

เคมีและฤทธิ์ทางชีวภาพของสารประกอบไดเทอร์ปีนอยด์จากเปล้าใหญ่

*Croton oblongifolius* Roxb.

นายประวิทย์ สิงห์โตทอง

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรดุษฎีบัณฑิต

สาขาวิชาเคมี ภาควิชาเคมี

บัณฑิตวิทยาลัย จุฬาลงกรณ์มหาวิทยาลัย

ปีการศึกษา 2542

ISBN 974-333-152-2

ลิขสิทธิ์ของบัณฑิตวิทยาลัย จุฬาลงกรณ์มหาวิทยาลัย

**CHEMISTRY AND BIOLOGICAL ACTIVITY OF DITERPENOID  
COMPOUNDS FROM *Croton oblongifolius* Roxb.**

**Mr. Pravit Singtothong**

**A Dissertation Submitted in Partial Fulfillment of the Requirements  
for the Degree of Doctor of Philosophy in Chemistry**

**Faculty of Science**

**Graduate School**

**Chulalongkorn University**

**Academic Year 1999**

**ISBN 974-333-152-2**

Thesis Title CHEMISTRY AND BIOLOGICAL ACTIVITY OF DITERPENOID  
COMPOUNDS FROM *Croton oblongifolius* Roxb.  
By Mr. Pravit Singtothong  
Department Chemistry  
Thesis Advisor Associate Professor Sophon Roengsumran, Ph.D.  
Thesis Co-advisor Associate Professor Amorn Petsom, Ph.D.

---

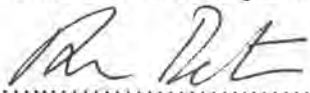
Accepted by the Graduate School, Chulalongkorn University in Partial  
Fulfillment of the Requirements for the Degree of Doctor of Philosophy.

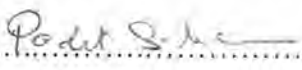
..... Dean of Graduate School  
(Associate Professor Suchada Kiranandana, Ph. D.)

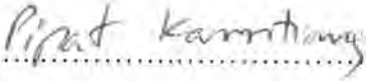
Thesis Committee

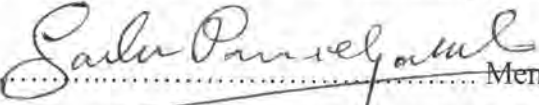
..... Chairman  
(Associate Professor Udom Kokpol, Ph.D.)


..... Thesis Advisor  
(Associate Professor Sophon Roengsumran, Ph.D.)

..... Thesis Co-advisor  
(Associate Professor Amorn Petsom, Ph.D.)

..... Member  
(Professor Padet Sidisunthorn, Ph.D.)

..... Member  
(Associate Professor Pipat Karntiang, Ph.D.)

..... Member  
(Associate Professor Sanha Panichajakul, Ph.D.)

..... Member  
(Associate Professor Siri Varothai, Ph.D.)

## C725433 : MAJOR CHEMISTRY

KEY WORD: CYTOTOXIC ACTIVITY / CYCLIC AMP PHOSPHODIESTERASE / DITERPENOID / CEMBRANE / LABDANE / CLERODANE / HALIMANE / *Croton oblongifolius* Roxb. PRAVIT SINGTOHONG : CHEMISTRY AND BIOLOGICAL ACTIVITY OF DITERPENOID COMPOUNDS FROM *Croton oblongifolius* Roxb. THESIS ADVISOR : ASSOC. PROF. SOPHON ROENGSUMRAN, Ph.D., THESIS CO-ADVISOR : ASSOC. PROF. AMORN PETSOM Ph.D. 285 pp. ISBN 974-333-152-2.

Chemical modification of crotocebraneic acid (1) and neocrotocebraneic acid (2) from *Croton oblongifolius* Roxb. had been investigated. Both 1 and 2 were esterified by reacting with diazomethane. The methyl esters were reduced with  $\text{LiAlH}_4$  to give the corresponding alcohols. The alcohols were oxidized with manganese dioxide to give the corresponding aldehydes, crotocebranal (1c), and neocrotocebranal (2c). All compounds gave expected spectral data.


*Croton oblongifolius* Roxb. from various locations in Thailand were subjected to chemical screening using proton NMR. The crude hexane extract of stem bark pointed out various types of chemical constituents. Plant specimens from selected locations were subjected to conventional extraction and isolation. Several diterpenoids were characterized including three new diterpenoids belonging to the halimane type. They were crotohalimaneic acid (7), benzoyl crotohalimanolic acid (8) and crotohalimoneic acid (9).

All compounds both natural and synthetic were subjected to biological activity tests. Many compounds exhibited cytotoxicity against panel of six cell lines which were LS 929 (fibroblast), S102 (hepatoma), HEP-G2 (heptatoma), SW 620 (colon), chago (lung), Kato-3 (gastric) and BT 474 (breast). Moreover, some diterpenoids were tested for cyclic AMP phosphodiesterase inhibition and it was found that 1 and 2 exhibit the highest enzyme inhibition.


