

การสังเคราะห์อนุพันธ์ของ 5-เอริล-3-เมทิล-1,2,3,4-เททระไฮโดรไอโซควิโนลิน



นาย วิสุจน์ วิจิตรนิเทศ

ศูนย์วิทยทรัพยากร

จุฬาลงกรณ์มหาวิทยาลัย

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาเภสัชศาสตรมหาบัณฑิต

สาขาวิชา เภสัชเคมี ภาควิชา เภสัชเคมี

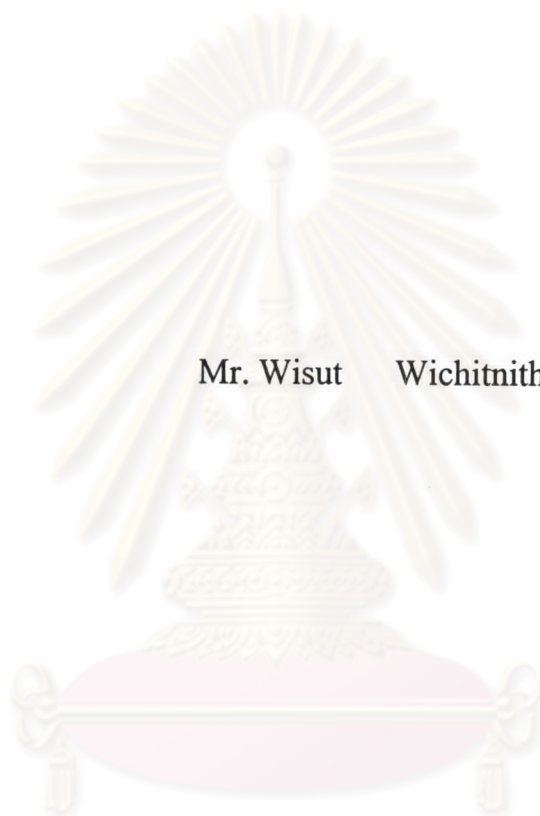
คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

ปีการศึกษา 2546

ISBN 974-17-5016-1

ลิขสิทธิ์ของจุฬาลงกรณ์มหาวิทยาลัย

SYNTHESIS OF 5-ARYL-3-METHYL-1,2,3,4-TETRAHYDRO-  
ISOQUINOLINE DERIVATIVES



Mr. Wisut Wichitnithad

ศูนย์วิทยทรัพยากร  
A Thesis Submitted in Partial Fulfillment of the Requirements  
for the Degree of Master of Science in Pharmacy in Pharmaceutical Chemistry

Department of Pharmaceutical Chemistry

Faculty of Pharmaceutical Sciences

Chulalongkorn University


Academic year 2003

ISBN 974-17-5016-1

Thesis Title           SYNTHESIS OF 5-ARYL-3-METHYL-1,2,3,4-TETRAHYDROISO-  
                                  QUINOLINE DERIVATIVES  
By                        Mr. Wisut Wichitnithad  
Field of Study         Pharmaceutical Chemistry  
Thesis Advisor        Assistant Professor Chamnan Patarapanich, Ph.D.  
Thesis Co-advisor    Associate Professor Sunibhond Pummangura, Ph.D.

---


Accepted by the Faculty of Pharmaceutical Sciences, Chulalongkorn University in  
Partial Fulfillment of the Requirements for the Master's Degree

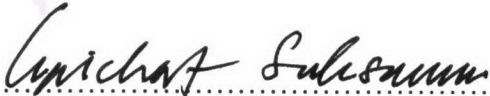
  
.....Dean of Faculty of Pharmaceutical Sciences  
(Associate Professor Boonyoung Tantisira, Ph.D.)

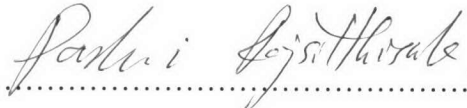
THESIS COMMITTEE

  
.....Chairman  
(Assistant Professor Mittr Pathipvanich, Ph.D.)

  
.....Thesis Advisor  
(Assistant Professor Chamnan Patarapanich, Ph.D.)

  
.....Thesis Co-Advisor  
(Associate Professor Sunibhond Pummangura, Ph.D.)

  
.....Member  
(Professor Apichart Suksamrarn, Ph.D.)

  
.....Member  
(Pornchai Rojsitthisak, Ph.D.)

วิสุจน์ วิจิตรนิเทศ : การสังเคราะห์อนุพันธ์ของ 5-เอริล-3-เมทิล-1,2,3,4-เททระไฮโดรไอโซควิโนลิน. (SYNTHESIS OF 5-ARYL-3-METHYL-1,2,3,4-TETRAHYDROISOQUINOLINE DERIVATIVES) อ. ที่ปรึกษา : ผศ. ดร. ชำนาญ ภัทรพานิช, อ.ที่ปรึกษาร่วม : รศ. ดร. สุนิพนธ์ ภูมมางกูร, 290 หน้า. ISBN 974-17-5016-1.

