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IRIDOLINARINS A, B, AND C: IRIDOID ESTERS OF AN IRIDOID GLUCOSIDE FROM *LINARIA JAPONICA*

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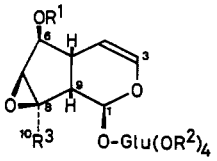
ABSTRACT.—Three iridoid esters of an iridoid glucoside, named iridolinarins A [**1**], B [**2**], and C [**3**], were isolated from whole plants of *Linaria japonica*. Their structures were determined by spectroscopic studies and chemical conversions.

Linaria japonica Miq. (Scrophulariaceae) is a perennial plant that grows in certain coastal areas of Japan. The whole plant extract is used in folk medicine as a diuretic and purgative. In earlier papers on this plant, the isolation of several iridoid glucosides was reported (1,2) and a recent reinvestigation of the same plant afforded four new iridoid glucosides (3). The present study on *L. japonica* has demonstrated the presence of three iridoid esters of an iridoid glucoside, named iridolinarins A, B, and C [**1–3**]. This paper deals with the structural determination of these esters.

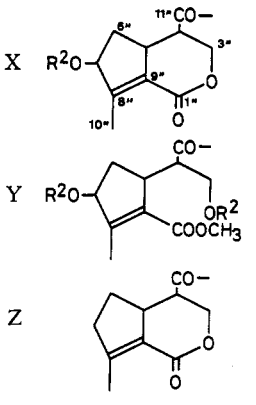
RESULTS AND DISCUSSION

Iridolinarins A, B, and C [**1–3**] were isolated from the *n*-BuOH-soluble fraction of a MeOH extract of *L. japonica* by a combination of various kinds of chromatography.

Iridolinarin A [**1**], $[\alpha]^{22}D$ −170.5°, was obtained as an amorphous powder, whose elemental composition was determined to be $C_{25}H_{32}O_{13}$ by negative-ion hrfabms. The uv spectrum showed the presence of an α,β-conjugated ketone (233 nm). The presence of an enol ether (1265 cm^{-1}) and a conjugated ester (1715 and 1645 cm^{-1}) was indicated by the ir spectrum. The ^{13}C-nmr spectrum of [**1**] consisted of a total of 25 signals. Of these, 6 were assignable to a β-D-glucopyranosyl moiety. The functionalities of the remaining 19 signals comprised two double bonds (disubstituted and tetrasubstituted), five carbons with oxygen substituents, and one acetalic, two carboxylic, two methyl, one methylene, and four methine groups (see Table 1). One of the methyl groups (δ_C 18.1) was expected to occur on one of the double bonds, probably the tetrasubstituted one, from its chemical shift in the ^1H-nmr spectrum (δ_H 2.18) and the appearance of two olefinic protons (δ_H 5.09 and 6.34), which were coupled to each other. The ^1H-^1H COSY



	R^1	R^2	R^3
1	X	H	CH_3
1a	H	H	CH_3
2	Y	H	CH_3
3	Z	H	CH_3
4	H	H	CH_2OH
5	X	Ac	CH_3
6	Y	Ac	CH_3
7	Z	Ac	CH_3



Glu: β-D-Glucopyranosyl

TABLE 1. ^{13}C-Nmr Data for Iridolinarins A (**1**), B (**2**), and C (**3**), **1a**, **1b**, and **3b** (CD_3OD, 100 MHz).

Carbon No.	1	2	3	1a (3a)	1b	3b
1	95.3	95.3	95.3	95.5		
3	142.6	142.3	142.6	141.7		
4	102.4	103.0	102.5	104.1		
5	36.9	37.5	36.8	39.4		
6	82.8	82.2	82.6	80.1		
7	62.7	62.7	62.7	65.2		
8	64.3	64.1	64.2	63.5		
9	45.8	46.0	45.8	46.5		
10	18.1	18.2	18.1	18.3		
1′	99.7	99.7	99.7	99.7		
2′	75.0	75.0	75.0	75.0		
3′	78.0	78.6	78.6	78.6		
4′	71.9	71.9	71.9	71.9		
5′	78.6	78.0	78.0	78.0		
6′	63.2	63.2	62.8	63.1		
1″	165.9	167.6	166.2		167.5	167.6
3″	71.3	60.9	70.8		61.0	60.8
4″	44.0	51.9	44.0		51.9	52.1
5″	43.9	44.8	46.0		44.8	47.5
6″	37.0	37.0	28.2		37.4	26.3
7″	79.8	80.1	39.2		80.0	40.2
8″	158.9	158.8	162.0		158.7	159.0
9″	126.8	130.5	124.0		130.6	129.2
10″	14.4	13.6	16.7		13.5	16.6
11″	172.4	175.2	172.7		175.8	176.1
CH_3O-(C-1″)		51.8			51.7	51.5
CH_3O-(C-11″)					52.2	52.1

