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A Stereoselective Synthesis of a Basic Skeleton of Amaryllidaceae Montanine-type Alkaloids, (±)-4a,11a-cis-11,11a-syn-5,11-Methanomorphanthridine Ring System

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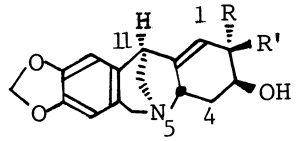
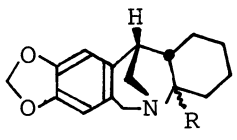
A title compound was synthesized by reductive cyclization of 4a,11a-cis-11,11a-syn-11-acetoxymethyl-N-p-tosylmorphanthridine or N-detosylated alcohol derived from a hydroxymethyl-p-tosylamide prepared by hydroboration-oxidation of cis-1-(p-tosylamido)-2-vinylcyclohexane derivative.

Recently, we reported a first synthesis[1] of (±)-4a,11a-cis-11,11a-anti-5,11-methanomorphanthridine (3) and its trans isomer (4), which are a basic skeleton of Amaryllidaceae montanine-type alkaloids, montanine (1)[2] and coccinine (2)[2] by reductive cyclization of 11-hydroxymethyl-N-tosylmorphanthridines with sodium bis(2-methoxyethoxy)aluminum hydride (SMEAH) in boiling toluene. In the methodology, however, stereoselective synthesis of a 4a,11a-cis-11,11a-syn compound (5), having the same stereochemistry to that at the 4a and 11 positions in 1 and 2, was not achieved. Therefore,



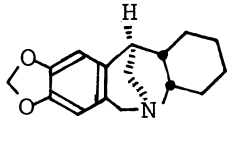
1 R=OMe, R'=H

2 R=H, R'=OMe



3 R=β-H

4 R=α-H



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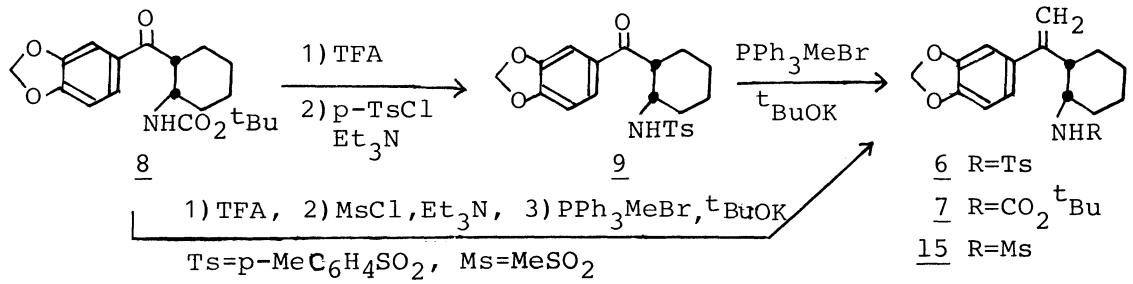
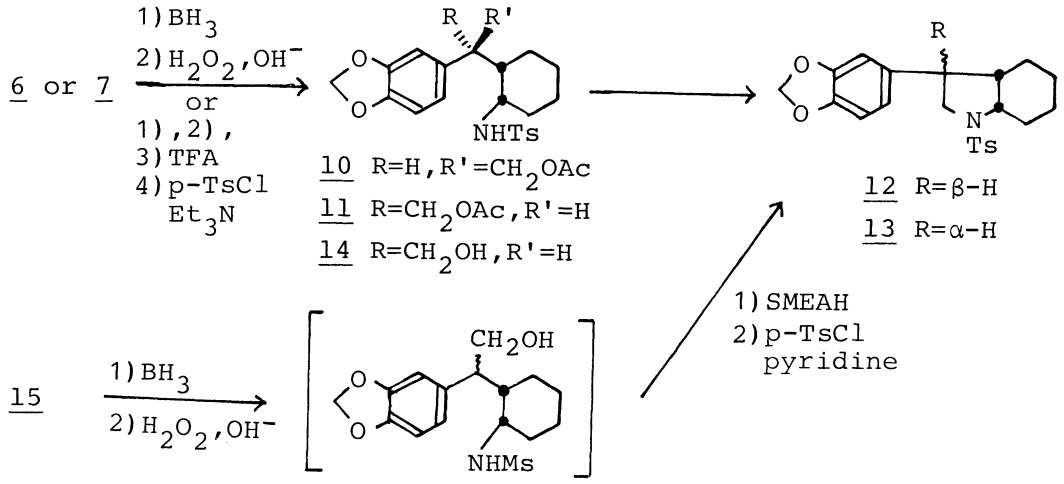
the development of the more efficient method for its stereoselective synthesis was explored. In the present paper, we wish to report a stereocontrolled effect of a p-tosyl group in hydroboration-oxidation[3] of 6 and a stereoselective synthesis of the title compound (5).



Terminal olefins (6 and 7) were prepared as follows. Reaction of cis-cyclohexane-1,2-dicarboxylic anhydride with 3,4-methylenedioxyphenylmagnesium bromide in THF at 0 °C gave cis-2-(3,4-methylenedioxybenzoyl)cyclohexane-1-carboxylic acid[4] (mp 168-169 °C), whose Curtius rearrangement furnished a carbamate (8)[4] (mp 138 °C; 61%). Conversion of 8 to a p-tosylamide (9)[4] (mp 173 °C) was performed in 91% yield. Wittig reaction of 8 and 9 gave 7[4] (mp 83.5 °C; 96%) and 6[4] (mp 173 °C; 84%), respectively.