แอนซิสโตรคาติน และ อนุพันธ์ของแนปทิลไอโซควิโนลิน ซึ่งมีรายงานว่ามียฤทธิ์ทางเภสัชวิทยาหลาย ๆ อย่างรวมทั้งฤทธิ์ต้านเชื้อมาลาเรีย ในงานวิจัยครั้งนี้เป็นการสังเคราะห์อนุพันธ์ของ 5-เอริล-3-เมทิล-1,2,3,4-เททระไฮโดรไอโซควิโนลิน ซึ่งเป็นสารอินทรีย์กลุ่มใหม่ที่ใช้ 5-แนปทิล-1,2,3,4-เททระไฮโดรไอโซควิโนลิน อัลคาลอยด์ เป็นสารต้นแบบ

สารประกอบในกลุ่มนี้ถูกสังเคราะห์ขึ้นโดยกระบวนการสังเคราะห์เริ่มจากการเตรียม อนุพันธ์ของ 1,2,3,4-เททระไฮโดรไอโซควิโนลิน โดยผ่านกระบวนการปัดวงแหวนผ่านสารตัวกลางที่เป็น เอน, โอ-อะซีทาว จากอนุพันธ์ของเฟนิลเอทิลเอมีน ซึ่งอนุพันธ์ของ 1,2,3,4-เททระไฮโดรไอโซควิโนลิน จะถูกนำไปทำปฏิกิริยา ไอโอดีเนชัน ได้เป็นอนุพันธ์ของ 5-ไอโอโด-3-เมทิล-1,2,3,4-เททระไฮโดรไอโซควิโนลิน ซึ่งได้เติมหมู่ เอริล กรุป ที่หลากหลาย โดยผ่านปฏิกิริยา ซูซูกิ คับบิง โดยมี เททระกิสไตรเฟนิลฟอสฟีน พาราเดียม เป็นตัวเร่งปฏิกิริยาในค่าที่เหมาะสม ซึ่งจะได้ผลิตภัณฑ์เป็น อนุพันธ์ต่าง ๆ ของ 5-เอริล-3-เมทิล-1,2,3,4-เททระไฮโดรไอโซควิโนลิน โดยสารที่สามารถสังเคราะห์ได้ในครั้งนี้สามารถพิสูจน์เอกลักษณ์ด้วยเทคนิคทาง สเปกโตรสโคปี (IR, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR และ 2-D NMR) และการวิเคราะห์องค์ประกอบของธาตุ

ศูนย์วิทยทรัพยากร  
จุฬาลงกรณ์มหาวิทยาลัย

ภาควิชา           เภสัชเคมี  
สาขาวิชา       เภสัชเคมี  
ปีการศึกษา 2546

ลายมือชื่อนิสิต.....  
ลายมือชื่ออาจารย์ที่ปรึกษา.....  
ลายมือชื่ออาจารย์ที่ปรึกษาร่วม.....



## 4576601333 : MAJOR PHARMACEUTICAL CHEMISTRY

KEY WORDS : SYNTHESIS / ANCISTROCLADINE / ANTIMALARIAL ACTIVITY /SUZUKI CROSS COUPING/ 5-ARYL-3-METHYL-1,2,3,4-TETRAHYDROISOQUINOLINE

WISUT WICHITNITHAD: SYNTHESIS OF 5-ARYL-3-METHYL-1,2,3,4-TETRAHYDROISOQUINOLINE DERIVATIVES. THESIS ADVISOR: ASST. PROF. CHAMNAN PATARAPANICH, Ph.D., THESIS CO-ADVISOR: ASSOC. PROF. SUNIBHOND PUMMANGURA, Ph.D., 290 pp. ISBN 974-17-5016-1.

Ancistrocladine and other naphthylisoquinoline alkaloids have been reported to possess various interesting biological activities including an antimalarial activity. The present investigation was to synthesize new series of 5-aryl-3-methyl-1,2,3,4-tetrahydroisoquinoline derivatives. These synthetic derivatives were designed using the 5-naphthyl-1,2,3,4-tetrahydroisoquinoline alkaloid as lead compound.

The synthetic procedure was started with the reaction of 1,2,3,4-tetrahydroisoquinoline derivatives (THIQ), prepared through *O,N*-acetal intermediates from the phenylethylamine derivative and consequently reacted with iodine to afford the corresponding 5-iodo-3-methyl-1,2,3,4-tetrahydroisoquinoline derivatives. Various aryl groups were introduced in to the position-5 of the THIQ via an efficient Suzuki coupling reaction in the presence of tetrakis (triphenylphosphine) palladium and a suitable base in toluene to give the corresponding 5-aryl-1,2,3,4-tetrahydroisoquinoline derivatives in good yields. The structures of synthetic products were identified by the spectroscopic techniques (IR,  $^1\text{H-NMR}$ ,  $^{13}\text{C-NMR}$  and 2-D NMR) and elemental analysis.

Department Pharmaceutical chemistry Student's signature.....*Wisut Wichitnithad*

Field of study Pharmaceutical chemistry Advisor's signature.....*Channa Patarapanich*

Academic year 2003

Co-advisor's signature.....*Sunibhond Pummangura*

## ACKNOWLEDGEMENT

First, I wish to express my sincerely indebted to my thesis advisor, Assistant Professor Chamnan Patarapanich, and my thesis co-advisor, Associate Professor Sunibhond Pummangura, for their valuable advice, continual guidance, kindness, and understanding throughout my graduate study period. His scientific open-mindedness encouraged me to successfully complete this unique research.

