MASTER'S THESIS

Chiral acetylenic sulfoxide in asymmetric synthesis ; Enantioselective synthesis of yohimbine alkaloids

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Date of Award:
1997

Chiral Acetylenic Sulfoxide in Asymmetric Synthesis.

Enantioselective Synthesis of Yohimbine Alkaloids

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A thesis submitted in partial fulfilment

of the requirements for the degree of

Master of Philosophy

September 1997

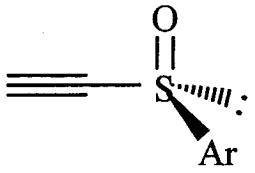
Hong Kong Baptist University

Abstract

Optically active sulfoxides are very useful synthons in asymmetric synthesis. The chirality of sulfinyl group can be used to influence the stereochemistry of an asymmetric process. In the first part of our research, chiral aryl acetylenic sulfoxides **11a-d** were prepared in optically pure form *via* the Anderson synthesis. The optically pure sulfinate precursors for the Andersen synthesis were either available commercially or synthesized from the corresponding sulfonyl chlorides using literature procedures.

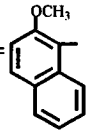
In our approach to the alkaloids syntheses, the chiral acetylenic sulfoxides used as two-carbon synthons were very good Michael acceptors for both primary and secondary amine. In part two of this thesis, the diastereoselectivity of Michael addition/cyclization in the construction of tetrahydro-β-carboline alkaloids skeleton was studied. We reveal that the stereoselectivity on the tetrahydro-β-carboline systems is highly influenced by several factors: substituents on the aromatic ring of the chiral acetylenic sulfoxides; acids used in the cyclization; and primary *verse* secondary amine as the first nucleophile.

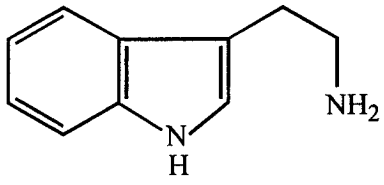
An enantioselective synthesis of yohimbine type intermediate **60** was achieved in the third part of this thesis. By a combination of reductive amination and Michael addition-cyclization with optically pure acetylenic sulfoixde, tryptamine **1** was converted to **22a'**. After protected with tosyl group, **22a'** underwent Pummerer cyclization in the presence of Lewis acid. Deprotection of the desulfurization product **59** afforded **60**. Compound **60** has been transformed to yohimbone and alloyohimbone in literature. They are the precursors of the natural alkaloids, yohimbinol, corynanthiene, alloyohimbine and rauwolscine.



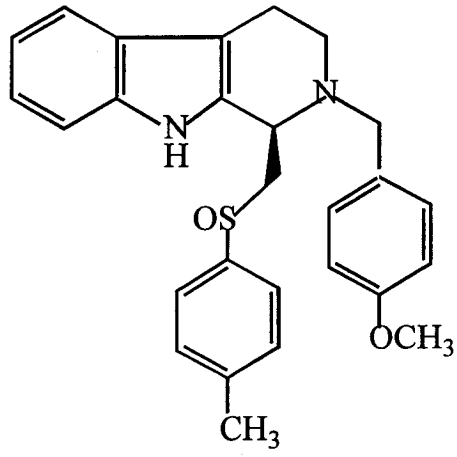
11

a Ar=*p*-BrC_6H_4 b Ar=*o*-$NO_2C_6H_4$

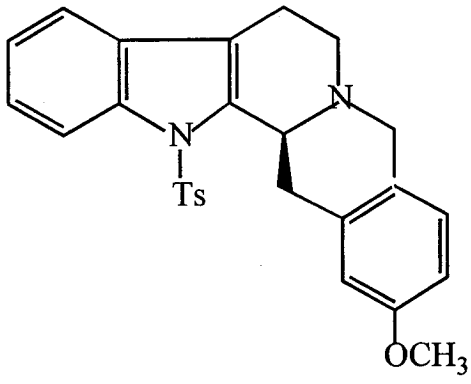
c Ar=*p*-$CH_3C_6H_4$ d Ar= 



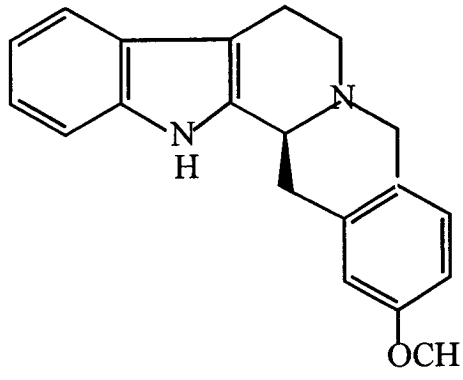
1



22a'



59



60

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