出席國際學術會議心得報告及發表之論文各一份

行政院國家科學委員會專題研究成果報告

柏科及杉科植物的成分研究

Chemical Studies of the Plants of Cupressaceae and Taxodiceae

計畫編號：NSC 89-2113-M-002-050

執行期限：89 年 8 月 1 日至 90 年 7 月 31 日

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計畫參與人員：文永順，江一民(博士生)

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一、中文摘要

台灣杉好建材有強的抗黴菌作用，其皮部主要骨架是雙萜及木酚素，由此部共分出三缺雙萜之 podocarpane 型共 11 個新化合物。山紅柿具有細胞毒 anthraquinone，而由其心材分出 6 種新的三萜化合物及一種已知化合物。狗肝葉是民間肝炎的草藥，由其全草找出 13 種已知苯的衍生物。台灣扁柏材是抗腐敗菌最好的木材，在分出一個新骨架 7（6→2）abeoabietane 雙萜物。

關鍵詞：台灣杉；山紅柿；正榕；狗肝葉；台灣扁柏。

Abstract

Taiwania cryptomerioides is a good building material due to strong resistant to antifungus. The components of its bark contain diterpenes and lignans. From this part, we have isolated eleven new trinorditerpene podocarpane derivatives. The heartwood of *Diospyros maritime* contains cytotoxic anthraquinones. In this time, six new lupane type triterpene were isolated from its heartwood. Aerial root of *Ficus microcarpa* has many kinds of diterpenes, four new triterpenes together with one known triterpene were purified and elucidation. Whole herb of *Dicliptera chinensis* was used as folk medicine of hepatitic disease, thirteen known benzenoids were isolated. *Chamaecyparis obtusa* var. *formosana* has been classified as a species with excellent durability, we have isolated again a novel skeleton, 7(6→2) abeoabietane compound.

keywords : *Taiwania cryptomerioides*; *Diospyros maritima*; *Ficus microcarpa*; *Dicliptera chinensis*; *Chaemaecyparis obtuse* var. *formosana*.

二、Purpose of Project

Taiwania cryptomerioides is a decay-resistant tree showing strong antifungus characteristic. The component, α-cadinol, has the best activity against *Coriolus versicolor* (white-rot fungi) and *Lactiporus sulphurens* (brown-rot fungi). The studies on its bark is tried to find antifungus components. Heartwood of *Diospyros maritime* is used as traditional treatment of rheumatic disease in Taiwan. The fruit of this plant has isolated ichthyotoxic, gemination inhibitory, and antifungal activities. In previous studies, we reported some new cytotoxic naphthoquinone, we try to find some potential cytotoxic principles. *Ficus microcarpa* is a popular ornamental tree of Maraceae. Due to strong vitality and antiplatelet activity of its aerial root extract caused us to study the chemical components. *Dicliptera chinensis* is a folk medicine for hepatitic disease, we hope to find the active principles. The wood of *Chamaecyparis obtuse* var. *formosana* is an important building material in Formosa attributable to its strong resistance to wood decaying fungi. It also led us to study the antifungus principles from its wood.

三、Content of Project

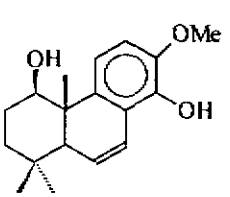
Taiwania cryptomerioides is a decay-resistant, economically important tree species indigenous to Taiwan. In the early days, the components of its heartwood, leaves and bark were studies extensively. Recently, many novel skeletons, and a podocarpane-type trinorditerpene, 1β,13,14-trihydroxy-8,11,13-podocarpatriene-7-one, was isolated for the first time from the leaves of this plant. Now we reported here eleven new podocarpane-type trinorditerpenes (**1**-**11**) were purified. And their structure were elucidated principally from spectral evidence.

The stem of *Diospyros maritima* are used to treat rheumatic disease locally in Taiwan, leading us to study the chemical constituent of this plant. In the previous report, we have isolated naphthoquinone and lupane-type triterpenes. In this time, we have purified six new lupane type triterpenes (**12**~**17**). Compounds **12** and **13** are novel skeletons.

