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CYCLOHEXYLETHANOIDS AND RELATED GLUCOSIDES FROM *MILLINGTONIA HORTENSIS*

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Key Word Index—*Millingtonia hortensis*; Bignoniaceae; flowers; cyclohexylethanoids; phenylethanoids; glucosides.

Abstract—From the dried flowers of *Millingtonia hortensis*, nine cyclohexylethanoids, including four glucosides were isolated along with 12 related known compounds. Biogenetic relationships between these compounds are discussed.

INTRODUCTION

Millingtonia hortensis is an important medicinal plant in Southeast Asia, ranging from India, Burma, Thailand, Vietnam, Southern China and Indonesia. In Thailand, the flower is called 'peep' and used for the treatment of asthma, sinusitis and as a cholagogue and tonic [1]. In previous chemical investigations of the flowers of this species, the isolation of four flavonoids, scutellarin and its galactoside [2], hispidulin [3] and cirsimaritin [4], along with a cyclohexylethanoid, isorengyol (**12**) [5], was reported. The present study has yielded nine new cyclohexylethanoids (**13**–**21**), including four glucosides, along with 12 related known compounds (**1**–**12**). Biogenetic relationships between these compounds are discussed.

RESULTS AND DISCUSSION

After repeated column chromatography, followed by HPLC, of a hot methanolic extract of the dried flowers of *Millingtonia hortensis*, 21 compounds (**1**–**21**) were isolated. Compounds **1**–**12** were identified as known compounds by means of their spectral data.

Compounds **1**–**4** were phenylethanoid glycosides. Compound **1** was salidroside previously isolated from *Carica papaya* [6] and many species of Salicaceae [7]. This compound was supposed to be a biogenetic precursor of cyclohexylethanoids through mimic chemical reaction [8]. Compound **2** was 2-phenethyl rutinoside previously isolated from *Citrus unshiu* [9]; the reported ^{13}C NMR data [9] of C-8 and C-4′ were corrected by DEPT measurement. Compound **3** was 2-(3,4-dihydroxyphenyl)-ethyl glucoside previously isolated from *Syringa vulgaris*, etc. [10]. Compound **4** was acteoside widely distributed in Scrophulariaceae, Acanthaceae, etc. [11]. Compounds **5** and **6** were phenylpropanoid glucosides, *p*-coumaryl alcohol glucoside (**5**) and isoeugenol glucoside (**6**), both of which have been obtained from *Lilium cordatum* [12]. Compounds **7**–**12** were cyclohexylethanoids identified as cornoside (**7**) [13], racemic rengyolone (**8**), rengyoside B (**9**), rengyol (**10**), rengyoside A (**11**) and isorengyol (**12**) [14, 15], respectively. Cornoside (**7**) has been isolated from *Cornus femina* and many other species, and compounds **8**–**12** are constituents of *Forsythia suspensa* ('rengyo' in Japanese). Except for **12**, the isolation of these cyclohexylethanoids from the Bignoniaceae has not been reported previously.

Compound **13**, $C_{14}H_{26}O_8$ showed 14 signals in its ^{13}C NMR spectrum, and six of them were attributed to a β-glucosyl moiety. Enzymatic hydrolysis of **13** with β-glucosidase afforded **12** and D-glucose. Comparison of the ^{13}C NMR spectra of **13** with **12**, revealed a glucosylation shift around C-8. Thus, the structure of **13** was characterized as 8-*O*-β-D-glucopyranosyl isorengyol.

Compound **14**, $C_8H_{12}O_3$ showed a similar ^{13}C NMR spectrum to that of **8**, but in place of the carbonyl carbon signal (δ196.9) of **8**, a carbinyl methine signal (δ65.9) appeared and double bond signals were shifted. Since the oxidation of **14** with CrO_3 afforded **8**, the basic structure of **14** was a 4-hydroxy congener of **8**. To deduce the configuration, **14** was hydrogenated to afford a saturated derivative (**15**), which was converted to its acetate **15a**. In the ^{1}H NMR of **15a**, NOE was observed between H-4 (δ4.76) and H-2 (δ3.77). Thus, the stereochemistry of **14** and **15** was 2,4-*cis*. The absolute configuration was not determined and needs to be clarified; the structure is tentatively illustrated as one of the enantiomers.

Naturally obtained **15**, $C_8H_{14}O_3$, was identical with the reduction compound of **14** by means of NMR. How-

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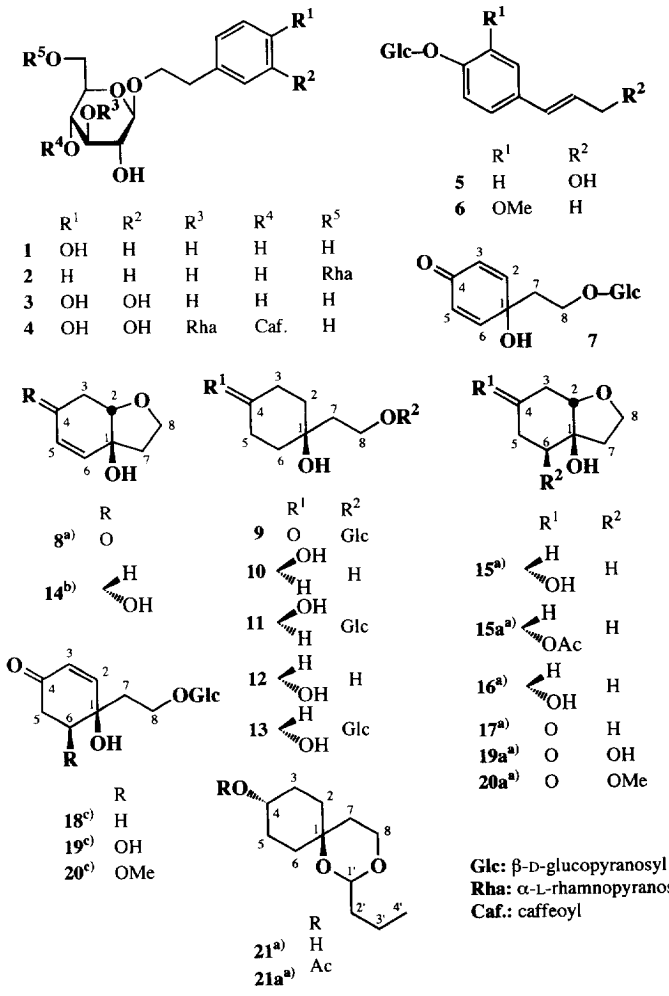

