provided by an alcoholic acetyl signal resonating at an anomalously high field (δ 1.57) in the ^{1}H-nmr spectrum of **14**. This could be explained by the ability of the acetates with an α-H at C-13a, such as methylisoalangiside tetraacetate, to adopt the conformation where the acetyl group lies over the plane of the aromatic system (8), and this suggestion was consistent with the observation that there were significant differences between **5** and **12** in the chemical shifts of C-6, C-12a, and C-13 in the ^{13}C-nmr spectra (Table 2). For final structural confirmation, methylisoalangiside and methylisoalangiside tetraacetate were prepared as follows. Secologanin [**13**] and dopamine were condensed in a buffer and subsequently lactamized under basic conditions to yield demethylalangiside [**11**] and demethylisoalangiside [**15**]. The latter, which was characterized as its acetate [**16**], was subjected to methylation with CH_2N_2/Et_2O followed by acetylation. The synthetic compounds, methylisoalangiside and methylisoalangiside tetraacetate, were thus com-

TABLE 2. ^{13}C-Nmr Spectral Data of Compounds **3–9**, **11**, **12**, and **15** in CD_3OD.

Carbon	Compound									
	3[a]	**4**[a]	**5**[a]	**6**[a]	**7**[a]	**8**[a]	**9**[a]	**11**[a]	**12**[a]	**15**[b]
C-1	113.3[c]	110.3	109.3	111.7	108.9	143.6	144.5	113.4	110.8	111.7
C-2	146.4	148.2	149.2[f]	146.2	147.9	144.4	147.4	145.3	149.4[j]	144.9[m]
C-3	148.0	146.5	149.9[f]	148.3	147.0	114.6	111.1	145.3	149.5[j]	145.6[m]
C-4	112.6[c]	116.1	114.1	113.6	117.1	120.3	120.2	116.0	113.2	117.0
C-4a	127.3[d]	128.9[e]	129.6[g]	127.9	129.6	128.5	129.9	127.4	128.7[k]	127.9[n]
C-5	29.5	29.4	29.3	29.2	29.1	30.3	30.4	29.3	29.6	28.9
C-6	41.0	40.8	43.8	43.9	43.8	40.5	40.5	41.1	40.7	43.9
C-8	166.0	166.0	166.7	166.6	166.6	166.1	166.2	166.0	166.0	166.6
C-8a	109.3	109.3	109.4	109.4	109.4	109.5	109.5	109.3	109.2	109.4
C-9	148.8	148.8	148.8	148.8	148.8	148.9	149.0	148.7	148.9	148.7
C-11	97.5	97.6	98.2	98.2	98.2	97.5	97.6	97.5	97.6	98.1
C-12	44.5	44.5	44.8	44.9	44.8	44.5	44.6	44.5	44.5	44.9
C-12a	27.8	27.9	24.4	24.4	24.4	28.5	28.6	27.7	27.9	24.3
C-13	35.1	35.3	28.4	28.3	28.4	32.8	32.8	35.0	35.2	28.2
C-13a	57.0	57.3	56.7	56.4	56.7	55.5	55.5	57.0	57.3	56.4
C-13b	130.3[d]	128.8[e]	130.3[g]	130.4	129.0	124.4	124.2	129.1	130.1[k]	129.1[n]
C-14	134.0	134.0	134.4	134.4	134.5	133.9	134.0	134.0	134.0	134.4
C-15	120.4	120.4	120.5	120.5	120.5	120.1	120.2	120.3	120.4	120.5
C-1′	99.7	99.7	100.6	100.6	100.6	99.6	99.7	99.7	99.7	100.6
C-2′	74.9	74.9	74.5	74.5	74.5	74.8	74.9	74.8	74.9	74.5
C-3′	78.0	78.1	78.1[h]	78.1[i]	78.1	78.0	78.0	78.0	78.1[l]	78.0[o]
C-4′	71.6	71.6	71.5	71.5	71.5	71.6	71.6	71.6	71.6	71.4
C-5′	78.4	78.4	78.3[h]	78.3[i]	78.3	78.3	78.4	78.3	78.4[l]	78.3[o]
C-6′	62.7	62.7	62.7	62.7	62.7	62.7	62.7	62.7	62.7	62.7
OMe	56.4	56.7	56.5	56.5	56.9	—	56.8	—	56.5	—
OMe	—	—	57.0	—	—	—	—	—	56.8	—

[a]Measured at 125 MHz.
[b]Measured at 75 MHz.
[c–o]Values with the same superscript are interchangeable.

pared with isolate **5** and its acetate **14**, respectively. Accordingly, compound **5** was established as methylisoalangiside.

Glucosides **6** and **7** were also obtained as amorphous powders. The hrsims measurements of **6** and **7** revealed the same molecular formula [$C_{25}H_{31}NO_{10}$] isomeric with alangiside [**3**] and 3-*O*-demethyl-2-*O*-methylalangiside [**4**]. The ^{1}H- and ^{13}C-nmr spectral features of **6** and **7** (Tables 1 and 2) were closely similar to those of methylisoalangiside [**5**], except for the absence of one aromatic methoxyl signal and the chemical shifts of the signals arising from the aromatic ring. The coupling constants between H_2-13 and H-13a, and the chemical shifts of C-6, C-12a, and C-13 implied that both compounds should possess the same configuration at C-13a as **5**. These results suggested **6** and **7** were two possible demethylates of methylisoalangiside [**5**], i.e., C-13a epimers of **3** and **4**. Further evidence of the α- disposition of H-13a in **6** and **7** was provided by the ^{1}H-nmr spectra of their acetates **17** and **18**, which exhibited characteristic acetyl signals at unusually high field (**17**: δ 1.64; **18**: δ 1.52), and by the resemblance of the cd curves of **6** and **7** to those of methylisoalangiside [**5**]. The placement of the methoxy group at C-3 in **6** and at C-2 in **7** was deduced from the fact that the chemical shifts of ^{1}H- and ^{13}C-nmr signals due to the aromatic moiety of **6** and **7** were in good accord with those of **3** and **4**, respectively (Tables 1 and 2). This was further corroborated by NOESY experiments with **6** and **7**. The nOe interactions between H-13 and H-1 and between H-5 and H-4 allowed us to assign two aromatic proton signals to H-1 and H-4, respectively, in each glucoside. The methoxy signal showed a strong interaction with H-4 in **6** and with H-1 in **7**, establishing the site of

the methoxyl group. Thus, structures **6** and **7** could unequivocally be assigned to isoalangiside and 3-*O*-demethyl-2-*O*-methylisoalangiside, respectively.