Ficus microcarpa was popular ornamental tree in the orient. The strong vitality of this plant as well as its antiplatelet activity led us to study its aerial root. The methanolic extract was concentrated to give a residue, which was supended in water. The aqueous solution was partitioned with EtOAc and *n*-BuOH, successively. The EtOAc soluble layer was separated with column chromatography and HPLC. Based on the physical and chemical evidence, two new cycloartane (**18**, **20**) and two new rare 13,17-cyclourasane-type triterpene (**21**, **22**) together one known (22*E*)-27-nor-3b-hydroxycycloart-23-en-25-one (**19**).

Whole herb of *Dicliptera chinensis* are used as diuretic, analgesic, antipyretic, antihepatitis, and antiimflammation locally in Taiwan. The methanolic extract from whole herb of *Dicliptera chinensis* was partitioned with ethyl acetate and water. The ethyl acetate solution fraction was separated by SiO_2 chromatography and HPLC. Thirteen know benzenoids (**23**-**35**) were isolated. Their structure were determined by physical methods including ^{1}H-, ^{13}C-NMR, UV, IR, and two dimensional NMR spectra.

The wood of *Chaemaecyparis obtuse* var. *formosana* is an important building material in Formosa due to its strong resistance to wood-decaying fungi. Previous chemical studies reported one novel diterpene (obtunone), three new diterpenes, 11,14-dihydroxy-8,11,13-abietatriene-7-one, obtuanhydride, and 18,19-*O*-isopropylidene -18,19-dihydroxyisopimara-8(14),115-diene. Further studies on same extract, we obtained an novel 7(6→2)abeoabietane diterpene, obtusanal (**36**), together with a known 12-hydroxy-3-6,7-secoabieta-8,11,13-triene-6,7-dial (**37**). The absolute configuration of **36** was determined as 5*S* by the CD spectrum method. The biotransformation **36** was proposed from **37**.



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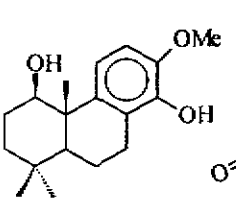

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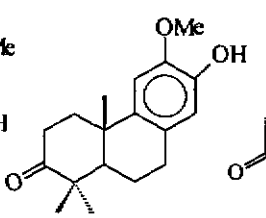

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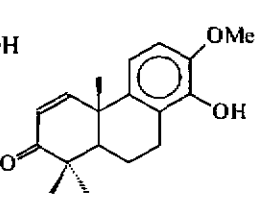

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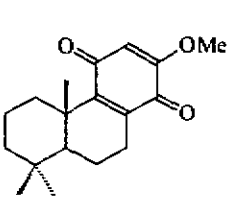

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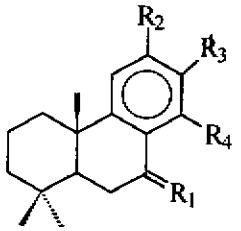
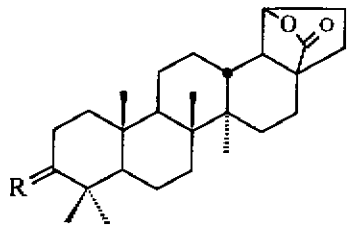
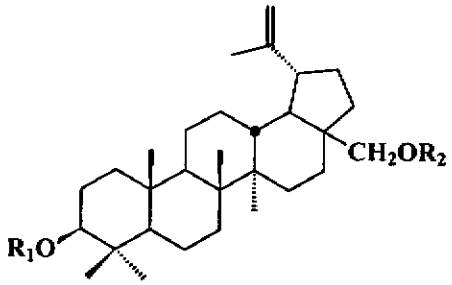
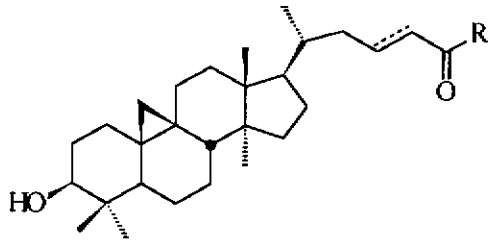