	R^1	R^2	R^3	R^4	R^5
1	OH	H	H	H	H
2	H	H	H	H	Rha
3	OH	OH	H	H	H
4	OH	OH	Rha	Caf.	H

	R^1	R^2
5	H	OH
6	OMe	H

	R
8[a)]	O
14[b)]	H, OH

	R^1	R^2
9	O	Glc
10	OH, H	H
11	OH, H	Glc
12	H, OH	H
13	H, OH	Glc

	R^1	R^2
15[a)]	H, OH	H
15a[a)]	H, OAc	H
16[a)]	H, OH	H
17[a)]	O	H
19a[a)]	O	OH
20a[a)]	O	OMe

	R
18[c)]	H
19[c)]	OH
20[c)]	OMe

	R
21[a)]	H
21a[a)]	Ac

a) Compounds were racemic mixtures.
b) 14 was chiral but needs to be clarified. The structure is tentatively illustrated as one of the enantiomers.
c) Aglycones of 18, 19 and 20 were racemic mixtures.

ever, the specific optical rotation of natural **15** was significantly smaller than that of **15** derived from **14**; natural **15** seemed to be racemic.

Compound **16** had the same molecular formula as **15** and the ^{13}C NMR data indicated that it was a 2,4-*trans* isomer of **15**, i.e. the 4-epimer of **15**. Since the specific optical rotation of **16** was small, it might be partially racemic. As in the case of **15**, the structure is tentatively illustrated as one of the enantiomers.

Compound **17**, $C_8H_{12}O_3$, had a similar ^{13}C NMR spectrum to that of **8**, except for the appearance of two methylene signals (δ 34.1 and 35.7) in place of the double bond carbon signals. From the ^{1}H NMR and ^{13}C NMR data, **17** was shown to be the saturated congener of **8**, as illustrated. Because of the small specific optical rotation and no Cotton effect in the CD spectrum, **17** appeared to be racemic.

Compound **18**, $C_{14}H_{22}O_8$, was a non-separable mixture of diastereomeric glucosides judging from a very close set of dual peaks in the ^{13}C NMR. Comparison of the ^{13}C NMR of **18** with that of **7**, the shown structure was suggested. Enzymatic hydrolysis of **18** with β-glucosidase afforded **17**. This was analogous to the reaction of **7** to form **8** [8]. Only one of the diastereomeric forms of **18** is illustrated.

Compound **19**, $C_{14}H_{22}O_9$, was also a mixture of diastereomeric glucosides showing dual signals. When the ^{13}C NMR of **19** was compared with that of **18**, the introduction of a hydroxyl group at C-6 was readily deduced. Compound **20**, $C_{15}H_{24}O_9$ was similarly characterized to be the C-6 methoxylated congener of **18**. To decide on the configuration, compounds **19** and **20** were enzymatically hydrolysed to afford the cyclic compounds **19a** ($C_8H_{12}O_4$) and **20a** ($C_9H_{14}O_4$), respectively. These compounds did not exhibit dual signals any more. In the ^{1}H NMR of **20a**, NOE were observed between H-6 and H-7, H-6 and H-8, H-2 and H-7, H-2 and H-8. Therefore, the junction of the two rings was *cis* and the 6-OMe was

Table 1. ^{13}C NMR spectral data for cyclohexylethanoids (**7**–**21**) in pyridine-d_5

C	7	8	9*	10*	11	12	13	14	15	16	17
1	68.2 *s*	74.8 *s*	69.1 *s*	70.1 *s*	69.1 *s*	71.3 *s*	70.2 *s*	77.5 *s*	77.5 *s*	75.2 *s*	76.7 *s*
2	153.7 *d*	81.9 *d*	37.7 *t*†	36.2 *t*	36.3 *t*†	34.5 *t*	34.4 *t*	84.0 *d*	83.1 *d*	82.2 *d*	84.4 *d*
3	127.1 *d*	40.4 *t*†	37.5 *t*†	31.8 *t*	31.8 *t*	31.2 *t*	31.0 *t*	40.3 *t*	37.1 *t*	36.6 *t*	42.3 *t*
4	185.8 *s*	196.9 *s*	211.3 *s*	69.8 *d*	69.8 *d*	67.4 *d*	67.1 *d*	65.9 *d*	67.2 *d*	65.9 *d*	209.7 *s*
5	127.1 *d*	127.9 *d*	37.5 *t*†	31.8 *t*	31.8 *t*	31.2 *t*	31.0 *t*	133.8 *d*	31.6 *t*†	31.7 *t*	34.1 *t*
6	153.7 *d*	150.2 *d*	37.6 *t*†	36.2 *t*	36.2 *t*†	34.5 *t*	34.3 *t*	131.2 *d*	32.3 *t*†	33.1 *t*	35.7 *t*
7	41.0 *t*	40.2 *t*†	42.0 *t*	45.2 *t*	43.0 *t*	43.2 *t*	41.2 *t*	40.2 *t*	39.5 *t*	39.7 *t*	40.8 *t*
8	65.2 *t*	66.3 *t*	66.5 *t*	58.9 *t*	66.7 *t*	58.8 *t*	66.6 *t*	67.7 *t*	65.8 *t*	65.3	66.1 *t*
Me											
CO											
1′	104.7 *d*		104.8 *d*		104.8 *d*		104.8 *d*				
2′	75.1 *d*		75.1 *d*		75.2 *d*		75.2 *d*				
3′	78.5 *d*†		78.6 *d*		78.6 *d*‡		78.6 *d*‡				
4′	71.6 *d*		71.7 *d*		71.7 *d*		71.6 *d*				
5′	78.4 *d*†		78.6 *d*		78.5 *d*‡		78.5 *d*‡				
6′	62.7 *t*		62.8 *t*		62.8 *t*		62.7 *t*				

