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ABSOLUTE STRUCTURE OF NEPETASIDE, A NEW IRIDOID GLUCOSIDE FROM *NEPETA CATARIA*

SHAN XIE, SHINICHI UESATO, HIROYUKI INOUYE, TETSURO FUJITA, FUJIO MURAI,* MOTOKO TAGAWA* and TETSURO SHINGU†

Faculty of Pharmaceutical Sciences, Kyoto University, Sakyo-Ku, Kyoto 606, Japan; *Laboratory of Chemistry, Aichi Medical University, Nagakute, Aichi 480-11, Japan; †Faculty of Pharmaceutical Sciences, Kobe-Gakuin University, Ikawadani, Nishi-Ku, Kobe 673, Japan

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Key Word Index—*Nepeta cataria*; Labiatae; iridoid glucoside; nepetaside.

Abstract—Besides an earlier reported 1,5,9-epideoxyloganic acid, a new iridoid glucoside, nepetaside, has been isolated from the aerial part of *Nepeta cataria*. Its absolute structure has been elucidated based on NMR spectroscopy and chemical conversions.

INTRODUCTION

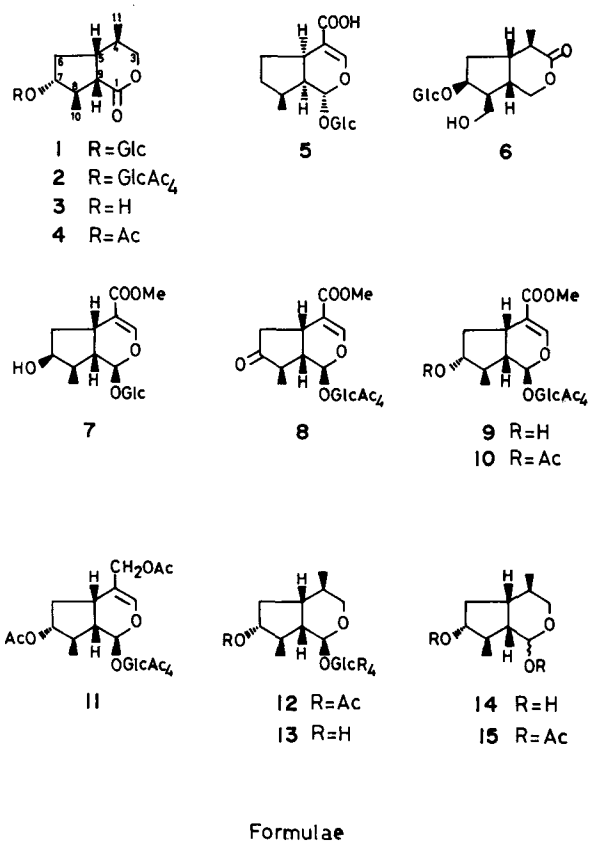
Previous investigations on the constituents of *Nepeta cataria* L. led to the isolation of five iridolactones and two iridoid glucosides: nepetalactone [1], 9-epinepetalactone [2], 5,9-dehydronepetalactone [3] (nepetalactone type), dihydronepetalactone, isodihydronepetalactone [4] (dihydronepetalactone type), 1,5,9-epideoxyloganic acid (**5**) [5] and nepetariaside [6] (glucoside type). This paper deals with the structure elucidation of a new glucoside, nepetaside (**1**), isolated from this plant.

RESULTS AND DISCUSSION

The methanolic extract of the fresh aerial parts of *N. cataria* was successively concentrated, diluted with water, and washed with ethyl acetate. The residue of the aqueous layer was fractionated into nepetaside (**1**) and 1,5,9-epideoxyloganic acid (**5**) by a combination of charcoal and silica gel column chromatography and preparative TLC as described in the Experimental.