nmr spectrum clearly indicated the presence of two series of proton spin-spin coupling systems, viz., system I: -O-CH=CH-CH(-CH-CH<$^{O-}_{O-}$)-CHOH-CH-O- and system II: -OCH_2-CH-CH-CH_2-CHOH-.

Because only partial structural determination was possible with the available spectroscopic data, **1** was subjected to mild alkaline hydrolysis, which yielded two compounds. The ^{13}C-nmr spectrum of the more polar one [**1a**], colorless needles, mp 215–220°, revealed that it included a β-glucopyranose moiety, and the remaining five signals were considered to form a dihydropyran ring, which is characteristic of the iridoid skeleton. The chemical shifts of the five carbons on the dihydropyran ring and three other carbons closely resembled those of catalpol [**4**] (4), except for the methyl signal (C-10) in **1** which was replaced by a carbinol function in **4**. The ^{1}H-^{1}H COSY nmr spectrum indicated the presence of the system I proton sequence and the coupling constants of the protons were similar to those of catalpol (see Table 2). As the cd spectra of **1** and **1a** showed a positive Cotton effect at 217 nm and a negative one at 191 nm, which were almost the same as those of catalpol, the structure of **1a**, including the absolute stereochemistry, was determined to be 10-deoxycatalpol. So far as is known, 10-deoxycatalpol itself has not been isolated from a natural source.

The other product [**1b**] from the hydrolysate was obtained as a colorless oil, $[\alpha]^{18}_D$ −38.8°. The presence of an α,β-unsaturated ester system was indicated by the ir (1700 cm^{-1}) and uv (227 nm) spectra. Compound **1b** was analyzed by hreims to comprise a total of 12 carbon atoms ($C_{12}H_{18}O_6$), which is two carbons greater than expected from the ^{13}C-nmr spectrum of **1**, probably due to the formation of methyl esters during hydrolysis (δ_C 51.7 and 51.8; δ_H 3.74 and 3.75). As also expected from the ^{13}C-nmr spectra of **1** and

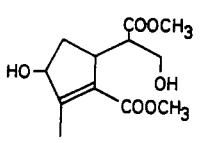
TABLE 2. ^{1}H-Nmr Data for Iridolinarins A–C (**1–3**) and **1a** (CD_3OD, 400 MHz).[a]