Table 1. *Continued*

C	18		19		19a	20		20a	21	21a
1	68.9	69.0 *s*	71.8	n *s*	78.9 *s*	71.8	71.9 *s*	79.0 *s*	71.6 *s*	71.2 *s*
2	155.9	156.0 *d*	153.2	153.4 *d*	83.8 *d*	154.0	154.1 *d*	83.8 *d*	24.3 *t*	24.3 *t*
3	127.6	127.7 *d*	128.4	128.6 *d*	42.6 *t*	128.0	128.1 *d*	42.9 *t*	28.6 *t*	25.2 *t*
4	198.8	n *s*	198.0	198.1 *s*	208.3 *s*	197.1	197.2 *s*	207.4 *s*	67.1 *d*	70.0 *d*
5	35.1	n *t*	43.9	44.0 *t*	43.7 *t*	39.9	n *t*	39.7 *t*	38.6 *t*	25.2 *t*
6	36.2	36.3 *t*	72.4	72.7 *d*	71.2 *d*	82.7	82.8 *d*	81.1 *d*	34.6 *t*	35.3 *t*
7	40.0	40.0 *t*	38.7	38.8 *t*	39.1 *t*	38.7	38.8 *t*	39.2 *t*	35.3 *t*	35.3 *t*
8	65.9	65.9 *t*	65.7	65.8 *t*	66.5 *t*	65.4	65.6 *t*	66.5 *t*	62.5 *t*	62.5 *t*
Me						57.5	57.5 *q*	57.8 *q*		21.4 *q*
CO										170.6 *s*
1′	104.6	104.7 *d*	104.6	104.7 *d*		104.6	104.7 *d*		94.9 *d*	95.1 *d*
2′	75.0	n *d*	75.1	75.1 *d*		75.1	n *d*		37.4 *t*	37.5 *t*
3′	78.5	78.5 *d*	78.6	78.6 *d*		78.6	n *d*		17.5 *t*	17.5 *t*
4′	71.6	n *d*	71.6	n d		71.6	n *d*		13.9 *q*	14.0 *q*
5′	78.4	n *d*	78.5	78.5 *d*		78.6	n *d*			
6′	62.6	n *t*	62.7	62.7 *t*		62.7	n *t*			

*In DMSO-d_6.
††Interchangeable values.
n = Not resolved.

oriented β. ^{1}H NMR spectra of **19a** and **20a** (*J* value of H-6, see Experimental) indicated that the configuration of C-6 was the same, which was also supported by the similarities of ^{13}C NMR spectra of mother compounds, **19** and **20**. Thus, the structures of **19**, **20** and their derivatives, were deduced as illustrated. It should be noted that both compounds are diastereomeric mixtures of enantiomeric aglycones, but not of diastereomeric aglycones. Accordingly, the derivatives, **19a** and **20a** are racemic but not diastereomeric. Only one of the diastereomeric forms is shown in the structures for **19** and **20**.

Compound **21**, $C_{12}H_{22}O_3$, seemed to be a related cyclohexylethanoid compound but its ^{13}C NMR showed an additional four signals. Among them, δ94.9 (*d*) was characteristic for an acetal carbon and 13.9 (*q*) was assigned to a methyl carbon. Acetylation of **21** afforded the monoacetate (**21a**). By means of ^{1}H–^{1}H and ^{1}H–^{13}C COSY experiments on **21a**, the partial structure (illustrated by thick lines in Fig. 1) was established. The HMBC spectrum clarified the correlation shown by arrows in Fig. 1. Since the suggested structure of **21** corresponded to the butanal acetal of **12**, **12** was reacted with 1-butanal in the presence of cation ion-exchange resin to afford **21**. Thus, the structure of **21** was established as shown. Since the optical rotation of natural **21** was nearly zero, it might be a racemic mixture.

Biogenesis-like transformation of **1** to **10** and its related cyclohexylethanoids isolated from *Forsythia suspensa* (Oleaceae) was reported and a plausible biogenetic route was suggested [8]. It is interesting to note that among the 23 compounds we isolated from *M. hortensis*, seven compounds (**1** and **7**–**12**) were common to both

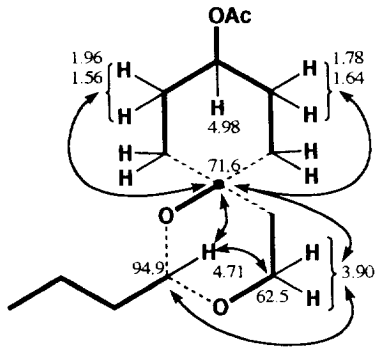

Fig. 1. Partial structure (thick line) and HMBC correlation (arrow) of **21a**.

species. If the biogenesis in both species is the same, our compounds can be reasonably interpolated into the proposed biogenetic route. An enone compound **18** could be the intermediate from **7** to **9**, which could be converted to **12** via **13** (glucoside of **12**). New bicyclic cyclohexylethanoids (**14**–**17**) could be biogenetically placed as shown in Fig. 2. Also 6-oxygenated compounds (**19** and **20**) could be derived from **7**.

Some of the compounds we isolated partially racemized and partially diastereomeric. Since our isolation procedure did not use strong acid or excessive heating, they seem to be natural products biosynthesized by various enzymes exhibiting different enzyme selectivity. This point needs to be clarified.

EXPERIMENTAL

Mps: uncorr. ^{1}H NMR and ^{13}C NMR (TMS as int. standard): 400 and 100 MHz, respectively in pyridine-d_5, unless otherwise stated. EIMS were recorded at 70 eV, FABMS: glycerol matrix.

Plant material. Millingtonia hortensis was collected in the surburbs of Khon Kaen City, Thailand. A voucher specimen is deposited at the Herbarium of Khon Kaen University, Thailand.

