

A FACILE SYNTHESIS OF (+)-TECOMANINE USING A CHIRAL
CYCLOPENTANE DERIVATIVE

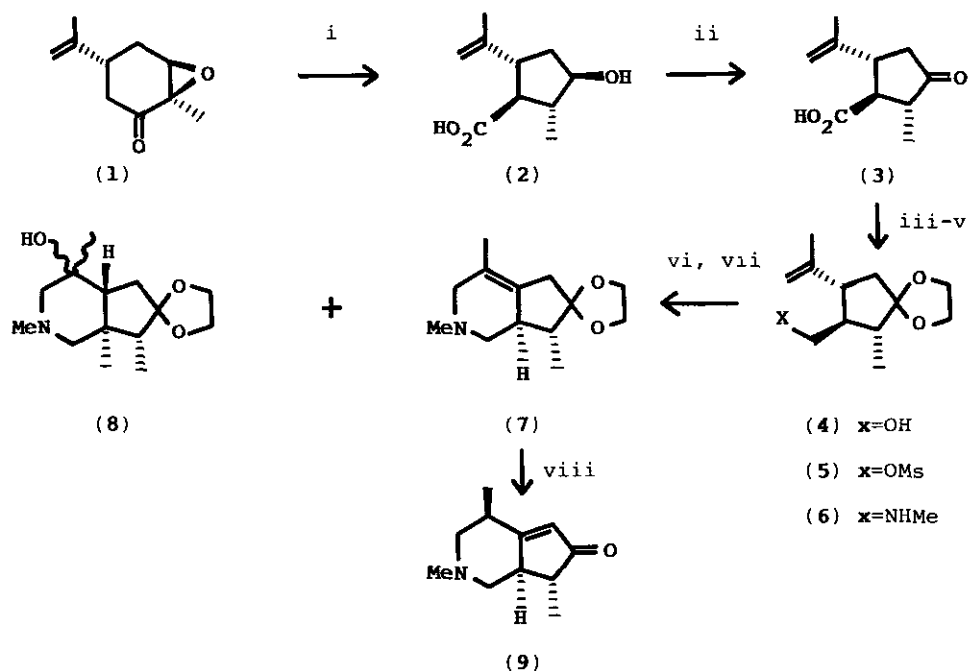
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Abstract ——— (-)-Carvone was efficiently converted into a
chiral cyclopentane derivative (3), which was utilized as a
starting material in the synthesis of (+)-tecomanine (9)
successfully.

Chiral cyclopentane derivatives have widely been employed as important starting materials in the syntheses of naturally occurring compounds.¹ Development of an efficient preparation of a chiral cyclopentane derivative from readily available substances with both (+)- and (-)-forms is therefore desirable.

In 1974, Asaka² reported the Favorskii-type rearrangement of (+)-carvone monoepoxide (1) using sodium ethoxide to furnish the tetra-substituted cyclopentane derivative (2). Although both enantiomers of carvone are commercially available and the product (2) seemed to be a useful chiral source for the synthesis of various types of natural products due to the presence of different functional groups on the ring, the conversion yield was rather low, and difficulties were mentioned in the isolation of the desired compound in this reaction according to our own reexamination.

First we therefore investigated the improved preparation of 3. One pot reaction of the Favorskii-type rearrangement of (+)-carvone monoepoxide (1) using sodium methoxide followed by hydrolysis and subsequent oxidation of the crude product afforded the ketone (3), in 60 % yield, as an easily isolable material. As we could establish the efficient conversion of carvone into the desired cyclopentane derivative (3), our attention was focused on its utilization in the synthesis of (+)-tecomanine, an antipodal form of natural product which is known to exhibit a hypoglycemic activity.³ Ketalization of 3 in a usual manner, followed by



Scheme Reagents and conditions: 1, NaOMe-MeOH, 3h, then addition of H_2O , 2h; ii, 4N-Jones reagent, acetone, 3h; iii, $HOCH_2CH_2OH$, H^+ , benzene, reflux, then $LiAlH_4$, THF, $0^\circ C$, 5h; iv, $MeSO_2Cl$, Et_3N , CH_2Cl_2 , $0^\circ C$, 10 min; v, 40 % $MeNH_2$ -MeOH, Na_2CO_3 , reflux, 3h; vi, NCS, CH_2Cl_2 , $0^\circ C$, 3 min; vii, Ag_2O , dioxane- H_2O (2:1), reflux, 2h, viii; 60 % $HClO_4$, acetone, 2h.

reduction with lithium aluminium hydride afforded the alcohol (4), in 73 % yield, whose methanesulfonylation gave rise to the mesylate (5). Treatment of 5 with methylamine in the presence of sodium carbonate provided the amine (6) in 83 % yield. N-Chlorination of 6 on treatment with N-chlorosuccinimide and subsequent cyclization⁴ of the chloride in dioxane-H₂O (2:1 v/v) in the presence of Ag₂O furnished the olefin (7) and the alcohol (8) in 21 % and 59 % yields, respectively. Deprotection of the ketal group of 7 with 60 % HClO₄ in acetone brought about the migration of the double bond to give (+)-tecomanine (9) $[[\alpha]_D^{25} + 146^\circ$ (c=0.84, CHCl₃) as picrate, mp 182.5 - 183.5 °C (lit.⁵ $[\alpha]_D^{25} - 175^\circ$ (c=1.17, CHCl₃), mp 179.5 - 180.5 °C], whose spectral data were identical with those of synthetic (±)-tecomanine.⁶ Thus we established an improved synthetic method of a chiral cyclopentane derivative (3) and succeeded in its utilization in the synthesis of (+)-tecomanine. The readily available cyclopentane derivative (3) will be a useful chiral starting material for the synthesis of a variety of natural products and its further application is under investigation.

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