Second, I am sincerely grateful to Professor Apichart suksamrarn and Dr. Pornchai Rojsitthisak for serving on my committee. Their valuable suggestions and discussions made this thesis more complete.

I would also like to acknowledge Professor Akinori Kubo and Dr. Naoki Saito for their valuable information suggestion and some reagent supply. In addition, I thank Dr. Khanit Suwanborirux for sharing his exceptional NMR interpreting skills and for providing so much help.

Furthermore, I would like to thank all staff members, including the scientists of the Department of Pharmaceutical Chemistry, Faculty of Pharmaceutical sciences, Chulalongkorn University for proving facilities during my study. I also grateful to all my friends for their encouragement throughout this graduate study.

Finally, I am grateful to my beloved parents for their love and understanding that enabled me to have willpower and inspiration to finish this work.

## LIST OF TABLES

Table	Page
1	IC <sub>50</sub> values of the 5-Naphthyl-1,2,3,4-Tetrahydroisoquinoline alkaloids (isolated from <i>Ancistrocladaceae sp.</i> ) on chloroquine resistant (K1) and susceptible (NF54) strains of <i>Plasmodium falciparum</i> . ....3
2	General methods for isoquinoline ring construction.....19
3	Reaction Conditions for Head-to-Tail Cross-Coupling.....36
4	The <sup>1</sup> H-NMR spectral data of CU-19-01, CU-19-02, CU-19-03, and CU-19-04.....265
5	The <sup>1</sup> H-NMR spectral data of CU-22-01.....266
6	The <sup>1</sup> H-NMR spectral data of CU-19-05, CU-19-10, CU-20-01, and CU-20-02.....275
7	Conditions and yield of Suzuki cross-coupling reaction.....279
8	The <sup>1</sup> H-NMR spectral data of CU-21-01, CU-21-02, CU-21-03, CU-21-04 and CU-21-05.....281
9	The <sup>1</sup> H-NMR spectral data of CU-21-06, CU-21-07, CU-21-08, CU-21-09 and CU-21-10.....282

ศูนย์วิทยทรัพยากร  
จุฬาลงกรณ์มหาวิทยาลัย

## CONTENTS

	Page
Thai Abstract.....	iv
English Abstract.....	v
Acknowledgement.....	vi
List of Tables.....	vii
List of Schemes.....	ix
List of Figures.....	xi
List of Abbreviation.....	xxxi
Chapter	
I.    Introduction.....	1
II.   Literature Review.....	16
III.  Experiments.....	42
IV.  Results and Discussion.....	257
V.   Conclusion.....	283
References.....	287
Vita.....	290

ศูนย์วิทยทรัพยากร  
จุฬาลงกรณ์มหาวิทยาลัย



## LIST OF SCHEMES

Schemes	Page
1 The synthetic procedures of <i>N</i> -benzyl-2-(3',5'-dimethoxyphenyl)-1-methylethylamine.....	13
2 The synthetic procedures for 6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline through <i>O,N</i> -acetal cyclization using paraformaldehyde..	13
3 The synthetic procedures for 6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline through <i>O,N</i> -acetal cyclization using butyl glyoxal.....	14
4 The synthetic procedure for the 5-iodo-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline derivatives using the aromatic iodination.....	14
5 The corresponding 5-aryl-3-methyl-1,2,3,4-tetrahydroisoquinoline derivatives synthesis via Suzuki Coupling reaction.....	15
6 The synthetic of <i>N</i> -benzyl-2-(3',5'-dimethoxyphenyl)-1-methylethylamine; a) $\text{CH}_3\text{CH}_2\text{NO}_2$ , $\text{NH}_4\text{OAc}$ , reflux; b) $\text{NaBH}_4$ , IPA/ $\text{CH}_2\text{Cl}_2$ , $\text{SiO}_2$ , room temperature; c) 10 % Pd/C, $\text{H}_2$ , EtOH; d) benzaldehyde, benzene, reflux; e) $\text{NaBH}_4$ , EtOH, room temperature.....	258
7 The synthetic routes of 2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline; f) HCHO, $\text{K}_2\text{CO}_3$ , EtOH, room temperature; g) 0.5 M TFA in $\text{CH}_2\text{Cl}_2$ , 0 °C.....	267
8 The synthetic routes of butyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate; h) $\text{Bu}^n\text{OCOCHO}$ , $\text{K}_2\text{CO}_3$ , $\text{Bu}^n\text{OH}$ , room temperature; i) 0.5 M TFA in $\text{CH}_2\text{Cl}_2$ , 0 °C.....	269



- 9 The synthetic routes of 5-iodo-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline derivatives; i)  $I_2$ ,  $AgNO_3$ ,  $EtOH/CH_2Cl_2$ , room temperature.....272
- 10 The synthetic routes of 5-aryl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline derivatives; j)  $ArB(OH)_2$ ,  $Pd(PPh_3)_4$ , toluene, sat.  $NaHCO_3$ ,  $110^\circ C$ .....276



