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Semburins and Swertiols, Novel 2,8-Dioxabicyclo[3.3.1]nonanes and Their Precursory Alcohols, from *Swertia japonica* Makino

Tsutomu Sakai,* Yoshiko Nakagawa, Takashi Iwashita,
Hideo Naoki, and Takeo Sakan
Suntory Institute for Bioorganic Research, Shimamoto-cho, Mishima-gun, Osaka 618

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The steam-volatile constituents of *Swertia japonica* Makino have been studied, and 71 components of the oil (comprising nearly 90% of the sample) have been identified. Structures of three novel 2,8-dioxabicyclo[3.3.1]nonanes (semburin, isosemburin, and neosemburin) and their precursory alcohols (swertiol, isoswertiol, and isoneoswertiol) have been established by spectroscopic analysis and chemical transformation data. The presence of 2-*epi*-isoneoswertiol, which was named neoswertiol, was detected by GC/MS. This is the first time that the 2,8-dioxabicyclo[3.3.1]nonane skeleton has been encountered in natur al products.

In 1967, Motomura[1)] reported the interesting observation that cats are attracted by volatile fractions of *Swertia japonica* Makino as well as by fractions of *Actinidia polygama* Miq.[2)] and *Nepeta cataria* L.,[3)] *etc.* During the course of our investigations on various plants which have a peculiar excitatory effect on cats and *Felidae*, we studied the volatile constituents of *Swertia japonica* Makino. *Swertia japonica* Makino (Gentianaceae; Japanese name, semburi) is a popular herb in Japan, the whole plant being widely used as a folk medicine for stomach complaints because of its characteristic strong bitter taste. The bitter principles of this plant have been studied by a number of workers.[4)] However, until recently no detailed study of the volatile components had been carried out. In a previous paper,[5)] we reported the isolation and structures of two novel 2,8-dioxabicyclo[3.3.1]nonanes, semburin and isosemburin, which constitute the major components isolated from the volatile oil. We now report the analysis of the volatile constituents by GC/MS, and the details of the isolation and structural elucidation of these and five new compounds.

Results and Discussion

Analysis of Volatile Constituents. The oils obtained by steam distillation of the fresh or air-dried *Swertia japonica* plant (collected in Miyagi Pref., 1980) and *via* methanol extraction of the air-dried commercial material showed similar gas chromatographic profiles. Figure 1 shows the gas chromatogram of the whole essential oil obtained from the air-dried commercial plant. This chromatogram was obtained by injecting 1.0 μl of the oil into a CP Wax 51 glass WCOT column. The column temperature was held initially at 100 °C for 10 min, then programmed at 2 °C per minute to 150 °C, and run isothermally at 150 °C until all the components had emerged.

Volatile constituents of *Swertia japonica* were identified as far as possible by GC/MS. The major components were isolated by preparative GC and by silica-gel column chromatography (CC) and their structures were confirmed by their spectral properties. Table 1 shows the compounds detected in the volatile oil.

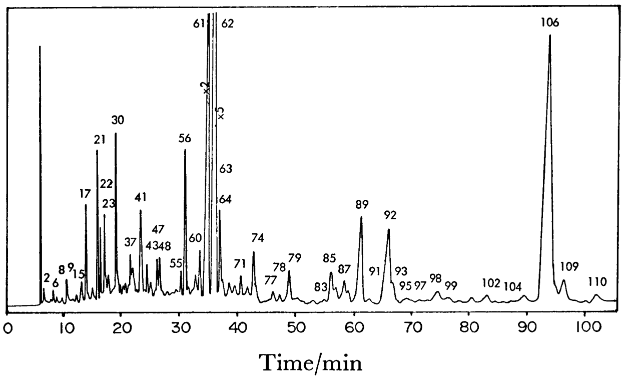


Fig. 1. Gas chromatogram of the volatile oil of *Swertia japonica* Makino.

Among the more than 110 component peaks observed in the chromatogram of the oil, seventy-one compounds were determined. Anethole and eugenol (peaks 62 and 106) were the main components in the oil (32% of the oil). A fraction containing aromatic oxygenated compounds constituted 11.2% of the oil, followed by terpenic oxygenated compounds (8.5%), terpenic hydrocarbons (7.1%), and aliphatic oxygenated compounds (5.9%). The existence of three new oxides and four new alcohols, which we have named semburins and swertiols, was revealed by GC/MS in both the volatile oil and the methanol extract. Semburins (peak 56, 61, and 64) and swertiols (peaks 91, 92, 93, and 98) accounted for 11.8% and 5.0% of the oil, respectively. Furthermore, a new lactone (peak 109, 1.39% of the oil) was obtained.

