KINGINOSIDE, A NEW ACYL GROUP CARRYING IRIDOID BIOSIDE FROM LONICERA MORROWII

Norio AIMI,* Hideo SEKI, Shin-ichiro SAKAI, and Joju HAGINIWA

Faculty of Pharmaceutical Sciences, Chiba University, 1-33 Yayoi-cho, Inage-ku, Chiba 263, Japan

A new iridoid glycoside , kinginoside, was isolated from *Lonicera morrowii* (Caprifoliaceae). Its structure was deduced to be sweroside-6'-*O*-(4"-*O*-feruloyl)-α-L-rhamnoside mainly by spectroscopic analysis. The structure was confirmed by chemical synthesis of the corresponding acetate from sweroside of known structure.

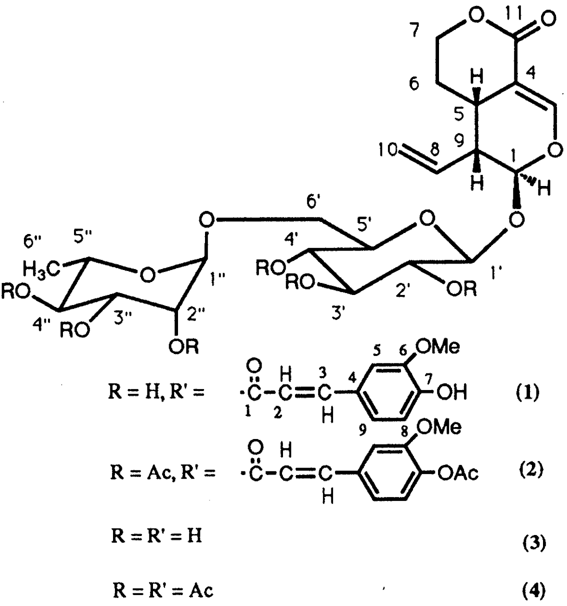
KEYWORDS kinginoside; *Lonicera morrowii*; Caprifoliaceae; iridoid glycoside; structure determination; chemical correlation

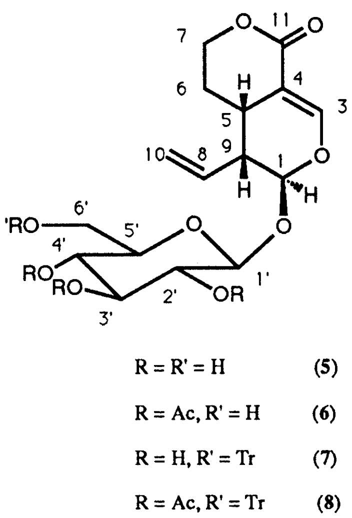
Lonicera morrowii is known as a source plant of secologanin, an iridoid glucoside of particular importance in biosynthesis of various types of monoterpenoid indole alkaloids. From this plant three other iridoid glycosides, morroniside, kingiside, and sweroside, were found.1) Recently the constituents of its fresh fruits, which are mentioned as toxic in authoritative books, have been thoroughly studied and six known iridoid glucosides and chlorogenic acid isolated.2) On our renewed study of the constituents of this plant we now found a new iridoid glycoside, kinginoside (**1**). This compound was proved to belong to a rare class of iridoids composed of seco-type iridoid aglycone, a biose unit, and an aroyl group. The structure of **1** was elucidated by use of spectral methods and regio- and stereoselective synthesis of kinginoside acetate (**2**).

The stem part of *Lonicere morrowii* was extracted with hot methanol, and the extract was partitioned between ether and water. The water layer was extracted with 1-butanol, and the butanol-soluble part was chromatographed over silica gel. The fraction eluted with $CHCl_3$-MeOH-H_2O was purified repeatedly by open column chromatography over silica gel and normal phase medium pressure liquid chromatography to give kinginoside (**1**)3) as an amorphous powder. High-resolution FAB-MS indicated the molecular formula to be $C_{32}H_{40}O_{16}$ (Observed m/z; 681.239 $(M+H)^+$, Calcd. for $C_{32}H_{41}O_{16}$, m/z; 681.239).

The UV spectrum of **1** showed the absorption maxima at 226, 230, 280, and 308(sh) nm and revealed the presence of a feruloyl residue as well as a β-alkoxy acrylic ester chromophore typical of iridoid moiety. This finding was chemically proved to be correct by the treatment of **1** with sodium methoxide, when ferulic acid and desferuloylkinginoside (**3**) were obtained. Compound **3** was shown to have the molecular formula $C_{22}H_{32}O_{13}$ by high-resolution FAB-MS (observed m/z 527.174 (100%); calcd. for $C_{22}H_{32}O_{13}Na$, m/z 527.174), suggesting it was composed of an iridoid aglycone, a hexose and a pentose unit. At this stage kinginoside (**1**) was thought to be one analogue of pericymenoside as reported in the literature4), $C_{33}H_{44}O_{18}$, which had been isolated from a species of genus *Lonicera*. But the following structural work indicated that they belong to different structural types.