ศูนย์วิทยทรัพยากร  
จุฬาลงกรณ์มหาวิทยาลัย

## LIST OF FIGURES

Figure	Page
1	5-naphthyl-1,2,3,4-tetrahydroisoquinoline alkaloids of <i>Ancistrocladaceae sp.</i> .....2
2	Diagram illustrated the versatile pharmacological activities of the 1,2,3,4 –THIQ derivatives.....5
3	Sites of structure modification of phenylethylamines.....6
4	The metabolism of norepinephrine and epinephrine by MAO and COMT..9
5	Simplification of the 5-naphthyl-1,2,3,4-tetrahydroisoquinoline structure to 5-aryl-3-methyl-1,2,3,4-tetrahydroisoquinoline derivatives to evaluate the antimalarial activity.....11
6	The chemical structures of target compounds.....11
7	The life cycle of malarial protozoa.....18
8	The general synthetic methods of 1,2,3,4-Tetrahydroisoquinoline.....20
9	The proposed mechanism of Bischler-Napieralski cyclization.....21
10	The proposed mechanism of Pictet-Spengler reaction.....22
11	The synthetic mechanism of THIQ derivatives through <i>N</i> -acyliminium from <i>N</i> -Oxide.....23
12	The synthetic mechanism of tetrahydroisoquinoline through <i>N</i> -acyliminium from azomethine.....24
13	The proposed mechanism of <i>O,N</i> -acetal cyclization reaction.....25
14	The oxidation reaction of the glycol by periodic acid.....28
15	The general catalytic cycle for cross-coupling.....33
16	The IR spectrum (KBr) of 2-(3',5'-dimethoxyphenyl)-1-methyl-1-nitroethene (CU-19-01).....87

Figure	Page
17	The 300 MHz <sup>1</sup> H-NMR spectrum of 2-(3',5'-dimethoxyphenyl)-1-methyl-1-nitroethene (CU-19-01).....88
18	The 75 MHz <sup>13</sup> C-NMR spectrum of 2-(3',5'-dimethoxyphenyl)-1-methyl-1-nitroethene (CU-19-01) .....89
19	The IR spectrum (KBr) of 2-(3',5'-dimethoxyphenyl)-1-methyl-1-nitroethane (CU-19-02).....90
20	The 300 MHz <sup>1</sup> H-NMR spectrum of 2-(3',5'-dimethoxyphenyl)-1-methyl-1-nitroethane (CU-19-02).....91
21	The 75 MHz <sup>13</sup> C-NMR spectrum of 2-(3',5'-dimethoxyphenyl)-1-methyl-1-nitroethane (CU-19-02).....92
22	The 75 MHz DEPT 135 spectrum of 2-(3',5'-dimethoxyphenyl)-1-methyl-1-nitroethane (CU-19-02).....93
23	The 75 MHz DEPT 135 and <sup>13</sup> C-NMR spectrum comparison of 2-(3',5'-dimethoxyphenyl)- 1-methyl-1-nitroethane (CU-19-02).....94
24	The IR spectrum (KBr) of 2-(3',5'-dimethoxyphenyl)- 1-methyl ethylamine (CU-19-03).....95
25	The 300 MHz <sup>1</sup> H-NMR spectrum of 2-(3',5'-dimethoxyphenyl)-1-methylethylamine (CU-19-03).....96
26	The 75 MHz <sup>13</sup> C-NMR spectrum of 2-(3',5'-dimethoxyphenyl)-1-methylethylamine (CU-19-03).....97
27	The 75 MHz DEPT 135 spectrum of 2-(3',5'-dimethoxyphenyl)-1-methylethylamine (CU-19-03).....98
28	The 75 MHz DEPT 135 and <sup>13</sup> C-NMR spectrum comparison of 2-(3',5'-dimethoxyphenyl)- 1- methylethylamine (CU-19-03).....99
29	The IR spectrum (KBr) of <i>N</i> -benzyl-2-(3',5'-dimethoxyphenyl)-1-methylethylamine (CU-19-04).....100

Figure	Page
30	The 300 MHz $^1\text{H}$ -NMR spectrum of <i>N</i> -benzyl-2-(3',5'-dimethoxyphenyl)-1-methylethylamine (CU-19-04).....101
31	The 75 MHz $^{13}\text{C}$ -NMR spectrum of <i>N</i> -benzyl-2-(3',5'-dimethoxyphenyl)-1-methylethylamine (CU-19-04).....102
32	The 75 MHz DEPT 135 spectrum of <i>N</i> -benzyl-2-(3',5'-dimethoxyphenyl)-1-methylethylamine (CU-19-04).....103
33	The 75 MHz DEPT 135 and $^{13}\text{C}$ -NMR spectrum comparison of <i>N</i> -benzyl-2-(3',5'-dimethoxyphenyl)-1-methylethylamine (CU-19-04).....104
34	The IR spectrum (KBr) of 2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-19-05).....105
35	The 300 MHz $^1\text{H}$ -NMR spectrum of 2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-19-05).....106
36	The 300 MHz $^1\text{H}$ -NMR spectrum of 2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-19-05) (Enlarged scale).....107
37	The 75 MHz $^{13}\text{C}$ -NMR spectrum of 2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-19-05).....108
38	The 75 MHz DEPT 135 spectrum of 2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-19-05).....109
39	The 75 MHz DEPT 135 and $^{13}\text{C}$ -NMR spectrum comparison of 2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-19-05) .....110
40	The 300 MHz HH COSY spectrum of 2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-19-05).....111