Extract and isolation. Dried flowers (300 g) were extracted with MeOH at room temp. to give 149 g of extract, part (71 g) of which was suspended in H_2O and

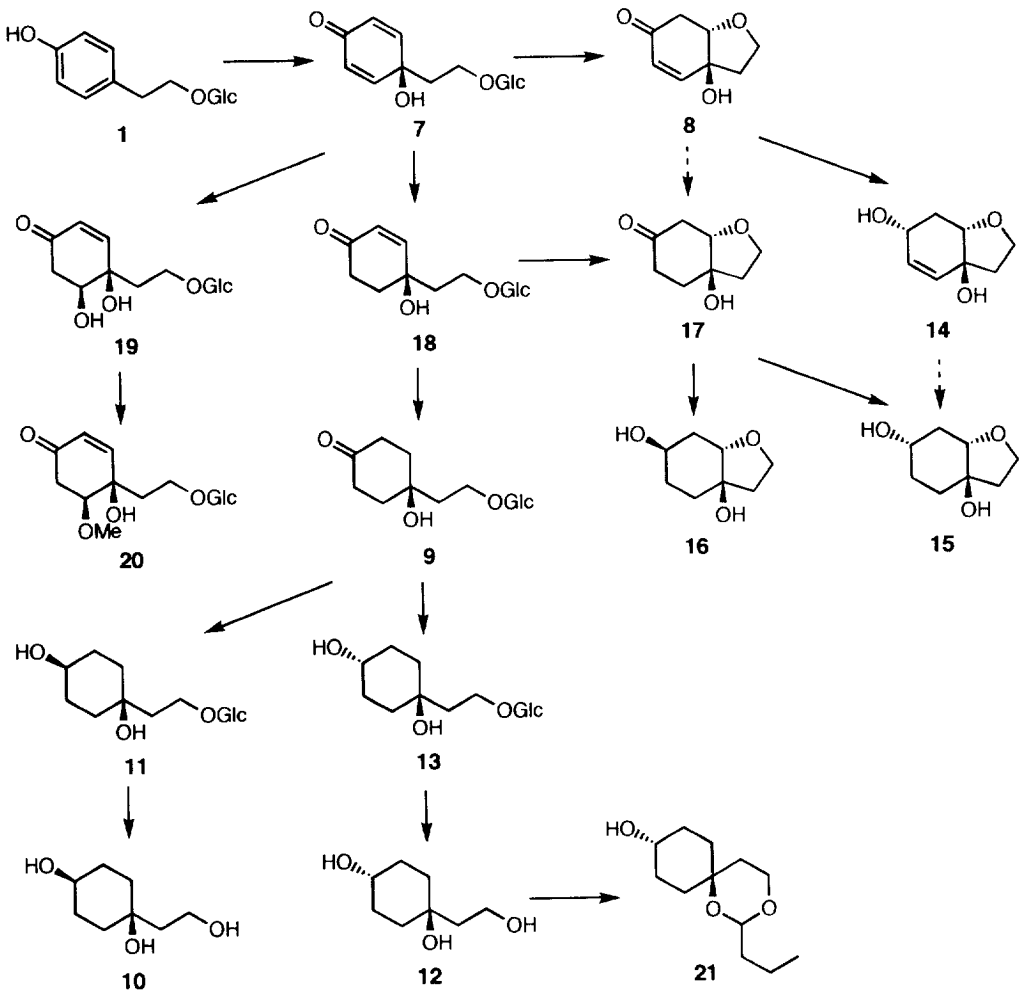

Fig. 2. Probable biogenesis of cyclohexylethanoids.

chromatographed on a column of Diaion HP-20 (Mitsubishi Chem. Ind.) eluted successively with H_2O, 40% MeOH, 80% MeOH, MeOH and Me_2CO. The 40% eluate was chromatographed on silica gel repeatedly followed by HPLC (YMC D-ODS-10: 20 mmϕ × 250 mm and TSK Amide 80:21.5 mmϕ × 300 mm) using MeOH–H_2O and/or MeCN–H_2O systems at a flow rate of 6 ml min^{-1} to afford **1** (254 mg), **9** (16 mg), **20** (24 mg), **7** (124 mg), **11** (26 mg), **13** (4 mg), **19** (7 mg) and **18** (21 mg).

The other part (79 g) of the first MeOH extract was suspended in H_2O and extracted with Et_2O to remove a nonpolar fr. (8.3 g). The aq. extract was chromatographed on a column of Diaion HP-20 eluted successively with H_2O, 40% MeOH, 80% MeOH, MeOH and Me_2CO. The aq. eluate was extracted with *n*-BuOH and the *n*-BuOH extract chromatographed on silica gel eluting with EtOAc–EtOH–H_2O to give 2 frs. From fr. 1, **21** (45 mg) was obtained. From fr. 2, **12** (428 mg), **14** (148 mg), **15** (13 mg), **10** (33 mg), **17** (18 mg) and **16** (147 mg) were obtained by MPLC (ODS AQ 120, YMC: 20 mmϕ × 150 mm) at 1.5 ml min^{-1} followed by HPLC (ODS and Polyamine; YMC). The 40% MeOH eluate was subjected to silica gel CC using $CHCl_3$–MeOH–H_2O to give frs 1–3. From fr. 1, **8** (44 mg) and **6** (7 mg) were obtained by MPLC (ODS) and Sephadex LH-20 CC. Fr. 2 afforded **5** (7 mg), **1** (280 mg), **3** (35 mg) and **2** (18 mg) after repeated silica gel CC and MPLC (ODS) and/or HPLC (ODS). Fr. 3 yielded **4** (158 mg) after silica gel CC.