	R_1	R_2	R_3	R_4
6	O	H	OMe	OH
7	H_2	OMe	OH	H
8	H_2	OH	OMe	H
9	H_2	H	OMe	OH
10	H_2	H	OH	H
11	O	H	OH	OH

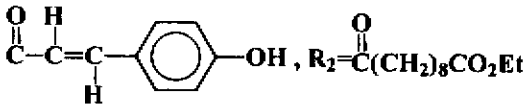


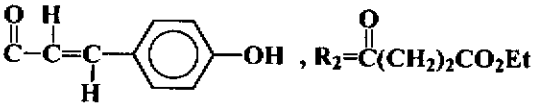
12 R=β-OH, α-H
13 R=O

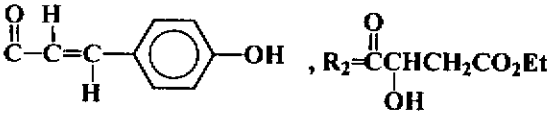


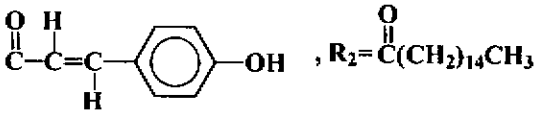


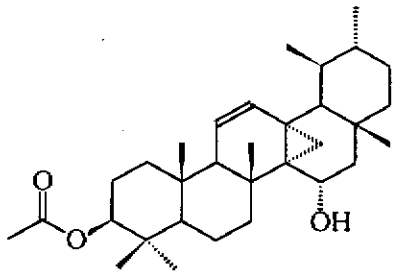
18 R=CH_3
19 R=CH_3, Δ^{23}
20 R=H, Δ^{23}

14 R_1= 

15 R_1= 

16 R_1= 

17 R_1= 



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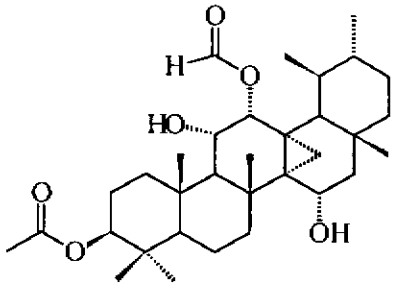

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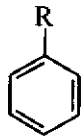
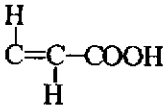
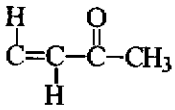
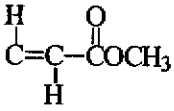


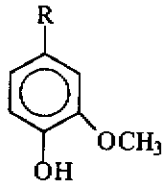
23 R= COOH

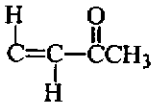
24 R= 

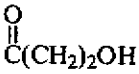
25 R= 

26 R= CHO

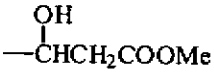
27 R= 

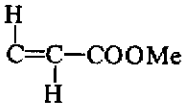


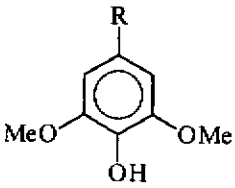
28 R= 

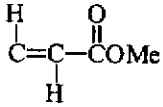
29 R= 

30 R= CHO

31 R= 

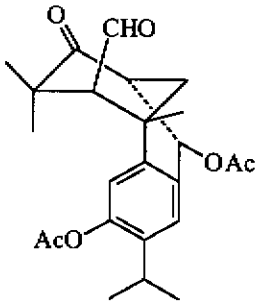
32 R= 



33 R= 

34 R= COOMe

35 R= CHO



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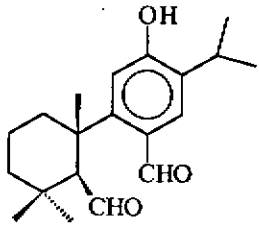

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新千禧年天然物研討會(Natural Products Research in the New Millennium)

郭悅雄 國立台灣大學化學系

一、參加會議

此次會議是第 48 屆藥用植物研究學會與第 6 屆國際藥理學會為了千禧年，聯合舉辦之研討會。在瑞士，蘇黎世之蘇黎世工業大學舉辦，蘇黎世工業大學與蘇黎世大學仳鄰在市中心，都不能算是很大的大學，校內古色古香。此次召開研討議題有六項。第一是新天然化合物，第二是色層分析之新方法，第三是決定結構之新方法，第四是植物生理及生合成研究，第五是細胞培養及生物技術，第六是其他項目。

此次研討會全部在蘇黎世工業大學內舉辦，有主演講，邀請演講 work shop 及壁報發表。大會共五日，由 9 月 3 日開始作登記，到 7 日結束，早上為主要演講及邀請演講，下午有邀請演講及口頭報告，而壁報論文皆排在下午 4：00 到 6：00 共三天（4 日，5 日，6 日）。

大會開幕儀式由著名物理化學家 R.R.Ernst 講新千禧年科學會有什麼不同。參加此會共有 6 百多名學者，以歐洲的國家參加人數最多，盛況空前，每個會場都無虛座。