Structures of Semburins. Three novel 2,8-dioxabicyclo[3.3.1]nonanes possessing the same molecular formula of $C_9H_{14}O_2$ were contained in a fraction eluted with ether–hexane (1:9) on silica gel CC. Each compound was isolated in the pure state by preparative GC and by repeated CC. The mass spectra of two major compounds (**1** and **2**) are almost identical, but differ slightly from that of the minor compound (**3**). (Scheme 1). The IR spectra of **1** and **2** are very similar and showed the absence of hydroxyl and carbonyl groups and the presence of a vinyl group. The IR spectrum of **3** is also similar to that of **1** and **2**, except for the absence of vinyl bands. These facts suggest that the second major compound **2** is a diastereoisomer of the major compound **1**, while the minor compound **3** is a double bond isomer of both **1** and **2**. These three new compounds have been named semburin (**1**), isosemburin (**2**), and

TABLE 1. CONSTITUENTS OF THE VOLATILE OIL FROM *Swertia japonica* MAKINO

Peak No.	Compound	Content %[a]	Peak No.	Compound	Content %[a]
2	Ethyl acetate	0.15	58	Phenylpropionaldehyde	0.29
3	Benzene	0.04	59	δ-Cadinene	0.64
6	Hexanal	0.26	60	α-Curcumene	1.07
8	Limonene	0.18	61	Semburin[b]	7.84
9	*trans*-2-Hexenal	0.35	62	Anethole	16.59
10	1,8-Cineol	0.09	63	α-Damascenone	0.42
16	*cis*-Rose oxide	0.05	64	Neosemburin[b]	1.59
17	2,4-Hexadienal	0.14	65	Geraniol	0.41
18	*trans*-Rose oxide	0.08	66	Calamenene	0.49
21	1-Octen-3-ol	1.53	67	Benzyl alcohol	0.22
22	Furfural	0.95	69	Safrole	0.50
23	2,4-Heptadienal	0.14	72	1-Methylnaphthalene	0.17
25	Menthone	0.13	73	α-Ionone	0.42
26	2-Furylacetaldehyde	0.48	74	Phenethyl alcohol	1.39
29	Benzaldehyde	0.36	77	Di-*t*-butyl-*p*-cresol	0.44
30	Linalool	2.07	78	α-Calacorene	0.37
31	α-Copaene	0.34	79	β-Ionone	1.17
32	Tagetone	0.27	83	Biphenyl	0.12
33	5-Methylfurfural	0.42	85	Epoxy-β-ionone	1.29
35	5-Methyl-2-acetylfuran	0.40	87	*p*-Anisaldehyde	0.96
37	Bornyl acetate	0.83	89	Cinnamaldehyde	3.38
38	4-Terpineol	0.86	90	3-Phenyl-1-propanol	0.38
40	α-Bergamotene	0.29	91	Neoswertiol[b]	0.37
41	Caryophyllene	2.16	92	Isoswertiol[b]	3.11
42	Phenylacetaldehyde	0.25	93	Isoneoswertiol[b]	0.74
43	Pulegone	0.68	95	Nerolidol	0.21
46	β-Farnesene	0.31	96	Cubenol	0.20
47	α-Terpineol	0.68	97	Epicubenol	0.28
48	Borneol	0.80	98	Swertiol[b]	0.74
49	α-Humulene	0.32	99	α-Cyperone	0.48
50	Verbenone	0.18	102	Ethyl cinnamate	0.57
52	Piperitone	0.10	104	γ-Eudesmol	0.14
53	Naphthalene	0.35	106	Eugenol	15.40
54	Zingiberene	0.24	109	3-Propylidene-5-pentanolide[b]	1.39
55	β-Bisabolene	0.66	110	Methyleugenol	0.24
56	Isosemburin[b]	2.39			

a) Based on relative peak areas of the GC analysis of the volatile oil; GC on CP Wax 51 glass WCOT column (50 m×0.24 mm i.d.), 100 °C to 150 °C programmed at 4 °C/min. b) New compound.

neosemburin (**3**).