ภาควิชา.....เคมี

สาขาวิชา.....เคมีอินทรีย์

ปีการศึกษา..... 2548

ลายมือชื่อนิสิต..... 

ลายมือชื่ออาจารย์ที่ปรึกษา..... 

ลายมือชื่ออาจารย์ที่ปรึกษาร่วม..... 

ประวิทย์ สิงห์โตทอง : เคมีและฤทธิ์ทางชีวภาพของสารประกอบไดเทอร์พีนอยด์จากเปล้าใหญ่

*Croton oblongifolius* Roxb. (CHEMISTRY AND BIOLOGICAL ACTIVITY OF

DITERPENOID COMPOUNDS FROM *Croton oblongifolius* Roxb.) อาจารย์ที่ปรึกษา :

รศ.ดร.โสภณ เรืองสำราญ, อาจารย์ที่ปรึกษาร่วม รศ.ดร.อมร เพชรสม; 285 หน้า. ISBN 974-333-152-2.

ได้ทำการดัดแปรทางเคมีของสารประกอบโครโตเซมบราเนอิก แอซิด (1) และ นิโอโครโตเซมบราเนอิก แอซิด (2) จากต้นเปล้าใหญ่ *Croton oblongifolius* Roxb. ทั้งสารประกอบ 1 และ 2 เปลี่ยนไปเป็นเอสเทอร์โดยการทำปฏิกิริยากับไดอะโซมีเทน รีดิทซ์เมทิลเอสเทอร์ด้วยลิเทียมอลูมิเนียมไฮไดรด์ได้แอลกอฮอล์ จากนั้นออกซิไดซ์แอลกอฮอล์ด้วยแมงกานีสไดออกไซด์จะได้แอลดีไฮด์ที่สอดคล้องกันคือ โครโตเซมบราเนล (1c) และนิโอโครโตเซมบราเนล (2c) สารประกอบทุกตัวให้ข้อมูลทางสเปกโทรสโกปีตามที่คาดไว้

ได้ทำการคัดกรอง *Croton oblongifolius* Roxb. จากแหล่งต่างๆ ในประเทศไทยด้วยโปรตอนเอ็นเอ็มอาร์ของสารสกัดเฮกเซนจากเปลือกต้นเปล้าใหญ่ ข้อมูลชี้ให้เห็นว่ามีองค์ประกอบทางเคมีหลายกลุ่มที่แตกต่างกัน เมื่อนำตัวอย่างพืชจากบางแหล่งที่เลือกไว้ไปทำการสกัดแยกตามกรรมวิธีทั่วไป ได้พบสารประกอบไดเทอร์พีนอยด์มากมายรวมถึงสารประกอบไดเทอร์พีนอยด์ชนิดใหม่สามชนิดที่อยู่ในกลุ่มฮาลิเมน สารประกอบเหล่านี้ได้แก่ โครโตฮาลิมาเนอิก แอซิด (7) เบนโซอิลโครโตฮาลิมาโนลิก แอซิด (8) และโครโตฮาลิโมนเนอิก แอซิด (9)

ได้นำสารประกอบทั้งหมดทั้งจากธรรมชาติและจากการสังเคราะห์ไปทดสอบฤทธิ์ทางชีวภาพ สารประกอบหลายชนิดแสดงฤทธิ์ยับยั้งเซลล์ลายน์ 6 ชนิด ซึ่งได้แก่ LS 929 (fibroblast), S102 (hepatoma), HEP-G2 (hepatoma), SW 620 (colon), chago (lung), Kato-3 (gastric) and BT 474 (breast) นอกจากนี้สารประกอบไดเทอร์พีนอยด์บางชนิดยังถูกนำไปทดสอบฤทธิ์การยับยั้งไซคลิกเอเอ็มพีฟอสโฟไดเอสเทอเรส และได้พบว่าสาร 1 และ 2 แสดงฤทธิ์การยับยั้งเอนไซม์ได้ดีที่สุด

ภาควิชา ..... เคมี

สาขาวิชา ..... เคมีอินทรีย์

ปีการศึกษา ..... 2542

ลายมือชื่อนิสิต .....

ลายมือชื่ออาจารย์ที่ปรึกษา .....

ลายมือชื่ออาจารย์ที่ปรึกษาร่วม .....

## ACKNOWLEDGEMENTS

I would like to express my deepest gratitude to my advisors, Associate Professor Sophon Roengsumran and Associate Professor Amorn Petsom, for their excellent instruction, guidance, encouragement and support throughout this dissertation. Without their kindness and understanding, this work could not be accomplished.

My gratitude is also extended to Professor Padet Sidisunthorn, Associate Professor Siri Varothai, Associate Professor Udom kokpol, Associate Professor Sanha Panichajakul, and Associate Professor Pipat Karntiang for serving as dissertation committee, for their valuable comments and also for useful suggestions. Moreover, I would like to thank Associate Professor Narongsak Chaichid (Department of Physics, Faculty of Science, Thammasat University) and Dr. Nongnuj Jaiboon (Department of Chemistry, Faculty of Science, Chulalongkorn University) for X-ray crystallographic work, Mrs. Songchan Poothong (The Institute of Biotechnology and Genetic Engineering, Chulalongkorn University) for cytotoxicity activity testing. Dr. Nattaya Ngamrojnavanich for cytotoxicity activity testing. Associate Chaiyo Chaichantipyuth for helpful discussion.