二、與會心得

此次大會的主題是 Ethnobotany, Ethnomedicine 及

Ethnopharmacology。也就是說明如何應用本土的植物，去作製藥及藥理的研究。另外是討論如何加速 High-Throughput screening 作為天然藥物之快速之發現，如何配合分離儀器如 LC-UV-ELSD，LD-IR 及 LCMS/MS 作快速分離。

至於天然藥物的研究，各式各樣之植物，有高等植物、低等植物、海洋植物及黴菌，都有人涉及其藥物成分。如低等植物之地衣有抗癌之成分。從 *Streptomyces spheroides* 找出抗生素，由 mushroom 可找出 thrombin inhibitor，此與心臟動脈有關，其他學者亦有由 mushroom 找出抗愛滋病毒之反轉錄酶。另在 *Strychnos icaja* 找出二種複雜結構之 bisindole alkaloid，對人類之 KB cell 有毒性。由本國來與會的有五位天然物專家，第一個發表 *Aristolochia cucurbitifolia* 分出 8 個新成分，具有細胞毒之效用。第二位是作 *Zanthoxylum schinifdium* 所找出的有 8 種新化合物，某些成分具有抗血小板凝聚及 HBV DNA replication activity。第三位亦是作有細胞毒之番石榴科之植物 *Annona muricata*。第四位也是從 *Lindera communis* 找出細胞毒之成分，著者是題目是由台灣扁柏材找出新的七個雙帖化合物，扁柏有抗癌防蟻之功能，是台灣最好且最貴之建材，我們的報告由材部分出 144 種成分，有 47 個新化合物，也證實其中有些成分有抗白腐菌與黑腐菌之功能，並找出對乙型肝炎之表面抗原有抑制作用之成分。

三、 建議

一種國際性會議是集合世界的先進國之工作發表會，了解最新研究的動向與情報，要鼓勵國內學者多參與國際性研討會可快速獲得最新有關自己研究的資料，建議國內各有關單位如想多獲得國外學者智慧結晶，則多舉辦一些不需很大的國際會議，可提高某些研究的水準。

四、 攜回資料

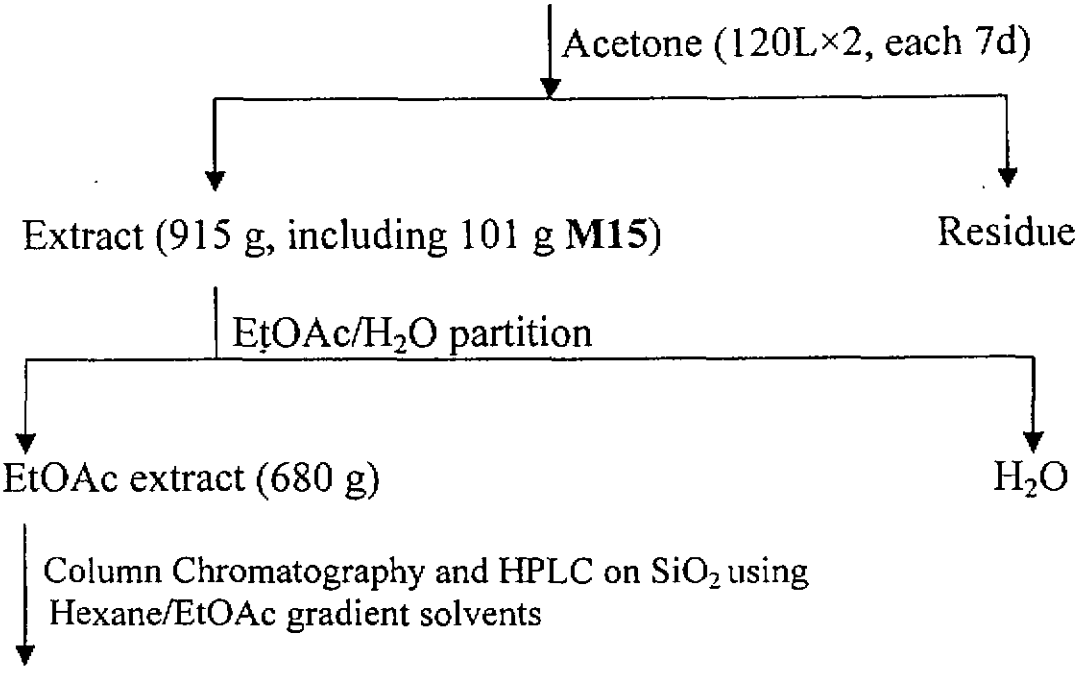
1.Book of Abstracts

Novel Diterpenes From The Heartwood of *Chamaecyparis obtusa* var. *formosana*

Yueh-Hsiung Kuo and Chia-Hsien Chen
Department of Chemistry, National Taiwan University,
Taipei, Taiwan, ROC