Semburin(**1**), $[\alpha]_D^{26}$ $-2.0°$, and isosemburin (**2**), $[\alpha]_D^{24}$ $-8.0°$, contain nine carbons: two CH_2's, one $=CH_2$, two OCH_2's, two CH's, one $=CH$, and one O–CH–O (^{13}C NMR). The IR and high resolution mass spectra of both **1** and **2** suggested the presence of a tetrahydropyran ring having a vinyl group: absorption bands at 3070, 1640, and 920 cm^{-1} ($CH_2=CH$) and fragment peaks at *m/z* 81.0320 ($C_5H_5O^+$, 98%), 109.0635 ($C_7H_9O^+$, 37%), and 124.0886 (M^+-CH_2O, 100%). These data coupled with the 360 MHz ^1H NMR and the 300 MHz ^1H–^1H 2-D chemical shift correlation spectra[6] (see Fig. 2), led to the 4-vinyl-2,8-dioxabicyclo[3.3.1]nonane skeleton for both semburin and isosemburin. The structure of **1** was confirmed by synthesis of (±)-**1**[7] *via* a pathway resembling its biogenesis from sweroside (**4**), a bitter principle of this plant. This synthesis verified the *cis* relationship of 4-H and 5-H. Furthermore, the absolute configuration at C-5 in both **1** and **2** was established as being identical with that of the asterisked carbon in structure **4** by synthesis of (−)-**1** and (−)-**2** from (*R*)-4-allyl-4-butanolide.[8] This synthesis also established that **1** and **2** are epimers.

The stereochemistry of **1** is evident from 360 MHz ^1H NMR analysis. Proton decoupling and 2-D *J* techniques[9] showed the presence of two W-type long range couplings between 5-H (δ 1.71)/1-H (δ 5.32)(1.5 Hz) and between 5-H/3′-H (δ 3.69)(2.0 Hz), indicating that the tetrahydropyran ring with the vinyl side-chain adopts a chair conformation. Irradiation of the 7′-H signal at δ 3.42 in **1** induced an NOE on the δ 1.36 9-H pattern, indicating a boat conformation for the other tetrahydropyran ring. Finally, the equa-

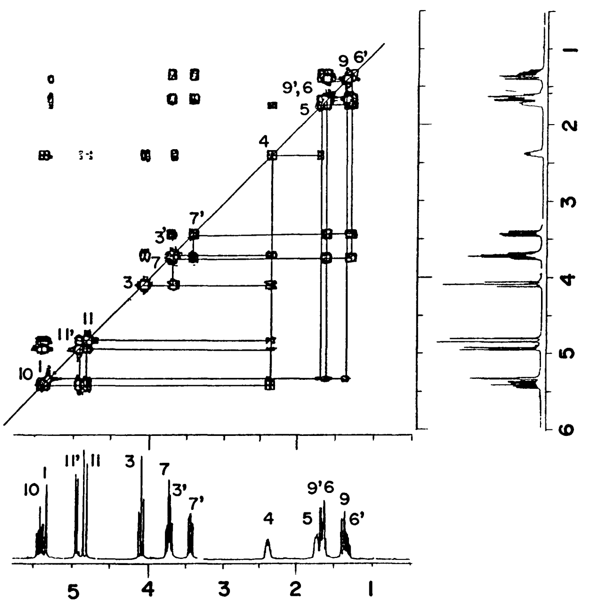


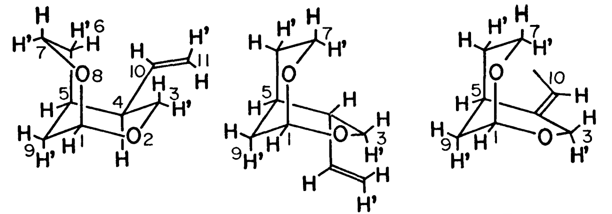
Fig. 2. ^{1}H–^{1}H 2-D chemical shift correlation map of semburin **1**.

torial nature of the vinyl group was established by noting a 12 Hz diaxial coupling between 4α-H and 3β-H. The NMR data (Fig. 2) unequivocally led to structure **1** with the chair/boat conformation **1a**.

The conformation of **2** was deduced to be half-chair/chair **2a** by carrying out similar experiments. Two W-type couplings between 5-H (δ 1.57)/1-H (δ 5.31)(1.5 Hz) and between 9-H (δ 1.30)/4-H (δ 2.10) (1.5 Hz) were observed upon proton decoupling of **2**. Irradiation of the 7′-H signal at δ 3.46 induced an NOE on the 4-H signal at δ 2.10. The coupling constants of the dddd pattern of the 4-H signal ($J_{4,3}$= 9 Hz, $J_{4,3'}$=7 Hz) indicated the presence of an axial vinyl side-chain on a half-chair tetrahydropyran ring.