Nepetaside (**1**) was obtained as colourless needles, mp 204–205°, $C_{16}H_{26}O_8$ $[\alpha]_D$ −52.5° (MeOH). Its IR spectrum showed absorption bands at 3400–3340 cm^{-1} due to hydroxyl groups and at 1728 cm^{-1} due to a δ-lactonized carbonyl group. The ^1H NMR spectrum of **1** exhibited two doublets at δ1.00 (J=6.6 Hz) and 1.20 (J=6.6 Hz) due to secondary methyl groups, as well as an AB part of an ABX system at 3.95 (*dd*, J=10.0, 10.9 Hz) and 4.20 (*dd*, J=3.4, 10.9 Hz) due to a methylene group in the lactone ring, characteristic of iridolactone glucosides such as villoside (nepetalactone type) [7] and gibboside (**6**) (iridomyrmecin type) [8]. Furthermore, the spectrum showed a doublet at 4.30 (J=7.6 Hz), assignable to the anomeric proton of a β-D-glucopyranosyloxy group. Acetylation of **1** gave tetraacetate **2**, mp 125–126°, $C_{24}O_{34}H_{12}$, $[\alpha]_D$ −35.5° ($CHCl_3$), which showed ^1H NMR signals due to four acetoxy groups (δ2.00–2.10) of the glucose moiety, suggesting that there is no hydroxyl group in the aglycone moiety.

Enzymatic hydrolysis of **1** with β-glucosidase gave D-glucose and aglycone **3**, $C_{10}H_{16}O_3$, $[\alpha]_D$ −24.2° (MeOH). Detailed proton decoupling experiments enabled us to deduce the proton-proton connectivities as shown in Fig. 1. This deduction was corroborated by the spin correlated two-dimensional spectrum (COSY). Subsequently, determination of the relative stereochemistry at asymmetric centres of **3** was accomplished by the inspection of differential nuclear Overhauser effects (NOEs) (Fig. 2). In particular, the presence of NOE between 4-methyl group and 5-H but no NOE between 4-H and 5-H demonstrated a *cis*-disposition for the



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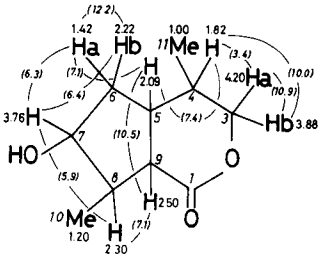

Fig. 1. The ^{1}H NMR spectral data and proton–proton coupling constants for nepetaside aglucone (**3**).

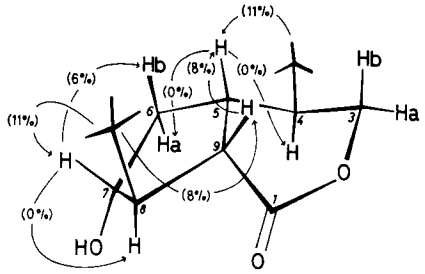

Fig. 2. Observed NOEs for nepetaside aglucone (**3**).

4-methyl group and 5-H. Furthermore, the presence of NOEs between 8-methyl group and 7-H, and 8-methyl group and 9-H, as well as the absence of NOE between 8-H and 7-H, indicated that the 8-methyl group is *cis* to 9-H and to 7-H. Hence the 8-methyl group is *trans* to the 7-hydroxyl group. The ^{13}C NMR spectrum of **3** revealing the presence of 10 carbons (see Experimental) also supports the above-mentioned evidence.