Proton	Compound			
	1	**2**	**3**	**1a**
1	5.09 (d, 9.0)	5.12 (d, 9.3)	5.10 (d, 9.2)	5.02 (d, 9.5)
3	6.34 (dd, 1.3, 7.0)	6.34 (dd, 1.9, 6.0)	6.34 (dd, 1.5, 6.2)	6.32 (dd, 1.8, 6.0)
4	4.83 (dd, 3.9, 7.0)	4.92 (dd, 4.4, 6.0)	4.84 (dd, 4.2, 6.2)	5.04 (dd, 4.4, 6.0)
5	2.07 (m)	2.47 (ddt, 1.9, 4.4, 7.7)	2.40 (m)	2.23 (ddt, 1.8, 4.4, 7.7)
6	4.87 (dd, 1.1, 6.6)	4.94 (dd, 1.3, 7.7)	4.89 (dd, 1.3, 7.9)	3.89 (dd, 1.1, 7.7)
7	3.45 (d, 1.1)	3.48 (br s)	3.45 (d, 1.1)	3.26 (br s)
9	2.36 (m)	2.41 (dd, 7.7, 9.3)	2.40 (m)	2.35 (dd, 7.7, 9.5)
10	1.52 (3H, s)	1.54 (3H, s)	1.52 (3H, s)	1.52 (3H, s)
1′.....	4.76 (d, 7.9)	4.78 (d, 7.9)	4.76 (d, 7.9)	4.76 (d, 7.9)
2′.....	3.23 (dd, 7.9, 9.5)	3.24 (dd, 7.9, 9.0)	3.23 (dd, 7.9, 9.2)	3.23 (dd, 7.9, 9.4)
3′.....	3.38 (t, 9.5)	3.39 (t, 9.0)	3.38 (t, 9.2)	3.38 (t, 9.4)
4′.....	3.21 (dd, 8.8, 9.5)	3.22 (dd, 9.0, 9.7)	3.21 (dd, 8.8, 9.2)	3.22 (dd, 8.8, 9.4)
5′.....	3.30 (ddd, 2.0, 7.0, 8.8)	*[b]	3.30 (ddd, 2.0, 6.8, 8.8)	3.30 (ddd, 2.0, 6.6, 8.8)
6′.....	3.60 (dd, 7.0, 11.9)	3.62 (dd, 6.8, 11.9)	3.60 (dd, 6.8, 11.9)	3.61 (dd, 6.6, 11.7)
	3.91 (dd, 2.0, 11.9)	3.92 (dd, 2.0, 11.9)	3.92 (dd, 2.0, 11.9)	3.91 (dd, 2.0, 11.7)
3″.....	4.51 (dd, 3.5, 11.9)	3.49 (dd, 4.6, 10.9)	4.46 (dd, 3.5, 11.9)	
	4.57 (dd, 2.0, 11.9)	3.78 (dd, 8.8, 10.9)	4.53 (dd, 2.6, 11.9)	
4″.....	3.14 (ddd, 2.0, 3.5, 5.5)	3.03 (dt, 4.6, 8.8)	3.12 (ddd, 2.6, 3.5, 5.9)	
5″.....	3.60 (m)	3.49 (m)	3.42 (m)	
6″.....	2.06 (m)	1.78 (ddd, 6.6, 9.3, 13.7)	1.75 (ddd, 9.9, 12.6, 19.8)	
	2.37 (m)	2.28 (ddd, 2.8, 7.5, 13.7)	2.21 (dddd, 1.6, 7.9, 11.0, 19.8)	
7″.....	4.52 (m)	4.65 (br t, 6.8)	2.40 (m)	
			2.58 (br qui, ca. 8)	
10″.....	2.18 (3H, dd, 0.6, 2.6)	2.08 (3H, br s)	2.17 (3H, t, 1.1)	
CH_3O-..		3.76 (s)		

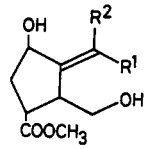
[a]The letters and figures in parentheses are multiplicities and coupling constants in Hz, respectively.
[b]Chemical shift not observed.

1a, **1b** had a tetrasubstituted double bond on which a methyl group occurred, as well as two carbomethoxyl, two methylene and three methine groups. One of the methylene and methine carbons was expected to have an electronegative substituent from its chemical shift, so the spin-spin coupling system II, revealed by the ^{1}H-^{1}H COSY experiment on **1**, should be, in part, **1b**. Several plausible structures for **1b**, deduced from one- and two-dimensional nmr spectroscopic and other physical data thus far available, are depicted as **1b**, **1b′a**, and **1b′b** in Figure 1. To determine which was the case, a 2D-INADEQUATE nmr experiment was performed. The connectivities of carbon atoms that were revealed by its spectrum are depicted as bold lines in the structure of **1b** in Figure 2. The 8″- and 9″-carbon atoms must be connected to form a double bond and the 9″-position was the only place where the remaining carbomethoxyl group could be located. Therefore, the structure of the extra iridoid portion, obtained from **1**, was that of **1b**. The absolute stereochemistries at the 4″-, 5″-, and 7″-positions remain to be determined.

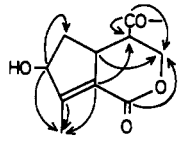
The elemental composition for **1** demanded that part **1b** should have a bicyclic system, when it exists in the molecule of **1**, with the formation of a lactone ring between the carbinol at C-3 and the carboxylic acid at C-1 being the most plausible. This was supported by the results of a long-range ^{13}C-^{1}H COSY nmr experiment indicating the correlation between the protons at the 3″-position and the carbonyl carbon at 1″ (**X** in Figure 1). When compound **1a** was compared to **1**, the ^{13}C-nmr signal of C-6 shifted downfield by 2.7 ppm, whereas the C-5 and C-7 resonances shifted upfield (−2.5 and −2.5 ppm, respectively), and the ^{1}H-nmr signal of H-6 also shifted downfield (δ_H 3.89→4.87). These data confirmed the notion that the extra iridoid was linked to the hydroxyl group at the 6-position. On acetylation, iridolinarin A formed a pentaacetate [**5**]. A fragment ion at *m/z* 331 (tetraacetyl-glucose oxonium) in the eims ruled out the possibility that the site of acylation occurred in the glucose moiety, thereby further