Figure	Page
41	The 300 MHz HH COSY spectrum of 2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-19-05) (Enlarged scale).....112
42	The 300 MHz HMQC spectrum of 2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-19-05).....113
43	The 300 MHz HMQC spectrum of 2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-19-05) (Enlarged scale).....114
44	The IR spectrum (KBr) of butyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-19-10).....115
45	The 300 MHz <sup>1</sup> H-NMR spectrum of butyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-19-10).....116
46	The 300 MHz <sup>1</sup> H-NMR spectrum of butyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-19-10) (Enlarged scale).....117
47	The 75 MHz <sup>13</sup> C-NMR spectrum of butyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-19-10).....118
48	The 75 MHz DEPT 135 spectrum of butyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-19-10).....119
49	The 75 MHz DEPT 135 and <sup>13</sup> C-NMR spectrum comparison of butyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-19-10).....120
50	The 300 MHz HH COSY spectrum of butyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-19-10).....121



Figure	Page
51	The 300 MHz HH COSY spectrum of butyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-19-10) (Enlarged scale).....122
52	The 300 MHz HMQC spectrum of butyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-19-10).....123
53	The 300 MHz HMQC spectrum of butyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-19-10) (Enlarged scale ).....124
54	The IR spectrum (KBr) of 5-iodo-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-20-01).....125
55	The 300 MHz <sup>1</sup> H-NMR spectrum of 5-iodo-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-20-01).....126
56	The 300 MHz <sup>1</sup> H-NMR spectrum of 5-iodo-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-20-01) (Enlarged scale).....127
57	The 75 MHz <sup>13</sup> C-NMR spectrum of 5-iodo-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-20-01).....128
58	The 75 MHz DEPT 135 spectrum of 5-iodo-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-20-01).....129
59	The 75 MHz DEPT 135 and <sup>13</sup> C-NMR spectrum comparison of 5-iodo-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-20-01).....130
60	The 300 MHz HH COSY spectrum of 5-iodo-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-20-01).....131
61	The 300 MHz HH COSY spectrum of 5-iodo-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-20-01) (Enlarged scale).....132

Figure	Page
62	The 300 MHz HMQC spectrum of 5-iodo-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-20-01).....133
63	The 300 MHz HMQC spectrum of 5-iodo-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-20-01) (Enlarged scale).....134
64	The 300 MHz HMBC spectrum of 5-iodo-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-20-01) (Enlarged scale).....135
65	The IR spectrum (KBr) of butyl-5-iodo-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-20-02).....136
66	The 300 MHz <sup>1</sup> H-NMR spectrum of butyl-5-iodo-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-20-02).....137
67	The 300 MHz <sup>1</sup> H-NMR spectrum of butyl-5-iodo-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-20-02) (Enlarged scale).....138
68	The 75 MHz <sup>13</sup> C-NMR spectrum of butyl-5-iodo-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-20-02).....139
69	The 75 MHz DEPT 135 spectrum of butyl-5-iodo-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-20-02).....140
70	The 75 MHz DEPT 135 and <sup>13</sup> C-NMR spectrum comparison of butyl-5-iodo-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-20-02).....141
71	The 300 MHz HH COSY spectrum of butyl-5-iodo-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-20-02).....142

Figure	Page
72	The 300 MHz HH COSY spectrum of butyl-5-iodo-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-20-02) (Enlarged scale).....143
73	The 300 MHz HMQC spectrum of butyl-5-iodo-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-20-02).....144
74	The 300 MHz HMQC spectrum of butyl-5-iodo-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-20-02) (Enlarged scale).....145
75	The 300 MHz HMBC spectrum of butyl-5-iodo-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-20-02) (Enlarged scale).....146
76	The IR spectrum (KBr) of 5-phenyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-01).....147
77	The 300 MHz <sup>1</sup> H-NMR spectrum of 5-phenyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-01).....148
78	The 300 MHz <sup>1</sup> H-NMR spectrum of 5-phenyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-01) (Enlarged scale).....149
79	The 75 MHz <sup>13</sup> C-NMR spectrum of 5-phenyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-01).....150
80	The 75 MHz DEPT 135 spectrum of 5-phenyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-01).....151
81	The 75 MHz DEPT 135 and <sup>13</sup> C-NMR spectrum comparison of 5-phenyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-01).....152



Figure	Page
82	The IR spectrum (KBr) of 5-(4''-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-02).....153
83	The 300 MHz <sup>1</sup> H-NMR spectrum of 5-(4''-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-02).....154
84	The 300 MHz <sup>1</sup> H-NMR spectrum of 5-(4''-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-02) (Enlarged scale).....155
85	The 75 MHz <sup>13</sup> C-NMR spectrum of 5-(4''-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-02).....156
86	The 75 MHz DEPT 135 spectrum of 5-(4''-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-02).....157
87	The 75 MHz DEPT 135 and <sup>13</sup> C-NMR spectrum comparison of 5-(4''-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-02).....158
88	The 300 MHz HH COSY spectrum of 5-(4''-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-02).....159
89	The 300 MHz HH COSY spectrum of 5-(4''-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-02) (Enlarged scale).....160
90	The 300 MHz HMQC spectrum of 5-(4''-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-02).....161
91	The 300 MHz HMQC spectrum of 5-(4''-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-02) (Enlarged scale).....162
92	The IR spectrum (KBr) of 5-(4''-methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-03).....163

