CHEMISTRY LETTERS, pp. 1257-1258, 1981. © The Chemical Society of Japan 1981

THE STRUCTURES OF SEMBURIN AND ISOSEMBURIN, 2,8-DIOXABICYCLO[3.3.1] NONANES ISOLATED FROM THE VOLATILE OIL OF *SWERTIA JAPONICA* MAKINO

Tsutomu SAKAI,* Hideo NAOKI, Kazutoshi TAKAKI,† and Hiromu KAMEOKA†
Suntory Institute for Bioorganic Research, Shimamoto-cho, Mishima-gun, Osaka 618
†Kinki University, Faculty of Science & Enginieering, Higashiosaka 577

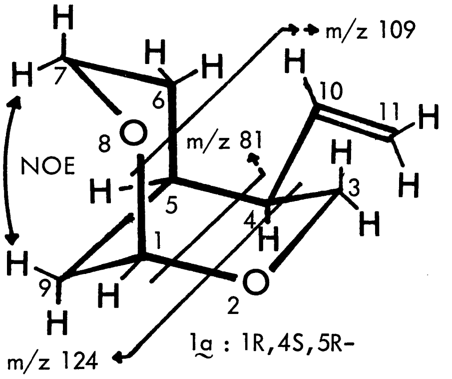
The structures of semburin and isosemburin isolated from the volatile oil of *Swertia japonica* Makino have been determined as **1** and **3**, respectively. It is the first time that the 2,8-dioxabicyclo[3.3.1] nonane skeleton has been encountered in natural products.

Swertia japonica Makino (Semburi in Japanese) is a popular herb widely used for its stomachic activity. Although the components of this plant have been investigated by a number of workers,1) past studies have dealt mainly with the bitter principle and little attention has been paid on the volatile components. In this communication we report the structures of two novel compounds, semburin and isosemburin, which constitute the major volatile components.

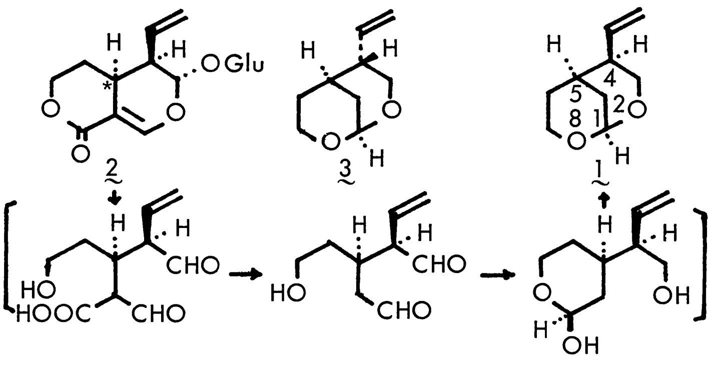
Steam distillation of the fresh whole plant (3 kg)2) and the air-dried material (0.5 kg) gave, respectively, 0.37 g and 0.27 g of volatile oils having similar GC profiles. Silica gel chromatography of the combined oil and elution with ether-hexane (10:90) yielded a mixture of two compounds (190 mg). Each compound was isolated in the pure state from the mixture by preparative gas chromatography.

Semburin, $[\alpha]_D^{24}$ +6.0° (c = 0.05, $CHCl_3$), the major component (28.0% of the volatile oil) was found to possess the composition $C_9H_{14}O_2$ (M^+, m/z 154); GC-MS exhibited major fragment peaks at m/z 124 ($M^+ - CH_2O$), 109 ($C_7H_9O^+$), and 81 (the base peak, $C_5H_5O^+$)(see **1a**). The IR spectrum of semburin showed the presence of a vinyl group (ν_{max} 3070, 1640, and 920 cm^{-1}) and the absence of hydroxy and ketone groups. The ^{13}C-NMR data (Table 1) indicated that the nine carbons consisted of two CH_2's, two CH's, two CH_2-O's, one O-CH-O, and one CH_2=CH-. This data coupled with the 360 MHz ^1H-NMR data (Table 1) led to the 4-ethenyl-2,8-dioxabicyclo[3.3.1]nonane structure as the sole expression for semburin. Decoupling studies showed the presence of long range couplings between 5-H (δ 1.71)/1-H (δ 5.32) and between 5-H/3a-H (δ 3.69) (W-type, see **1a**). The configuration of the vinyl group (at C-4) is equatorial, *i.e.*, 4-H is axial on the basis of its dddd pattern ($J_{4,3}$ = 12, $J_{4,3'}$ = 6 Hz)(Table 1, also see data for the 4-epimer described below). Irradiation of the 7-H signal at 3.42 ppm induced an NOE on the 1.36 ppm 9-H pattern.3) These NMR data unequivocally lead to the bicyclic chair/boat skeletal structure **1** (**1a**).