Compound **8** was recognized as an isomer of demethylalangiside [**11**], $C_{24}H_{29}NO_{10}$, from its mass spectrum. Its ^{1}H-nmr spectral features [H-9 at δ 7.45, a terminal vinyl at δ 5.15, 5.22, and 5.50] indicated its structural analogy to **11**, although there were remarkable differences in the spectra, with the aromatic protons of **8** appearing as a pair of ortho-coupled doublets (J=8.0 Hz) at δ 6.48 and 6.65 instead of two singlets as in **11**. Acetylation of **8** afforded a hexaacetate **19**, whose ^{1}H-nmr spectrum showed two phenolic acetyl signals but not the anomalous acetyl signal typical of the acetates with 13a*R* configuration. These results, along with biogenetic considerations, suggested a structure for **8** with two phenolic hydroxyl groups at C-1 and C-2 in the same manner as for neoipecoside [**20**], which we have isolated previously from *Cephaelis ipecacuanha* (4). This substitution pattern was confirmed by HMBC experiments with **8**, which revealed a ^3J interaction between the signal at δ 6.48 and C-5 (δ 30.3), allowing us to assign the aromatic proton signal to H-4, and thereby its coupled signal at δ 6.65 to H-3. Final absolute structural confirmation was obtained from the fact that **19** was identical with neoipecoside lactam hexaacetate derived from neoipecoside (4).

The ^{1}H- and ^{13}C-nmr data (Tables 1 and 2) indicated that **9** has a structure similar to **8** but with an additional aromatic methoxyl group. Furthermore, its sims showed a quasi-molecular ion peak $[M+H]^+$ at *m/z* 506, indicating an increase of 14 mass units in comparison with that of **8**. These findings suggested that the new isolated compound should be a methylated derivative of **8**. The substitution of the hydroxyl at C-1 and methoxyl at C-2 was ascertained by a correlation between H-4 (δ 6.61) and C-5 (δ 30.4) in its HMBC spectrum and a cross-peak between H-3 (δ 6.81) and OMe (δ 3.84) in the NOESY spectrum. The absolute configuration of C-13a in **9** was determined to be the same as that of **8** i.e., *R*, based upon the following observations: (a) the coupling constants between H-13a and H_2-13 were nearly the same [**9**: 11.0 and 2.5 Hz; **8**: 11.0 and 2.0 Hz], (b) an nOe interaction was observed between H-13a and H-12a in each glucoside, (c) the cd spectra of **8** and **9** exhibited a negative Cotton effect around 245 nm. Accordingly, the structure of isolate **9** was established as the 2-*O*-methyl derivative of **8** and the glucosides **8** and **9** were designated as demethylneoalangiside and neoalangiside, respectively.

Compound **10** was obtained as an amorphous powder. Its hrsims indicated a molecular formula of $C_{26}H_{30}N_2O_9$ for **10**. It showed uv maxima at 231.5, 277 (sh), and 311 (sh) nm, and ir bands at 3394 (OH), 1653 (NCO) and 1577 (Ar) cm^{-1}. Its ^{1}H-nmr data suggested that the structure of **10** was analogous with demethylalangiside [**11**], but significant differences were noted for the aromatic proton signals, which appeared as an ABX system at δ 6.64 (dd,J=8.5 and 2.5 Hz), 6.80 (d,J=2.5 Hz), and 7.12 (d,J=8.5 Hz). The ^{13}C-nmr spectrum showed eight aromatic carbon signals (δ 151.5 C, 135.4 C, 133.2 C, 128.7 C, 112.5 CH, 112.3 CH, 108.5 C, 103.4 CH). These features, together with its molecular formula and uv spectrum, indicated the presence of a hydroxy-indole ring in **10** instead of a dihydroxy-benzene ring as in **11**. This was also supported by analysis of the sims spectrum of **10**, which showed fragment peaks at *m/z* 353 and 187 (9,10). As a result of an HMBC experiment on **10**, where an interaction between H-9 (δ 6.80) and C-7 (δ 108.5) was seen, it was predicted that the hydroxyl group was located at C-10 on the indole ring. This argument received further support from the agreement of the aromatic carbon signals in the ^{13}C-nmr spectra of **10** with the corresponding signals of 10-hydroxystrictosidine lactam [**21**] (9). A remaining point of possible ambiguity was the absolute configuration at C-3. To establish the stereochemistry of this asymmetric center, the ^{13}C-nmr spectrum of **10** was compared with those of vincoside

