

MASTER'S THESIS

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

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**Chiral Acetylenic Sulfoxide in Asymmetric
Synthesis.**

Enantioselective Synthesis of Yohimbine Alkaloids

MO Tian

**A thesis submitted in partial fulfilment
of the requirements for the degree of
Master of Philosophy**

September 1997

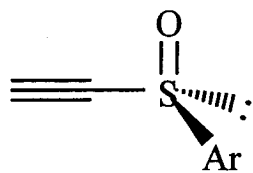
Hong Kong Baptist University

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.

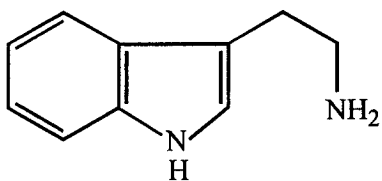
An enantioselective synthesis of yohimbine type intermediate **60** was achieved in the third part of this thesis. By a combination of reductive amination and Michael addition-cyclization with optically pure acetylenic sulfoxide, tryptamine **1** was converted to **22a'**. After protected with tosyl 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, corynanthine, alloyohimbine and rauwolscine.



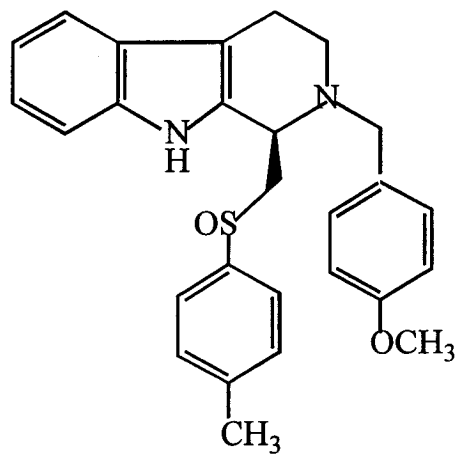
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a Ar=*p*-BrC₆H₄ b Ar=*o*-NO₂C₆H₄

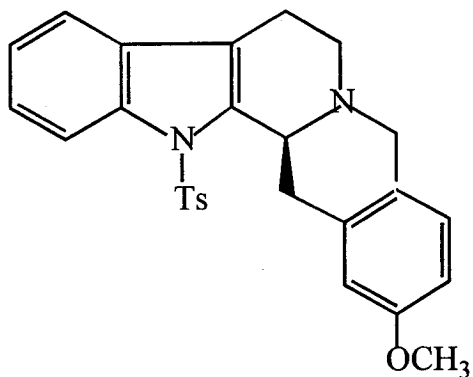
c Ar=*p*-CH₃C₆H₄ d Ar=



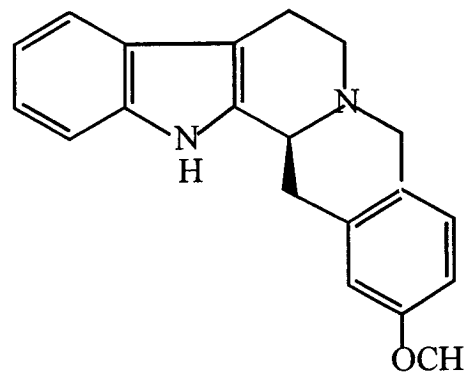
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22a'



59



60

Table of Contents

Declaration.....	i
Abstract.....	ii
Acknowledgments.....	iv
Table of Contents.....	v
List of Tables.....	vii
List of Abbreviations.....	viii
List of Schemes and Diagram.....	x
List of Selected Spectrum.....	xii
Chapter 1. Chiral Acetylenic Sulfoxide and Asymmetric Synthesis.....	1
1.1 Introduction.....	2
1.1.1 Asymmetric Synthesis.....	2
1.1.2 Chiral Sulfoxide in Asymmetric Synthesis.....	7
1.2 Chiral Acetylenic Sulfoxide in Asymmetric Synthesis.....	10
1.2.1 Preparation of the Diastereomerically Pure Sulfinate Esters from Sulfonyl Chlorides.....	12
1.2.2 Synthesis of Chiral Acetylenic Sulfoxide.....	14
Chapter 2. Chiral Acetylenic Sulfoxide in Enantioselective Synthesis of Tetrahydro-β-carboline Alkaloids.....	16
2.1 Introduction.....	17
2.2 Results and Discussion.....	19
2.2.1 Studies on the Diastereoselectivity of Michael Addition/Cyclization Reaction Sequence in the Construction of Tetrahydro- β -carboline Alkaloid Skeleton.....	19
2.2.1.1 Primary Amine <i>versus</i> Secondary Amine Cyclization in Protic Acids	25
2.2.1.2 Effect of Different Substituents on the Aromatic Ring of Chiral Acetylenic Sulfoxides.....	30
2.2.1.3 Uses of Lewis Acids in the Cyclization.....	34
2.3 Summary.....	37
Chapter 3. Formal Enantioselective Synthesis of Yohimbine Alkaloids, Yohimbinol and Corynantheine.....	38
3.1 Introduction.....	39
3.2 Enantioselective Synthesis of Yohimbine Alkaloids.....	44
Chapter 4. Conclusion.....	61

Chapter 5. Experimental	63
References	93
Appendix: Spectroscopic Data	97
VITA	185