The third minor compound (**3**), neosemburin ($[\alpha]^{25}_{D}$ +8.3°), showed the presence of a $CH_3CH{=}C$ group (δ 1.30, 3H, dddd; δ 5.08, 1H, dddq) instead of a $CH_2{=}CH{-}CH$ group in its ^{1}H NMR spectrum. Decoupling studies of the 360 MHz ^{1}H NMR spectrum showed **3** to be 4-ethylidene-2,8-dioxabicyclo[3.3.1]-nonane. The absolute configurations of C-1 and C-5 are assumed to be the same as in **1** and **2**. The geometry of the trisubstituted double bond in **3** was assigned a *Z* configuration, since irradiation of the 3-H resonance at δ 4.10 and the 10-Me signal at δ 1.30 enhanced the 10-H (δ 5.08) and the 5-H (δ 2.49) patterns, respectively. A W-type coupling between 5-H (δ 2.49)/ 7-H (δ 3.52)(1.5 Hz) was observed, indicating the conformation of **3** also to be half-chair/chair **3a** as in the case of **2a**. (Fig. 3).

Structures of Swertiols. Two pairs of new isomeric compounds also possessing the semburin molecular formula ($C_9H_{14}O_2$) were contained in a fraction eluted with ether–hexane (3:7) on silica gel CC. Three of these have been isolated in the pure state by preparative GC and CC.



1a **2a** **3a**

Fig. 3.

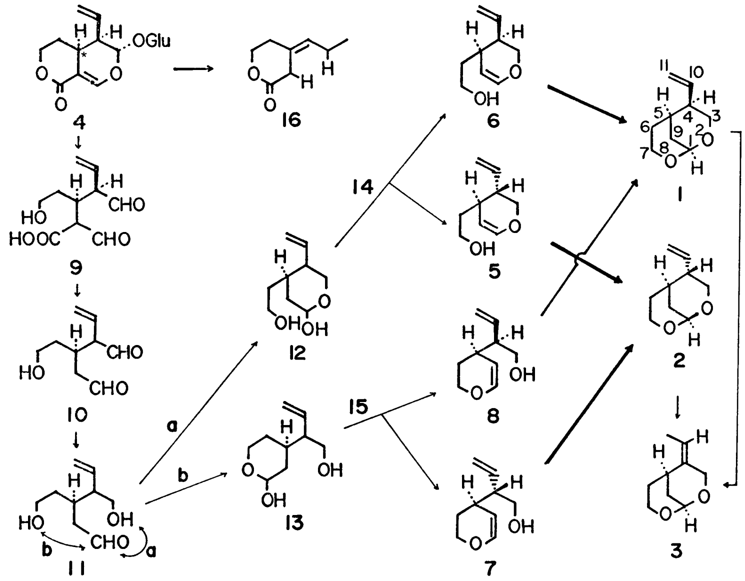
The major compound, isoswertiol (**5**)($[\alpha]^{24}_{D}$ +54.2°), had IR absorption bands for a hydroxyl (3360 cm^{-1}), a vinyl (3020, 1640, and 920 cm^{-1}), and a $CH{=}CH{-}O{-}CH_2$ (1240 cm^{-1}) group. The ^{13}C and ^{1}H NMR spectra of **5** indicated the presence of a 3,4-dihydro-2*H*-pyran moiety (δ 3.52 and 3.81, each 1H, dd, 2-H_2; δ 6.39, 1H, dd, 6-H; δ 4.55, 1H, dd, 5-H; δ 2.01, 2H, m, 3-H and 4-H), and $-CH_2CH_2OH$ (δ 1.20 and 1.56, each 1H, dddd, 7-H_2; δ 3.33, 2H, m, 8-H_2; δ 0.64, 1H, br s, OH) and $CH{=}CH_2$ groups (δ 5.40, 1H, ddd, 9-H; δ 4.92 and 4.93, each 1H, ddd, 10-H_2). The mass spectrum of **5** also supported the presence of these groups: *m*/*z* 109 ($M^+-CH_2CH_2OH$, 58%), 83 ($C_5H_7O^+$, 77%), and 54 ($C_4H_6^+$, 100%). On the basis of these data, **5** is 3-vinyl-4-(2-hydroxyethyl)-3,4-dihydro-2*H*-pyran. The smooth conversion of **5** into isosemburin (**2**) by treatment with *p*-toluenesulfonic acid confirmed the structure of **5**, and also established the absolute configurations at C-3 and C-4 in **5** to be the same as in **2**.

The minor compound (**6**) exhibited IR and mass spectra very similar to **5**. No NMR measurements were carried out due to the limited amount of sample. However, transformation of **6** into semburin (**1**) by treatment with *p*-toluenesulfonic acid established the structure of **6**, swertiol, as being the 3-epimer of isoswertiol (**5**).

