

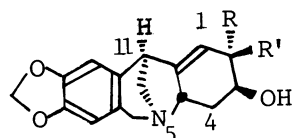
A Stereoselective Synthesis of a Basic Skeleton of Amaryllidaceae
Montanine-type Alkaloids, ($\pm$)-4a,11a-cis-11,11a-syn-5,11-
Methanomorphanthridine Ring System

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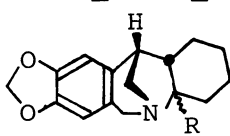
A title compound was synthesized by reductive cyclization of 4a,11a-cis-11,11a-syn-11-acetoxymethyl-N-p-tosylmorphanthridine or N-detosylated alcohol derived from a hydroxymethyl-p-tosylamide prepared by hydroboration-oxidation of cis-1-(p-tosylamido)-2-vinylcyclohexane derivative.

Recently, we reported a first synthesis¹⁾ of ($\pm$)-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,



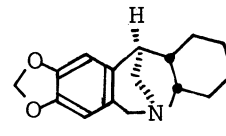
1 R=OMe, R'=H

2 R=H, R'=OMe



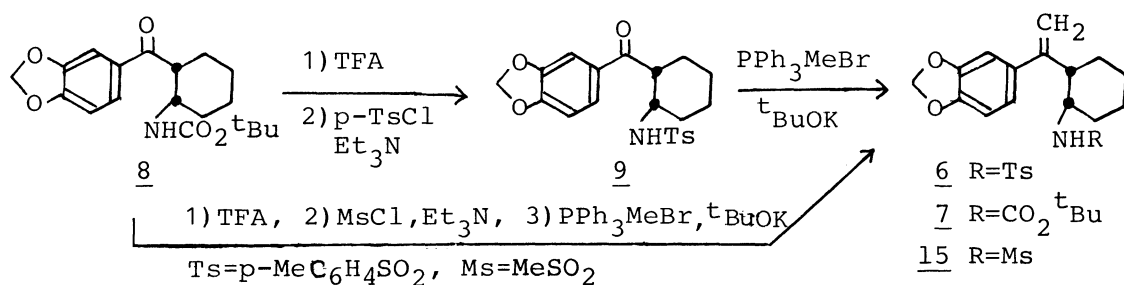
3 R= β -H

4 R= α -H



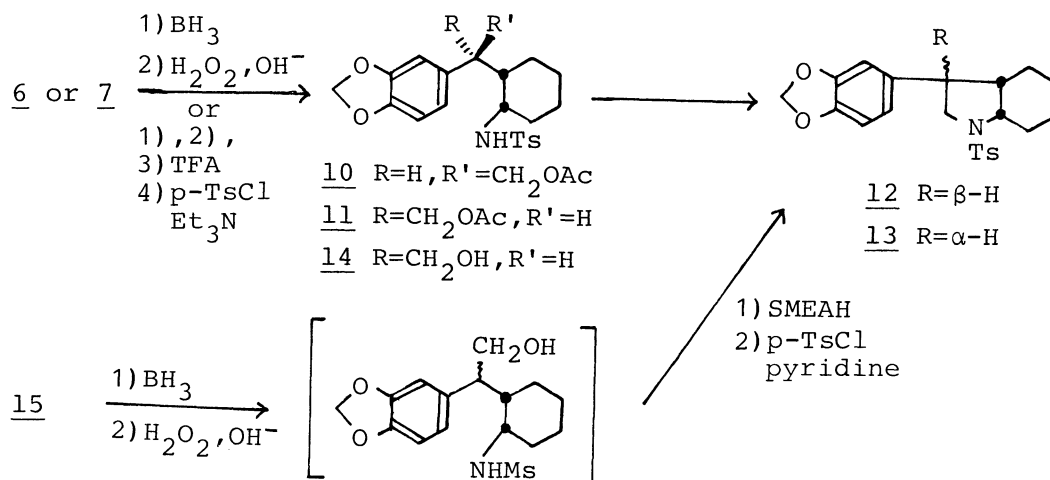
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the development of the more efficient method for its stereoselective synthesis was explored. In the present paper, we wish to report a stereocontrolled effect of a p-tosyl group in hydroboration-oxidation³⁾ of 6 and a stereoselective synthesis of the 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 acid⁴⁾ (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 7⁴⁾ (mp 83.5 °C; 96%) and 6⁴⁾ (mp 173 °C; 84%), respectively.

Hydroboration-oxidation of 7 followed by acetylation gave a mixture of acetoxycarbamates, which were similarly converted to a separable mixture of p-tosylamides 10⁴⁾ (mp 125-126 °C) and 11⁴⁾ (mp 172-173 °C) in a ratio of 1:11.8⁵⁾ (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-



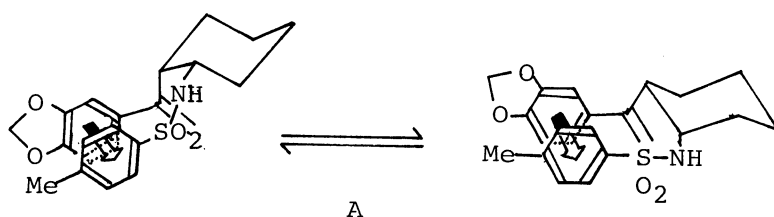
thylenedioxyphenyl)indolines¹⁾ (12 and 13).

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 1:4.3⁵⁾ (23% overall yield) as expected, although the stereoselectivity was poor.

The remarkable difference is attributable to the steric hindrance, which would occur because of the formation of the charge-transfer complex⁷⁾

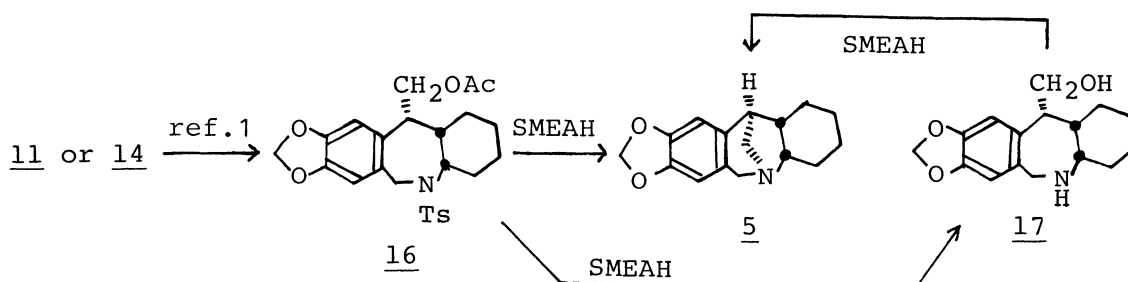


(e.g. A) between 3,4-methylenedioxyphenyl and p-tosyl groups in 6, although a sulfonamide-

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.

Conversion of 11 obtained above to 5 was performed as follows. Cyclization of 11 under the same conditions as reported previously¹⁾ 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 those⁸⁾ 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 compounds gave satisfactory chemical and mass and ¹H-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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