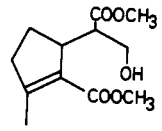
1b



	R^1	R^2
1b'a	$COOCH_3$	CH_3
1b'b	CH_3	$COOCH_3$



X



3b

FIGURE 1. Structures for extra iridoid portions and selected results of the ^{13}C-^{1}H long-range COSY nmr experiment. Compounds **1b**, **1b'a**, and **1b'b** represent possible structures for the extra iridoid portion in the methanolyzates of iridolinarins A and B [**1** and **2**], and compound **3b** represents that of iridolinarin C [**3**]. Arrows in **X** indicate long-range correlations (J=7.5 Hz) between carbons (arrow tails) and protons (arrowheads).

confirming the proposed structure. Therefore, the structure of iridolinarin A was determined as **1**.

Iridolinarin B [**2**], $[\alpha]^{22}D$ −110.8°, was obtained as a colorless amorphous powder. The molecular formula of $C_{26}H_{36}O_{14}$ analyzed by hrfabms was 32 mass units greater than that of **1**. Iridolinarin B formed a hexaacetate [**6**]. Alkaline hydrolysis of **2** gave 10-deoxycatapol [**1a**] and **1b**. Thus, the difference in molecular weight of 32 should be due to the addition of an element of MeOH to **1**, and the appearance of methoxyl signals in the ^{13}C- and ^{1}H-nmr spectra (δ_C 51.8 and δ_H 3.76, respectively) indicated the opening of the lactone ring of the extra iridoid portion forming a methyl ester. Accordingly, the

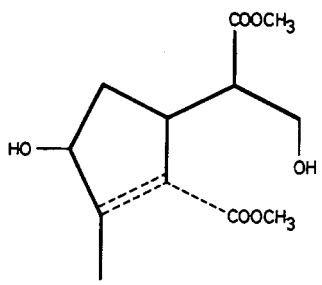


FIGURE 2. The C-C bonds of **1b**, as revealed by a 2D-INADEQUATE nmr experiment, are depicted as bold solid lines. The ^{13}C-^{13}C-INADEQUATE nmr spectrum of **1b** acquired on a 130 mg of sample and recorded in CD_3OD with τ=4.5 msec (J=55 Hz). The matrix used had 128×2048 data points and was zero-filled to 256×4096 data points. Bonds with dotted lines were not confirmed by nmr spectroscopy, but must theoretically be connected.

same rationale for the structural determination of **1** was essentially adopted for iridolinarin B, which was therefore assigned as [**2**].

Iridolinarin C [**3**], $[\alpha]^{18}D$ −162.1°, was also obtained as a colorless amorphous powder, whose molecular formula was $C_{25}H_{32}O_{12}$. This corresponded to one oxygen atom less than found in the elemental formula of **1**. Iridolinarin C formed a tetraacetate [**7**]. On alkaline hydrolysis, 10-deoxycatalpol [**1a**] and an extra iridoid portion [**3a**], whose spectroscopic features were similar to those of **1b**, were isolated. The one- and two-dimensional nmr spectra of **3b** indicated that the methine carbon (C-7″) with the hydroxyl group in **1a** was replaced by a methylene, which meant the loss of an oxygen atom. Thus, iridolinarin C is 7″-deoxyiridolinarin A [**3**].

Iridolinarin B [**2**] is believed to be a natural product, because methanolysis of **3** (during extraction and purification) should yield a similar ring-opened compound. No such compound could be detected on tlc analysis of the *n*-BuOH-soluble fraction.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—The instruments used were as follows: 400 MHz ^{1}H nmr and 100 MHz ^{13}C nmr, JEOL GX-400; ms, JEOL SX-102 (fabms matrix: glycerol for non-acetates and *m*-nitrobenzyl alcohol for acetates; eims: 70 eV); optical rotations, Union Giken PM-101; ir, Shimadzu IR-400S; uv, Shimadzu UV-160S; dccc (droplet counter-current chromatography), Tokyo Rikakikai DCC-A with 500 glass columns; rpcc (reversed-phase open column chromatography), ODS (Cosmosil, 40 mm×220 mm); Si gel 60 (70–230 mesh, Merck) and prep. tlc, Si gel (Merck, 0.5 mm thickness) on glass plates.