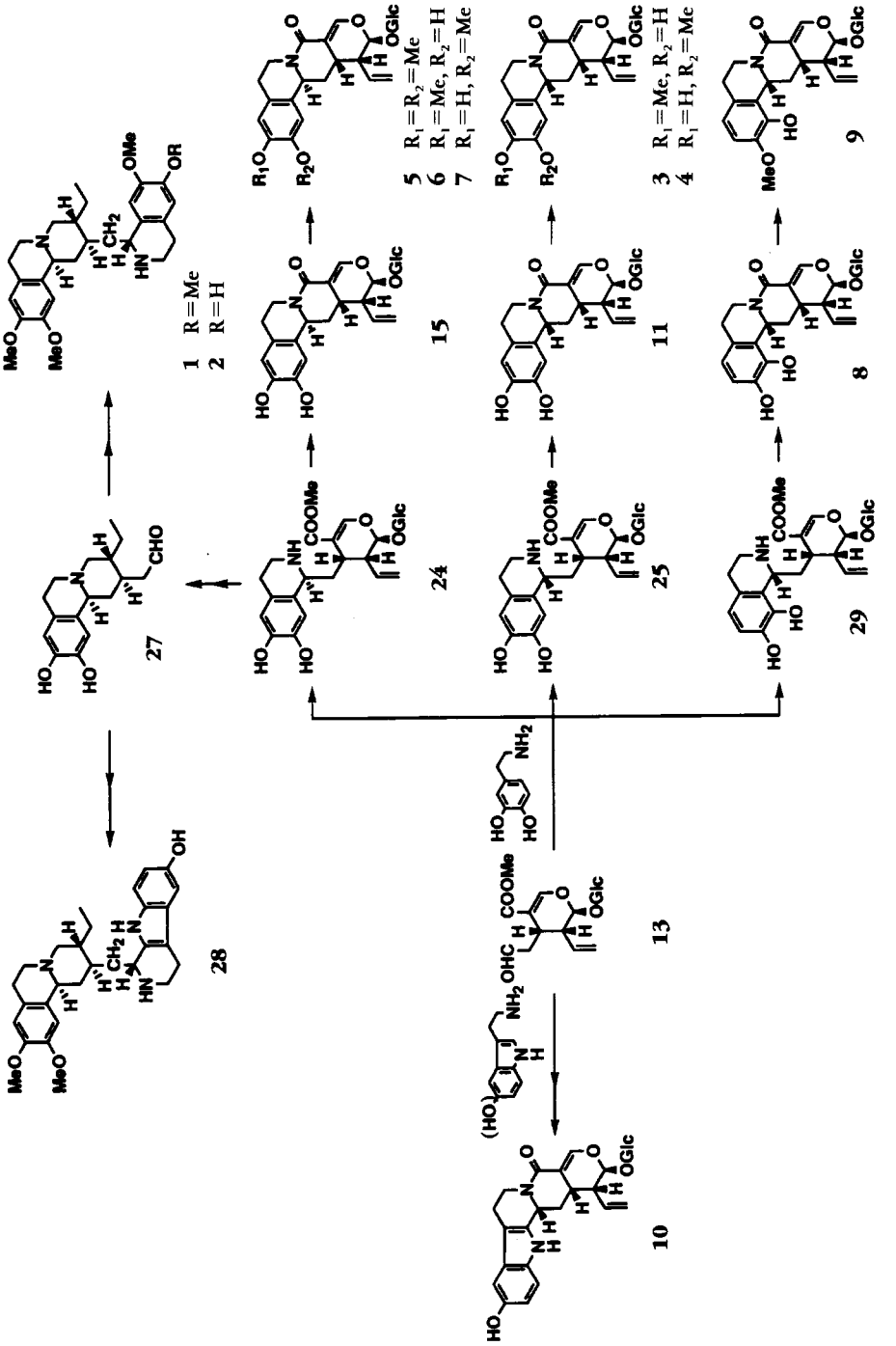
TABLE 3. ^{13}C-Nmr Spectral Data of Compounds **10** and **21–23** in CD_3OD.

Carbon	Compound			
	10[a]	**21**[b]	**22**[b]	**23**[b]
C-2	135.4	135.6	134.6	134.8
C-3	54.9	55.1	54.9	55.1
C-5	41.3	44.8	41.3	44.7
C-6	22.1	22.1	22.1	22.1
C-7	108.5	109.6[c]	109.3[e]	110.3
C-8	128.7	129.4	128.0	128.7
C-9	103.4	103.2	118.9	118.7
C-10	151.5	151.5	120.0	120.2
C-11	112.3	112.8[d]	122.6	122.5
C-12	112.5	112.3[d]	112.0	112.3
C-13	133.2	132.5	138.3	137.8
C-14	32.7	27.2	32.7	27.3
C-15	27.4	24.9	27.4	24.9
C-16	109.4	109.2[c]	109.1[e]	109.2
C-17	149.0	149.1	149.1	149.1
C-18	120.5	120.6	120.5	120.6
C-19	134.0	134.3	134.0	134.3
C-20	44.6	44.7	44.6	44.7
C-21	97.5	98.1	97.4	98.1
C-22	166.1	167.0	166.1	167.1
C-1′	99.7	100.5	99.6	100.5
C-2′	74.9	74.3	74.9	74.3
C-3′	78.0	78.2	78.4	78.2
C-4′	71.6	71.3	71.6	71.4
C-5′	78.4	77.9	78.0	78.0
C-6′	62.7	62.6	62.7	62.6

[a]Measured at 125 MHz.
[b]Data taken from Ref. (9). Measured at 75 MHz.
[c–e]Values with the same superscript are interchangeable.

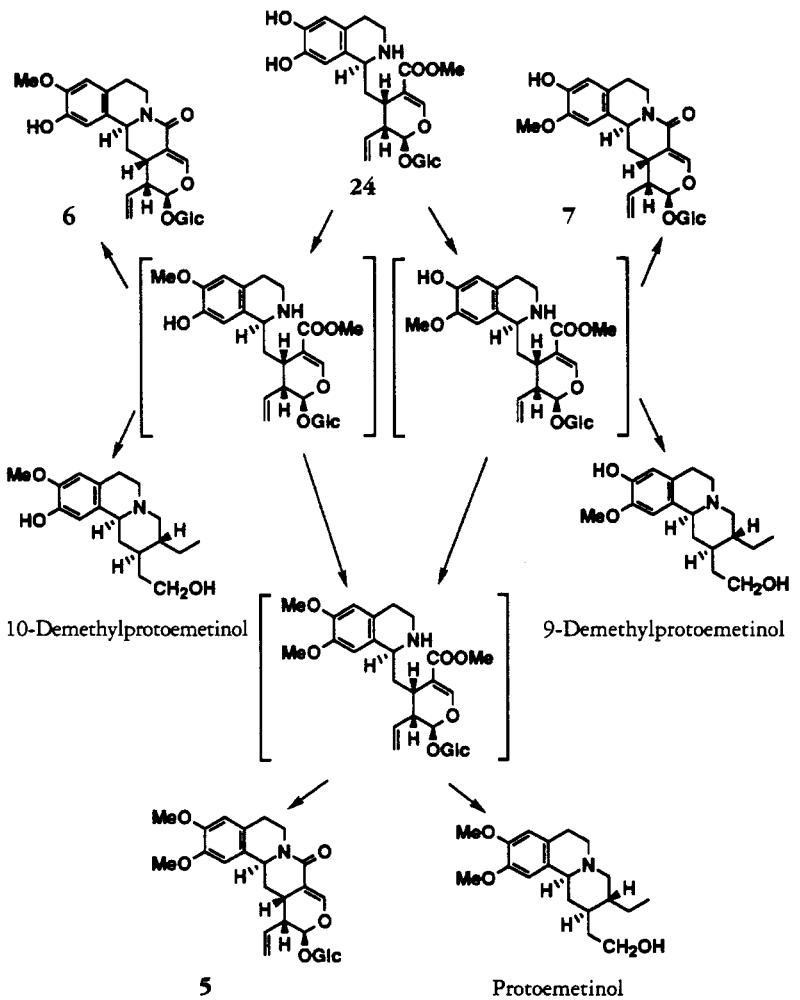
lactam [**22**] and strictosidine lactam [**23**] (9). There were significant differences between **10** and **23** in the chemical shifts of C-5, C-14, and C-15 in the ^{13}C-nmr spectra (Table 3), while these same signals of **10** and **22** resonated at nearly identical frequencies. The cd spectrum of **10** showed a negative Cotton effect at 271 nm, indicating the *R* configuration at C-3 (11). Thus, compound **10** was elucidated as 10-hydroxyvincoside lactam.

