摘 要

本篇論文主要探討利用分子對稱的觀念來協助一些□引□朵生物鹼之合成研究。我們使用了 Pictet–Spengler 反應，以色胺與具有對稱性的醛來建立這類天然物之 tetrahydro–β–carboline 之架構。

(i) Tangutorine **1** 之全合成：經由關鍵的中間體**2**；化合物**2**具有與**1** 相同的立體化學。**2** 本身是由色胺與醛**3** 一從對稱的 1,3-環己二酮製備一以 Pictet–Spengler 及分子內 Michael 加成反應來製造。

(ii) Eburnamonine **7** 之全合成：經由螺環中間體**12**。

(iii) Vallesamidine **20** 之 formal 合成：經由中間體**25**。

Aspidospermidine **39** 之合成研究：經由螺環中間體**47** 。

(iv) Oxogambirtannine **40** 之合成研究:經由中間體**55**。

化合物 **12**, **25**, **47**及**55** 的製備都使用 Pictet–Spengler 反應由色胺及對稱的醛，分別是**11c**, **24c**, **49c** 及 **51** 來製造。

ABSTRACT

Synthetic studies towards several indole alkaloids were pursued, utilizing molecular symmetry to guide the synthetic design. All tetrahydro-β-carbolines intermediates described in this dissertation were constructed by reacting tryptamine with symmetrical aldehydes *via* acid-induced Pictet-Spengler reaction:

- Total synthesis of tangutorine **1** started from the reaction of tryptamine with aldehyde **3** - derived from symmetrical 1,3-cyclohexadione - to build the key intermediate **2** that has the correct stereochemistry of tangutorine **1**.
- Total synthesis of Eburnamonine **7** was conducted *via* a spirocyclic intermediate **12,** formed by reacting tryptamine with symmetrical 5-membered ring aldehyde **11c**.
- Formal synthesis of vallesamidine **20** was conducted *via* intermediate **25**, formed by reacting tryptamine with symmetrical 7-membered ring aldehyde **24**.
- Synthetic study on aspidospermidine **39** was conducted *via* a spirocyclic intermediate **47**, formed by reacting tryptamine with symmetrical tetrahydropyranyl aldehyde **49c**.
- Synthetic study on oxogambirtannine **40** was conducted by reacting tryptamine with symmetrical 2-aryl substituted acetaldehyde **51**.

PREFACE

Prelog wrote in his '*My 132 Semesters of Chemistry Studies*' that the best way to learn science is as an apprentice to a master who is a model both in his field and in his personal characteristics. He also emphasized that it was important for a chemist to be confronted with reality and that sometimes it is better to follow the maxim, "*Work now, understand later*", later than the reverse.

I could still remember my discussion with Prof. Ho Tse-lok when I took a leave from BASF in Indonesia and returned to Taiwan for possibility of pursuing PhD programme under his guidance. It was in December 2001. About half years later, after being involved in colorants (pigments and dyes) for nearly 5 years, I resigned and started my PhD programme. The research did not work out as smooth as was expected. I was not in touch with organic chemistry and its laboratory experiments for about 7 years. My job experience in the colorants, included formulation development, but I was involved mainly in the application area, where the main emphasis is on how to grind, disperse the colorants and stabilize the dispersion; basically, no chemical reactions are welcomed during the process, as when they happened, that meant you destroyed the colorants. During those years in colorants, as I was busy with day-to-day management work, I was used to delegate all my ideas on formulation development to my fully-trained laborants. So it took some time before I could accustom myself back to the 'normal' life of organic chemistry experiments.

Time went so fast. After about 3 years, finally this research has come to an end. I could say that after several years of living a colorful life with colorants, I have also experienced another 'colorful' life with organic synthesis. To this, I would like to express my deep appreciation and thanks to my mentor, Prof. Ho Tse-lok for his advice and in-time (painstaking) guidance, especially when I encountered 'bottle-necked' problems in my projects. Also for the arrangement of the financial support from National Science Council of

Republic of China.

I would like also to express my thanks to all the members of my examination committee for their suggestions and corrections: Dr. Chung Wen-Sheng, Dr. Tsai Yeun-Min, Dr. Tony Mong and Dr. Chiu Sheng-Hsien.

This research would not be completed without strong supports from my beloved mother and my family. Special gratitude to my late father, who died several months after the tragic racial 1998 incident in Jakarta, Indonesia.

I also would like to express my thanks to Grace Wu for her constant support and understanding during the whole process, especially sharing my problems during difficult moments.

Last but not least, I would like to express how delightful I have been to enjoy the company of all the laboratory colleagues of Prof. Ho Tse-lok's laboratory, present and past. And also to Ms. Chang of NCTU Instrument Center for her NMR service, Ms. Li for her LRMS and EA, Ms. Lin and Ms. Tsai of NTHU Instrument Center for their HRMS service.

CONTENTS

LIST OF NMR SPECTRA

page

ABBREVIATIONS

Ac	acetyl
Ar	aryl
Bn	benzyl
BOC	*t*-butoxycarbonyl
Bz	benzoyl
DIBAL-H	diisobutylaluminum hydride
DMAP	4-(*N*,*N*-dimethylamino)pyridine
DMF	dimethylformamide
DMSO	dimethyl sulfoxide
LAH	lithium aluminum hydride
LDA	lithium diisopropylamide
LTA	lead tetraacetate
MCPBA	*m*-chloroperbenzoic acid
Ms	methanesulfonyl
NMO	*N*-methylmorpholine *N*-oxide
PCC	pyridinium chlorochromate
PDC	pyridinium dichromate
PTSA	*p*-toluenesulfonic acid
Py	pyridine
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TMS	trimethylsilyl
TLC	thin layer chromatography