Salidroside (**1**). Crystals from MeOH–$CHCl_3$, mp 158–159°. $[\alpha]_D^{18}$ −22.2° (H_2O; *c* 1.36). ^{13}C NMR: (from C-1 to C-8): δ 129.5, 130.5, 116.2, 157.4, 116.2, 130.5, 36.0, 71.2; (from Glc-1 to 6) 104.8, 75.2, 78.6, 71.7, 78.6, 62.8; ^{1}H NMR: δ 7.19 (2H, *d*, *J* = 8.4 Hz, H-2,6), 7.12 (2H, *d*, *J* = 8.4 Hz, H-3,5), 4.92 (1H, *d*, *J* = 7.9 Hz, H-1′), 4.33 and 3.92 (1H each, *dt*, *J* = 9.3 and 7.6 Hz, H-8), 3.01 (2H, *d*, *J* = 7.6 Hz, H-7) [6].

Compound **2**. Oil. $[\alpha]_D^{16}$ −59° (MeOH; *c* 0.47). ^{13}C NMR δ (from C-1 to 8): 139.5, 128.7, 129.4, 126.4, 129.4, 128.7, 36.7, 70.5; (from Glc-1 to 6): 104.7, 75.0, 78.6, 71.8, 77.1, 68.3; (from Rha-1 to 6): 102.5, 72.3, 72.8, 74.1, 69.8, 18.6; ^{1}H NMR: δ 5.54 (1H, *d*, *J* = 1.7 Hz, Rha-1), 4.85 (1H, *J* = 7.7 Hz, Glc-1) [9].

Compound **3**. Oil. $[\alpha]_D^{18}$ −18.1° (MeOH; *c* 0.54). ^{13}C NMR δ (from C-1 to 8): 130.5, 116.5, 145.6, 147.1, 117.5, 120.5, 36.3, 71.3; (from Glc-1 to 6): 104.7, 75.2, 78.5, 71.6, 78.5, 62.7; ^{1}H NMR: δ 7.21 (1H, *d*, *J* = 1.5 Hz, H-2), 7.18 (1H, *d*, *J* = 8 Hz, H-5), 6.76 (1H, *dd*, *J* = 1.5 and 8 Hz, H-6), 4.89 (1H, *d*, *J* = 7.9 Hz, Glc-1), 3.02 (2H, t, *J* = 7.6 Hz, H-7) [10].

Acteoside (**4**). Powder. $[\alpha]_D^{18}$ −78.1° (MeOH; *c* 2.7). ^{13}C NMR (DMSO-d_6) δ (from C-1 to 8): 129.1, 116.3, 145.0, 143.6, 115.5, 119.6, 35.0, 70.3; (from Glc-1 to 6): 102.3, 74.5, 79.1, 69.2, 74.5, 60.8; (from Rha-1 to 6): 101.2, 70.5, 70.4, 71.7, 68.7, 18.2; (from Caf-1 to 9): 125.5, 114.7, 145.6, 148.5, 115.8, 121.5, 145.0, 113.6, 165.7. ^{1}H NMR (DMSO-d_6) in agreement with lit. values [11].

Compound **5**. Powder. $[\alpha]_D^{17}$ −50° (MeOH; *c* 0.40). ^{13}C NMR (DMSO-d_6) δ (from C-1 to 9): 130.7, 127.1, 116.3, 156.7, 116.3, 127.1, 128.8, 128.0, 61.6; (from Glc-1 to 6): 100.4, 73.2, 77.0, 69.7, 76.6, 60.7; ^{1}H NMR (DMSO-d_6): δ 7.34 (2H, *d*, *J* = 8.7 Hz, H-3, 5), 6.97 (2H, *d*, *J* = 8.7 Hz, H-2, 6), 6.48 (1H, *br d*, *J* = 15.9 Hz, H-7), 6.24 (1H, *dt*, *J* = 15.9 and 5.2 Hz, H-8), 5.30 (1H, *d*, *J* = 4.8 Hz, OH), 5.09 (1H, *d*, *J* = 4.8 Hz, OH), 5.02 (1H, *d*, *J* = 5.1 Hz, OH), 4.84 (1H, *d*, *J* = 7.5 Hz, H-1′), 4.81 (1H, *t*, *J* = 5.2 Hz, OH-9), 4.56 (1H, *t*, *J* = 5.8 Hz, OH-6′), 4.08 (2H, *br t*, *J* = 5.2 Hz, H-9) [12].

β-D-*Glucosyl isoeugenol* (**6**). Powder. $[\alpha]_D^{20}$ −42° (MeOH; *c* 0.40). ^{13}C NMR (DMSO-d_6) δ (from C-1 to 8): 132.8, 110.4, 143.0, 147.2, 116.5, 119.2, 131.2, 124.0, 18.3; 55.9 (OMe); (from Glc-1 to 6): 102.2, 74.8, 78.8, 71.2, 78.8, 62.3; ^{1}H NMR (DMSO-d_6): δ 7.52 (1H, *d*, *J* = 8.3 Hz, H-5), 7.09 (1H, *d*, *J* = 2.0 Hz, H-2), 6.95 (1H, *dd*, *J* = 2.0 and 8.3 Hz, H-6), 6.35 (1H, *dq*, *J* = 15.8 and 1.6 Hz, H-7), 6.10 (1H, *dq*, *J* = 15.8 and 6.6 Hz, H-8), 5.66 (1H, *d*, *J* = 6.6 Hz, H-1′), 3.74 (3H, *s*, 3-OMe), 1.73 (3H, *dd*, *J* = 1.6 and 6.6 Hz, H-9) [12].

Cornoside (**7**). Oil. $[\alpha]_D^{25}$ −19.5° (EtOH; *c* 1.5). ^{1}H NMR: δ 7.24 and 7.12 (each 1H, *dd*, *J* = 2.9 and 10.4 Hz, H-2 and H-6), 6.26 and 6.23 (each 1H, *dd*, *J* = 2.9 and 10.4 Hz, H-2 and H-6), 6.26 and 6.23 (each 1H, *dd*, *J* = 2.9 and 10.4 Hz, H-3 and H-5), 4.89 (1H, *d*, *J* = 7.9 Hz, Glc-1), 4.42 and 4.04 (each 1H, *dt*, *J* = 9.9 and 6.8 Hz, H-8), 2.30 (2H, *t*, *J* = 6.8 Hz, H-7). ^{13}C NMR: Table 1.