The occurrence of the glucosides **5–7** gives important information about the biosynthesis of ipecac alkaloids represented by emetine [**1**] and cephaeline [**2**]. Previous biosynthetic investigations (12) demonstrated that secologanin [**13**] is condensed with dopamine in a Pictet-Spengler manner to form two epimers, deacetylisoipecoside [**24**] and deacetylipecoside [**25**]. Deacetylisoipecoside [**24**] was exclusively transformed to the ipecac alkaloids without change of configuration. Deacetylipecoside [**25**] is not an intermediate for the alkaloids but is acetylated in *Cephaelis ipecacuanha* to give ipecoside [**26**], or is transformed in *A. lamarckii* to alangiside [**3**]. However, all of the tetrahydroisoquinoline-monoterpene glucosides isolated so far have had a β-H at the chiral center, but no glucoside with an α-H such as **5–7** has been isolated from natural sources. This is the first instance of the isolation of glucosides with the same stereochemistry as ipecac alkaloids, and it strongly supports the intermediacy of deacetylisoipecoside [**24**] in the biosynthetic pathway to ipecac alkaloids and their related compounds (Scheme 1). The intermediate **24** could be further transformed, most likely via **27**, to



SCHEME 1. Proposed biosynthetic sequence for the biosynthesis of the alkaloids and nitrogenous glucosides in *Alangium lamarckii*.

alkaloids such as **1**, **2**, and tubulosine [**28**] or cyclized to demethylisoalangiside [**15**]. The new glucosides with an unusually cyclized isoquinoline nucleus, demethylneoalangiside [**8**] and neoalangiside [**9**], are obviously biosynthesized via deacetylneoipecoside [**29**], which was previously postulated as a precursor for neoipecoside [**20**] (4). It could therefore be assumed that three different types of condensation of dopamine and secologanin [**13**] could take place in *Alangium* plants in the same way as in *C. ipecacuanha*. It is also noteworthy that all of the isolated compounds possess a lactam ring. No glucoside with an *N*-acyl group like ipecoside has been found in *Alangium*, although some glucosides with an *O*-acyl group in the glucose moiety were isolated (13). We suppose therefore that *N*-acylation is not involved in this group of plants. The glucosides **5**–**9** may be derived from deacetylisoipecoside or deacetylneoipecoside through lactamization and subsequent *O*-methylation as in the case of alangiside and 3-*O*-demethyl-2-*O*-methylalangiside. However, we could not rule out an alternative plausible pathway to **5**–**7**, where deacetylisoipecoside is methylated prior to lactamization (Scheme 2). If 2-*O*- and 3-*O*-methylated deacetylisoipecosides could be further deglucosylated, recyclized and reduced, we could reasonably account for the co-



SCHEME 2. An alternative biosynthetic sequence for the glucosides **5**–**7** and demethylprotoemetinols.

occurrence of demethylprotoemetinols in this plant (14). Therefore, the possibility should be taken into account that the methylation of a phenolic hydroxyl group takes place at the glucoside level in the biosynthetic sequence for ipecac alkaloids. It is also interesting that 10-hydroxyvincoside lactam was isolated. This constitutes the first isolation of a tetrahydro-β-carboline monoterpene glucoside from *A. lamarckii*, which could be biosynthesized through condensation of secologanin with tryptamine (or serotonin) instead of with dopamine.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Mps were recorded on a Büchi melting point apparatus and are reported uncorrected. Uv spectra were recorded on a Shimadzu UV-240 spectrophotometer and ir spectra on a Shimadzu Ftir-8200 or a Hitachi 270-30 infrared spectrophotometer. Optical rotations were measured on a Jasco DIP-370 digital polarimeter. Ms and hrms were obtained with a Hitachi M-4100 mass spectrometer. For sims, glycerol was used as the matrix. The nmr experiments were performed with Varian VXR-500, Varian Gemini-300, and Varian Gemini-200 spectrometers, with TMS as internal standard. Hplc was performed using a Waters system (600E multisolvent delivery system, 486 tunable absorbance detector). Cc was carried out with Si gel 60 (70–230 mesh, Nacalai Tesque). Tlc was performed on precoated Kieselgel 60F_{254} plates (Merck) and spots were visualized under uv light.

PLANT MATERIAL.—The dried fruits of *Alangium lamarckii*, collected in India, were purchased from Mikuni, Osaka, Japan. A voucher specimen (KPFY-921) is deposited in our laboratory.

