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# SYNTHESIS OF (±)-SEMBURIN

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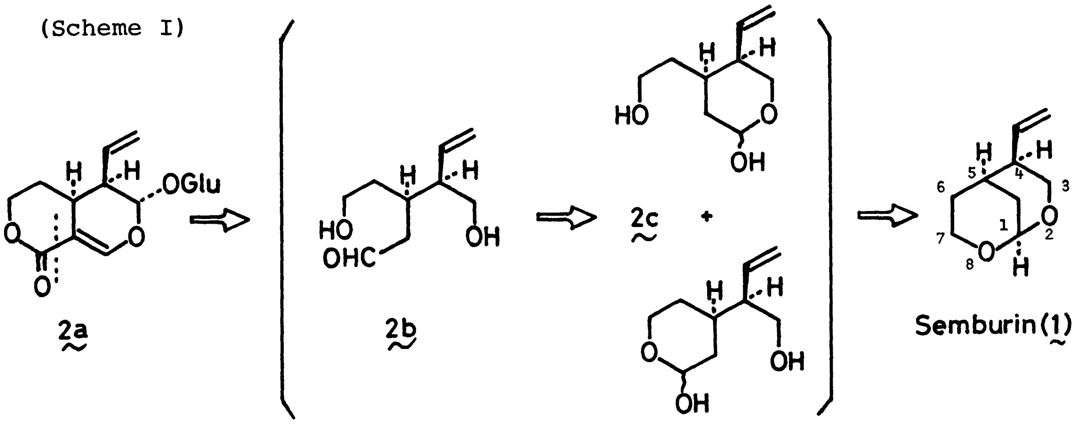
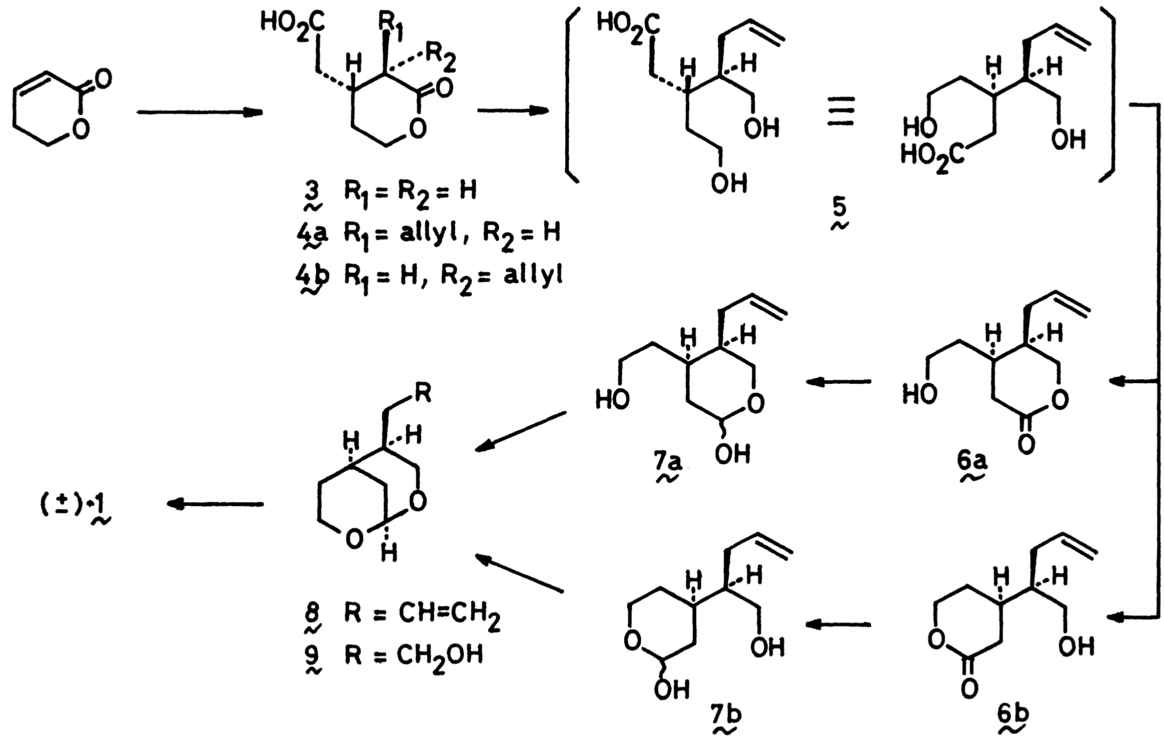
Semburin, a new 2,8-dioxabicyclo[3,3,1]nonane skeleton, has been synthesized in the stereoselective manner from α-pyrone.