Figure	Page
93	The 300 MHz <sup>1</sup> H-NMR spectrum of 5-(4''-methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-03).....164
94	The 300 MHz <sup>1</sup> H-NMR spectrum of 5-(4''-methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-03) (Enlarged scale).....165
95	The 75 MHz <sup>13</sup> C-NMR spectrum of 5-(4''-methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-03).....166
96	The 75 MHz DEPT 135 spectrum of 5-(4''-methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-03).....167
97	The 75 MHz DEPT 135 and <sup>13</sup> C-NMR spectrum comparison of 5-(4''-methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-03).....168
98	The 300 MHz HH COSY spectrum of 5-(4''-methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-03).....169
99	The 300 MHz HH COSY spectrum of 5-(4''-methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-03) (Enlarged scale).....170
100	The 300 MHz HMQC spectrum of 5-(4''-methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-03).....171
101	The 300 MHz HMQC spectrum of 5-(4''-methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-03) (Enlarged scale).....172
102	The IR spectrum (KBr) of 5-(4''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-04).....173
103	The 300 MHz <sup>1</sup> H-NMR spectrum of 5-(4''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-04).....174



104	The 300 MHz $^1\text{H}$ -NMR spectrum of 5-(4''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-04) (Enlarged scale).....	175
105	The 75 MHz $^{13}\text{C}$ -NMR spectrum of 5-(4''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-04)....	176
106	The 75 MHz DEPT 135 spectrum of 5-(4''-methoxyphenyl)-2-benzy-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-04).....	177
107	The 75 MHz DEPT 135 and $^{13}\text{C}$ -NMR spectrum comparison of 5-(4''-Methoxyphenyl)-2- benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-04).....	178
108	The 300 MHz HH COSY spectrum of 5-(4''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-04)...	179
109	The 300 MHz HH COSY spectrum of 5-(4''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-04) (Enlarged scale).....	180
110	The 300 MHz HMQC spectrum of 5-(4''-methoxyphenyl)-2-benzy-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-04).....	181
111	The 300 MHz HMQC spectrum of 5-(4''-methoxyphenyl)-2-benzy-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-04) (Enlarged scale).....	182
112	The IR spectrum (KBr) of 5-(3'',4''-methoxyphenyl)-2-benzy-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05).....	183
113	The 500 MHz $^1\text{H}$ -NMR spectrum of 5-(3'',4''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05).....	184

114	The 500 MHz $^1\text{H}$ -NMR spectrum of 5-(3'',4''-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05) (Enlarged scale 1).....	185
115	The 500 MHz $^1\text{H}$ -NMR spectrum of 5-(3'',4''-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05) (Enlarged scale 2).....	186
116	The 500 MHz $^1\text{H}$ -NMR spectra of 5-(3'',4''-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05) at 25 °C, 20 °C, 10 °C, and 0 °C.....	187
117	The 500 MHz $^1\text{H}$ -NMR spectra of 5-(3'',4''-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05) at 25 °C, 20 °C, 10 °C, and 0 °C.(Enlarged scale).....	188
118	The 125 MHz $^{13}\text{C}$ -NMR spectrum of 5-(3'',4''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05).....	189
119	The 125 MHz $^{13}\text{C}$ -NMR spectrum of 5-(3'',4''-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05) (Enlarged scale).....	190
120	The 125 MHz DEPT -90 and 135 spectrum of 5-(3'',4''-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05).....	191
121	The 125 MHz DEPT-90 and 135 spectrum of 5-(3'',4''-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroiso-quinoline (CU-21-05) (Enlarged scale).....	192

Figure	Page
122	The 125 MHz DEPT -90 and 135 spectrum of 5-(3'',4''-dimethoxy phenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroiso-quinoline (CU-21-05) (Enlarged scale).....193
123	The 500 MHz HH COSY spectrum of 5-(3'',4''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05)....194
124	The 500 MHz HH COSY spectrum of 5-(3'',4''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline(CU-21-05) (Enlarged scale).....195
125	The 500 MHz HMQC spectrum of 5-(3'',4''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05).....196
126	The 500 MHz HMQC spectrum of 5-(3'',4''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05) (Enlarged scale 1).....197
127	The 500 MHz HMQC spectrum of 5-(3'',4''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05) (Enlarge scale 2).....198
128	The 500 MHz NOESY spectrum of 5-(3'',4''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05).....199
129	The 500 MHz NOESY spectrum of 5-(3'',4''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05) (Enlarged scale).....200
130	The IR spectrum (KBr) of butyl-(5-phenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-06).....201
131	The 300 MHz <sup>1</sup> H-NMR spectrum of butyl-(5-phenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-06).....202