The remaining problems, the position of the glucosyl linkage and the absolute structure of nepetaside (**1**), were surmised on the basis of the glycosylation shift rule, which had been established by the ^{13}C NMR spectroscopic studies of saponins [9–12]: glycosydation of an aglycone causes downfield shifts on both the carbinyl-carbon signal (α-C) of the aglycone alcohol and the anomeric-carbon signal (C-1′) of a sugar moiety. Furthermore, the signals of the α-C of a monoglycoside and C-1′ (the chirality of this carbon is represented by the configuration of the corresponding carbon in a free sugar) of its sugar moiety with different chiralities appear 10–11 ppm and 6–8 ppm downfield, respectively, whereas those with the same chiralities appear 6–7 ppm and 3–4 ppm downfield, respectively, in comparison with the corresponding carbons of a free aglycone and monosaccaride. Application of this rule to gibboside (**6**) and its aglycone (Table 1) showed that the rule is also suitable for such iridoids as those bearing a five membered ring. Thus, ^{13}C chemical shifts for nepetaside (**1**) were compared with those for its aglucone **3** and D-glucose. The C-7 (α-C) and C-1′ of **1** were found to be shifted downfield by 6.5 ppm and 3.9 ppm, respectively, relative to the corresponding carbons of **3** and the D-glucose. These data indicated that (i) the β-D-glucosyloxy group is situated at the C-7 position in **1**; (ii) the C-7 centre, possessing the same *R*-chirality as the C-1′ of a D-glucose, should have a α-hydroxyl group. The absolute configuration of nepetaside (**1**) was therefore deduced to be as presented in the formula, i.e. 4*R*,5*S*,7*R*,8*R* and 9*S*.

Table 1. Chiralities of C-7 (α-C) deduced from glucosylation shifts for nepetaside (**1**) and gibboside (**6**)

	Δδ		Chirality	
	C-7*	C-1′†	C-7	C-1 ‡
1	+6.5	+3.9	*R*	*R*
6	+9.1	+6.3	*S*	*R*

*$\Delta\delta_{C-7} = \delta_{glucoside} - \delta_{aglucone}$.
†$\Delta_{C-1'} = \delta_{glucoside} - \delta$-$_{glucose}$.
‡β-D-Glucose.

In order to confirm the absolute structure **1**, chemical conversion of loganin (**7**) with defined structure into nepetaside (**1**) was attempted. Thus, loganin (**7**) was oxidized with Jones reagent followed by acetylation to yield 7-ketologanin tetraacetate (**8**) [13], which was then reduced with sodium borohydride to 7-epiloganin tetraacetate (**9**) [13]. This compound, after acetylation to 7-epiloganin pentaacetate (**10**) [13], was reduced with $LiAlH_2(OMe)_2$ and the product was acetylated to give the hexaacetate **11**. The acetate was hydrogenated over Pd-C to give compound **12**. Observation of NOE between the 4-methyl group and 5-H in the ^{1}H NMR spectrum of **12** indicated a *cis*-relationship between these groups. The deacetylation product **13** of **12** was successively hydrolysed with Taka-diastase (to aglucone **14**) and acetylated to yield **15**. Conversion of **15** into lactone **3** was accomplished by treating with Jones reagent. Finally, the lactone was glucosidated in the presence of trimethylsilyl trifluoromethanesulphonate to give glucoside **1**. The absolute structure of nepetaside (**1**) was therefore established.

EXPERIMENTAL

General procedures. Mps: uncorr. ^{1}H NMR spectra were recorded at 200 MHz and ^{13}C NMR spectra at 50.10 MHz with TMS as an int. standard. EIMS were measured at 75 eV. Column chromatography was carried out using activated charcoal or silica gel MN-60. Si gel 60 GF_{254} and PF_{254} were used for TLC and prep. TLC, respectively, and spots and bands were detected by irradiation with UV light (254 nm) or by exposure to I_2 vapour. Bands due to free glucosides were extracted with $CHCl_3$–MeOH (7:3), and the ones due to their acetates with $CHCl_3$–MeOH (98:2).

Plant material. Nepeta cataria was collected in the Medicinal Plant Garden, Faculty of Pharmaceutical Sciences, Kyoto University in June, 1982. The voucher specimen of *Nepeta cataria* (S. Xie and S. Uesato No. 1) has been deposited in the Herbarium of the Institute of Botany, Faculty of Science, Kyoto University (KYO), Kitashirakawa-oiwake-cho, Sakyo-Ku, Kyoto 606, Japan.

