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นางสาวศรีรัตน์ กสิวงศ์

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SESQUITERPENE LACTONES FROM MICHELIA RAJANIANA STEM BARK AND GRANGEA MADERASPATANA

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ศรีรัตน์ กสิวงศ์ : เซสควิเทอร์ปีนแลคโทนจากเปลือกต้นจำปีหลวง และต้นพญามุตติ (SESQUITERPENE LACTONES FROM MICHELIA RAJANIANA STEM BARK AND GRANGEA MADERASPATANA) อ. ที่ปรึกษา : รศ. นิจศิริ เรืองรังษี, ๑๔๙ หน้า.

สามารถพบสารเซสควิเทอร์ปีนแลคโทนกลุ่มอีปอกซีเยอร์มาคราโนไลด์ ๕ ชนิด จากสารสกัดเปลือกต้นจำปีหลวง คือ parthenolide, bisparthenolidine, paramicholide, N-acetylparthenolidine และ N-acetyl-8α-hydroxyparthenolidine สาร ๓ ชนิดหลังเป็นสารใหม่ยังไม่เคยมีรายงานมาก่อน สำหรับสาร ๒ ชนิดแรกเคยมีการทดลองให้ผลต้านเนื้องอก ส่วนสารชนิดที่ ๖ เป็นสารกลุ่มออกโซอปอร์ฟีนอยด์อัลคาลอยด์ ชื่อ Liriodenine

จากการสกัดต้นพญามุตติพบสารเซสควิเทอร์ปีนแลคโทน กลุ่มยูเดสมาโนไลด์ ๓ ชนิด คือ frullanolide, 7α-hydroxyfrullanolide และ 3α, 7α-dihydroxydihydrofrullanolide สารชนิดแรกเคยมีรายงานว่าเป็นสารที่ทำให้เกิดอาการแพ้ ส่วนสาร ๒ ชนิดหลังเป็นสารใหม่ยังไม่เคยมีรายงานมาก่อน

การกำหนดสูตรโครงสร้าง ใช้เครื่องมือโปรตอน และคาร์บอน ๑๓ นิวเคลียร์ แมกเนติกเรโซแนนซ์ ที่มีประสิทธิภาพสูง และมีการทดลองแบบ ๒ มิติ ทำให้ทำนายสูตรโครงสร้างได้แม่นยำมากขึ้น

ภาควิชา เภสัชเวท ลายมือชื่อนิสิต .....

สาขาวิชา เภสัชเวท

ปีการศึกษา ๒๕๓๑ ลายมือชื่ออาจารย์ที่ปรึกษา .....

SRIRAT KASIWONG : SESQUITERPENE LACTONES FROM MICHELIA RAJANIANA STEM BARK AND GRANGEA MADERASPATANA. THESIS ADVISOR : ASSO. PROF. NIJSIRI RUANGRUNGSI, Ed. D. 149 PP.

Examination of the stem bark of *Michelia rajaniana* Craib. (Magnoliaceae) revealed the presence of five epoxy germacranolides, parthenolide, bisparthenolidine, paramicholide, N-acetylparthenolidine and N-acetyl-8α-hydroxy-parthenolidine. The latter three components were found to be unusual germacranolides which have not been reported previously while the former two were demonstrated to possess antitumor activity. In addition, the sixth component was oxoaporphinoid alkaloid liriodenine.

The present investigation was also undertaken to further study of sesquiterpene lactones from *Grangea maderaspatana* Poir. (Compositae). Three eudesmanolides were isolated and their structures were determined. The first component was allergenic lactone named frullanolide whilst the other two were unusual 7-hydroxy eudesmanolide named 7α-hydroxy-frullanolide and 3α, 7α-dihydroxydihydrofrullanolide

^{1}H-NMR ^{13}C-NMR Structural elucidations have been established through high field spectroscopy and 2D-COSY experiment. A detailed discussion on the elucidation of chemical structures is included.

ภาควิชา เภสัชเวท ลายมือชื่อนิสิต .....