I also would like to thank The National Science and Technology Development Agency, Ministry of Science, Technology and Environment, National Research Council of Thailand, and The Asahi Foundation for partial financial support.

Thank Department of Chemistry and The Institute of Biotechnology and Genetic Engineering for research facilities. Sincere thanks are extended to all staff members and friends of the Chemistry Department for their assistance and friendship.

## CONTENTS

	Page
ABSTRACT IN THAI.....	iv
ABSTRACT IN ENGLISH .....	v
ACKNOWLEDGEMENT.....	vi
CONTENTS .....	vii
LIST OF TABLES .....	xi
LIST OF FIGURES .....	xiv
LIST OF SCHEME .....	xxi
LIST OF ABBREVIATIONS .....	xxii
CHAPTER II INTRODUCTION .....	1
1.1 Botanical aspects of <i>Croton oblongifolius</i> Roxb. ....	2
1.2 The chemical constituents of <i>Croton oblongifolius</i> Roxb. ....	4
1.3 Significance of the Problem .....	7
1.4 The objectives of this research .....	10
CHAPTER II LITERATURE REVIEWS .....	11
2.1 Literature reviews of cembranoid diterpene compounds .....	12
CHAPTER III EXPERIMENTAL .....	36
3.1 General experimental procedures .....	36
3.2 Preliminary screening of crude hexane from .....	37
stem bark of <i>Croton oblongifolius</i> Roxb.	
3.3 Extraction and isolation .....	37
3.3.1 Extraction and isolation of stem bark of <i>Croton oblongifolius</i> .37	
Roxb. from Amphur Vicheinburi, Petchaboon province	
3.3.2 Extraction and isolation of stem bark of <i>Croton oblongifolius</i> .39	
Roxb. from Amphur Sai Yok, Kanchanaburi province	
3.3.3 Extraction and isolation of stem bark of <i>Croton oblongifolius</i> .40	
Roxb. from Amphur Muang, Prachuabkirikhan province	



3.3.4	Extraction and isolation of stem bark of <i>Croton oblongifolius</i> Roxb. from Amphur Sai Yok, Kanchanaburi province (location 2)	41
3.3.5	Extraction and isolation of stem bark of <i>Croton oblongifolius</i> Roxb. from Amphur Pakchong, Nakornratchasima province	42
3.3.6	Extraction and isolation of stem bark of <i>Croton oblongifolius</i> Roxb. from Amphur Panusnikom, Chonburi province	43
3.4	Purification and Properties of the Compounds from <i>Croton oblongifolius</i> Roxb.	44
3.4.1	Purification and properties of compound <u>1</u>	44
3.4.2	Purification and properties of compound <u>2</u>	45
3.4.3	Purification and properties of compound <u>3</u>	46
3.4.4	Purification and properties of compound <u>4</u>	47
3.4.5	Purification and properties of compound <u>5</u>	47
3.4.6	Purification and properties of compound <u>6</u>	48
3.4.7	Purification and properties of compound <u>7</u>	49
3.4.8	Purification and properties of compound <u>8</u>	50
3.4.9	Purification and properties of compound <u>9</u>	50
3.4.10	Purification and properties of compound <u>10</u>	51
3.4.11	Purification and properties of compound <u>11</u>	52
3.5	Modification of compound from <i>Croton oblongifolius</i> Roxb.	53
3.5.1	Modification of compound <u>1</u>	53
3.5.1.1	Methylation of compound <u>1</u>	53
3.5.1.2	Reduction of compound <u>1a</u>	53
3.5.1.3	Oxidation of compound <u>1b</u>	54
3.5.2	Modification of compound <u>2</u>	55
3.5.2.1	Methylation of compound <u>2</u>	55
3.5.2.2	Reduction of compound <u>2a</u>	55
3.5.2.3	Oxidation of compound <u>2b</u>	56