The absolute configuration is based on the biogenetic consideration shown in Scheme 1. Namely, it has been assumed that the C-5 configuration is the same as that of the asterisked carbon in structure **2** of sweroside,4) a bitter principle isolated from this plant.



$\underset{\sim}{1a}$: 1R,4S,5R-



Scheme 1. Biogenesis of Semburin

Table 1. The ^{13}C- and ^{1}H-NMR Spectral Data of Semburin ($\underset{\sim}{1}$) and Isosemburin ($\underset{\sim}{3}$). (in C_6D_6)

Compound	No.	1	3	4	5	6	7	9	10	11
Semburin (1)	^{13}C	92.5d	61.5t	44.0d	25.9d	23.9t	60.4t	30.3t	137.8d	115.7t
	^{1}H	5.32dt	3.69dd 4.08dd	2.37dddd	1.71m	1.29dddd 1.63dddd	3.42ddd 3.72ddd	1.36dddd 1.63dddd	5.40ddd	4.89ddd 4.94ddd
Isosemburin(3)	^{13}C	93.1d	62.7t	44.1d	27.5d	26.3t	57.3t	32.0t	139.6d	114.5t
	^{1}H	5.31dt	3.26dd 3.89dd	2.10dt	1.57m	1.07m 1.60m	3.46ddd 4.03ddd	1.30dddd 1.55m	5.53ddd	4.88ddd 4.89ddd

Isosemburin, $[\alpha]_D^{24}$ -8.0° (c = 0.05, $CHCl_3$), the minor component which is 5% of the volatile oil, showed the same mass spectrum as that of semburin ($\underset{\sim}{1}$) and analysed for $C_9H_{14}O_2$. The IR spectrum of isosemburin was also very similar to that of $\underset{\sim}{1}$. The NMR data of isosemburin (Table 1) similarly lead to structure $\underset{\sim}{3}$. The pattern of the 4-H signal ($J_{4,3}$= 9, $J_{4,3'}$ = 7 Hz) shows that the vinyl side-chain is axial, *i. e.*,4-H is equatorial. This is supported by the higher shift of the C-6 signal (23.9 ppm) in $\underset{\sim}{1}$ as compared to that (26.3 ppm) in $\underset{\sim}{3}$ due to a γ-upfield shift in the former case. The differences seen in the shifts of some other ^{13}C signals are probably due to γ-upfield effects as well as anti-γ-carbon shielding effects reported earlier for 2-substituted bicyclo [3.3.1] nonan-9-ones.[5] Although the 2,8-dioxabicyclo [3.3.1] nonane skeleton has already been obtained as the aglycone of secologanin,[6] this is the first time it has been encountered in natural products.

References

1) H. Inouye, S. Ueda, and Y. Nakamura, Tetr. Lett., 1967, 3221; T. Kubota and Y. Tomita, Tetr. Lett., 1961, 176.

2) We are deeply indebted to Dr. Genjiro Kusano of Tohoku University for supplying "Semburi", harvested in Oct. 1979 at Miyagi Pref.

3) Since the 9-H and 6-H signals overlapped at 1.63 ppm (Table 1), the technique of "NOE Difference Spectra" was employed for NOE measurements: L.D. Hall and J.K.M. Sanders, J. Am. Chem. Soc., 102, 5703 (1980).

4) H. Inouye, T. Yoshida, Y. Nakamura, and S. Tobita, Chem. Pharm. Bull., 18, 1889 (1970).

5) A. Heumann and H. Kolshorn, Tetrahedron, 31, 1571 (1975).

6) R.T. Brown and C.L. Chapple, Tetr. Lett., 1976, 787.

(Received June 30, 1981)