The second major compound, isoneoswertiol (**7**)($[\alpha]^{22}_{D}$ −52.8°), had IR absorption bands for a hydroxyl (3340 cm^{-1}), a vinyl (3050, 1630, and 905 cm^{-1}), and a $CH{=}CH{-}O{-}CH_2$ (1240 cm^{-1}) group. The ^{13}C and ^{1}H NMR spectra of **7** showed the presence of a 3,4-dihydro-2*H*-pyran moiety (δ 3.66 and 3.74, each 1H, ddd, 2-H_2; δ 1.43, 2H, m, 3-H_2; δ 4.47, 1H, dddd, 5-H; δ 6.39, 1H, dd, 6-H), and $-CH_2OH$ (δ 3.30, 1H, dd, 8-H; δ 3.49, 1H, br dd, 8-H; δ 0.80, 1H, br s, OH) and $-CH{=}CH_2$ (δ 5.40, 1H, ddd, 9-H; δ 4.89 and 4.97, each 1H, ddd, 10-H_2) groups. The mass spectrum also confirmed the presence of these groups: *m*/*z* 83 ($C_5H_7O^+$, 100%) and 124 (M^+-CH_2OH, 1.5%). These data indicated that **7** is 2-(3,4-dihydro-2*H*-pyran-4-yl)-3-buten-1-ol. The conversion of **7** into isosemburin (**2**) established the structure and the absolute configuration at C-2 and C-4′.

The remaining counterpart of the second pair could not be isolated, but was assumed to be the 2-epimer of isoneoswertiol (**7**); we named it neoswertiol (**8**), since its mass spectrum (by GC/MS) is identical with that of isoneoswertiol (**7**).

A possible biogenetic route from sweroside (**4**) to semburins (**1** and **2**) is illustrated in Scheme 1. Acid-catalyzed cleavage of sweroside (**4**) would provide the hydroxydial acid (**9**). Decarboxylation and racemi-



Scheme 1. Biosynthesis of semburins and swertiols from sweroside.

zation at the α-position of the carbonyl in **9** then gives the hydroxydials **10**, the reduction of which leads to epimeric diols **11**. Compound **11** is an important intermediate because the absolute configuration at C-5 in **4** remains unaltered. Cyclization of **11** in two directions **a** and **b** would provide two hemiacetals **12** and **13**. Semburins **1** and **2** could be obtained directly from both hemiacetals **12** and **13** by dehydration-cyclization, or *via* the dihydropyran alcohols **14** and **15**. These dihydropyran alcohols **14** and **15** correspond to the four new compound **5**—**8** isolated from both the volatile oil and the methanol extract of plant.

A number of studies concerning the role of loganin and secologanin in the biosynthesis of terpenoids and indole alkaloids have been reported, but possible key intermediates postulated in the biogenetic sequence from iridoids to alkaloids have not been isolated or confirmed. It is possible that the compounds discussed might be efficient precursors in the biosynthesis of the Corynanthe-type indole alkaloids.

Although the 2,8-dioxabicyclo[3.3.1]nonane skeleton has already been obtained as the aglycone of secologanin,[10] this is the first time it has been encountered in natural products.

*Structure of a New Lactone **16**.* From the fraction containing swertiols, a new lactone (peak 109 in Table 1, 1.39% of the oil), 3-propylidene-5-pentanolide (**16**) was obtained. Its mass spectrum showed a molecular ion at *m/z* 140 corresponding to $C_8H_{12}O_2$. The IR and ^1H NMR spectra showed the presence of a δ-lactone moiety (1740 cm^{-1}) and a $CH_3CH_2CH=C$ group [δ 0.74 (3H, t, $J=7.5$ Hz), 1.59 (2H, ddq, $J=7.5$, 7.0, 1.0 Hz), and 4.86 (1H, ttt, $J=7.0$, 1.5, 1.5 Hz)]. Irradiation of the 3-H_2 signal at δ 2.87 induced an NOE on the 8-H_2 (δ 1.59) pattern. Thus, the configuration of the trisubstituted double bond was determined as *Z*. It is also presumed that this compound is derived from sweroside (**4**). (see Scheme 1)

Experimental

The IR spectra were obtained on a Hitachi EPI G2 infrared spectrophotometer as thin films between NaCl plates. The optical rotations were measured on a Perkin-Elmer 141 polarimeter. The NMR spectra were taken by Nicolet NT-360 (360 MHz ^1H NMR), Nicolet NT-300 (300 MHz ^1H–^1H 2-D *J* correlation), and JEOL FX-100 (^{13}C NMR). GC/MS spectra were determined with a Hitachi M-80 GC/MS spectrometer equipped with 50 m×0.24 mm i.d. glass WCOT column of CP Wax 51. The preparative GC conditions, using a model 920 Varian Aerograph fitted with a thermal-conductivity detector, were as follows: a 3 m× 10 mm aluminum column containing 10% Thermon 1500 on Chromosorb W; He carrier gas, 60 ml/min; oven temp at 130—150 °C.