Rengyolone (**8**). Oil. $[\alpha]_D^{19}$ −1.8° (MeOH; *c* 2.4) (lit. [14] +0.26° also racemic); no Cotton effect in CD. ^{1}H NMR: δ 6.96 (1H, *dd*, *J* = 1.8 and 10.1 Hz, H-6), 6.16 (1H, *dd*, *J* = 0.6 and 10.1 Hz, H-5), 4.51 (1H, *ddd*, *J* = 1.8, 4.3 and 4.8 Hz, H-2), 4.07 (1H, *ddd*, *J* = 5.6, 8.5 and 8.7 Hz, H-8a), 3.89 (1H, *ddd*, *J* = 7.2, 7.8 and 8.5 Hz, H-8b), 3.00 (1H, *dd*, *J* = 4.3 and 16.6 Hz, H-3b), 2.87 (1H, *ddd*, *J* = 0.6, 4.8 and 16.6 Hz, H-3a), 2.46 (1H, *ddd*, *J* = 7.2, 8.7 and 12.7 Hz, H-7a), 2.21 (1H, *ddd*, *J* = 5.6, 7.8 and 12.7 Hz, H-7b). ^{13}C NMR: Table 1.

Rengyoside B (**9**). Oil. $[\alpha]_D^{18}$ −17.6° (EtOH; *c* 0.80). ^{1}H NMR: δ 4.87 (1H, *d*, *J* = 7.7 Hz, H-1′). ^{13}C NMR: Table 1.

Rengyol (**10**). Powder. ^{1}H NMR: δ 4.20 (2H, *t*, *J* = 6.8 Hz, H-8), 3.91 (1H, *tt*, *J* = 4.0 and 10.1 Hz, H-4), 2.01 (2H, *t*, *J* = 6.8 Hz, H-7). ^{13}C NMR: Table 1.

Rengyoside A (**11**). Oil. $[\alpha]_D^{17}$ −21° (MeOH; *c* 0.18). ^{1}H NMR: δ 4.92 (1H, *d*, *J* = 7.7 Hz, H-1′). ^{13}C NMR: Table 1.

Isorengyol (**12**). Crystals from MeOH–$CHCl_3$, mp 103–105°. ^{1}H NMR: δ 4.24 (2H, *t*, *J* = 6.5 Hz, H-8), 2.14 (2H, *t*, *J* = 6.5 Hz, H-7). ^{13}C NMR: Table 1.

Compound **13**. Oil. $[\alpha]_D^{17}$ −21.0° (MeOH; *c* 0.4), HR-FAB-MS (negative) $[M-H]^-$ *m/z* 321.1565, $C_{14}H_{26}O_8$-H requires 321.1550. ^{1}H NMR: δ 4.87 (1H *d*, *J* = 7.7 Hz, H-1′), 4.55 and 4.13 (1H, each, *dt*, *J* = 9.8 and 7.0 Hz, H-8), 3.9–4.6 (7H, H-4 and H-2′–6′), 1.7–2.3 (10H, H-2, 3, 5, 6 and 7). ^{13}C NMR: Table 1.

Enzymatic hydrolysis of **13**. An aq. soln of **13** (1 mg in 1 ml) was incubated with almond β-glucosidase (Sigma, 1 mg) at 37° for 14 hr. The reaction mixt. was treated with Molcut II UFP1 LCC BK to remove protein. The filtrate was analysed by TLC (silica gel $CHCl_3$–MeOH–H_2O,

6:4:1, R_f = 0.54 for **12** and 0.18 for glucose) and HPLC (YMC-pak R-ODS-10 S-5 120A, 4.0 mm ID × 25 cm eluting with MeOH–H_2O (3:97), R_t = 7.4 min for **12**) to identify **12** and glucose.

Compound **14**. Crystals from $CHCl_3$–benzene, mp 97–98°. $[\alpha]_D^{21}$ + 102° (MeOH; *c* 1.2). HR-FAB-MS (negative) $[M-H]^+$ *m/z* 155.0690, $C_8H_{12}O_3$ – H requires 155.0708. ^{1}H NMR: δ6.82 (1H, *br s*, 1-OH), 6.31 (1H, *br d*, *J* = 5.6 Hz, 4-OH), 6.18 (1H, *ddd*, *J* = 1.1, 1.9 and 10.1 Hz, H-5), 6.12 (1H, *dd*, *J* = 1.9 and 10.1 Hz, H-6), 4.61 (1H, *br s*, changed to 4.63 *dddd*, *J* = 1.9, 1.9, 4.8 and 9.6 Hz on addition of D_2O, H-4), 4.52 (1H, *dd*, *J* = 4.9 and 11.9 Hz, H-2), 4.34 (1H, *ddd*, *J* = 6.6, 7.9 and 9.8 Hz, H-8a), 4.14 (1H, *ddd*, *J* = 3.0, 7.9 and 8.4 Hz, H-8b), 2.58 (1H, *dddd*, *J* = 1.1, 4.8, 4.9 and 12.3 Hz, H-3a), 2.27 (1H, *ddd*, *J* = 3.0, 6.6 and 12.5 Hz, H-7a), 2.17 (1H, *ddd*, *J* = 8.4, 9.8 and 12.5 Hz, H-7b), 2.05 (1H, *ddd*, *J* = 9.6, 11.0 and 12.3 Hz, H-3b). ^{13}C NMR: Table 1.

Oxidation of **14** *to* **8**. Compound **14** (50 mg) was oxidized with CrO_3 (100 mg) in dry pyridine (2 ml) at room temp. for 15 hr. Usual work-up afforded **8** (8 mg). $[\alpha]_D^{15}$ + 58° (MeOH; *c* 0.53). ^{1}H NMR and ^{13}C NMR identical to naturally obtained **8**.