EXTRACTION AND ISOLATION.—Dried fruits (4.5 kg) of *A. lamarckii* were crushed and extracted with hot MeOH. The MeOH extracts were concentrated *in vacuo* and the resulting residue (854.7 g) was suspended in H_2O and extracted successively with $CHCl_3$ and *n*-BuOH. A part (71.7 g) of the residue (159.2 g) from the *n*-BuOH layers was chromatographed on a Si gel column. Elution with $CHCl_3$/MeOH mixtures of the indicated MeOH content gave 11 fractions, 1 (7–10%, 2.27 g), 2 (10%, 17.47 g), 3 (10%, 14.00 g), 4 (10%, 1.89 g), 5 (12%, 2.04 g), 6 (12%, 2.67 g), 7 (12%, 1.98 g), 8 (15%, 4.85 g), 9 (15%, 4.08 g), 10 (15%, 3.45 g), 11 (20–30%, 2.92 g). Fraction 1 was submitted to reversed-phase mplc and elution with MeOH-H_2O (35:65–40:60) and MeOH-H_2O (40:60) gave fraction 1/a (66.9 mg) and fraction 1/b (162.9 mg), respectively. Fraction 1/a was purified by prep. hplc (μBondasphere 5 μm C_{18}–100 Å, MeOH-H_2O, 1:1), affording **A** (7.0 mg), **B** (5.6 mg), **5** (3.1 mg), and **C** (12.9 mg). Fraction 1/b was also purified by prep. hplc (MeOH-H_2O, 1:1) to yield **5** (8.7 mg), **C** (70.4 mg), and **D** (25.0 mg). Fraction 2 was rechromatographed on a Si gel column and an eluate from $CHCl_3$-MeOH (93:7) was further purified by prep. tlc ($CHCl_3$-MeOH, 3:1, and EtOAc-C_6H_6-EtOH, 4:1:1.2) and by prep. hplc (μBondasphere 5 μm C_{18}-100 Å, MeOH-H_2O, 1:1) to afford **9** (5.3 mg). In the same way, the following fractions were purified by a combination of Si gel cc with $CHCl_3$-MeOH (92:8–85:15), prep. tlc with $CHCl_3$-MeOH (4:1 or 3:1) or EtOAc-C_6H_6-EtOH (4:1:1), reversed-phase mplc with MeOH-H_2O (25:75–40:60) and prep. hplc with MeOH-H_2O (40:60–55:45). Fraction 3 yielded sweroside (78.5 mg), **E** (173.1 mg), **F** (31.1 mg), **G** (19.7 mg), **4** (1.02 g), **3** (6.80 g), **H** (97.9 mg), **I** (24.3 mg), **6** (28.1 mg), **7** (11.1 mg); fraction 4: **4** (50.2 mg), **3** (268.4 mg), **I** (3.0 mg), **6** (5.1 mg); fraction 5: **11** (96.2 mg), **8** (68.4 mg), **E** (1.3 mg), **4** (25.8 mg), **3** (202.3 mg), **I** (1.9 mg); fraction 6: phenethyl alcohol xylopyranosyl (1→6) glucopyranoside (32.0 mg), **11** (427.4 mg), **10** (2.3 mg), **8** (51.2 mg), **4** (14.6 mg), **3** (121.1 mg); fraction 7: **11** (288.1 mg), **10** (13.5 mg), **3** (105.9 mg). Compounds **A**–**I** were unidentified glucosides, which will be subjected to further investigation.

Methylisoalangiside [**5**].—Colorless amorphous powder, $[\alpha]^{25}D$ −141° (*c*=0.28, MeOH); uv (MeOH) λ max (log ε) 235 (4.31), 282 (3.65), 292 (sh, 3.52) nm; ir (KBr) ν max 3406, 1657, 1589, 1516, 899 cm^{-1}; ^{1}H-nmr data, see Table 1; ^{13}C-nmr data, see Table 2; sims *m/z* $[M+Na]^+$ 542, $[M+H]^+$ 520, 358, 192; hrsims *m/z* $[M+H]^+$ 520.2179 (calcd for $C_{26}H_{34}NO_{10}$, 520.2184); cd (MeOH) Δε −8.65 (224), +1.46 (242), −0.18 (255), +0.12 (274) nm.

Isoalangiside [**6**].—Colorless amorphous powder, $[\alpha]^{25}D$ −118° (*c*=0.86, MeOH); uv (MeOH) λ max (log ε) 233 (4.26), 284.5 (3.64) nm; ir (KBr) ν max 3400, 1660, 1592, 1516, 900 cm^{-1}; ^{1}H-nmr data, see Table 1; ^{13}C-nmr data, see Table 2; sims *m/z* $[M+Na]^+$ 528, $[M+H]^+$ 506, 344, 178; hrsims *m/z* $[M+H]^+$ 506.2023 (calcd for $C_{25}H_{32}NO_{10}$, 506.2027); cd (MeOH) Δε −5.62 (224), +1.33 (240), −0.68 (254), +0.49 (280) nm.

3-O-Demethyl-2-O-methylisoalangiside [**7**].—Colorless amorphous powder, $[\alpha]^{28}D$ −169° (*c*=0.45, MeOH); uv (MeOH) λ max (log ε) 234 (4.25), 284 (3.61) nm; ir (KBr) ν max 3400, 1653, 1578, 1516, 901 cm^{-1}; ^{1}H-nmr data, see Table 1; ^{13}C-nmr data, see Table 2; hrsims *m/z* $[M+H]^+$ 506.2024 (calcd for $C_{25}H_{32}NO_{10}$, 506.2027); cd (MeOH) Δε −9.93 (225), +0.30 (243), −1.00 (254), −0.65 (283) nm.

Demethylneoalangiside [**8**].—Colorless crystals (MeOH/H_2O): mp 193–195°; $[\alpha]^{28}D$ −9.8° (*c*=1.0, MeOH); uv (MeOH) λ max (log ε) 231 (sh, 4.24), 238.5 (4.25), 287 (sh, 3.37) nm; ir (KBr) ν max 3416, 1654, 1570, 1506, 882 cm^{-1}; ^1H-nmr data, see Table 1; ^{13}C-nmr data, see Table 2; sims *m/z* $[M+Na]^+$ 514, $[M+H]^+$ 492, 330; hrsims *m/z* $[M+Na]^+$ 514.1697 (calcd for $C_{24}H_{29}NO_{10}Na$, 514.1690); $[M+H]^+$ 492.1882 (calcd for $C_{24}H_{30}NO_{10}$, 492.1871); cd (MeOH) Δε −11.65 (243), +2.96 (283) nm.

Neoalangiside [**9**].—Colorless amorphous powder, $[\alpha]^{23}D$ +7.7° (*c*=0.25, MeOH); uv (MeOH) λ max (log ε) 230 (sh, 4.27), 234 (4.27), 286 (sh, 3.38) nm; ir (KBr) ν max 3405, 1653, 1558, 1508, 881 cm^{-1}; ^1H-nmr data, see Table 1; ^{13}C-nmr data, see Table 2; sims *m/z* $[M+Na]^+$ 528, $[M+H]^+$ 506, 344, 178; hrsims *m/z* $[M+H]^+$ 506.2021 (calcd for $C_{25}H_{32}NO_{10}$, 506.2027); cd (MeOH) Δε −11.23 (245), +3.13 (282) nm.