Isolation of Iridoids. Fresh aerial parts of *N. cataria* (790.0 g) were extracted with boiling MeOH (15 l × 3) for 1 hr. The residue (119.2 g) of the combined extracts was taken up in H_2O, and the insoluable materials were filtered off. The filtrate after washing with AcOEt was concd to yield a residue (83.2 g), which was chromatographed on a charcoal (500 g) column, eluted with MeOH–H_2O with increasing MeOH contents. The 50% MeOH eluate afforded 1,5,9-epideoxyloganic acid (**5**), $[\alpha]_D^{22}$ +80.8°

(MeOH). The residue of the 80% MeOH eluate was purified by prep. TLC and recrystallized from EtOH to yield nepetaside (**1**) (0.10 g) as colourless needles. Mp 204–205°; $[\alpha]_D^{22}$ −52.5° (MeOH; *c* 0.60); IR ν_{max}^{KBr} cm^{-1}: 3400–3340, 1728, 1068; ^{1}H NMR (CD_3OD): δ1.00 (*d*, *J* = 6.6 Hz, H_3-11), 1.20 (*d*, *J* = 6.6 Hz, H_3-10), 3.95 (*dd*, *J* = 10.0, 10.9 Hz, H_b-3), 4.20 (*dd*, *J* = 3.4, 10.9 Hz, H_a-3), 4.30 (*d*, *J* = 7.6 Hz, H-1′); ^{13}C NMR: δ 15.8 (*q*, C-11), 18.5 (*q*, C-10), 36.1 (*d*, C-4), 37.0 (*t*, C-6′), 41.1 (*d*, C-5), 44.5 (*d*, C-9), 48.7 (*d*, C-8), 62.9 (*t*, C-6′), 71.4 (*d*, C-4′), 74.3 (*t*, C-3), 75.1 (*d*, C-2′), 78.0 (*d*, C-3′), 78.1 (*d*, C-5′), 84.8 (*d*, C-7), 102.7 (*d*, C-1′), 177.2 (*s*, C-1); HRMS: $[M]^+$ 346.16400; $C_{16}H_{26}O_8$ requires: 346.16274.

Acetylation of **1**. Nepetaside (**1**) (8.0 mg) was acetylated and recrystallized from MeOH to yield nepetaside tetraacetate (**2**) (15.8 mg) as colourless needles. Mp 125–126°; $[\alpha]_D^{25}$ −35.5° ($CHCl_3$; *c* 1.00); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1750, 1230, 1040; ^{1}H NMR ($CDCl_3$): δ0.97 (*d*, *J* = 6.8 Hz, H_3-11), 1.22 (*d*, *J* = 6.6 Hz, H_3-10), 1.72 (*m*, H-4), 2.00–2.10 (4 × OAc), 3.88 (*t*, *J* = 10.5 Hz, H_b-3), 4.20 (*dd*, *J* = 4.6, 10.5 Hz, H_a-3), 4.54 (*d*, *J* = 7.8 Hz, H-1′), 4.90–5.25 (*m*, H_3-2′,3′,4′); ^{13}C NMR: δ15.5 (*q*, C-11), 18.0 (*q*, C-10), 34.7 (*d*, C-4), 36.3 (*t*, C-6), 41.1 (*d*, C-5), 43.3 (*d*, C-9), 46.9 (*d*, C-8), 62.1 (*t*, C-6′), 68.6 (*d*, C-4′), 71.4 (*d*, C-2′), 71.8 (*d*, C-3′), 72.9 (*t*, C-3) 72.9 (*d*, C-5′), 84.7 (*d*, C-7), 99.5 (*d*, C-1′), 173.4 (*s*, C-1). (Found: C, 55.86; H, 6.72. $C_{24}H_{34}O_{12}$ requires: C, 56.02; H, 6.66%.)