Structure **1** containing the novel 2,8-dioxabicyclo[3,3,1]nonane skeleton has been assigned to semburin, a component of the volatile fraction of <u>Swertia japonica</u> Makino ("semburi" in Japanese).[1)] We wish to report the synthesis of (±)-semburin (**1**) <u>via</u> a pathway which resembles the proposed biogenetic route from sweroside (**2a**) → **2b** → **2c** → **1** (Scheme I).[1)]

(Scheme I)



1,4-Addition of diethyl malonate (NaH, benzene) to α-pyrone followed by decarboxylation with concd HCl gave the 3-carboxymethyl-5-pentenolide (**3**)[2)] in 40% yield: mp 63∿64 °C; IR($CHCl_3$) 1735, 1720 $cm^{-1}$. Since the vinyl group contained in the natural product (**1**) was not considered to withstand the synthetic reaction conditions, an allyl group was introduced instead and was modified later. Thus, treatment of **3** with 2 equiv LDA, 2 equiv HMPA and allyl bromide (THF, -78 °C) gave a 4:1 mixture of the desired **4a**[2)] and undesired **4b**[2)] (oil; 56% yield), the major isomer resulting from attack of the alkylating reagent from the less hindered β-side.[3)] The <u>trans</u>-acid (**4a**) was converted <u>via</u> the three step sequence (i) diisobutylaluminum hydride(DIBAL)/toluene, -78 °C; (ii) $NaBH_4$/EtOH, 0 °C; and (iii) p-TsOH/benzene, reflux, into a mixture of pentenolides (**6a**) and (**6b**)(1:1), (88% from **4a**). The mixture without separation was reduced with DIBAL (toluene, -78 °C) to hemiacetals (7a) and (7b), which were cyclized with p-TsOH (or PPTS, $CH_2Cl_2$) to the 2,8-dioxabicyclo[3,3,1]-nonane (8)[2] in 40% yield from 6a/6b: oil; IR($CHCl_3$) 3060, 1635 $cm^{-1}$; $^1H$ NMR(360MHz in $C_6D_6$) δ5.49(ddt, 1H, J=10.7, 17.2, 6.5Hz), 5.33(bs, 1H), 4.93(ddd, 1H, J=10.7, 2.0, 1.0 Hz), 4.89(ddd, 1H, 17.2, 2.0, 1.5 Hz), 3.81(dd, 1H, J=11.8 Hz), 3.70(ddd, 1H, J=5.4, 6.5, 11.9 Hz), 3.63(dd, 1H, J=5.6, 11.8 Hz), 3.47(ddd, 1H, J=6.5, 8.6, 11.9 Hz); mass spectrum, m/e 168 ($M^+$). Ozonolysis of the side chain followed by $NaBH_4$ reduction yielded the alcohol (9)[2] which was converted to (±)-semburin by Grieco's method[4] [ o-nitrophenyl selenocyanate, n-$Bu_3P$, THF-pyridine (1:1), room temperature, 2 h; 30% $H_2O_2$, $CH_2Cl_2$, room temperature, 1 h]. The $^1H$ NMR(360MHz), IR, mass and TLC behaviour of synthetic 1 were identical with those of the natural specimen.[5]



References

1) T. Sakai, H. Naoki, K. Takaki, and H. Kameoka, Chem. Lett., 1981, 1257.

2) Satisfactory spectroscopic data as well as elementary analytical data were obtained for this compound.

3) The configuration of the allyl group of isomers (4a) and (4b) were determined by NMR lanthanide shift studies of the respective methyl esters.

4) P. A. Grieco, S. Gilman, and M. Nishizawa, J. Org. Chem., 41, 1485 (1976).

5) We thank Professor Koji Nakanishi, Director of Suntory Institute for Bioorganic Research, for discussions.

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