Chamaecyparis obtusa var. *formosana*

(Taiwan Hinoki, 台灣扁柏, Heartwood, 11 Kg)



M：Monoterpenoid 25	(3 New comp;	7 Skeletons;	1 Novel skeleton)
S：Sesquiterpenoid 42	(8 New comp;	9 Skeletons	)
D：Diterpenoid 53	(25 New comp;	13 Skeletons;	4 Novel skeletons)
St：Steroid 5	(	1 Skeleton	)
L：Lignoid 27	(16 New comp;	5 Skeletons;	1 Novel skeleton)
O：Other 7	(3 New comp;	4 Skeletons;	1 Novel skeleton)

Total 159 Compounds; 55 New comp; 39 Skeletons; 7 Novel skeletons

Two Novel and Two New Diterpenes, Obtusadione, Obtusanal, Chamanonol and Isochamanonol from the Heartwood of *Chamaecyparis obtusa* var. *formosana*

Yueh-Hsiung Kuo* and Chia-Hsien Chen

Department of Chemistry, National Taiwan University, Taipei, Taiwan, ROC

Abstract

Two novel diterpenes, obtusadione (**4**), and obtusanal (**5**), and two new diterpene, chamanonol (**1**) and isochamanonol (**2**) together with a known 12-hydroxy-6,7-secoabieta-8,11,13-triene-6,7-dial (**3**) isolated from the heartwood of *Chamaecyparis obtusa* var. *formosana*, were elucidated on the basis of 2D-NMR methods. Compounds **4** and **5** are 14(8→9)abeoabietane and 7(6→2)abeoabietane-type diterpene, respectively. Via biotransformation, **4** and **5** were proposed deriving from **1** and **3**, respectively. By acidic treatment, **1** and **2** yielded same product, 6,7-dehydroferrugiol.

Keywords: *Chamaecyparis obtusa* var. *formosana*; 14(8→9)abeoabietane-type diterpene; 7(6→2)abeoabietane-type diterpene; dehydroabietane.

The years old of *Chamaecyparis obtusa* var. *formosana* (Taiwan hinoki; Cupressaceae) is always over one thousand. It is a huge wood indigenous to Taiwan and grows at an altitude of 1,300 – 2,800 m above sea. With regard to the decay and white-ant resistance, it is classified into the excellent durability species in Taiwan. Previous chemical studies of the reported only essential oil and acidic components.[1] We have investigated the principles of this wood and found one novel diterpene and three new abietane-type diterpenes.[2] Further detailed reinvestigation of the same extract from heartwood has yielded two new abietane diterpenes, chamanonol (**1**) and isochamanonol (**2**), one known 6,7-secoabietane diterpene, 12-hydroxy-6,7-secoabieta-8,11,13-triene-6,7-dial (**3**), and two novel abeoabietane diterpenes, obtusadione (**4**) and obtusanal (**5**). Based on the following spectral evidence, the structures of four new diterpenes were elucidated as follows.