	<b>Page</b>
3.5.3 Modification of compound <u>5</u> .....	56
3.5.3.1 Methylation of compound <u>5</u> .....	56
3.5.3.2 Reduction of compound <u>5a</u> .....	57
3.5.3.3 Oxidation of compound <u>5b</u> .....	58
3.5.4 Modification of compound <u>6</u> .....	58
3.5.4.1 Oxidation of compound <u>6</u> .....	58
3.5.4.2 Oxidation of compound <u>6a</u> .....	59
3.5.4.3 Methylation of compound <u>6b</u> .....	60
3.5.5 Methylation of compound <u>7</u> .....	60
3.5.6 Methylation of compound <u>9</u> .....	61
CHAPTER IV RESULTS AND DISCUSSIONS .....	62
4.1 Structure elucidation of the isolated compounds from .....	62
the stem barks of <i>Croton oblongifolius</i> Roxb.	
4.1.1 Structure elucidation of compound <u>1</u> .....	62
4.1.2 Structure elucidation of compound <u>2</u> .....	67
4.1.3 Structure elucidation of compound <u>3</u> .....	70
4.1.4 Structure Elucidation of compound <u>4</u> .....	73
4.1.5 Structure elucidation of compound <u>5</u> .....	76
4.1.6 Structure Elucidation of compound <u>6</u> .....	78
4.1.7 Structure Elucidation of compound <u>7</u> .....	82
4.1.8 Structure Elucidation of compound <u>8</u> .....	84
4.1.9 Structure Elucidation of compound <u>9</u> .....	87
4.1.10 Structure Elucidation of compound <u>10</u> .....	91
4.1.11 Structure Elucidation of compound <u>11</u> .....	93
4.2 Modification of compound from <i>Croton oblongifolius</i> Roxb.....	96
4.2.1 Modification of compound <u>1</u> .....	96
4.2.1.1 Methylation of compound <u>1</u> .....	96
4.2.1.2 Reduction of compound <u>1a</u> .....	97
4.2.1.3 Oxidation of compound <u>1b</u> .....	98

	Page
4.2.2 Modification of compound <u>2</u> .....	101
4.2.2.1 Methylation of compound <u>2</u> .....	101
4.2.2.2 Reduction of compound <u>2a</u> .....	102
4.2.2.3 Oxidation of compound <u>2b</u> .....	103
4.2.3 Modification of compound <u>5</u> .....	106
4.2.3.1 Methylation of compound <u>5</u> .....	106
4.2.3.2 Reduction of compound <u>5a</u> .....	107
4.2.3.3 Oxidation of compound <u>5b</u> .....	108
4.2.4 Modification of compound <u>6</u> .....	110
4.2.4.1 Oxidation of compound <u>6</u> .....	110
4.2.4.2 Oxidation of compound <u>6a</u> .....	111
4.2.4.3 Methylation of compound <u>6b</u> .....	112
4.2.5 Methylation of compound <u>7</u> .....	115
4.2.6 Methylation of compound <u>9</u> .....	116
4.3 Chemical diversity of <i>Croton oblongifolius</i> Roxb. in Thailand .....	118
CHAPTER V BIOLOGICAL ACTIVITY .....	121
5.1 Biological assay .....	121
5.1.1 Cytotoxicity test .....	121
5.1.2 Inhibition of cyclic 3, 5-adenosinemonophosphate .....	122
phosphodiesterase (cyclic AMP phosphodiesterase)	
5.2 Result of biological activity test .....	123
5.2.1 Cytotoxic activity against 6 cell lines .....	123
5.2.2 Inhibition of cyclic-AMP phosphodiesterase .....	125
CHAPTER VI CONCLUSION .....	126
REFERENCES .....	128
APPENDIX .....	135
BIOGRAPHY.....	285

## LIST OF TABLES

	Page
<b>Table 1</b> The chemical constituents of <i>Croton oblongifolius</i> Roxb.....	5
<b>Table 2</b> The IR absorption band assignment of compound <u>1</u> .....	62
<b>Table 3</b> <sup>1</sup> H-, <sup>13</sup> C-NMR and 2D long range <sup>1</sup> H- <sup>13</sup> C correlation in the HMBC spectrum data of compound <u>1</u> .....	66
<b>Table 4</b> The IR absorption band assignment of compound <u>2</u> .....	67
<b>Table 5</b> <sup>1</sup> H-, <sup>13</sup> C-NMR and 2D long range <sup>1</sup> H- <sup>13</sup> C correlation in the HMBC spectrum data of compound <u>2</u> .....	69
<b>Table 6</b> The IR absorption band assignment of compound <u>3</u> .....	70
<b>Table 7</b> <sup>1</sup> H-, <sup>13</sup> C-NMR and 2D long range <sup>1</sup> H- <sup>13</sup> C correlation in the HMBC spectrum data of compound <u>3</u> .....	72
<b>Table 8</b> The IR absorption band assignment of compound <u>4</u> .....	73
<b>Table 9</b> <sup>13</sup> C-NMR chemical shifts of compound <u>4</u> and Crovatin .....	75
<b>Table 10</b> The IR absorption band assignment of compound <u>5</u> .....	76
<b>Table 11</b> <sup>13</sup> C-NMR chemical shifts of compound <u>5</u> and Poilaneic acid .....	77
<b>Table 12</b> The IR absorption band assignment of compound <u>6</u> .....	78
<b>Table 13</b> <sup>1</sup> H-NMR spectrum data of compound <u>6</u> and Isokolavenol .....	81
<b>Table 14</b> The IR absorption band assignment of compound <u>7</u> .....	82
<b>Table 15</b> <sup>1</sup> H-, <sup>13</sup> C-NMR and 2D long range <sup>1</sup> H- <sup>13</sup> C correlation in the HMBC spectrum data of compound <u>7</u> .....	83
<b>Table 16</b> The IR absorption band assignment of compound <u>8</u> .....	84
<b>Table 17</b> <sup>1</sup> H-, <sup>13</sup> C-NMR and 2D long range <sup>1</sup> H- <sup>13</sup> C correlation in the HMBC spectrum data of compound <u>8</u> .....	86
<b>Table 18</b> The IR absorption band assignment of compound <u>9</u> .....	87
<b>Table 19</b> <sup>1</sup> H-, <sup>13</sup> C-NMR and 2D long range <sup>1</sup> H- <sup>13</sup> C correlation in the HMBC spectrum data of compound <u>9</u> .....	90