Material and Isolation. Steam distillations of the fresh whole plant (3 kg, collected in Sendai, Miyagi Pref., Oct. 1980), its air-dried material (0.5 kg), and a commercial air-dried material (5 kg, collected in Tohoku District) gave, respectively, 0.37 g, 0.27 g, and 2.0 g of volatile oils. The commercial material (0.4 kg) was extracted with MeOH for 2 weeks. The crude extract (44.8 g) was obtained.

The volatile oil (2.0 g) of the commercial material was chromatographed on silica gel (70 g, 2.5 cm i.d.×60 cm column). Elution with hexane, hexane–ether mixture, ether, and MeOH gave 7 fractions: fraction I (hexane, 0.53 g), II (hexane–ether, 95:5, 0.12 g), III (9:1, 0.46 g), IV (85:15, 0.30 g), V (7:3, 0.19 g), VI (ether, 0.23 g), and VII (MeOH, 0.08 g). Fraction III was rechromatographed, yielding 3 fractions: III-1 (0.17 g), III-2 (0.13 g), and III-3 (0.15 g). Three semburins were contained in fraction III-3. Four swertiols were contained in fraction V. Each compound was isolated by prep. GC and CC: semburin, 5.0 mg, prep. GC Rt (oven temp 130°) 20.5 min; isosemburin, 1.5 mg, 16.0 min; neosemburin, 1.0 mg, 23.0 min; isoswertiol, 9.0 mg, 20 min (oven temp 150 °C); isoneoswertiol, 3.9 mg, 20 min; swertiol, 30 min.

*Semburin (**1**).* $[\alpha]_D^{26}$ $-2.0°$ ($CHCl_3$, $c=0.10$); IR ν_{max}^{film} cm^{-1}: 3070, 1640, 1000, 920; ^{13}C NMR (25 MHz, C_6D_6): δ 23.9 (t, C-6), 25.9 (d, C-5), 30.3 (t, C-9), 44.0 (d, C-4), 60.4 (t, C-7), 61.6 (t, C-3), 92.5 (d, C-1), 115.7 (t, C-11),

TABLE 2. ^{1}H NMR SPECTRAL DATA OF SEMBURINS **1**, **2**, AND **3** (IN C_6D_6)

Proton	Semburin(**1**)	Isosemburin(**2**)	Neosemburin(**3**)
1-H	5.32 ddd	5.29 ddd	5.47 br
3-H	4.08 dd	3.89 dd	4.10 m
3′-H	3.69 ddd	3.26 dd	
4-H	2.38 dddddd	2.11 ddddd	—
5-H	1.72 m	1.58 m	2.49 br s
6-H	1.63 m	1.61 dddd	1.61 dddd
6′-H	1.30 dddd	1.09 dddd	1.23 br d
7-H	3.72 ddd	3.46 dddd	3.52 dddd
7′-H	3.41 ddd	4.03 ddd	4.16 ddddd
9-H	1.63 m	1.31 ddd	1.50 m
9′-H	1.36 ddd	1.55 ddd	
10-H	5.40 ddd	5.55 ddd	5.08 dddq
11-H	4.93 ddd	4.89 ddd	1.30 dddd
11′-H	4.81 ddd	4.89 ddd	

Coupling constants. Semburin(**1**): 1,5 = 1.5 Hz; 1,9 = 1,9′ = 1.5 Hz; 3,3′ = 7,7′ = 11.6 Hz; 3,4 = 11.8 Hz; 3′,4 = 5,9′ = 5.5 Hz; 3′,5 = 2.0 Hz; 4,5 = 3.0 Hz; 4,10 = 6.3 Hz; 4,11 = 4,11′ = 1.6 Hz; 5,6′ = 9.0 Hz; 6,6′ = 15.2 Hz; 6,7 = 6.9 Hz; 6,7′ = 10.0 Hz; 6′,7 = 4.2 Hz; 6′,7′ = 6.0 Hz; 9,9′ = 13.0 Hz; 10,11 = 10.8 Hz; 10,11′ = 17.1 Hz; 11,11′ = 1.6 Hz. Isosemburin(**2**): 1,5 = 5,7 = 1.5 Hz; 1,9 = 1,9′ = 5,9′ = 2.0 Hz; 3,3′ = 7,7′ = 12.0 Hz; 3,4 = 6.5 Hz; 3′,4 = 8.5 Hz; 4,9 = 1.5 Hz; 4,10 = 6.8 Hz; 4,11 = 4,11′ = 1.0 Hz; 5,6 = 5.5 Hz; 5,6′ = 2.2 Hz; 5,9 = 3.0 Hz; 6,6′ = 14.0 Hz; 6,7 = 3.5 Hz; 6,7′ = 10.0 Hz; 6′,7 = 6.0 Hz; 6′,7′ = 5.0 Hz; 9,9′ = 12.9 Hz; 10,11 = 9.8 Hz; 10,11′ = 16.0 Hz; 11,11′ = 1.0 Hz. Neosemburin(**3**): 1,7′ = 0.5 Hz; 3,10 = 3,10′ = 3′,10 = 3,11 = 3′,11 = 1.5 Hz; 5,6 = 3.8 Hz; 5,7 = 1.0 Hz; 5,7′ = 0.5 Hz; 5,10 = 2.0 Hz; 5,11 = 1.0 Hz; 6,6′ = 13.0 Hz; 6,7 = 5.5 Hz; 6,7′ = 13.0 Hz; 6′,7 = 1.5 Hz; 6′,7′ = 3.5 Hz; 7,7′ = 11.5 Hz; 10,11 = 7.0 Hz.