The molecular formula of chamanonol (**1**) was established as $C_{20}H_{30}O_2$ by HRMS. The IR spectrum of **1** showed bands attributable to a hydroxy group (3398 cm^{-1}), geminal dimethyl group (1373, 1381 cm^{-1}), and conjugated carbonyl group (1658, 1629 cm^{-1}). UV absorption at λ_{max} 242 nm corresponded to an α,β-unsaturated ketone with β,β- or α,β-disubstituents. The ^1H NMR spectrum showed three singlet of methyl groups [δ 0.86, 0.92, and 1.34 (H-18, H-19, and H-20)], an isopropyl group [δ 1.01, 1.03 (each 3H, d, J = 7.0 Hz), 2.77 (1H, sep, J = 7.0 Hz)], and two singlet vinyl protons [δ 5.96 (H-11) and 6.35 (H-14)]. Compound **1** exhibited five methyl ^{13}C NMR signals [δ 20.2, 21.3, 21.8, 21.8, 33.5], one crossed dieneone signals [δ 121.9 (C-11), 141.7 (C-13), 145.6 (C-14), 169.1 (C-9), and 184.4 (C-12), and a quaternary carbon [δ 69.2 (C-8)] attached to hydroxy group. Comparison of ^{13}C NMR data with ferruginol derivatives[4] suggested that **1** possesses the same carbon skeleton with oxo-function locating at C-12, and two double bonds at C-9 (11) and C-11 (14). H-15/C-12, H-14/C-12, H-11/C-12, H-11 (δ 5.96)/C-8 (δ 69.2), H-14 (δ 6.35)/C-8 are all exhibited HMBC correlation. This result suggested the hydroxy group located at C-8. This hydroxyl group was judged at β-orientation due to the 1,3-diaxial effect causing the H-20 downfield shifting to δ 1.34. By the HMBC and NOESY techniques, chamanonol (**1**) was assigned as 8β-hydroxyabieta-9 (11),13-dien-12-one which was not previously isolated from natural sources, though it had prepared from ferrugiol by oxidizing with phenyl seleninic anhydride or benzoyl peroxide.[5]

The MS of isochamanonol (**2**) gave an exact mass at *m/z* 302.2243, indicating the molecular formular $C_{20}H_{30}O_2$. The UV maxima at 239 nm indicated a conjugated olefinic carbonyl with β,β- or α,β-disubstituents, while the IR spectrum of **2** exhibited hydroxy, olefinic, conjugated cyclohexanone groups absorption bonds. The ^{1}H NMR spectrum was consistent with abieta-9 (11),13-dien-12-one. Three singlets at δ 0.85, 0.86 and 1.09 (H-20), an isopropyl attached on an olefine [δ 0.95, 0.99 (each 3H, d, J = 6.9 Hz), and 2.79 (1H, sep, J = 6.9 Hz)], and two singlet vinyl protons [δ 5.97, 6.29] are all similar to compound **1**. A quaternary carbon (δ 68.1) (see Table 1) supposed carring a hydroxyl group has HMBC correlation with H-11 (δ 5.97), H-14 (δ 6.29), and H-15 (δ 2.79). This evidence suggested that the hydroxyl group locates at C-8. Comparison of ^{1}H NMR and ^{13}C NMR (Table 1) data with compound **1**, isochamanonol (**2**) is an isomer of **1** with C-8 epimer. Due to no hydroxy group deshielding effect, H-20 (δ 1.09) in **2** is at higher field than corresponded proton (δ 1.34) in **1**. In addition of the aid of HMBC and NOESY methods, the structure of isochamanonol (**2**) can be assigned as 8α-hydroxyabieta-9 (11),13-dien-12-one.

Obtusadione (**4**) was given the molecular formula $C_{20}H_{30}O_2$ on the basis of HRMS (M^+ *m/z* 302.2243). No hydroxy absorption was observed in its IR spectrum, only one carbonyl (1712 cm^{-1}) and one olefinic (1610 cm^{-1}) absorptions presented. The UV λ_{max} at 223, 245 nm indicated conjugated carbonyl system. Compound (**4**) has twenty ^{13}C NMR signals (Table 1), from which two carbonyl signals (δ 207.3, 208.8) and two olefinic signals [δ 153 (C), 152.3 (CH)] were observed. One carbonyl absorption at 1712 cm^{-1} together with two carbonyl ^{13}C NMR signal and conjugated UV absorptions indicated that one cyclohexane and one cyclopentenone. A singlet with very lower field signal of vinyl proton at δ 7.26 suggested that it is a β-olefinic proton in cyclopentenone system unambigusuly. An isopropyl group attached on α-olefin of cyclopentenone system attributable to their ^{1}H NMR signals [δ 1.05, 1.09 (each 3H, d, J = 6.9 Hz), and 2.60 (1H, sep, J = 6.9 Hz)]. Three singlet methyl groups [δ 0.87 (H-20), 0.89 (H-19), and 1.02 (3H, H-18)] addition of an isopropyl proposed the skeleton of **4** is similar to abietane-type diterpene. Two methylene protons at δ 2.57 (1H, ddd, J = 14.6, 7.4, 6.4 Hz, H-7), and 2.49 (1H, ddd, J = 14.6, 5.3, 2.1 Hz, H-7) was assigned as linked between a methylene group and cyclohexanone ketone (δ 208.8) discerning from their coupling pattern and HMBC correlation to ketone (δ 208.8). A pair of doublets at δ 3.21 (1H, d, J = 18.7 Hz, H-11) and 2.13 (1H, d, J = 18.7 Hz, H-11) was considered to position between a quaternary carbon (δ 67.8) and cyclopentenone ketone (δ 207.3) attributable to having HMBC correlation with δ 207.3 and 67.8. This quaternary carbon was assigned to C-9 (spirocarbon) due to showing HMBC correlation with H-20, H-14, H-7. From the HMBC analysis (see structures **6**). The structure of **4** was judged as 14(8→9)abeoabieta-14-ene-8,12-dione. As to its relative stereochemistry was clear from NOESY (see structure **7**) technique. The NOSEY correlation (see structure **7**), H-5/H-14 and H-5/H-18, confirmed the double bond conneted to α-axial orientation, meanwhile it can demonstrate Ha-11 and Hb-11 having larger different chemical shift due to Ha-11 receiving deshielding effect from carbonyl of cyclohexanone. Compound (**4**) was considered deriving from chamanonol (**1**) (Chart 1) via biotransformation. We try to prove the biotransformation by using chemical method and treated **1** with TsOH in THF two days at room temperature. The product is only recover. As the reaction was heated under reflux 6 hour, 5,6-dehydroferrugiol (**8**)[5] is the only product. (see Chart 1)

