

## MASTER'S THESIS

### Chiral acetylenic sulfoxide in asymmetric alkaloid synthesis

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**Chiral Acetylenic Sulfoxide in Asymmetric Alkaloid Synthesis**

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**A thesis submitted in partial fulfillment of the requirements**

**for the degree of**

**Master of Philosophy**

**Principal supervisor: Prof. Albert W. M. LEE**

**Hong Kong Baptist University**

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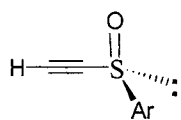
## Abstract

The use of chiral acetylenic sulfoxide as a two-carbon synthon in asymmetric synthesis was explored. Enantiomerically pure acetylenic sulfoxides **1a-c** with different aryl substituents were synthesized in optically pure forms from the corresponding sulfinate precursors *via* the Anderson synthesis.

Enantioselective syntheses of  $\beta$ -carboline and tetrahydroisoquinoline skeletons were outlined. Factors affecting the diastereoselectivity such as aryl substituents in the chiral acetylenic sulfoxide, primary *vs.* secondary amine and the reaction temperature were investigated.

Reactions of L-tryptophan methyl ester and its  $N_b$ -benzylated derivative with chiral acetylenic sulfoxides built the  $\beta$ -carboline skeleton with good diastereoselectivity. In this double asymmetric induction approach, the *trans* isomers (**3-5** and **3-6**) could be purified as the predominant products. Attempted synthesis of the Cook's ketone **3-19**, which is a key intermediate for the syntheses of sarpagine and related alkaloids, *via*  $N_a$ -methylated *trans* isomers failed.

Tetrahydroisoquinoline could be enantioselectively synthesized from chiral acetylenic sulfoxides. Further functional group transformations completed a total synthesis of (*S*)-calycotomine (**4-20**). Attempted synthesis of (*R*)-(-)-cryptaustoline (**4-22**) is also presented.

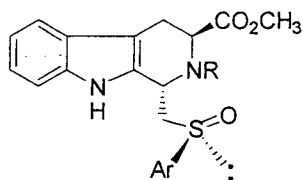


(*R*)-(+)-1

1a, Ar = *p*-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>

1b, Ar = *p*-BrC<sub>6</sub>H<sub>4</sub>

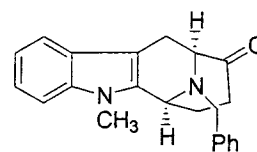
1c, Ar = *o*-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>



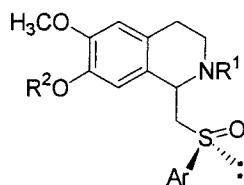
$\beta$ -carboline

R = H, 3-5

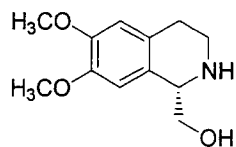
R = Bn, 3-6



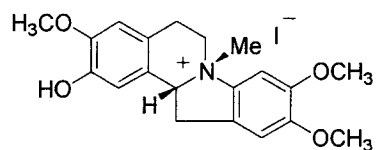
Cook's ketone 3-19



Tetrahydroisoquinoline



(*S*)-(+)-calycotomine 4-20



(*R*)-(-)-cryptaustoline 4-22

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