TABLE 3. ^{1}H NMR SPECTRAL DATA OF ISOSWERTIOL (**5**) AND ISONEOSWERTIOL (**7**)

Proton	Isoswertiol(**5**)	Isoneoswertiol(**7**)
2-H	3.52 dd	3.66 ddd
2′-H	3.81 dd	3.74 ddd
3-H	2.01 m	1.42 m
3′-H	—	
4-H	2.01 m	1.99 ddddd
5-H	4.55 dd	4.47 dddd
6-H	6.39 dd	6.39 dd
7-H	1.56 dddd	1.85 dddddd
7′-H	1.20 dddd	—
8-H	3.33 m	3.30 dd
8′-H		3.49 br dd
9-H	5.40 ddd	5.40 ddd
10-H	4.92 ddd	4.87 ddd
10′-H	4.93 ddd	4.97 ddd
O-H	0.64 br s	0.80 br s

Coupling constants. Isoswertiol (**5**): 2,2′ = 10.5 Hz; 2,3 = 10.0 Hz; 2′,3 = 3.0 Hz; 3,9 = 7.7 Hz; 3,10 = 3,10′ = 0.5 Hz; 4,5 = 2.3 Hz; 4,6 = 1.8 Hz; 4,7 = 7.3 Hz; 4,7′ = 8.9 Hz; 5,6 = 6.2 Hz; 7,7′ = 13.3 Hz; 7,8 = 7.3 Hz; 7,8′ = 4.2 Hz; 7′,8′ = 8.9 Hz; 9,10 = 17.0 Hz; 9,10′ = 10.2 Hz; 10,10′ = 2.0 Hz. Isoneoswertiol (**7**): 2,2′ = 11.0 Hz; 2,3 = 6.5 Hz; 2,3′ = 4.5 Hz; 2′,3 = 5.0 Hz; 2′,3′ = 5.5 Hz; 3,4 = 1.0 Hz; 3′,4 = 7.0 Hz; 3,5 = 3′,5 = 0.5 Hz; 4,5 = 3.0 Hz; 4,6 = 2.0 Hz; 4,7 = 12.5 Hz; 5,6 = 6.5 Hz; 7,8 = 5.0 Hz; 7,8′ = 7.5 Hz; 7,9 = 9.0 Hz; 7,10 = 1.0 Hz; 7,10′ = 0.5 Hz; 8,8′ = 10.5 Hz; 9,10 = 17.0 Hz; 9,10′ = 10.5 Hz; 10,10′ = 2.0 Hz.

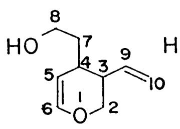
137.8 (d, C-10); ^{1}H NMR (360 MHz, C_6D_6): see Table 2; MS m/z (rel int. %): 154 (M^+, 1), 124(49), 109(46), 95(14), 91(12), 81 ($C_5H_5O^+$, 100), 80(61), 67(50), 53(49), 41(90). High resolution (H. R.) MS; Found: M^+ m/z 154.0967. Calcd for $C_9H_{14}O_2$: M^+ m/z 154.0992.

Isosemburin (2). $[\alpha]^{25}_{D}$ −8.0° ($CHCl_3$, c=0.05); IR ν^{film}_{max} cm^{-1}: 3070, 1640, 1000, 920; ^{13}C NMR (25 MHz, C_6D_6): δ 26.3 (t, C-6), 27.5 (d, C-5), 32.0 (t, C-9), 44.1 (d, C-4), 57.3 (t, C-7), 62.7 (t, C-3), 93.1 (d, C-1), 114.5 (t, C-11), 139.6 (d, C-10); ^{1}H NMR (360 MHz, C_6D_6): see Table 2; MS m/z (rel int. %): the same as those of **1**.