Obtusanal (**5**) suggested the presence of phenolic acetyl, acetoxyl, aldehyde, cyclohexanone, and phenyl groups ascribing to its IR absorption bands at 1757, 1734, 1725, 1706, 1610, and 1514 cm^{-1}.

respectively. ^{1}H NMR spectrum indicated the presence of two singlet methyl groups [δ 0.44 (H-18), 1.01 (H-19)], an isopropyl group attached on phenyl [δ 1.16, 1.17 (each 3H, d, J = 6.9 Hz, H-16, H-17), 2.96 (1H, sep, J = 6.9 Hz)], two acetyl groups [δ 2.12, 2.32], and aldehyde group [δ 9.76 (d, J = 6.9 Hz)], three methine protons [δ 2.48 (dd, J = 6.9, 1.9 Hz, H-5), 3.39 (dd, J = 7.4, 4.7 Hz, H-2), and 6.15 (d, J = 7.4 Hz, H-7)], two methylene protons [δ 2.09 (1H, dd, J = 14.3, 1.9 Hz, H-1$_\alpha$), 2.53 (1H, dd, J = 14.3, 4.7 Hz, H-1$_\beta$)]. The MS of **5** had an exact mass of *m/z* 414.2050 indicating the molecular formula $C_{24}H_{30}O_6$. Removal of two acetyl unit from the formula $C_{24}H_{30}O_6$ of **5** would afford a parent diterpene with two methyl groups one isopropylphenol moiety and an aldehyde group. The skeleton of **5** is similar to 6,7-secodehydroabietane as **3**, but the aldehyde linked to phenyl must be converted to acetoxy and benzyl carbon connected to ring A. The COSY spectrum exhibited the result as follows: H-5/H-6, H-2/H-1, -7, H-1$_\alpha$/H-1$_\beta$, -5. The carbonyl absorption at 1706 cm^{-1} and H-5 having W-form coupling (J = 1.9 Hz) with H-1$_\alpha$ confirmed it has a moiety of cyclohexanone. The ^{13}C NMR data (Table 1) exhibited four methyl groups, one phenyl with one oxygenated, two acetyl, two carbonyl groups signals. Two methyl groups (δ 1.01 and 0.44) and methine proton (δ 3.39) showed HMBC correlation with cyclohexanone carbonyl indicating there are neighboring to this ketone. The following HMBC correlation, H-18,-19/C-5, H-5/C-9, H-20/C-9, H-7/C-8,-9, H-1/C-3, -9, could decribe the correct structure of **5**. As to its relative stereochemistry, it can be demonstrated by NOESY (see 9) technique (H-6/H-1$_\beta$, H-5/H-18, -19, CH_3COO-C-7/H-1α, -2, H-7/H-14, H-17/H-14 showing NOESY correlation). H_3-18 appeared at high field (δ 0.44) due to position at α-axial orientation which shielded from aromatic group. The structure of **5** is a novel skeleton being 7(6→2)abcoabietane. The proposed retrobiotransform of **5** was shown as in Chart 2. The precussor of **5** is diol **10** which was converted to 12-hydroxy-3-oxo-6,7-secoabieta-8,11,13-triene-6,7-dial (**11**) via retroaldol condensation. Compound 11 is a biooxidative product from **3**.