สาขาวิชา เภสัชเวท

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LIST OF STRUCTURES

structure

1 isoprene unit

2 α-methylene γ-lactone

3 germacrolides

4 melampolides

5 heleangolides

6 *cis,cis*-germacranolides

7 costunolide

8 costunolide cation

9 α-cyclocostunolide

10 β-cyclocostunolide

11 epitulipinolide

12 tanacin

13 herbolide B

14 eriofertin

15 dihydroparthenolide 4,5-epoxide

16 cation of 15

17 guaianolides

18 parthenolide

19 lanuginolide

20 peroxyferolide

21 peroxycostunolide

22 peroxyparthenolide

23 (-)-frullanolide

24 (+)-frullanolide

25 eriolanin

26 eriolangin

structure

27 ivangulin

28 lumisantonin

29 vernodesmin

30 alantolactone

31 isoalantolactone

32 eudalene

33 saussurea lactone

34 1,2-epoxide of 33

35 3,4-epoxide of 33

36 dihydrosantamarin

37 dihydroreynosin

38 alcohol derivative

39 ambrosanolide

40 helenanolide

41 acetyl CoA

42 acetoacetyl CoA

43 3-hydroxy methyl glutaryl CoA

44 mevalonic acid

45 mevalonic acid pyrophosphate

46 isopentenylpyrophosphate

47 3,3-dimethylallylpyrophosphate

48 geranylpyrophosphate

49 *trans,trans*-farnesylpyrophosphate

50 *trans,trans*-germacradiene

51 germacrene

52 epoxide intermediate

53 hydroperoxide

54 alcohol

structure

55 aldehyde

56 acid derivative

57 inunolide

58 costunolide 1,10-epoxide

59 reynosin

60 santamarin

61 intermediate cation

62 eudesmanolides hydroperoxide

63 aldehyde derivative

64 germacrolide-4,5-epoxide

65 guaianolide cation

66 guaianolide diol

67 xanthanolide

68 guaianolide dienol

69 cyclopropane guaianolide

70 ivaxillarin

71 tamaulipin acetate

72 chair-like transition state

73 divinylcyclohexane

74 guaianolide type cation

75 ambrosanolide derivatives

76 damsin

77,77' melampolide-4,5-epoxide

78 intermediate cation

79 eudesmanolides

80 eremophilanolides

81 furanoeremophilane

structure

82 intermediate of 83 and 84

83 furan derivative

84 eremophilenolide

85 furanolactone

86 furanodilactone

87 fukinone

88 α,β-epoxyketone

89 ring contraction product

90 bakkenolide A

ABBREVIATION

AcOH	= acetic acid
br	= broad
°C	= degree Celsius
C	= carbon
^{13}C-NMR	= carbon-13 nuclear magnetic resonance
cm	= centimetre
CoA	= coenzyme A
d	= doublet
d.b.	= double bond
EIMS	= electron impact mass spectrometry
ent	= enantiomer
EtOH	= ethanol
g	= gram
^{1}H-NMR	= proton nuclear magnetic resonance
hRf	= $\frac{\text{distance of spot centre from start point}}{\text{distance of solvent front from start point}} \times 100$
$h\nu$	= photon
Hz	= Hertz
IR	= infrared
kg	= kilogram
L	= litre
lactoniz.	= lactonization
m	= metre
m	= multiplet
M^+	= molecular ion
m/z	= mass to charge ratio

continued

mg	= milligram
MHz	= megahertz
ml	= millilitre
mm	= millimetre
m.p.	= melting point
N	= normality
nm	= nanometre
OAc	= acetyl
OAng	= angelate
OH	= hydroxy
OPP	= pyrophosphate
oxidat.	= oxidation
p.	= page
PD-C	= palladium-carbon
ppm	= part per million
Py	= pyridine
q	= quartet
s	= singlet
Se	= selenium
sp.(spp.)	= species
t	= triplet
TLC	= thin-layer chromatogram
UV-visible	= ultraviolet-visible

CHEMICAL FORMULAE

BF_3	=borontrifluoride
CCl_4	=carbontetrachloride
$CDCl_3$	=deuterated-chloroform
CH_2N_2	=diazine
$CrCl_2$	=chromium dichloride
HCl	=hydrochloric acid
$HClO_4$	=perchloric acid
H_2O	=water
H_2O_2	=hydrogen peroxide
K_2CO_3	=potassium carbonate
MeOH	=methanol
MnO_2	=manganese dioxide
$NaBH_4$	=sodium borohydride
RCO_3O	=peroxy acid
SeO_2	=selenium dioxide
$SOCl_2$	=thionyl chloride