PLANT MATERIAL.—Whole *Linaria japonica* plants were collected in July 1990, at coastal areas of Tottori Prefecture, Japan. A voucher specimen (90-LJ-Tottori) has been deposited at the Herbarium of the Department of Pharmacognosy, Institute of Pharmaceutical Sciences, Hiroshima University School of Medicine.

EXTRACTION AND ISOLATION.—Air-dried whole plants of *Linaria japonica* were extracted with MeOH (15 liters×2). The concentrated MeOH extract was adjusted to 95% aqueous MeOH by the addition of H_2O (1.5 liters) and then extracted with *n*-hexane (1.5 liters×2, 35.0 g). The MeOH layer was concentrated and suspended in 1.5 liters of H_2O, and then extracted with EtOAc (1.5 liters×2, 49.7 g) and *n*-BuOH (1.5 liters×3, 151 g).

The *n*-BuOH extract (150 g) was chromatographed over a column of a highly porous synthetic resin (Diaion HP-20; Nippon Rensui Co., Tokyo; 80 mm×600 mm) with a stepwise increase of MeOH content in H_2O (9 liters each of 20, 40, 60, 80 and 100% MeOH, with fractions of 3 liters being collected). The 40% MeOH eluate (fractions 5 and 6, 10.94 g) was subjected to Si gel (450 g) column chromatography with $CHCl_3$ (2 liters), and 2.5% MeOH (2 liters), 5% MeOH (3 liters), 10% MeOH (9 liters), 15% MeOH (6 liters) and 20% MeOH (3 liters) in $CHCl_3$, with fractions of 500 ml being collected. The residue (2.67 g) from fractions 19–26 was further purified by 5 dccc runs using the solvent $CHCl_3$-MeOH-H_2O-1-PrOH (9:12:8:2), with fractions of 5 g being collected. Iridolinarins A [**1**] and B [**2**] were concentrated in fractions 75–100. These fractions were finally subjected to rpcc with MeOH-H_2O (1:9, 1 liter)→MeOH-H_2O (1:1, 1 liter), with fractions of 10 g being collected. Iridolinarin A [**1**] was obtained in fractions 95–102 (760 mg) and B [**2**] in fractions 122–133 (380 mg).

The 60% MeOH eluate (fractions 8 and 9, 14.30 g) obtained on Diaion HP-20 chromatography was subjected to Si gel (450 g) column chromatography with $CHCl_3$ (2 liters), and 1% MeOH (3 liters), 2% MeOH (3 liters), 4% MeOH (3 liters), 6% MeOH (6 liters), 8% MeOH (6 liters), 10% MeOH (6 liters), 12.5% MeOH (3 liters), and 15% MeOH (3 liters) in $CHCl_3$, with fractions of 500 ml being collected. An aliquot (503 mg) of the residue (2.36 g) from fractions 30–36 was purified by dccc to give 264 mg of iridolinarin C [**3**].

IRIDOLINARIN A [**1**].—Colorless amorphous powder; $[\alpha]^{22}D$ −170.5° (*c*=0.78, MeOH); ir ν max (KBr) 3400, 2850, 1715, 1645, 1405, 1265, 1150, 1055, 1010, 920, 855, 825, 755 cm^{-1}; uv λ max (MeOH) (log ϵ) 204 (4.04), 233 (3.96) nm; ^{13}C and ^{1}H nmr see Tables 1 and 2; hrfabms (negative-ion) *m/z* 539.1808 $[M-H]^-$, $C_{25}H_{31}O_{13}$ requires 539.1764.

IRIDOLINARIN B [**2**].—Colorless amorphous powder; $[\alpha]^{22}D$ −110.8° (*c*=0.69, MeOH); ir ν max (KBr) 3450, 2900, 1710, 1650, 1435, 1225, 1080–1000, 925, 860, 830, 730 cm^{-1}; uv λ max (MeOH) (log ϵ) 204 (3.99), 227 (3.93) nm; ^{13}C and ^{1}H nmr see Tables 1 and 2; hrfabms (negative-ion) *m/z* 571.2056 $[M-H]^-$, $C_{26}H_{35}O_{14}$ requires 571.2027.