Catalytic hydrogenation of **14** to **15**. Compound **14** (50 mg) in EtOH was hydrogenated with 5% Pd/C to afford **15** (36 mg) as an oil. $[\alpha]_D^{18}$ –23° (MeOH; *c* 1.5). ^{1}H NMR and ^{13}C NMR data identical to natural **15** (*vide ante*). Compound **15** derived from **14** was acetylated with Ac_2O–pyridine at room temp. for 4 hr to afford **15a** (7 mg) as an oil. $[\alpha]_D^{19}$ –22° ($CHCl_3$; *c* 0.47). FAB-MS (negative) *m/z* 199 $[M-H]^-$. ^{1}H NMR ($CDCl_3$): δ4.76 (1H, *dddd*, *J* = 4.1, 4.1, 10.0 and 10.4 Hz, H-4), 4.06 (1H, *ddd*, *J* = 8.3, 8.3 and 8.6 Hz, H-8a), 4.00 (1H, *ddd*, *J* = 4.2, 8.6 and 9.5 Hz, H-8b), 3.77 (1H, *dd*, *J* = 6.2, 9.6 Hz, H-2), 2.21 (1H, *ddd*, *J* = 8.3, 9.5 and 13.2 Hz, H-7a), 2.11 (1H, *ddd*, *J* = 4.3, 9.1 and 14.1 Hz, H-6a), 2.09 (1H, *dddd*, *J* = 2.0, 4.1, 6.2 and 13.1 Hz, H-3a), 2.02 (3H, *s*, Ac), 1.95 (1H, *ddddd*, *J* = 2.0, 4.1, 4.3, 9.1 and 13.2 Hz, H-5a), 1.85 (1H, *ddd*, *J* = 4.2, 8.3 and 13.2 Hz, H-7b), 1.72 (1H, *ddd*, *J* = 4.3, 12.1 and 14.1 Hz, H-6b), 1.48 (1H, *dddd*, *J* = 4.3, 10.0, 12.1 and 13.2 Hz, H-5b), 1.46 (1H, *ddd*, *J* = 9.6, 10.4 and 13.1 Hz, H-3b).

Compound **15**. Oil. $[\alpha]_D^{16}$ – 6.0° (MeOH; *c* 0.57). HR-FAB-MS (negative) $[M-H]^+$ *m/z* 157.0872, $C_8H_{14}O_3$ – H requires 157.0865. ^{1}H NMR: δ4.25 (1H, *ddd*, *J* = 8.1, and 8.4 Hz, H-8a), 4.20 (1H, *dd*, *J* = 6.1, 9.2 Hz, H-2), 4.07 (1H, *ddd*, *J* = 3.7, 8.1 and 9.3 Hz, H-8b), 4.02 (1H, *dddd*, *J* = 3.7, 3.9, 9.3 and 9.9 Hz, H-4), 2.44 (1H, *dddd*, *J* = 2.0, 3.9, 6.1 and 13.0 Hz, H-3a), 2.30 (1H, *ddd*, *J* = 4.0, 7.6 and 14.0 Hz, H-6a), 2.29 (1H, *ddd*, *J* = 8.4, 9.3 and 12.5 Hz, H-7a), 2.15 (1H, *ddddd*, *J* = 2.0, 3.7, 4.2, 7.6 and 13.0 Hz, H-5a), 2.00 (1H, *ddd*, *J* = 4.2, 11.5 and 14.0 Hz, H-6b), 1.98 (1H, *ddd*, *J* = 3.7, 8.1 and 12.5 Hz, H-7b), 1.83 (1H, *ddd*, *J* = 9.2, 9.9 and 13.0 Hz, H-3b), 1.74 (1H, *dddd*, *J* = 4.0, 9.3, 11.5 and 13.0 Hz, H-5b). ^{13}C NMR: in Table 1.

Compound **16**. Powder. $[\alpha]_D^{13}$ –2.6° (MeOH; *c* 1.7). HR-FAB-MS (negative) $[M-H]^-$ *m/z* 157.0865, $C_8H_{14}O_3$-H requires 157.0865. ^{1}H NMR: δ4.35 (1H, *dddd*, *J* = 4.0, 4.0, 9.4 and 9.5 Hz, H-4), 4.25 (1H, *dd*, *J* = 3.9, 4.1 Hz, H-2), 4.06 (1H, *ddd*, *J* = 4.8, 8.5 and 9.7 Hz, H-8a), 3.95 (1H, *ddd*, *J* = 7.3, 8.5 and 8.4 Hz, H-8b), 2.43 (1H, *dddd*, *J* = 1.6, 3.9, 4.0 and 13.9 Hz, H-3a), 2.24 (1H, *ddd*, *J* = 4.1, 9.5 and 13.9 Hz, H-3b). ^{13}C NMR: Table 1.

Compound **17**. Oil. $[\alpha]_D^{11}$ – 5.6° (MeOH; *c* 0.95), no Cotton effect in CD spectrum. HR-FAB-MS (negative) $[M-H]^-$ *m/z* 155.0702, $C_8H_{12}O_3$ -H requires 155.0708. ^{1}H NMR 4.28 (1H, *dd*, *J* = 4.3, and 4.5 Hz, H-2), 3.93 (2H, *m*, H-8), 2.95 (1H, *dd*, *J* = 4.5 and 15.8 Hz, H-3), 2.78 (1H, *ddd*, *J* = 0.9, 4.3 and 15.8 Hz, H-3), 2.66 (1H, *ddd*, *J* = 4.8, 8.4 and 16.8 Hz, H-5), 2.35 (1H, *dddd*, *J* = 0.9, 4.9, 8.6 and 16.8 Hz, H-5), 2.24 (1H, *ddd*, *J* = 5.3, 6.2 and 12.6 Hz, H-7a), 2.21 (2H, *m*, H-6), 2.07 (1H, *ddd*, *J* = 8.3, 8.3 and 12.6 Hz, H-7b). ^{13}C NMR: Table 1.