	Page
<b>Table 20</b> The IR absorption band assignment of compound <u>10</u> .....	91
<b>Table 21</b> <sup>13</sup> C-NMR chemical shifts of compound <u>10</u> and Hardwickiic acid .....	92
<b>Table 22</b> The IR absorption band assignment of compound <u>11</u> .....	93
<b>Table 23</b> <sup>1</sup> H-NMR chemical shifts of compound <u>11</u> and Nidorellol .....	95
<b>Table 24</b> The IR absorption band assignment of compound <u>1a</u> .....	97
<b>Table 25</b> The IR absorption band assignment of compound <u>1b</u> .....	98
<b>Table 26</b> The IR absorption band assignment of compound <u>1c</u> .....	99
<b>Table 27</b> <sup>13</sup> C-NMR chemical shift of compound <u>1</u> and derivatives .....	100
<b>Table 28</b> The IR absorption band assignment of compound <u>2a</u> .....	102
<b>Table 29</b> The IR absorption band assignment of compound <u>2b</u> .....	103
<b>Table 30</b> The IR absorption band assignment of compound <u>2c</u> .....	104
<b>Table 31</b> <sup>13</sup> C-NMR chemical shift of compound <u>2</u> and derivatives .....	105
<b>Table 32</b> The IR absorption band assignment of compound <u>5a</u> .....	107
<b>Table 33</b> The IR absorption band assignment of compound <u>5b</u> .....	108
<b>Table 34</b> The IR absorption band assignment of compound <u>5c</u> .....	109
<b>Table 35</b> The IR absorption band assignment of compound <u>6a</u> .....	111
<b>Table 36</b> The IR absorption band assignment of compound <u>6b</u> .....	112
<b>Table 37</b> The IR absorption band assignment of compound <u>6c</u> .....	113
<b>Table 38</b> <sup>13</sup> C-NMR chemical shifts of compound <u>6</u> and derivatives.....	114
<b>Table 39</b> The IR absorption band assignment of compound <u>7a</u> .....	115
<b>Table 40</b> The IR absorption band assignment of compound <u>9a</u> .....	116
<b>Table 41</b> Cytotoxic activity against P 388 cell line of cembranoid compounds ....	123
from <i>C. oblongifolius</i> .Roxb.	
<b>Table 42</b> Cytotoxic activity against cell line of some compounds .....	124
from <i>C. oblongifolius</i> .Roxb.	
<b>Table 43</b> Inhibitory Activity of Some Compound from <i>C. oblongifolius</i> Roxb. ....	125
on cyclic AMP Phosphodiesterase.	
<b>Table 44</b> Crystal data and structure refinement for crotohalimoneic acid ( <u>9</u> ).....	278

<b>Table 45</b> Atomic coordinates and equivalent isotropic displacement parameters ( $\text{Å}^2 \times 10^3$ ) for crotohalimoneic acid (9) .....	279
<b>Table 46</b> Bond lengths (Å) for crotohalimoneic acid (9).....	280
<b>Table 47</b> Bond angles (deg) for crotohalimoneic acid (9) .....	281
<b>Table 48</b> Anisotropic displacement parameters ( $\text{Å}^2 \times 10^3$ ) for..... crotohalimoneic acid (9)	282
<b>Table 49</b> Hydrogen coordinates and isotropic and isotropic displacement parameters ( $\text{Å}^2 \times 10^3$ ) for crotohalimoneic acid (9) .....	283

## LIST OF FIGURES

Figure	Page
1. <i>Croton oblongifolius</i> Roxb.....	3
2. The structures of diterpenoid compounds from <i>Croton oblongifolius</i> Roxb.....	6
3. The structures of diterpenoid compounds from <i>Croton oblongifolius</i> Roxb..... in Thailand.	9
4. The HMBC correlation of compound <u>1</u> .....	64
5. The COSY correlation of compound <u>1</u> .....	64
6. The NOESY correlation of compound <u>1</u> .....	65
7. The Structure of compound <u>2</u> .....	68
8. The structure of compound <u>3</u> .....	71
9. The structure of compound <u>4</u> .....	74
10. The structure of compound <u>5</u> .....	78
11. The HMBC correlation of compound <u>6</u> .....	79
12. The COSY correlation of compound <u>6</u> .....	80
13. The NOESY correlation of compound <u>6</u> .....	81
14. The structure of compound <u>7</u> .....	83
15. The HMBC correlation of compound <u>8</u> .....	85
16. The COSY correlation of compound <u>8</u> .....	85
17. The NOESY correlation of compound <u>8</u> .....	85
18. The HMBC correlation of compound <u>9</u> .....	88
19. The COSY correlation of compound <u>9</u> .....	88
20. The NOESY correlation of compound <u>9</u> .....	89
21. ORTEP drawing of compound <u>9</u> .....	89
22. The structure of compound <u>10</u> .....	93
23. The structure of compound <u>11</u> .....	94
24. The structure of compound <u>7a</u> .....	116
25. The structure of compound <u>9a</u> .....	117