IRIDOLINARIN C [**3**].—Colorless amorphous powder; $[\alpha]^{18}D$ −162.1° (*c*=0.85, MeOH); ir ν max (KBr) 3400, 2875, 1700, 1630, 1150, 1090–1000, 925, 830, 760 cm^{-1}; uv λ max (MeOH) (log ε) 240 (3.86) nm; ^{13}C and ^{1}H nmr see Tables 1 and 2; hrfabms (negative-ion) *m/z* 523.1804 $[M-H]^-$, $C_{25}H_{31}O_{12}$ requires 523.1815.

MILD ALKALINE HYDROLYSIS OF **1**.—Iridolinarin A (**1**, 508 mg) was treated with 20 ml of 0.1 N methanolic NaOH at 20° for 3 h, and the resultant products separated by Si gel (50 g) column chromatography with $CHCl_3$-MeOH (9:1, 200 ml, and then 7:3, 200 ml, with fractions of 12.5 ml being collected) to give **1a** (fractions 8 and 9) (137 mg, 46%) and **1b** (fractions 28–33) (152 mg, 69%).

10-DEOXYCATALPOL [**1a**].—Colorless fine needles, mp 215–220° (MeOH); $[\alpha]^{18}D$ −101.8° (*c*=0.69, MeOH); ir ν max (KBr) 3450, 3300, 2875, 1655, 1495, 1375, 1315, 1270, 1225, 1130–1010, 990, 950, 915, 825, 755 cm^{-1}; ^{13}C and ^{1}H nmr see Tables 1 and 2; fabms *m/z* 347 $[M+H]^+$, 369 $[M+Na]^+$ (+NaI), 385 $[M+K]^+$ (+KI); cd λ ext (nm) (Δε) 191 (−3.40), 199 (0), 207 (+1.88) (*c*=0.0224, double distilled H_2O) [catalpol [**4**], cd λ ext (nm) (Δε) 190 (−2.13), 196 (0), 205 (+2.51) (*c*=0.0642, double distilled H_2O)]; *anal.* found C 51.51, H 6.43; $C_{15}H_{22}O_9$ requires C 52.02, H 6.40.

COMPOUND **1b**.—Colorless liquid, $[\alpha]^{18}D$ −38.8° (*c*=0.88, MeOH); ir ν max (liquid film) 3375, 2950, 1715, 1700, 1645, 1435, 1220, 1035 cm^{-1}; uv λ max (MeOH) (log ε) 227 (3.90) nm; ^{13}C nmr see Table 1; ^{1}H nmr (CD_3OD) δ 1.78 (1H, ddd, *J*=6.6, 9.3, and 13.7 Hz, H-6″a), 2.07 (1H, t, *J*=1.3 Hz, H-10″), 2.27 (1H, ddd, *J*=2.4, 7.5, and 13.7 Hz, H-6″b), 2.91 (1H, ddd, *J*=4.4, 5.0, and 9.0 Hz, H-4″), ca. 3.4 (1H, m, H-5″), 3.48 (1H, dd, *J*=4.4 and 11.0 Hz, H-3″a), 3.67 (3H, s, 11″-$COOCH_3$), 3.74 (3H, s, 1″-$COOCH_3$), 3.76 (1H, dd, *J*=9.0 and 11.0 Hz, H-3″b), 4.63 (qt, *J*=1.0 and 7.0 Hz, H-6″); hreims *m/z* 258.1161 $[M]^+$, $C_{12}H_{18}O_6$ requires 258.1103.