Enzymatic hydrolysis of compound **1**. β-D-Glucosidase (4.5 mg) was added to nepetaside (**1**) (25.3 mg) in an acetate buffer soln (pH 4.9) (3.5 ml). After standing at 37° for 24 hr, the reaction soln was saturated with NaCl and extracted with AcOEt. The extract was successively washed with satd NaCl, dried with $MgSO_4$ and concd *in vacuo* to yield D-glucose (8.4 mg) and aglycone **3** (11.2 mg) both as a white powder. Compound **3**: $[\alpha]_D^{24}$ −24.2° (MeOH; *c* 1.00); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400–3300, 3000–2900, 1720, 1390, 1052; ^{1}H NMR ($CDCl_3$): δ1.00 (*d*, *J* = 6.6 Hz, H_3-11), 1.20 (*d*, *J* = 6.6 Hz, H_3-10), 1.42 (*m*, H_a-6), 1.82 (*m*, H-4), 2.09 (*m*, H-5), 2.22 (*dd*, *J* = 6.4, 12.2 Hz, H_b-6), 2.30 (*m*, H-8), 2.50 (*dd*, *J* = 7.1, 10.5 Hz, H-9), 3.76 (*m*, H-7), 3.88 (*dd*, *J* = 10.0, 10.9 Hz, H_b-3), 4.20 (*dd*, *J* = 3.4, 10.9 Hz, H_a-3); ^{13}C NMR: δ15.8 (*q*, C-11), 17.6 (*q*, C-10), 35.6 (*d*, C-4), 39.0 (*t*, C-6), 40.4 (*d*, C-5), 45.7 (*d*, C-9), 47.0 (*d*, C-8), 72.8 (*t*, C-3), 78.3 (*d*, C-7), 174.3 (*s*, C-1); HRMS $[M]^+$ 184.11006; $C_{10}H_{16}O_3$ requires: 184.10993.

Acetylation of compound **3**. Nepetaside aglucone (**3**) (8.0 mg) was acetylated to give monoacetate **4** (6.4 mg) as an oily compound. $[\alpha]_D^{22}$ −51.0° ($CHCl_3$; *c* 1.00); ^{1}H NMR ($CDCl_3$): δ1.00 (*d*, *J* = 6.8 Hz, H_3-11), 1.17 (*d*, *J* = 6.6 Hz, H_3-10), 2.03 (*s*, OAc), 3.90 (*dd*, *J* = 10.2, 10.9 Hz, H_b-3), 4.18 (*dd*, *J* = 3.4, 10.9 Hz, H_a-3), 4.68 (*m*, H-7); ^{13}C NMR: δ15.7 (*q*, C-11), 17.9 (*q*, C-10), 35.5 (*d*, C-4), 36.1 (*t*, C-6), 40.9 (*d*, C-5), 42.5 (*d*, C-9), 46.7 (*d*, C-8), 72.8 (*t*, C-3), 79.7 (*d*, C-7), 173.6 (*s*, C-1). (Found: C, 63.53; H, 8.15. $C_{12}H_{18}O_4$ requires: C, 63.68; H, 8.02%.)

Jones oxidation of loganin (**7**). A soln of compound **7** (12.03 g) in H_2O (60 ml) and Me_2CO (800 ml) was stirred with Jones reagent (28 ml) for 1 hr at room temp and then neutralized with satd $NaHCO_3$ soln. The insoluble materials was filtered off, and the filtrate on concn gave a residue, which was chromatographed on a charcoal (75 g) column and eluted with H_2O (1.5 l) and EtOH (3 l). After concn, the residue of the EtOH elute was transferred to a silica gel (270 g) column, eluted with MeOH–$CHCl_3$ with increasing MeOH contents. The residue of the combined 8–10% MeOH eluates was acetylated to yield 7-ketologanin tetraacetate (**8**) (5.54 g) as colourless needles, mp 106–107°, $[\alpha]_D^{22}$ −134° ($CHCl_3$; *c* 1.00).