Figure	Page
132	The 300 MHz $^1\text{H}$ -NMR spectrum of butyl-(5-phenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-06) (Enlarged scale).....203
133	The 75 MHz $^{13}\text{C}$ -NMR spectrum of butyl-(5-phenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-06).....204
134	The 75 MHz DEPT 135 spectrum of butyl-(5-phenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-06).....205
135	The 75 MHz DEPT 135 and $^{13}\text{C}$ -NMR spectrum comparison of butyl-(5-phenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-06).....206
136	The IR spectrum (KBr) of butyl-(4'''-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-07).....207
137	The 300 MHz $^1\text{H}$ -NMR spectrum of butyl-5-(4'''-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-07).....208
138	The 300 MHz $^1\text{H}$ -NMR spectrum of butyl-5-(4'''-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-07) (Enlarged scale).....209
139	The 75 MHz $^{13}\text{C}$ -NMR spectrum of butyl-5-(4'''-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-07).....210

Figure	Page
140	The 75 MHz DEPT 135 spectrum of butyl-5-(4 <sup>'''</sup> -biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-07).....211
141	The 75 MHz DEPT 135 and <sup>13</sup> C-NMR spectrum comparison of Butyl-5-(4 <sup>'''</sup> -biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-07).....212
142	The 300 MHz HH COSY spectrum of butyl-5-(4 <sup>'''</sup> -biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-07).....213
143	The 300 MHz HH COSY spectrum of butyl-5-(4 <sup>'''</sup> -biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-07) (Enlarged scale).....214
144	The 300 MHz HMQC spectrum of butyl-5-(4 <sup>'''</sup> -biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-07).....215
145	The 300 MHz HMQC spectrum of butyl-5-(4 <sup>'''</sup> -biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-07) (Enlarged scale).....216
146	The IR spectrum (KBr) of butyl-5-(4 <sup>'''</sup> -methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-08).....217
147	The 300 MHz <sup>1</sup> H-NMR spectrum of butyl-5-(4 <sup>'''</sup> -methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-08).....218



Figure	Page
148	The 300 MHz $^1\text{H}$ -NMR spectrum of butyl-5-(4 <sup>'''</sup> -methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-08) (Enlarged scale).....219
149	The 75 MHz $^{13}\text{C}$ -NMR spectrum of butyl-5-(4 <sup>'''</sup> -methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-08).....220
150	The 75 MHz DEPT 135 spectrum of butyl-5-(4 <sup>'''</sup> -methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-08).....221
151	The 75 MHz DEPT 135 and $^{13}\text{C}$ -NMR spectrum comparison of butyl-5-(4 <sup>'''</sup> -methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate(CU-21-08).....222
152	The 300 MHz HH COSY spectrum of butyl-5-(4 <sup>'''</sup> -methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-08).....223
153	The 300 MHz HH COSY spectrum of butyl-5-(4 <sup>'''</sup> -methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-08) (Enlarged scale).....224
154	The 300 MHz HMQC spectrum of butyl-5-(4 <sup>'''</sup> -methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-08).....225
155	The 300 MHz HMQC spectrum of butyl-5-(4 <sup>'''</sup> -methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate(CU-21-08) (Enlarged scale).....226

Figure	Page
156	The IR spectrum (KBr) of butyl-5-(4'''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-09).....227
157	The 300 MHz <sup>1</sup> H-NMR spectrum of butyl-5-(4'''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-09) .....228
158	The 300 MHz <sup>1</sup> H-NMR spectrum of butyl-5-(4'''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-09) (Enlarged scale).....229
159	The 75 MHz <sup>13</sup> C-NMR spectrum of butyl-5-(4'''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate(CU-21-09) .....230
160	The 75 MHz DEPT 135 spectrum of butyl-5-(4'''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-09).....231
161	The 75 MHz DEPT 135 and <sup>13</sup> C-NMR spectrum comparison of butyl-5-(4'''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-09).....232
162	The 300 MHz HH COSY spectrum of butyl-5-(4'''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-09).....233
163	The 300 MHz HH COSY spectrum of butyl-5-(4'''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-09) (Enlarged scale).....234

Figure	Page
164	The 300 MHz HMQC spectrum of butyl-5-(4 <sup>'''</sup> -methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-09).....235
165	The 300 MHz HMQC spectrum of butyl-5-(4 <sup>'''</sup> -methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-09) (Enlarged scale).....236
166	The IR spectrum (KBr) of butyl-5-(3 <sup>'''</sup> , 4 <sup>'''</sup> -dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-10).....237
167	The 300 MHz <sup>1</sup> H-NMR spectrum of butyl-5-(3 <sup>'''</sup> , 4 <sup>'''</sup> -dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-10).....238
168	The 300 MHz <sup>1</sup> H-NMR spectrum of butyl-5-(3 <sup>'''</sup> , 4 <sup>'''</sup> -dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-10) (Enlarged scale).....239
169	The 75 MHz <sup>13</sup> C-NMR spectrum of butyl-5-(3 <sup>'''</sup> , 4 <sup>'''</sup> -dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-10) .....240
170	The 75 MHz DEPT 135 spectrum of butyl-5-(3 <sup>'''</sup> , 4 <sup>'''</sup> -dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-10) .....241
171	The 75 MHz DEPT 135 and <sup>13</sup> C-NMR spectrum comparison of butyl-5-(3 <sup>'''</sup> , 4 <sup>'''</sup> -dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-10).....242