MILD ALKALINE HYDROLYSIS OF **3**.—Iridolinarin C (**3**, 100 mg) was hydrolyzed with alkali in a similar manner to **1** to afford 49 mg of **3a** (74%) and 20 mg of **3b** (43%). The more polar compound [**3a**] was identified as 10-deoxycatalpol [**1a**] by comparison of its physical data. The physical properties of the less polar compound [**3b**] are as follows: colorless liquid, $[\alpha]^{18}D$ +20.3° (*c*=1.33, MeOH), ir ν max (liquid film) 3450, 2995, 1705, 1635, 1435, 1355, 1220, 1115, 1050 cm^{-1}; uv λ max (MeOH) (log ε) 231 (3.96) nm; ^{13}C nmr see Table 1; ^{1}H nmr (CD_3OD) δ 1.81 (1H, tdd, *J*=3.9, 8.8 and 13.4, H-6″a), 1.94 (1H, dtd, *J*=7.9, 9.5 and 13.4 Hz, H-6″b), 2.08 (1H, q, *J*=1.3 Hz, H-10″), 2.38 (1H, qddd, *J*=0.9, 3.8, 9.5 and 18.1 Hz, H-7″a), 2.52 (1H, qui, td, *J*=1.3, 9.0 and 18.1 Hz, H-7″b), 2.98 (1H, ddd, *J*=4.0, 4.9 and 9.2 Hz, H-4″), ca. 3.37 (1H, v br s, $W_{1/2}$=20 Hz, H-5″), 3.51 (1H, dd, *J*=4.0 and 10.8 Hz, H-3″a), 3.67 (3H, s, 11″-$COOCH_3$), 3.72 (3H, s, 1″-$COOCH_3$), 3.83 (1H, dd, *J*=9.3 and 10.8 Hz, H-3″b); hr eims *m/z* 242.1163 $[M]^+$, $C_{12}H_{18}O_5$ requires 242.1154, 224.1028 $[M-H_2O]^+$, $C_{12}H_{16}O_4$ requires 224.1048, 211.0991 $[M-CH_3O]^+$, $C_{11}H_{15}O_4$ requires 211.0970.

ACETYLATION OF **1–3**.—Iridolinarins A [**1**] (21 mg), B [**2**] (22 mg), and C [**3**] (20 mg) were acetylated with a mixture of Ac_2O (1 ml) and pyridine (1 ml) for 16 h at 18°. The reaction mixtures were poured into ice-H_2O and then the precipitates were purified by prep. tlc [developed with C_6H_6-$(CH_3)_2CO$ (9:1), and eluted with $CHCl_3$-MeOH (9:1)] to give 22 mg (76%), 27 mg (84%), and 16 mg (62%) of the respective acetates. Iridolinarin A pentaacetate [**5**], $[\alpha]^{17}D$ −112.8° (*c*=1.46, $CHCl_3$); ^{1}H nmr ($CDCl_3$) δ 2.01, 2.03, 2.05, 2.07, 2.08 (3H each, s, CH_3CO-×5); ^{13}C nmr ($CDCl_3$) δ 20.6 (×2), 20.70, 20.71, 21.0 (CH_3CO-×5), 169.4, 169.4, 170.2, 170.4, 170.5, 170.7 (CH_3CO-×5 and C-11″); fabms *m/z* 773 $[M+Na]^-$, 713, 591, 331 (+NaI), 789 $[M+K]^+$, 729, 535, 331 (+KI); eims *m/z* 331 (56) [Glu(OAc)$_4$ oxonium ion]$^-$, 256 (7), 169 (100), 104 (61). Iridolinarin B hexaacetate [**6**], $[\alpha]^{17}D$ −57.4° (*c*=1.79, $CHCl_3$); ^{1}H nmr ($CDCl_3$) δ 2.01, 2.02, 2.04, 2.06, 2.07, 2.09 (3H each, s, CH_3CO-×6); ^{13}C nmr ($CDCl_3$) δ 20.6 (×2), 20.7 (×3), 21.0 (CH_3CO-×6), 169.39, 169.43, 170.2, 170.5 (×2), 170.6, 172.2 (CH_3CO-×6 and C-11″); fabms *m/z* 847 $[M+Na]^-$, 787, 623, 591, 371 (+NaI), 863 $[M+K]^-$, 803, 331 (+KI); eims *m/z* 331 (100) [Glu(OAc)$_4$ oxonium ion]$^-$, 253 (17), 193 (27), 169 (96), 133 (100), 104 (55). Iridolinarin C tetraacetate [**7**], $[\alpha]^{17}D$ −91.7° (*c*=1.05, $CHCl_3$); ^{1}H nmr ($CDCl_3$) δ 2.01, 2.04, 2.06, 2.08 (3H each, s, CH_3CO-×4); ^{13}C nmr ($CDCl_3$) δ 20.6 (×2), 20.7 (×2) (CH_3CO-×4), 169.39, 169.43, 170.2, 170.5, 170.9 (CH_3CO-×4 and C-11″); fabms *m/z* 715 $[M+Na]^+$, 655 (+NaI), 731 $[M+K]^+$ (+KI); eims *m/z* 331 (77) [Glu(OAc)$_4$ oxonium ion]$^+$, 289 (53), 229 (94), 187 (60), 169 (100), 127 (100), 104 (82).

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