Conversion of tetraacetate **8** *into 7-epiloganin pentaacetate* (**10**). $NaBH_4$ (1.24 g) was added to a soln of acetate **8** (5.54 g) in MeOH (200 ml) under ice cooling. After stirring for 30 min at room temp., the reaction mixt. was neutralized with 20% AcOH and concd. The residue was taken up in $CHCl_3$, and the extract was dried with $MgSO_4$ and concd. The crude product (4.48 g) was transferred to a silica gel (100 g) column and eluted successively with $CHCl_3$ (1 l), 1% MeOH–$CHCl_3$ (2 l) and 2% MeOH–$CHCl_3$ (1 l). Combined 1–2% MeOH–$CHCl_3$ eluates were concd and the residue was recrystallized from EtOH to yield 7-epiloganin tetraacetate (**9**) (2.03 g) as colourless needles, mp 154–154.5°, $[\alpha]_D^{27}$ −98.7° ($CHCl_3$; *c* 1.00). An aliquot (1.24 g) of this compound was acetylated and the product was recrystallized from MeOH to yield pentaacetate **10** (0.92 g) as colourless needles, mp 144.5–145°, $[\alpha]_D^{27}$ −150.3° ($CHCl_3$; *c* 1.00).

Conversion of pentaacetate **10** *into* 11*-alcohol hexaacetate* **11**. A soln of pentaacetate **10** (1.20 g) in dry THF (40 ml) was added to a stirred suspension of $LiAlH_2(OMe)_2$ [prepared from $LiAlH_4$ (1.42 g) and dry MeOH (2.9 ml) in dry THF (60 ml)] over a period of 20 min at −25°, and the stirring was continued for a further 1.5 hr at the same temp. The reaction soln was treated according to ref. [14] to yield an alcohol (0.54 g), which was acetylated followed by recrystallization from EtOH to yield hexaacetate **11** (0.83 g) as colourless needles. Mp 87–87.5°; $[\alpha]_D^{27}$ −127.2° ($CHCl_3$; *c* 1.00); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1750, 1236, 1040; ^{1}H NMR ($CDCl_3$): δ 1.13 (*d*, *J* = 6.4 Hz, H_3-10), 2.00–2.10 (6 × OAc), 5.19 (*br s*, H-1), 6.25 (*br s*, H-3). (Found: C, 54.73; H, 6.31. $C_{28}H_{38}O_{15}$ requires: C, 54.70; H, 6.24%.)

Catalytic reduction of hexaacetate **11**. A soln of **11** (0.93 g) in MeOH was hydrogenated over 5% Pd-C (0.63 g) until the absorption of hydrogen had ceased. After removal of the catalyst, the filtrate was concd *in vacuo*. The residue was subjected to prep. TLC and recrystallized from EtOH to yield compound **12** (0.90 g) as colourless needles. Mp 146–147°; $[\alpha]_D^{27}$ −60.5° ($CHCl_3$; *c* 1.00); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1752, 1732, 1251, 1040; ^{1}H NMR ($CDCl_3$): δ0.75 (*d*, *J* = 5.9 Hz, H_3-11), 1.10 (*d*, *J* = 6.8 Hz, H_3-10), 2.00–2.10 (5 × OAc), 5.09 (*br s*, H-1); ^{13}C NMR ($CDCl_3$): δ15.2 (*q*, C-11), 17.0 (*q*, C-10), 30.8 (*d*, C-4), 35.7 (*t*, C-6), 39.5 (*d*, C-5), 40.3 (*d*, C-9), 48.0 (*d*, C-8), 62.0 (*t*, C-6′), 64.6 (*d*, C-4′), 68.5 (*d*, C-2′), 71.2 (*t*, C-3), 72.0 (*d*, C-5′), 73.0 (*d*, C-3′), 81.9 (*d*, C-7), 93.8 (*d*, C-1′), 94.8 (*d*, C-1). (Found: C, 55.15; H, 6.82. $C_{26}H_{38}O_{13} \cdot 1/2H_2O$ requires: C, 55.00; H, 6.93%).