Neosemburin (3). $[\alpha]^{25}_{D}$ +8.3° ($CHCl_3$, c=0.06), ^{1}H NMR (360 MHz, C_6D_6): see Table 2; MS m/z (rel int. %): 154 (M^+, 25), 136(7), 125(25), 93(56), 91(29), 83 ($C_5H_7O^+$, 100), 79(62), 70(51), 69(69), 67(51), 55(76), 53 (47), 41(85), 39(62).

Isoswertiol (5). $[\alpha]^{24}_{D}$ +54.2° (MeOH, c=0.66); IR ν^{film}_{max} cm^{-1}: 3350, 3050, 1635, 1240, 915; ^{13}C NMR (25 MHz, C_6D_6): δ 32.9 (d, C-4), 37.6 (t, C-7), 43.3 (d, C-3), 60.0 (t, C-8), 68.0 (t, C-2), 103.7 (d, C-5), 116.7 (t, C-10), 138.3 (d, C-9), 143.8 (d, C-6); ^{1}H NMR (360 MHz, C_6D_6): see Table 3; MS m/z (rel int. %): 154(M^+, 15), 139(1), 136(3), 124(10), 109(58), 99(48), 83(77), 81(39), 79(31), 67(14), 54($C_4H_6^+$, 100), 41(28), 39(22). H.R. MS; Found: M^+ m/z 154.1002. Calcd for $C_9H_{14}O_2$: M^+ m/z 154.0992.

Swertiol (6). IR ν^{film}_{max} cm^{-1}: 3350, 3050, 1635, 1240, 915; MS m/z (rel int. %): 154(M^+, 14), 135(2), 121(3), 109(25), 99(40), 91(10), 81(21), 79(16), 69(6), 67(5), 54 ($C_4H_6^+$, 100), 41(20), 39(18).



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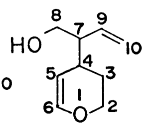

7

Isoneoswertiol (7). $[\alpha]^{22}_{D}$ −52.8° (MeOH, c=0.18); IR ν^{film}_{max} cm^{-1}: 3400, 3050, 1630, 1240, 905; ^{13}C NMR (25 MHz, C_6D_6): see Table 3; MS m/z (rel int. %): 154(M^+, 2), 124 (1.5), 83 ($C_5H_7O^+$, 100), 67(15), 55(55), 39(26). H.R. MS; Found: M^+ m/z 154.0987. Calcd for $C_9H_{14}O_2$: M^+ m/z 154.0992.

Neoswertiol (8). MS m/z (rel int. %): 154(M^+, 3), 124(1), 83($C_5H_7O^+$, 100), 67(15), 55(55), 39(26).

3-Propylidene-5-pentanolide (16). IR ν^{film}_{max} cm^{-1}: 1740, 1660, 1625; ^{1}H NMR (360 MHz, C_6D_6): δ 0.73 (3H, t, J=7.5 Hz, 8-H_3), 1.58 (2H, dqt, J=7.5, 7.5, 1.0 Hz, 7-H_2), 1.74 (2H, br t, J=7.0 Hz, 4-H_2), 2.87 (2H, br quint, J= 1.0 Hz, 2-H_2), 3.54 (2H, dd, J=6.0, 6.0 Hz, 5-H_2), 4.86 (1H, ttt, J=7.0, 2.0, 2.0 Hz, 7-H); MS m/z (rel int. %): 140(M^+, 18), 112(M^+−CO, 10), 95(6), 82($C_6H_{10}^+$, 100), 67(10), 53(7), 39(11).

Conversion of 5 to 2. To a solution of **5** (0.3 mg) in benzene (0.5 ml) was added a solution of *p*-toluenesulfonic acid (1 mg) in benzene (1 ml). The mixture was allowed to stand at room temperture overnight in a sealed tube. After the usual work-up, the residue was subjected to GC/MS analysis. The only product of cyclization was identified as isosemburin (**2**).

Conversion of 7 to 2. **7** (0.2 mg) was cyclized in a similar manner to that described above to give **2**. The identification of the product was carried out by GC/MS.

Proton J-correlation Spectra (COSY) of 1 and 2. They were viewed in the contour mode. Quadrature detection was employed in both dimensions to collect a 512×1K data matrix, with 16 acquisitions for each t_1 delay (evolution period). Dwell times for each dimension (t_1 and t_2) were set to 332 s. Both dimensions were resolution enhanced by a sine multiplication; the second dimension (F_1) is presented in power mode.

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