Figure	Page
26. The IR spectrum of compound <u>1</u> .....	136
27. The <sup>1</sup> H-NMR spectrum of compound <u>1</u> .....	137
28. The DEPT-90 and DEPT-135, <sup>13</sup> C-NMR spectrum of compound <u>1</u> .....	138
29. The HMQC-NMR spectrum of compound <u>1</u> .....	139
30. The COSY-NMR spectrum of compound <u>1</u> .....	140
31. The HMBC-NMR spectrum of compound <u>1</u> .....	141
32. The EI MS spectrum of compound <u>1</u> .....	142
33. The IR spectrum of compound <u>2</u> .....	143
34. The <sup>1</sup> H-NMR spectrum of compound <u>2</u> .....	144
35. The DEPT-90 and DEPT-135, <sup>13</sup> C-NMR spectrum of compound <u>2</u> .....	145
36. The HMQC-NMR spectrum of compound <u>2</u> .....	146
37. The COSY-NMR spectrum of compound <u>2</u> .....	147
38. The NOESY-NMR spectrum of compound <u>2</u> .....	148
39. The HMBC-NMR spectrum of compound <u>2</u> .....	149
40. The EI MS spectrum of compound <u>2</u> .....	150
41. The IR spectrum of compound <u>3</u> .....	151
42. The <sup>1</sup> H-NMR spectrum of compound <u>3</u> .....	152
43. The DEPT-90 and DEPT-135, <sup>13</sup> C-NMR spectrum of compound <u>3</u> .....	153
44. The HMQC-NMR spectrum of compound <u>3</u> .....	154
45. The COSY-NMR spectrum of compound <u>3</u> .....	155
46. The NOESY-NMR spectrum of compound <u>3</u> .....	156
47. The HMBC-NMR spectrum of compound <u>3</u> .....	157
48. The EI MS spectrum of compound <u>3</u> .....	158
49. The IR spectrum of compound <u>4</u> .....	159
50. The <sup>1</sup> H-NMR spectrum of compound <u>4</u> .....	160
51. The DEPT-90 and DEPT-135, <sup>13</sup> C-NMR spectrum of compound <u>4</u> .....	161
52. The HMQC-NMR spectrum of compound <u>4</u> .....	162
53. The COSY-NMR spectrum of compound <u>4</u> .....	163
54. The NOESY-NMR spectrum of compound <u>4</u> .....	164
55. The HMBC-NMR spectrum of compound <u>4</u> .....	165



Figure	Page
56. The EI MS spectrum of compound <u>4</u> .....	166
57. The IR spectrum of compound <u>5</u> .....	167
58. The <sup>1</sup> H-NMR spectrum of compound <u>5</u> .....	168
59. The DEPT-90 and DEPT-135, <sup>13</sup> C-NMR spectrum of compound <u>5</u> .....	169
60. The EI MS spectrum of compound <u>5</u> .....	170
61. The IR spectrum of compound <u>6</u> .....	171
62. The <sup>1</sup> H-NMR spectrum of compound <u>6</u> .....	172
63. The DEPT-90 and DEPT-135, <sup>13</sup> C-NMR spectrum of compound <u>6</u> .....	173
64. The HMQC-NMR spectrum of compound <u>6</u> .....	174
65. The COSY-NMR spectrum of compound <u>6</u> .....	175
66. The NOESY-NMR spectrum of compound <u>6</u> .....	176
67. The HMBC-NMR spectrum of compound <u>6</u> .....	177
68. The EI MS spectrum of compound <u>6</u> .....	178
69. The IR spectrum of compound <u>7</u> .....	179
70. The <sup>1</sup> H-NMR spectrum of compound <u>7</u> .....	180
71. The DEPT-90 and DEPT-135, <sup>13</sup> C-NMR spectrum of compound <u>7</u> .....	181
72. The HMQC-NMR spectrum of compound <u>7</u> .....	182
73. The COSY-NMR spectrum of compound <u>7</u> .....	183
74. The NOESY-NMR spectrum of compound <u>7</u> .....	184
75. The HMBC-NMR spectrum of compound <u>7</u> .....	185
76. The EI MS spectrum of compound <u>7</u> .....	186
77. The IR spectrum of compound <u>8</u> .....	187
78. The <sup>1</sup> H-NMR spectrum of compound <u>8</u> .....	188
79. The DEPT-90 and DEPT-135, <sup>13</sup> C-NMR spectrum of compound <u>8</u> .....	189
80. The HMQC-NMR spectrum of compound <u>8</u> .....	190
81. The COSY-NMR spectrum of compound <u>8</u> .....	191
82. The NOESY-NMR spectrum of compound <u>8</u> .....	192
83. The HMBC-NMR spectrum of compound <u>8</u> .....	193
84. The EI MS spectrum of compound <u>8</u> .....	194
85. The IR spectrum of compound <u>9</u> .....	195