10-Hydroxyvincoside lactam [**10**].—Colorless amorphous powder, $[\alpha]^{24}D$ −120° (*c*=0.79, MeOH); uv (MeOH) λ max (log ε) 231.5 (4.43), 277 (sh, 3.98), 311 (sh, 3.43) nm; ir (KBr) ν max 3394, 1653, 1577, 1456, 905 cm^{-1}; ^1H nmr (CD_3OD) δ 1.44 (1H, td, *J*=13.0 and 11.5 Hz, H-14), 2.43 (1H, dt, *J*=13.0 and 3.5 Hz, H-14), 2.67–2.73 (3H, m, H_2-6, H-20), 2.92 (1H, ddd, *J*=12.5, 9.0, and 6.5 Hz, H-5), 3.20 (1H, dd, *J*=9.0 and 8.0 Hz, H-2′), 3.68 (1H, dd, *J*=12.0 and 5.5 Hz, H-6′), 3.90 (1H, dd, *J*=12.0 and 2.0 Hz, H-6′), 4.70 (1H, d, *J*=8.0 Hz, H-1′), 5.04 (1H, dt, *J*=12.5 and 3.0 Hz, H-5), 5.19 (1H, dd, *J*=10.5 and 2.0 Hz, H-18), 5.29 (1H, dd, *J*=17.0 and 2.0 Hz, H-18), 5.50 (1H, d, *J*=1.5 Hz, H-21), 5.54 (1H, dt, *J*=17.0 and 10.5 Hz, H-19), 6.64 (1H, dd, *J*=8.5 and 2.5 Hz, H-11), 6.80 (1H, d, *J*=2.5 Hz, H-9), 7.12 (1H, d, *J*=8.5 Hz, H-12), 7.44 (1H, d, *J*=2.5 Hz, H-17); ^{13}C-nmr data, see Table 3; sims *m/z* $[M+H]^+$ 515, 353, 187; hrsims *m/z* $[M+H]^+$ 515.2027 (calcd for $C_{26}H_{31}N_2O_9$, 515.2031); cd (MeOH) Δε −14.58 (237.5), −8.23 (271), +0.99 (310) nm.

ACETYLATION OF **5**.—Conventional acetylation of methylisoalangiside [**5**] (2.8 mg) and subsequent purification by prep. tlc ($CHCl_3$-MeOH, 98:2) afforded methylisoalangiside tetraacetate [**14**] (1.9 mg) as a colorless amorphous powder: ^1H nmr ($CDCl_3$) δ 1.57, 1.96, 2.01, 2.09 (12H, each s, 4×Ac), 1.99 (1H, ddd, *J*=14.0, 11.0, and 5.0 Hz, H-13), 2.22 (1H, ddd, *J*=14.0, 5.5, and 4.0 Hz, H-13), 2.62 (1H, ddd, *J*=10.0, 5.5, and 1.5 Hz, H-12), 2.64 (1H, ddd, *J*=15.0, 10.5, and 2.0 Hz, H-5), 2.75 (1H, quint. of d, *J*=5.5 and 2.5 Hz, H-12a), 2.94–3.04 (2H, m, H-5, H-6), 3.71 (1H, ddd, *J*=9.5, 4.5, and 2.5 Hz, H-5′), 3.85, 3.90 (6H, each s, 2×OMe), 4.12 (1H, dd, *J*=12.5 and 2.5 Hz, H-6′), 4.28 (1H, dd, *J*=12.5 and 4.5 Hz, H-6′), 4.64 (1H, br t, *J*=4.5 Hz, H-13a), 4.75 (1H, m, H-6), 4.84 (1H, d, *J*=8.0 Hz, H-1′), 4.90 (1H, dd, *J*=9.5 and 8.0 Hz, H-2′), 5.05 (1H, t, *J*=9.5 Hz, H-4′), 5.18 (1H, t, *J*=9.5 Hz, H-3′), 5.27 (1H, d, *J*=1.5 Hz, H-11), 5.32 (1H, dd, *J*=10.0 and 1.5 Hz, H-15), 5.36 (1H, dd, *J*=17.0 and 1.5 Hz, H-15), 5.64 (1H, dt, *J*=17.0 and 10.0 Hz, H-14), 6.62 (1H, s, H-4), 6.63 (1H, s, H-1), 7.33 (1H, d, *J*=2.5 Hz, H-9); eims *m/z* $[M]^+$ 687 (15), 356 (7), 340 (12), 331 (23), 286 (20), 192 (12), 169 (100), 109 (53).

PREPARATION OF **11** AND **15** FROM **13** AND DOPAMINE.—A solution of secologanin [**13**] (1 g) and dopamine.HCl (0.5 g) in citrate-phosphate buffer (15 ml, pH 5.0) was incubated for 3.5 days at room temperature. The reaction mixture was rinsed with EtOAc (×3), and the aqueous layer was made basic with 10% aqueous Na_2CO_3 solution (2.0 ml) and stirred for 3 h at room temperature. The reaction mixture was extracted successively with EtOAc and *n*-BuOH. The combined *n*-BuOH layers were evaporated *in vacuo* and the resulting residue was then redissolved in MeOH. After removal of the precipitate by filtration, the filtrate was evaporated *in vacuo* and purified with prep. tlc ($CHCl_3$-MeOH, 7:3) and prep. hplc (μBondasphere $5C_{18}$-100Å, MeOH-H_2O, 45:55) to yield demethylalangiside [**11**] (224.9 mg) and demethylisolangiside [**15**] (33.5 mg).

Demethylalangiside [**11**].—Colorless needles (H_2O): mp 182–184°; $[\alpha]^{21}D$ −78° (*c*=1.0, MeOH); ^1H-nmr data, see Table 1; ^{13}C-nmr data, see Table 2; cd (MeOH) Δε −12.80 (242) nm.