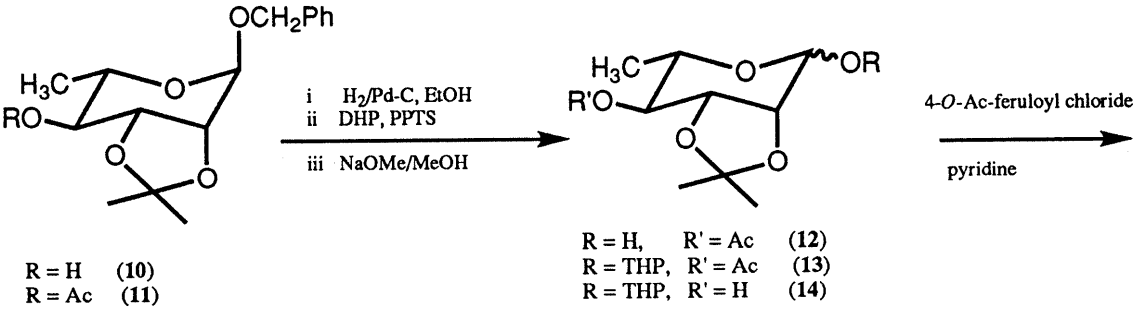
^{13}C-NMR spectra of kinginoside and its derivatives showed the molecule to consist of sweroside aglycone, a rhamnoglycoside moiety, and a feruloyl group. Thus the ^{13}C-NMR signals of iridoid part of **1** are almost superimposable on those of the aglycone part of sweroside (**5**). The chemical shifts of the carbons C1'-C4' of the glucose part of **1** were also quite similar to those of sweroside (**5**) but C5' (δ 77.2) and C6' (δ 67.4) of **1** were shown to be highfield and lowfield shifts, respectively, compared to the corresponding signals of the glucose part of **5** (**5**; C5' δ 78.1; C6' δ 62.6). This observation clearly indicated that the second sugar in **1** is linked at the C6' position of the glucose part of **5**. Careful inspection of ^{1}H- and ^{13}C-NMR suggested that the second sugar was rhamnose and the glycoside linkage was α-oriented. Furthermore, the feruloyl group was suggested to be at the C4" position by the observed downfield shift of the ^{13}C NMR signal due to C-4" (C4" in **1**; δ 75.6; C-4 in methyl α-rhamnoside; δ 73.9). Thus the structure shown below was deduced to **1**:

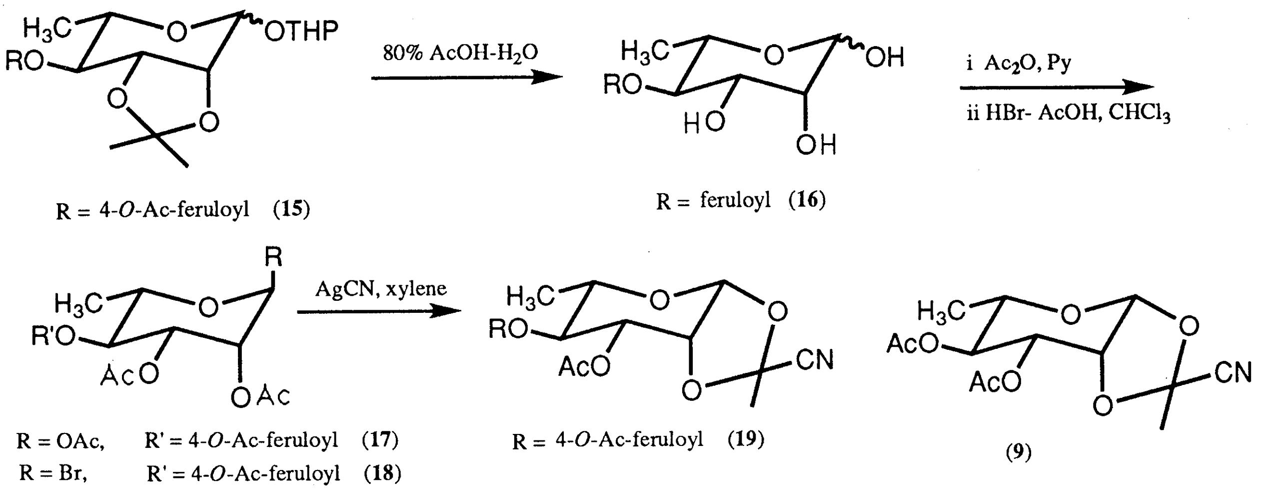




To prove the correctness of this structure assignment, a synthetic study was undertaken. First planned was condensation between 2',3',4'-tri-*O*-acetylsweroside (**6**) and nitril (**9**). To prepare **6**, the primary hydroxyl group in **5** was tritylated to **7** and then **7** was acetylated to **8**. Removal of the trityl group of **8** with HCl (AcCl-MeOH), however, resulted in the formation of a 3:1 mixture of desired **6** and acyl migration products. Therefore direct condensation between **8** and **9** using Betaneli's method[5)] was attempted. Thus **9**, prepared from L-rhamnose through 3 steps, was heated with **8** in methylene chloride in the presence of triphenylmethilium perchlorate and the expected condensation product (**4**) was obtained with the yield of 33 %.