Figure	Page
86. The $^1\text{H}$ -NMR spectrum of compound <u>9</u> .....	196
87. The DEPT-90 and DEPT-135, $^{13}\text{C}$ -NMR spectrum of compound <u>9</u> .....	197
88. The HMQC-NMR spectrum of compound <u>9</u> .....	198
89. The COSY-NMR spectrum of compound <u>9</u> .....	199
90. The NOESY-NMR spectrum of compound <u>9</u> .....	200
91. The HMBC-NMR spectrum of compound <u>9</u> .....	201
92. The EI MS spectrum of compound <u>9</u> .....	202
93. The IR spectrum of compound <u>10</u> .....	203
94. The $^1\text{H}$ -NMR spectrum of compound <u>10</u> .....	204
95. The DEPT-90 and DEPT-135, $^{13}\text{C}$ -NMR spectrum of compound <u>10</u> .....	205
96. The EI MS spectrum of compound <u>10</u> .....	206
97. The IR spectrum of compound <u>11</u> .....	207
98. The $^1\text{H}$ -NMR spectrum of compound <u>11</u> .....	208
99. The DEPT-90 and DEPT-135, $^{13}\text{C}$ -NMR spectrum of compound <u>11</u> .....	209
100. The HMQC-NMR spectrum of compound <u>11</u> .....	210
101. The COSY-NMR spectrum of compound <u>11</u> .....	211
102. The NOESY-NMR spectrum of compound <u>11</u> .....	212
103. The HMBC-NMR spectrum of compound <u>11</u> .....	213
104. The EI MS spectrum of compound <u>11</u> .....	214
105. The IR spectrum of compound <u>1a</u> .....	215
106. The $^1\text{H}$ -NMR spectrum of compound <u>1a</u> .....	216
107. The DEPT-90 and DEPT-135, $^{13}\text{C}$ -NMR spectrum of compound <u>1a</u> .....	217
108. The EI MS spectrum of compound <u>1a</u> .....	218
109. The IR spectrum of compound <u>1b</u> .....	219
110. The $^1\text{H}$ -NMR spectrum of compound <u>1b</u> .....	220
111. The DEPT-90 and DEPT-135, $^{13}\text{C}$ -NMR spectrum of compound <u>1b</u> .....	221
112. The EI MS spectrum of compound <u>1b</u> .....	222
113. The IR spectrum of compound <u>1c</u> .....	223
114. The $^1\text{H}$ -NMR spectrum of compound <u>1c</u> .....	224
115. The DEPT-90 and DEPT-135, $^{13}\text{C}$ -NMR spectrum of compound <u>1c</u> .....	225

Figure	Page
116. The EI MS spectrum of compound <u>1c</u> .....	226
117. The IR spectrum of compound <u>2a</u> ... ..	227
118. The <sup>1</sup> H-NMR spectrum of compound <u>2a</u> .....	228
119. The DEPT-90 and DEPT-135, <sup>13</sup> C-NMR spectrum of compound <u>2a</u> .....	229
120. The EI MS spectrum of compound <u>2a</u> .....	230
121. The IR spectrum of compound <u>2b</u> ... ..	231
122. The <sup>1</sup> H-NMR spectrum of compound <u>2b</u> .....	232
123. The DEPT-90 and DEPT-135, <sup>13</sup> C-NMR spectrum of compound <u>2b</u> .....	233
124. The EI MS spectrum of compound <u>2b</u> .....	234
125. The IR spectrum of compound <u>2c</u> ... ..	235
126. The <sup>1</sup> H-NMR spectrum of compound <u>2c</u> .....	236
127. The DEPT-90 and DEPT-135, <sup>13</sup> C-NMR spectrum of compound <u>2c</u> .....	237
128. The EI MS spectrum of compound <u>2c</u> .....	238
129. The IR spectrum of compound <u>5a</u> ... ..	239
130. The <sup>1</sup> H-NMR spectrum of compound <u>5a</u> .....	240
131. The DEPT-90 and DEPT-135, <sup>13</sup> C-NMR spectrum of compound <u>5a</u> .....	241
132. The EI MS spectrum of compound <u>5a</u> .....	242
133. The IR spectrum of compound <u>5b</u> ... ..	243
134. The <sup>1</sup> H-NMR spectrum of compound <u>5b</u> .....	244
135. The DEPT-90 and DEPT-135, <sup>13</sup> C-NMR spectrum of compound <u>5b</u> .....	245
136. The EI MS spectrum of compound <u>5b</u> .....	246
137. The IR spectrum of compound <u>5c</u> ... ..	247
138. The <sup>1</sup> H-NMR spectrum of compound <u>5c</u> .....	248
139. The DEPT-90 and DEPT-135, <sup>13</sup> C-NMR spectrum of compound <u>5c</u> .....	249
140. The EI MS spectrum of compound <u>5c</u> .....	250
141. The IR spectrum of compound <u>6a</u> ... ..	251
142. The <sup>1</sup> H-NMR spectrum of compound <u>6a</u> .....	252
143. The DEPT-90 and DEPT-135, <sup>13</sup> C-NMR spectrum of compound <u>6a</u> .....	253
144. The EI MS spectrum of compound <u>6a</u> .....	254
145. The IR spectrum of compound <u>6b</u> ... ..	255

