CHEMISTRY LETTERS, pp. 933-934, 1982.

ENANTIOSELECTIVE SYNTHESES OF (-)-SEMBURIN AND (-)-ISOSEMBURIN

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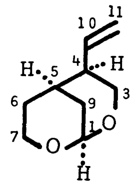
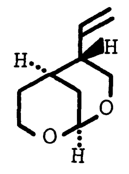
Validity of the proposed structures of (-)-semburin(1) and (-)-isosemburin(2), isolated from Swertia japonica Makino, has been established by the enantioselective total syntheses starting from the known chiral lactone(3).

The structures of (-)-semburin and (-)-isosemburin, both the constituents of the volatile oil of Swertia japonica Makino, were proposed to be unique 2,8-dioxabicyclo[3.3.1]nonane frameworks (1) and (2), respectively, based on NMR spectroscopy and biogenetic considerations.1)-3) We now report here the enantioselective syntheses of both (-)-semburin(1) and (-)-isosemburin(2), starting from the chiral lactone(3)4) with known absolute configuration, which could unambiguously confirm the appropriateness of the proposed structures.

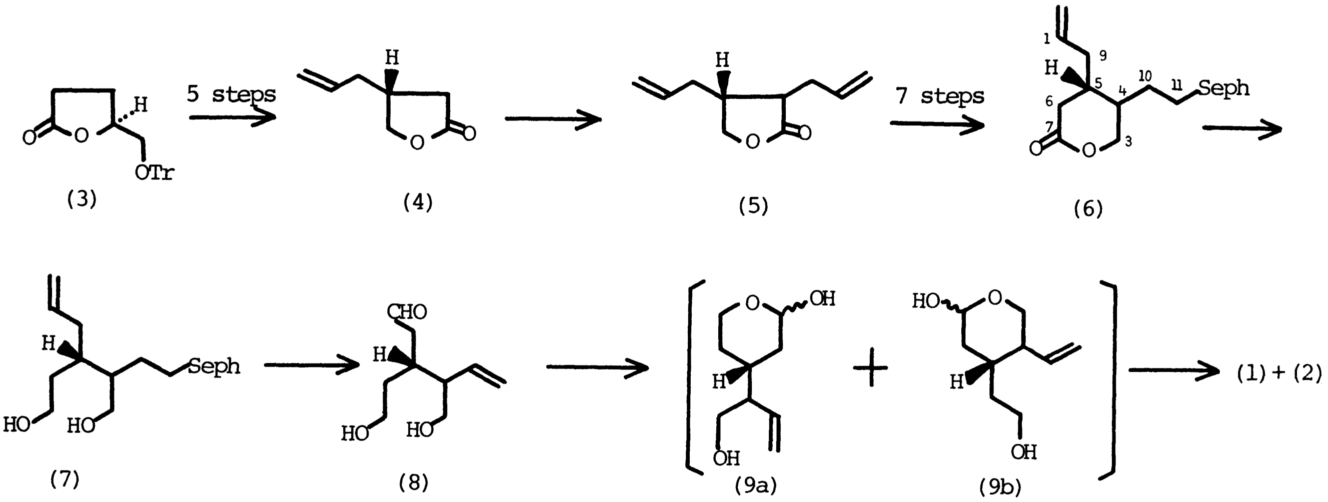
According to the established thirteen step procedure,5) the γ-lactone(3) was converted into the δ-lactone(6:4(α)H) along with a minor amount of its 4(β)H-epimer (6:4(β)H) owing to imperfect stereoselectivity in the second alkylation stage((4)→(5)). The obtained epimeric mixture, without separation, was reduced with diisobutylaluminum hydride(THF, -78°C - room temperature), followed by sodium borohydride to give the diol(7)6) as an epimeric mixture. The epimeric diol(7) was ozonized(MeOH, -78°C), followed by treating with an excess of triethylamine7)(-78°C - room temperature) to yield the vinyl-aldehyde(8) which formed a mixture of the hemiacetals, (9a) and (9b), spontaneously during the work-up. The mixture, upon reflux azeotropically in benzene in the presence of a catalytic amount of p-toluenesulfonic acid, yielded a mixture of (-)-semburin(1) and (-)-isosemburin(2) as an oil possessing camphor like odor. Separation of the mixture using a preparative gas chromatography(10% Thermon-1500 on Chromosorb W(AW-DMCS)) gave (-)-semburin(1), $[\alpha]_D^{23.5}$ -1.89°(c=0.53, $CHCl_3$)(natural, $[\alpha]_D^{25.5}$ -2.00°(c=0.10,



(1)



(2)



Scheme

CHCl$_3$)), as a major component and (−)-isosemburin(2), $[\alpha]_D^{23.5}$ −9.71°(c=0.35, CHCl$_3$) (natural, $[\alpha]_D^{25}$ −8.0°(c=0.05, CHCl$_3$)), as a minor component. Their GC and spectroscopic(IR, ^{1}H-NMR(360MHz), MS) properties were all identical with those of the corresponding natural products.

Acknowledgment We thank Drs. Katsuya Endo and Yoshiteru Oshima, Pharmaceutical Institute, Tohoku University, for their helpful assistance.

References

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3. Synthsis of racemic semburin(1) has been recently accomplished by employing the fundamentally different approach: Y. Ohfune, K. Takaki, H. Kameoka, and T. Sakai, Chemistry Lett., 1982, 209.
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6. Reduction using lithium aluminum hydride alone in THF also gave the diol(7) accompanied by a considerable amount of deselenated by-products.
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(Received April 14, 1982)