Compound **18**. Oil. HR-FAB-MS (negative) $[M-H]^-$ *m/z* 317.1248, $C_{14}H_{24}O_8$ -H requires 317.1237. UV λ_{max}^{MeOH} 219 nm (log ε = 3.9); ^{1}H NMR: δ7.16 and 7.10 (each 1H, *d*, *J* = 10.3 Hz, H-2), 6.00 and 5.99 (each 1H, *d*, *J* = 10.3 Hz, H-3), 4.92 (1H × 2, *d*, *J* = 7.7 Hz, H-1'). ^{13}C NMR: Table 1.

Enzymatic hydrolysis of **18**. An aq. soln of **18** (10 mg in 1 ml) was incubated with almond β-glucosidase (Sigma, 10 mg) at 37° for 10 hr. The reaction mixt. was chromatographed on silica gel (EtOAc–EtOH–H_2O, 8:2:1) to afford **17**, identified by ^{1}H NMR.

Compound **19**. Oil. HR-FAB-MS (negative) $[M-H]^-$ *m/z* 333.1199. $C_{14}H_{22}O_9$ -H requires 333.1186. UV λ_{max}^{MeOH} 217 nm (log ε = 3.8); ^{1}H NMR: δ7.15 and 7.06 (each 1H, *dd*, *J* = 1.6 and 10.3 Hz, H-2), 6.11 and 6.11 (each 1H, *d*, *J* = 10.3 Hz, H-3), 4.94 and 4.92 (each 1H, *d*, *J* = 7.7 Hz, H-1'). ^{13}C NMR: Table 1.

Enzymatic hydrolysis of **19**. An aq. soln of **19** (6 mg in 1 ml) was incubated with almond β-glucosidase (Sigma, 6 mg) at 37° for 24 hr. The reaction mixt. was chromatographed on silica gel (EtOAc) to afford **19a** (2 mg) as an oil. HR-EI-MS $[M]^+$ *m/z* 172.0782, $C_8H_{12}O_4$ requires 712.0736. ^{1}H NMR: δ4.34 (1H, *dd*, *J* = 3.5 and 6.8 Hz, H-6), 4.32 (1H, *dd*, *J* = 3.8 and 4.4 Hz, H-2), 3.19 (1H, *dd*, *J* = 4.4 and 16.4 Hz, H-3a), 2.97 (1H, *dd*, *J* = 6.8 and 16.6 Hz, H-5a), 2.83 (1H, *dd*, *J* = 3.5 and 16.6 Hz, H-5a), 2.80 (1H, *dd*, *J* = 3.8 and 16.4 Hz, H-3b), 4.3 (2H, *m*, H-8), 2.2–2.3 (2H, *m*, H-7). ^{13}C NMR: Table 1.

Compound **20**. Oil. HR-FAB-MS (negative) $[M-H]^-$ *m/z* 347.1342, $C_{15}H_{24}O_9$-H requires 347.1342. UV λ_{max}^{MeOH} 220 nm (log ε = 4.1). ^{1}H NMR: δ7.07 and 6.97 (each 1H, *dd*, *J* = 1.6 and 10.3 Hz, H-2), – 6.04 and 6.03 (each 1H, *d*, *J* = 10.3 Hz, H-3), 4.93 and 4.92 (each 1H, *d*, *J* = 7 Hz, H-1'), 3.33 and 3.30 (each 3H, *s*, 6-OMe). ^{13}C NMR; Table 1.

Enzymatic hydrolysis of **20**. An aq. soln of **20** (12 mg in 2 ml) was incubated with almond β-glucosidase (Sigma, 12 mg) at 37° for 24 hr. The reaction mixt. was chromatographed on silica gel (EtOAc) to afford **20a** (2 mg) as an oil. HR-EI-MS $[M]^+$ *m/z* 186.0892, $C_9H_{14}O_4$ requires 186.0892. ^{1}H NMR: δ4.22 (1H, *dd*, *J* = 3.8 and 4.7 Hz, H-2), 3.9–4.0 (2H, *m*, H-8), 3.64 (1H, *dd*, *J* = 3.3 and 6.5 Hz, H-6), 3.32 (3H, *s*, 6-OMe), 3.01 (1H, *dd*, *J* = 4.7 and 16.2 Hz, H-3a), 2.97 (1H, *dd*, *J* = 6.5 and 16.7 Hz, H-5a), 2.73 (1H, *dd*, *J* = 3.3 and 16.7 Hz,

H-5b), 2.72 (1H, *dd*, J = 3.8 and 16.2 Hz, H-3b), 2.1–2.2 (2H, *m*, H-7). ^{13}C NMR: in Table 1.

Compound **21**. Oil. HR-FAB-MS (negative) $[M - H]^+$ m/z 213.1499, $C_{12}H_{22}O_3$-H requires 213.1491. ^{1}H NMR ($CDCl_3$): δ4.72 (1H, *t*, J = 5.2 Hz, H-1′), 3.95 (1H, *m*, H-4), 3.8–3.9 (2H, *m*, H-8), 1.3–2.0 (15H), 0.92 (3H, *t*, J = 7.4 Hz, H-4′). ^{13}C NMR: Table 1.

Synthesis of **21**. Compound **12** (40 mg in 5 ml dioxane) was reacted with 1-butanal (50 μl) in the presence of ion-exchange resin (Dowex 50W-X8) and $CaSO_4$ at room temp. for 1 hr. The reaction mixt. was purified by HPLC to afford **21** (36 mg).

Acetylation of **21**. Compound **21** (12 mg) was acetylated with Ac_2O and pyridine to give the acetate (**21a**). $[\alpha]_D^{19}$ + 2.1° ($CHCl_3$; c 0.67). FAB-MS m/z 255 $[M - H]^-$. ^{1}H NMR ($CDCl_3$): δ4.98 (1H, *m*, H-4), 4.72 (1H, *t*, J = 5.3 Hz, H-1′), 3.9 (2H, *m*, H-8), 2.05 (3H, *s*, Ac), 1.2–2.2 (14H), 0.92 (3H, *t*, J = 7.3 Hz, H-4′). ^{13}C NMR: Table 1.

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