Figure	Page
146. The <sup>1</sup> H-NMR spectrum of compound <u>6b</u> .....	256
147. The DEPT-90 and DEPT-135, <sup>13</sup> C-NMR spectrum of compound <u>6b</u> .....	257
148. The EI MS spectrum of compound <u>6b</u> .....	258
149. The IR spectrum of compound <u>6c</u> .....	259
150. The <sup>1</sup> H-NMR spectrum of compound <u>6c</u> .....	260
151. The DEPT-90 and DEPT-135, <sup>13</sup> C-NMR spectrum of compound <u>6c</u> .....	261
152. The EI MS spectrum of compound <u>6c</u> .....	262
153. The IR spectrum of compound <u>7a</u> .....	263
154. The <sup>1</sup> H-NMR spectrum of compound <u>7a</u> .....	264
155. The DEPT-90 and DEPT-135, <sup>13</sup> C-NMR spectrum of compound <u>7a</u> .....	265
156. The HMQC-NMR spectrum of compound <u>11</u> .....	266
157. The COSY-NMR spectrum of compound <u>11</u> .....	267
158. The NOESY-NMR spectrum of compound <u>11</u> .....	268
159. The HMBC-NMR spectrum of compound <u>11</u> .....	269
160. The EI MS spectrum of compound <u>7a</u> .....	270
161. The IR spectrum of compound <u>9a</u> .....	271
162. The <sup>1</sup> H-NMR spectrum of compound <u>9a</u> .....	272
163. The DEPT-90 and DEPT-135, <sup>13</sup> C-NMR spectrum of compound <u>9a</u> .....	273
164. The EI MS spectrum of compound <u>9a</u> .....	274
165. The proton profile of crude hexane from <i>Croton oblongifolius</i> Roxb. : .....	275
Labdane diterpenoid compounds	
166. The proton profile of crude hexane from <i>Croton oblongifolius</i> Roxb. : .....	276
Clerodane diterpenoid compounds	
167. The proton profile of crude hexane from <i>Croton oblongifolius</i> Roxb. : .....	277
Cembranoid diterpene compounds	
168. Chemical distribution of <i>Croton oblongifolius</i> Roxb. from .....	278
various locations in Thailand	

## LIST OF SCHEMES

	Page
<b>Scheme 1</b> Extraction and isolation of the stem bark of <i>C. oblongifolius</i> Roxb. ....38 from Amphur Vicheinburi, Petchaboon province.	
<b>Scheme 2</b> Extraction and isolation of the stem bark of <i>C. oblongifolius</i> Roxb. ....39 from Amphur Sai Yok, Kanchanaburi province.	
<b>Scheme 3</b> Extraction and isolation of the stem bark of <i>C. oblongifolius</i> Roxb. ....40 from Amphur Muang, Prachuabkirikhan province.	
<b>Scheme 4</b> Extraction and isolation of the stem bark of <i>C. oblongifolius</i> Roxb. ....41 from Amphur Sai Yok, Kanchanaburi province (location 2).	
<b>Scheme 5</b> Extraction and isolation of the stem bark of <i>C. oblongifolius</i> Roxb. ....42 from Amphur Pakchong, Nakornratchasima province.	
<b>Scheme 6</b> Extraction and isolation of the stem bark of <i>C. oblongifolius</i> Roxb. ....43 from Amphur Panusnikom, Chonburi province.	
<b>Scheme 7</b> Modification pathway of compound <u>1</u> .....96	
<b>Scheme 8</b> Modification pathway of compound <u>2</u> .....101	
<b>Scheme 9</b> Modification pathway of compound <u>5</u> .....106	
<b>Scheme 10</b> Modification pathway of compound <u>6</u> .....110	

## LIST OF ABBREVIATIONS

$\delta$	Chemical shift
$\text{cm}^{-1}$	reciprocal centimeter (unit of wave number)
ppm	part per million
d	doublet (NMR)
dd	double doublet
dt	double triplet
m	multiplet (NMR)
s	singlet (NMR)
t	triplet (NMR)
br	broad
s	strong
m	medium
w	weak
$M^+$	molecular ion
$m/z$	mass to charge ratio
$\nu_{\text{max}}$	the reciprocating wavelength (IR)
$\lambda_{\text{max}}$	the wavelength at maximum absorption (UV)
ml	milliliter (s)
mg	milligram
Hz	Hertz
TMS	Tetramethylsilane
DEPT	Distortionless Enhancement by Polarization Transfer
HMQC	Heteronuclear Multiple Quantum Correlation
HMBC	Heteronuclear Multiple Bond Correlation
COSY	Correlated Spectroscopy
NOESY	Nuclear Overhauser Enhancement Spectroscopy