Zemplén reaction of compound **12**. Methanolic NaOMe (0.26 N, 1.05 ml) was added to a soln of **12** (0.90 g) in dry MeOH (50 ml) under ice cooling and the mixture was refluxed for 1.5 hr. After cooling, the reaction soln was neutralized with Amberlite IR-120 (H^+-form) and concd *in vacuo*. The residue (0.57 g) was chromatographed on a charcoal (10 g) column, eluted successively with H_2O (400 ml) and MeOH (300 ml). The MeOH eluate on concn gave free glucoside **13** (0.47 g) as an amorphous powder. $[\alpha]_D^{27}$ −80.9° (MeOH; *c* 1.00) IR ν_{max}^{KBr} cm^{-1}: 3400, 1440, 1380, 1080; ^{1}H NMR (CD_3OD): δ0.79 (*d*, *J* = 6.1 Hz, H_3-11), 1.05 (*d*, *J* = 6.6 Hz, H_3-10), 4.53 (*br s*, H-1); ^{13}C NMR: δ15.4 (*q*, C-11), 17.0 (*q*, C- 10), 33.6 (*d*, C-4), 38.9 (*t*, C-6), 40.2 (*d*, C-5), 43.5 (*d*, C-9), 48.2 (*d*, C-8), 62.6 (*t*, C-6′), 65.5 (*d*, C-4′), 71.6 (*d*, C-2′), 74.7 (*t*, C-3), 78.0 (*d*, C-5′), 78.2 (*d*, C-3′), 80.7 (*d*, C-7), 95.0 (*d*, C-1), 98.5 (*d*, C-1′). (Found: C, 53.75; H, 8.32. $C_{16}H_{28}O_8 \cdot 1/2H_2O$ requires: C, 53.75; H, 8.18%.)

Enzymatic hydrolysis of glucoside **13** *with Taka-diastase and subsequent acetylation of the hydrolysate*. The soln of Taka-diastase (7.5 ml) was added to a soln of glucoside **13** (0.07 g) in H_2O (4 ml). After standing for 24 hr at 37°, the mixt. was satd with NaCl and extracted with EtOAc. The extract was successively washed with satd NaCl, dried and concd *in vacuo* to afford aglycone **14** (0.03 g) as an oily compound, $[\alpha]_D^{22}$ −26.0° ($CHCl_3$; *c* 1.00); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500–3300, 2900, 1378, 1205. This substance was immediately accetylated to give diacetate **15** (0.04 g) as an oily compound, $[\alpha]_D^{22}$ −31.6° ($CHCl_3$; *c* 1.00); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2900, 1722, 1375, 1244; ^{1}H NMR (CD_3OD): δ0.89 (*d*, *J* = 6.8 Hz, H_3-11), 1.17 (*d*, *J* = 7.1 Hz, H_3-10), 2.04 (*s*, OAc), 5.32 (*br s*, H-1).

Jones oxidation of compound **15**. Jones reagent was added to a soln of **15** (0.04 g) in Me_2CO (4 ml) under ice cooling. After

stirring for 3 hr at room temp, the mixture was diluted with H_2O (10 ml) and then extracted with $CHCl_3$. The extract was successively washed with satd NaCl, dried and concd *in vacuo* to yield lactone (0.04 g) as an oil, $[\alpha]_D^{27}$ −48.3° ($CHCl_3$; *c* 1.00), identical with **4** in IR, ^1H NMR and ^{13}C NMR.