Demethylisoalangiside [**15**].—Colorless needles (H_2O): mp 177–179°; $[\alpha]^{24}D$ −166° (*c*=0.71, MeOH); uv (MeOH) λ max (log ε) 233.5 (4.29), 287.5 (3.70) nm; ir (KBr) ν max 3387, 1649, 1583, 901 cm^{-1}; ^1H-nmr data, see Table 1; ^{13}C-nmr data, see Table 2; sims *m/z* $[M+H]^+$ 492, 330, 164; hrsims *m/z* $[M+H]^+$ 492.1866 (calcd for $C_{24}H_{30}NO_{10}$, 492.1871); cd (MeOH) Δε −7.60 (226), −0.39 (250), −0.16 (292) nm.

ACETYLATION OF **15**.—Demethylisoalangiside [**15**] (9.0 mg) was acetylated and purified by prep. tlc ($CHCl_3$-MeOH, 98:2) to afford demethylisoalangiside hexaacetate [**16**] (10.5 mg) as a colorless amorphous powder: $[\alpha]^{24}D$ −159° (*c*=1.05, $CHCl_3$); ^1H nmr ($CDCl_3$) δ 1.61, 1.96, 2.01, 2.09, 2.27, 2.31 (18H, each s, 6×Ac), 2.00 (1H, ddd, *J*=14.0, 11.5, and 5.0 Hz, H-13), 2.22 (1H, dt, *J*=14.0 and 4.5 Hz, H-13), 2.62 (1H, ddd, *J*=10.0, 5.5, and 1.5 Hz, H-12), 2.70–2.77 (2H, m, H-5, H-12a), 3.01 (2H, m, H-5, H-6), 3.71 (1H, ddd, *J*=10.0, 4.5, and 2.0 Hz, H-5′), 4.12 (1H, dd, *J*=12.5 and 2.0 Hz, H-6′), 4.26 (1H, dd, *J*=12.5 and 4.5 Hz, H-6′), 4.67 (1H, br t, *J*=4.5 Hz, H-13a), 4.75 (1H, m, H-6), 4.83 (1H, d, *J*=8.0 Hz, H-1′), 4.90 (1H, dd, *J*=9.5 and 8.0 Hz, H-2′), 5.03 (1H, br t, *J*=9.5 Hz, H-4′), 5.18 (1H, t, *J*=9.5 Hz, H-3′), 5.26 (1H, d, *J*=1.5 Hz, H-11), 5.32 (1H, dd, *J*=10.0 and 1.5 Hz, H-15), 5.35 (1H, dd, *J*=17.0 and 1.5

Hz, H-15), 5.60 (1H, dt, J=17.0 and 10.0 Hz, H-14), 7.00, 7.01 (2H, each s, H-1, H-4), 7.34 (1H, d, J=2.5 Hz, H-9).

METHYLATION OF **11** AND **15**.—A solution of **11** (20 mg) in MeOH (3 ml) was treated with CH_2N_2/Et_2O and kept for 5 h. The reaction mixture was concentrated *in vacuo*, and the resulting residue was subjected to prep. tlc ($CHCl_3$-MeOH, 8:2), giving rise to **12** (20 mg) as colorless needles (MeOH/Et_2O), mp 167–169°. The product was identified as methylalangiside prepared from natural alangiside [**3**] [uv, ir, ^{1}H nmr, sims, $[\alpha]^{25}D$ −67° (c=0.8, MeOH), cd (MeOH) $\Delta\epsilon$ −15.10 (238) nm]. In a similar manner, demethylisoalangiside [**15**] (10 mg) was methylated and purified by prep. hplc (μBondasphere $5C_{18}$-100Å, MeOH-H_2O, 1:1) to afford methylisoalangiside (7.6 mg), which was identical to the isolated compound [**5**] [uv, ir, ^{1}H nmr, sims, $[\alpha]^{24}D$ −158° (c=0.5, MeOH), cd (MeOH) $\Delta\epsilon$ −9.72 (224), +2.47 (242), −0.77 (255), +0.07 (274) nm]. Methylisoalangiside (5.2 mg) was acetylated to afford methylisoalangside tetraacetate (6.9 mg), which was identical with **14** prepared from the isolate **5** [^{1}H nmr].

ACETYLATION OF **6**.—Isoalangiside [**6**] (4.5 mg) was acetylated in the usual way and the crude acetate (3.6 mg) was purified with prep. tlc (EtOAc-C_6H_6, 2:1) to give isoalangiside pentaacetate [**17**] (3.1 mg) as a colorless amorphous powder: $[\alpha]^{26}D$ −126° (c=0.5, $CHCl_3$); uv (MeOH) λ max (log ε) 230 (4.25), 275 (sh, 3.57), 286 (sh, 3.39) nm; ir ($CHCl_3$) ν max 1757, 1661, 1603, 1512 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ 1.64, 1.96, 2.01, 2.09, 2.33 (15H, each s, 5×Ac), 1.96 (1H, m, H-13), 2.18 (1H, dt, J=14.0 and 4.5 Hz, H-13), 2.61 (1H, ddd, J=10.0, 5.5, and 2.0 Hz, H-12), 2.71 (2H, m, H-5, H-12a), 2.97 (1H, td, J=12.0 and 3.5 Hz, H-6), 3.04 (1H, ddd, J=15.5, 12.0, and 5.5 Hz, H-5), 3.71 (1H, ddd, J=9.5, 4.5, and 2.0 Hz, H-5′), 3.80 (3H, s, OMe), 4.12 (1H, dd, J=12.5 and 2.0 Hz, H-6′), 4.26 (1H, dd, J=12.5 and 4.5 Hz, H-6′), 4.64 (1H, br t, J=4.5 Hz, H-13a), 4.76 (1H, ddd, J=12.0, 5.5, and 2.0 Hz, H-6), 4.84 (1H, d, J=8.0 Hz, H-1′), 4.89 (1H, dd, J=9.5 and 8.0 Hz, H-2′), 5.04 (1H, t, J=9.5 Hz, H-4′), 5.18 (1H, t, J=9.5 Hz, H-3′), 5.24 (1H, d, J=2.0 Hz, H-11), 5.31 (1H, dd, J=10.0 and 2.0 Hz, H-15), 5.34 (1H, dd, J=17.0 and 2.0 Hz, H-15), 5.61 (1H, dt, J=17.0 and 10.0 Hz, H-14), 6.72 (1H, s, H-4), 6.83 (1H, s, H-1), 7.32 (1H, d, J=2.5 Hz, H-9); eims m/z $[M]^+$ 715 (18), 673 (16), 384 (9), 368 (13), 331 (56), 314 (18), 169 (100), 109 (20); hreims m/z $[M]^+$ 715.2477 (calcd for $C_{35}H_{41}NO_{15}$, 715.2478).