Hydroboration-oxidation of 7 followed by acetylation gave a mixture of acetoxy carbamates, which were similarly converted to a separable mixture of p-tosylamides 10[4] (mp 125-126 °C) and 11[4] (mp 172-173 °C) in a ratio of 1:11.8[5] (71% overall yield). Structures of the p-tosylamides (10 and 11) were determined by their transformation to the known N-(p-tosyl)-3-(3,4-me-



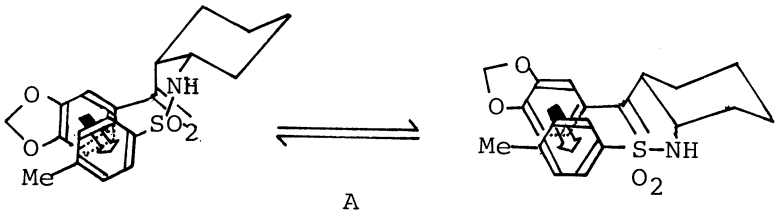
thylenedioxyphenyl) indolines[1] (12 and 13).

On the other hand, the similar reaction of 6 gave exclusively a hydroxymethyl-p-tosylamide (14)[4] (mp 184 °C; 100%), whose acetylation gave 11.

In order to explore the effect of the sulfonamide group in the hydroboration, a mesylamide (15)[4] (mp 103-104 °C; 71%) was used. The similar reaction of mesylamide (15) as noted above gave a diastereomeric mixture of hydroxy mesylamides in 93% yield, a ratio of which was undeterminable. Therefore, the mixture was converted in the usual manner to a diastereomeric mixture of 12 and 13. Surprisingly, the ratio of 12 and 13 was 17:1,[5] showing the reverse of the results obtained in the case of 6 and 7. This finding suggested the hydroboration to occur intramolecularly by the sulfonamide-borane complex,[6] which would be formed initially by reaction of acidic sulfonamido group with borane.

To confirm the supposition, reaction of 15 in the presence of n-butyllithium (one equivalent) was similarly carried out to give a diastereomeric mixture of 12 and 13 in a ratio of 1:4.3[5] (23% overall yield) as expected, although the stereoselectivity was poor.

The remarkable difference is attributable to the steric hyndrance, which would occur because of the formation of the charge-transfer complex[7] (e.g. A) between 3,4-methylenedioxyphenyl and p-tosyl groups in 6, although a sulfonamide-borane complex might be formed. Furthermore, the less stereoselectivity of 7 and 15 would be explained in terms of the lack of the complex. Thus, a dramatic stereocontrolled effect of p-tosyl group in hydroboration-oxidation of a terminal olefin (6) was observed.



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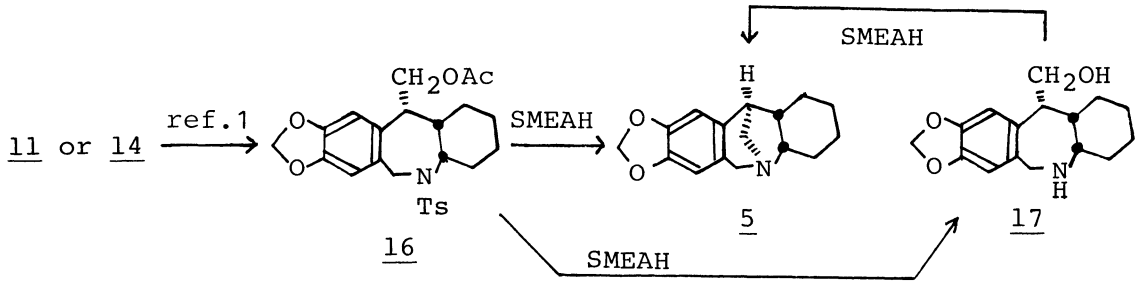
Conversion of 11 obtained above to 5 was performed as follows. Cyclization of 11 under the same conditions as reported previously[1] gave an 11-acetoxymethyl-N-tosylmorphanthridine (16)[4] (mp 136 °C; 77%), which was also

obtained (46%) from 14 under the same conditions.



Treatment of 16 with SMEAH in boiling toluene for 5 h gave 5 [mp 100 °C; 77%; MS m/z: 275 (M), 175 (base peak)], while reaction for 3 h yielded only an N-detosylated alcohol (17)[4] (mp 179-180 °C; 45%), which was cyclized to 5 (43%) by the similar treatment (3 h) as noted for 16. Structure of 5 was determined by comparison of its mass spectral data with those[8] reported and those described for its isomers.[1]

Thus, a stereoselective synthesis of 5 was accomplished.

References

1) O. Hoshino, M. Ishizaki, K. Saito, and K. Yumoto, J. Chem. Soc., Chem. Commun., 1990, 420.

2) Y. Inubushi, H. M. Fales, E. W. Warnhoff, and W. C. Wildman, J. Org. Chem., 25, 2153(1960).

3) Cf. There are reports on stereochemistry of hydroboration of terminal olefins, such as 2-substituted methylenecyclohexanes and methylenecyclopentanes [Y. Senda, S. Kamiyama, and S. Imaizumi, Tetrahedron, 33, 2933(1977)]. However, the reaction does not always proceed stereoselectively.

4) All new compouds gave satisfactory chemical and mass and ^{1}H-NMR spectral analyses.

5) A ratio was estimated by gas-liquid chromatography.

6) Formation of β-hydroxysulfoximines-borane complex is reported: C. R. Johnson and C. J. Stark, Tetrahedron Lett., 1979, 4713.

7) A p-tosyl group is known to behave as a π-acceptor: M. D. Bentley and M. J. S. Dewar, Tetrahedron Lett., 1967, 5043.

8) W. C. Wildman and C. L. Brown, J. Am. Chem. Soc., 90, 6439(1968).

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