Figure	Page
172	The 300 MHz HH COSY spectrum of butyl-5-(3 <sup>'''</sup> , 4 <sup>'''</sup> -dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-10).....243
173	The 300 MHz HH COSY spectrum of butyl-5-(3 <sup>'''</sup> , 4 <sup>'''</sup> -dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-10) (Enlarged scale).....244
174	The 300 MHz HMQC spectrum of butyl-5-(3 <sup>'''</sup> , 4 <sup>'''</sup> -dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-10).....245
175	The 300 MHz HMQC spectrum of butyl-5-(3 <sup>'''</sup> , 4 <sup>'''</sup> -dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-10) (Enlarged scale).....246
176	The IR spectrum (KBr) of 1-phenyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-22-01).....247
177	The 300 MHz <sup>1</sup> H-NMR spectrum of 1-phenyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-22-01).....248
178	The 300 MHz <sup>1</sup> H-NMR spectrum of 1-phenyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-22-01) (Enlarged scale).....249
179	The 75 MHz <sup>13</sup> C-NMR spectrum of 1-phenyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-22-01) .....250
180	The 75 MHz DEPT 135 spectrum of 1-phenyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-22-01).....251
181	The 75 MHz DEPT 135 and <sup>13</sup> C-NMR spectrum comparison of 1-phenyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-22-01).....252

Figure	Page
182	The 300 MHz HMQC spectrum of 1-phenyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-22-01).....253
183	The 300 MHz HMQC spectrum of 1-phenyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-22-01) (Enlarged scale).....254
184	The 300 MHz NOESY spectrum of 1-phenyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-22-01).....255
185	The 300 MHz NOESY spectrum of 1-phenyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-22-01) (Enlarged scale).....256
186	The reaction mechanism of the condensation between 3,5-dimethoxy benzaldehyde and nitroethane.....259
187	The reaction mechanism of the dimerization of nitrostyrene.....258
188	The reaction mechanism to synthesis of <i>N</i> -benzyl-2-(3,5-dimethoxyphenyl)-1-methylethylamine and 1-phenyl-1,2,3,4-THIQ.....261
189	Structure of 1-phenyl -3-methyl-6,8-dimethoxy-1,2,3,4-THIQ in three dimensions.....262
190	The reaction mechanism of ring cyclization of <i>N</i> -benzyl-2-(3,5-dimethoxyphenyl)-1-methylethylamine to generate the 1,2,3,4-tetrahydroisoquinoline with paraformaldehyde.....266
191	Sterically hindered “benzyl group” controlling <i>trans</i> -diastereoselective through <i>O,N</i> -acetal cyclization.....268
192	The reaction mechanism of ring cyclization of <i>N</i> -benzyl-2-(3,5-dimethoxyphenyl)-1-methylethylamine to generate the 1,2,3,4-tetrahydroisoquinoline with butyl glyoxal.....269
193	<sup>1</sup> H and <sup>13</sup> C NMR Chemical Shift to prove 5-position substitution of iodination.....271

- 194 The reaction mechanism of iodination of the 2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline derivatives.....272
- 195 A mechanistically catalytic cycle for cross-coupling of 5-iodo-2-benzyl-(6,8-dimethoxy)-3-methyl-1,2,3,4-THIQ derivatives.....278



ศูนย์วิทยทรัพยากร  
จุฬาลงกรณ์มหาวิทยาลัย



## LIST OF ABBREVIATIONS

%	percent
$\nu$	stretching vibration (for IR spectra)
$\nu_{as}$	asymmetrical stretching (for IR spectra)
$\nu_s$	symmetrical stretching (for IR spectra)
$\mu\text{l}$	micro liter
$\mu\text{M}$	micro molar
$^{\circ}\text{C}$	degree celsius
$^{13}\text{C-NMR}$	carbon-13-nuclear magnetic resonance
$\text{cm}^{-1}$	reciprocal centimeter (for IR spectra)
d	doublet (for NMR spectra)
dd	doublet of doublet (for NMR spectra)
eq.	equation or equivalent
$^1\text{H-NMR}$	proton nuclear magnetic resonance
HMBC	Heteronuclear Multiple Bond Coherence
HMQC	Heteronuclear Multiple Quantum Coherence
h	hour
Hz	hertz
IR	infrared spectrometry
$J$	coupling constant (for NMR spectra)
$J_{vic}$	vicinal coupling constant (for NMR spectra)
$J_{gem}$	geminal coupling constant (for NMR spectra)
m	multiplet (for NMR spectra)
mg	milligram
min	minute
MHz	megahertz
ml	milliliter

Mmol	millimole
m.p.	melting point
NOE	nuclear overhauser effect
Pd/C	palladium on activated charcoal
PNMT	phenylethanolamine <i>N</i> -methyltransferase
ppm	part(s) per million
rt	room temperature
s	singlet (for NMR spectra)
SAM	S-adenosylmethionine
SAH	S-adenosylhomocysteine
t	triplet (for NMR spectra)
THIQ	tetrahydroisoquinoline



ศูนย์วิจัยทรัพยากร  
จุฬาลงกรณ์มหาวิทยาลัย