ACETYLATION OF **7**.—*3-O*-Demethyl-*2-O*-methylisoalangiside [**7**] (5.5 mg) was acetylated in the usual way and the crude acetate (8.0 mg) was subjected to prep. tlc (EtOAc-C_6H_6, 2:1), giving rise to *3-O*-demethyl-*2-O*-methylisoalangiside pentaacetate [**18**] (6.3 mg) as a colorless amorphous powder: $[\alpha]^{28}D$ −149° (c=0.63, $CHCl_3$); uv (MeOH) λ max (log ε) 229 (4.27), 278 (sh, 3.62), 286 (sh, 3.51) nm; ir ($CHCl_3$) ν max 1755, 1661, 1597, 1510 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ 1.52, 1.96, 2.01, 2.09, 2.30 (15H, each s, 5×Ac), 2.03 (1H, ddd, J=14.0, 12.0, and 5.0 Hz, H-13), 2.27 (1H, ddd, J=14.0, 5.0, and 4.0 Hz, H-13), 2.63 (1H, ddd, J=10.0, 5.5, and 1.5 Hz, H-12), 2.67 (1H, ddd, J=15.5, 3.5, and 2.5 Hz, H-5), 2.78 (1H, dddd, J=12.0, 5.5, 5.0, and 2.5 Hz, H-12a), 2.98 (1H, ddd, J=15.5, 11.5, and 6.0 Hz, H-5), 3.01 (1H, td, J=11.5 and 3.5 Hz, H-6), 3.72 (1H, ddd, J=9.5, 4.5, and 2.0 Hz, H-5′), 3.87 (3H, s, OMe), 4.12 (1H, dd, J=12.5 and 2.0 Hz, H-6′), 4.28 (1H, dd, J=12.5 and 4.5 Hz, H-6′), 4.66 (1H, br t, J=4.5 Hz, H-13a), 4.71 (1H, ddd, J=11.5, 6.0, and 2.5 Hz, H-6), 4.82 (1H, d, J=8.0 Hz, H-1′), 4.91 (1H, dd, J=9.5 and 8.0 Hz, H-2′), 5.04 (1H, t, J=9.5 Hz, H-4′), 5.18 (1H, t, J=9.5 Hz, H-3′), 5.28 (1H, d, J=1.5 Hz, H-11), 5.33 (1H, dd, J=10.0 and 1.5 Hz, H-15), 5.36 (1H, dd, J=17.0 and 1.5 Hz, H-15), 5.63 (1H, dt, J=17.0 and 10.0 Hz, H-14), 6.73 (1H, s, H-1), 6.83 (1H, s, H-4), 7.35 (1H, d, J=2.5 Hz, H-9); eims m/z $[M]^+$ 715 (71), 673 (22), 384 (7), 368 (14), 331 (57), 314 (12), 169 (100), 109 (19); hreims m/z $[M]^+$ 715.2471 (calcd for $C_{35}H_{41}NO_{15}$, 715.2478).

ACETYLATION OF **8**.—Demethylneoalangiside [**8**] (19.4 mg) was acetylated with Ac_2O in pyridine and the crude acetate (30.0 mg) was purified by prep. tlc with $CHCl_3$-MeOH (98:2) to afford demethylneoalangiside hexaacetate [**19**] (15.3 mg) as a colorless amorphous powder: $[\alpha]^{27}D$ −7.1° (c=0.96, $CHCl_3$); uv (MeOH) λ max (log ε) 223 (sh, 4.24), 237 (4.26) nm; ir ($CHCl_3$) ν max 1762, 1662, 1598, 1494 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ 1.34 (1H, td, J=13.0 and 11.0 Hz, H-13), 1.97, 2.01, 2.04, 2.10, 2.28, 2.38 (18H, each s, 6×Ac), 2.25 (1H, ddd, J=13.0, 4.5, and 2.0 Hz, H-13), 2.66 (1H, ddd, J=10.0, 5.5, and 2.0 Hz, H-12), 2.68 (1H, td, J=12.5 and 2.0 Hz, H-6), 2.72 (1H, dt, J=15.5 and 2.0 Hz, H-5), 2.83 (1H, ddd, J=15.5, 12.5, and 4.0 Hz, H-5), 2.90 (1H, dddd, J=13.0, 5.5, 4.5, and 2.5 Hz, H-12a), 3.77 (1H, ddd, J=9.5, 4.5, and 2.0 Hz, H-5′), 4.14 (1H, dd, J=12.5 and 2.0 Hz, H-6′), 4.33 (1H, dd, J=12.5 and 4.5 Hz, H-6′), 4.71 (1H, br d, J=11.0 Hz, H-13a), 4.94 (1H, d, J=8.5 Hz, H-1′), 5.01 (1H, ddd, J=12.5, 4.0, and 2.0 Hz, H-6), 5.04 (1H, dd, J=9.5 and 8.5 Hz, H-2′), 5.10 (1H, t, J=9.5 Hz, H-4′), 5.17 (1H, dd, J=10.0 and 1.5 Hz, H-15), 5.22 (1H, dd, J=17.0 and 1.5 Hz, H-15), 5.26 (1H, t, J=9.5 Hz, H-3′), 5.30 (1H, d, J=2.0 Hz, H-11), 5.44 (1H, dt, J=17.0 and 10.0 Hz, H-14), 7.07 (2H, s, H-3, H-4), 7.49 (1H, d, J=2.5 Hz, H-9); hrsims m/z $[M+H]^+$ 744.2505 (calcd for $C_{36}H_{42}NO_{16}$, 744.2505); cd (MeOH) $\Delta\epsilon$ −12.62 (238), −0.38 (282) nm; cd (EtOH) $\Delta\epsilon$ −12.97 (237) nm.

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