Then the synthesis of a compound having a feruroyl moiety at the correct position was undertaken. Thus 1-α-*O*-benzyl-L-rhamnose-2,3-*O*-acetonide (**10**)[6)] was acetylated to **11**. The resulting benzylether was converted to THP derivative (**13**) by use of dihydropyrane (DHP) and pyridinium *p*-toluenesuphonate (PPTS). After introducing feruloyl group to C-4 position in acetonide (**14**), THP and isopropylidene groups were removed with 80 % AcOH-H_2O at room temperature and the product (**16**) was acetylated to give **17**. Treatment of **17** with HBr followed by refluxing in xylene with AgCN afforded the desired nitrile (**19**). Condensation between **8** and **19** was performed by stirring the solution of the two compounds in dry





R = 4-*O*-Ac-feruloyl (**15**)

R = feruloyl (**16**)

R = OAc, R' = 4-*O*-Ac-feruloyl (**17**)

R = Br, R' = 4-*O*-Ac-feruloyl (**18**)

R = 4-*O*-Ac-feruloyl (**19**)

(**9**)

methylene chloride in the presence of triphenylmethylium perchlorate for 66 h. at room temperature. Final treatment of the resulting product with Ac_2O, Py. gave rise to the desired **2** (32%), which was shown to be identical (EI-MS, IR, ^{1}H-NMR) with kinginoside hexaacetate (**2**) derived from natural **1**.

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3) A colorless amorphous powder, $C_{32}H_{40}O_{16}$, HR-FAB-MS, m/z; Found, 681.239 $(M+H)^+$, Calcd. for $C_{32}H_{41}O_{16}$, 681.239. IR ν_{max}(KBr): 3700 - 3100 (OH); 1710, 1695 (C=O); 1620 (C=C); 1515 cm^{-1}.^{1}H-NMR (270 MHz, CD_3OD) δ; 1.16 (3H, d, J= 6.4 Hz, H_3-6"), 1.55 - 1.75 (3H, m, H-5, 6a, 6b), 2.60 - 2.75 (m, H-9), 3.23 (dd, J= 7.9, 9.5 Hz, H-2'), 3.23 (dd, J= 7.9, 7.9 Hz, H-4'), 3.3 - 3.4 (overlapped with solvent peak, H-3', 5', 2", 3"), 3.75 (dd, J= 11.0, 4.9 Hz, H-6'a), 3.89 (3H, s, H-fer-OMe), 3.95 (m, H-5"), 4.00 (dd, J= 11.0, 2.0 Hz, H-6'b), 4.2 - 4.5 (2H, m, H- 7a, 7b), 4.70 (d, J= 7.9 Hz, H-1'), 4.79 (brs, H-1"), 5.04 (dd, J= 9.5, 9.5 Hz, H-4"), 5.22 - 5.30 (2H, m, H-10a, 10b), 5.44 (d, J= 1.5 Hz, H-1), 5.48 - 5.56 (m, H-8), 6.39 (d, J= 15.9 Hz, H-fer-2), 6.82 (d, J= 8.2 Hz, H-fer-8), 7.09 (dd, J= 8.2, 1.5 Hz, H-fer-9), 7.20 (d, J= 1.5 Hz, H-fer-5), 7.58 (d, J= 2.4 Hz, H-3), and 7.65 (d, J= 15.9 Hz, H-fer-3). ^{13}C-NMR (67.8 MHz, CD_3OD) δ; 18.3 (C-6"), 25.1 (C-6), 27.8 (C-5), 43.1 (C-9), 56.6 (C-fer-OMe), 67.4 (C-6'), 67.9 (C-7), 70.4 (C-5"), 71.2 (C-4'), 72.2 (C-2"), 74.7 (C-3"), 74.8 (C-2'), 75.6 (C-4"), 77.2 (C-5'), 78.3 (C-3'), 97.8 (C-1), 100.9 (C-1'), 102.3 (C-1"),105.3 (C-4), 111.5 (C-fer-5), 116.8 (C-fer-2), 116.8 (C-fer-8), 120.2 (C-10), 126.5 (C-fer-9), 127.1 (C-fer-4), 132.6 (C-8), 145.7 (C-fer-3), 145.7 (C-fer-7), 151.2 (C-fer-6), 152.5 (C-3), 165.0 (C-11), 167.4 (C-fer-CO).

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