Basic hydrolysis of compound **4**. Methanolic NaOH soln (N, 0.2 ml) was added to a soln of **4** (0.04 g) in dry MeOH (2 ml) under ice cooling and the mixture was stirred for 40 min at room temp. The reaction soln was neutralized with dil. AcOH and then concd *in vacuo*. The product was purified by prep. TLC ($CHCl_3$–MeOH 98:2) to give aglucone **3** (0.02 g) as a white powder, $[\alpha]_D^{27}$ −27.0° (MeOH; *c* 1.00).

Conversion of lactone **3** *into glucoside* **1**. A soln of trimethylsilyl trifluoromethanesulphonate (0.06 ml) in dry CH_2Cl_2 (1 ml) was added to a stirred suspension of **3** (0.046 g), β-D-glucose pentaacetate (0.095 g) and molecular sieves 4A (powder) (0.209 g) in dry CH_2Cl_2 (4 ml) under ice cooling. After stirring for 3 hr at 20°, the reaction soln was neutralized with triethylamine and filtered. The filtrate was successively washed with satd NaCl, dried and concd to yield a residue, which was fractionated by prep. TLC ($CHCl_3$–MeOH: 98:2) to give aglycone monoacetate **4** (0.022 g) and a tetraacetate (0.014 g), $[\alpha]_D^{27}$ −34.2° ($CHCl_3$; *c* 1.00), the latter being identical in IR and ^1H and ^{13}C NMR spectra with the derivative (**2**) derived from nepetaside (**1**). Subsequently, methanolic $NaOCH_3$ (0.26 N, 0.02 ml) was added to a soln of **2** (0.014 g) in dry MeOH (2 ml) under ice cooling and the mixt. was refluxed for 20 min. After neutralization with Amberlite IR-120 (H^+ form), the reaction soln was concd to yield free glucoside **1** (0.006 g), $[\alpha]_D^{27}$ −30.1° (MeOH; *c* 0.37), identical in spectral data with nepetaside isolated from the plants.

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REFERENCES

1. McElvain, S. M., Bright, R. D. and Johnson, P. R. (1941) *J. Am. Chem. Soc.* **63**, 1558.
2. Bates, R. B., Eisenbraun, E. J. and McElvain, S. M. (1958) *J. Am. Chem. Soc.* **80**, 3420.
3. Sastry, S. D., Springstube, W. R. and Waller, G. R. (1972) *Phytochemistry* **11**, 453.
4. Sakan, T., Isoe, S., Hyeon, S. B., Katsumura, R. and Maeda, T. (1965) *Tetrahedron Letters* **46**, 4097.
5. Murai, F., Tagawa, M., Damtoft, S., Jensen, S. R. and Nielsen, B. J. (1984) *Chem. Pharm. Bull.* **32**, 2809.
6. Murai, F., Tagawa, M., Inouye, H., Ishida, T. and Inoue, M. (1987) *Chem. Pharm. Bull.* (In press).
7. Taguchi, H., Yokokawa, Y. and Endo, T. (1973) *Yakugaku Zasshi* **93**, 607.
8. Uesato, S., Xie, S., Inouye, H., Shingu, T., Inoue, M. and Doi, M. (1987) *Phytochemistry* **26**, 561.
9. Kasai, R., Suzuo, M., Asakawa, J. and Tanaka, O. (1977) *Tetrahedron Letters* **2**, 175.
10. Tori, K., Seo, S., Yoshimura, Y., Arita, H. and tomita, Y. (1977) *Tetrahedron Letters* **2**, 179.
11. Itano, K., Yamasaki, K., Kihara, C. and Tanaka, O. (1980) *Carbohydr. Res.* **87**, 27.
12. Tanaka, O. (1985) *Yakugaku Zasshi* **105**, 323.
13. Inouye, H., Yoshida, T., Tobita, S. and Okigawa, M. (1970) *Tetrahedron* **26**, 3905.
14. Uesato, S., Kobayashi, K. and Inouye, H. (1982) *Chem. Pharm. Bull.* **30**, 927.