Acknowledgements

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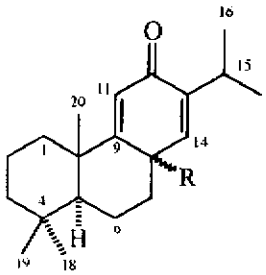
6. Physical data of all compounds: Compound **1**: mp 178-179℃; $[\alpha]_D$ -140 °(*c* 3.2, $CHCl_3$); HR-EIMS *m/z* 302.2244 (calcd $C_{20}H_{30}O_2$); UV(MeOH) λ_{max} nm (log ε): 240(4.10); EIMS *m/z* (%): 302(M^+, 27), 178 (40), 165 (100), 149 (30). Compound **2**: mp 177-178℃; $[\alpha]_D$ +73.7 ° (*c* 0.5, $CHCl_3$); HR-EIMS *m/z* 302.2243 (calcd 302.2246 for $C_{20}H_{30}O_2$); UV(MeOH) λ_{max} nm (log ε): 239(4.03); EIMS *m/z* (%): 302(M^+, 13), 178 (30), 165 (100), 149 (20). Compound **4**: liquid; $[\alpha]_D$ –79.1 °(*c* 0.3, $CHCl_3$); HR-EIMS *m/z* 302.2243 (calcd 302.2246 for $C_{20}H_{30}O_2$) ;

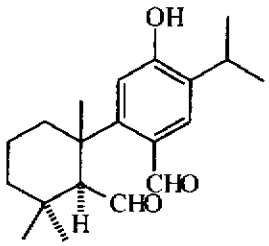
UV(MeOH) λ_{max} nm (log ε): 223(3.89), 245 (3.93); EIMS *m/z* (%): 302(M^+, 42), 241 (31), 166 (31), 88 (32), 73 (36), 70 (76), 61 (100). Compound **5**: liquid; $[\alpha]_D$ +5.5 ° (*c* 0.3, $CHCl_3$); HR-EIMS *m/z* 414.2050 (calcd 414.2042 for $C_{24}H_{30}O_6$); EIMS *m/z* (%): 414(M^+, 12), 242 (25), 200 (100), 185 (23), 159 (28).

Table 1 ^{13}C NMR (100 MHz) of 1, 2, 4 and 5

C	1	2	4	5
1	39.9	39.5	33.7	34.1
2	18.5	19.2	18.3	46.5
3	41.7	41.8	41.7	212.5
4	34.2	39.9	33.6	44.1
5	54.7	42.2	47.1	69.6
6	17.6	16.1	23.4	202.5
7	34.6	28.9	39.0	71.9
8	69.2	68.1	208.8	131.9
9	169.1	172.0	67.8	143.4
10	41.3	33.3	44.0	35.4
11	121.9	123.8	37.8	119.7
12	187.4	187.3	207.3	148.5
13	141.7	142.1	153.3	140.1
14	145.6	143.7	152.3	125.4
15	25.5	25.7	24.9	27.5
16	21.3	21.6	21.1	22.8
17	21.8	21.7	21.4	22.8
18	33.5	33.5	33.8	25.7
19	21.8	21.5	22.0	29.7
20	20.2	25.0	17.6	27.2
AcO-C-7				170.8
AcO-C-12				169.4



1 R = β–OH
2 R = α–OH



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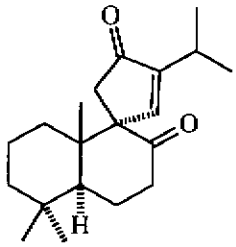

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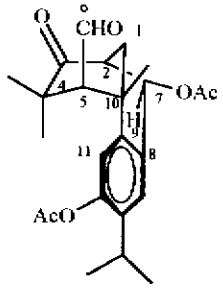

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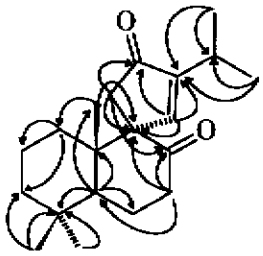
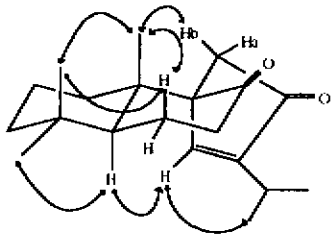
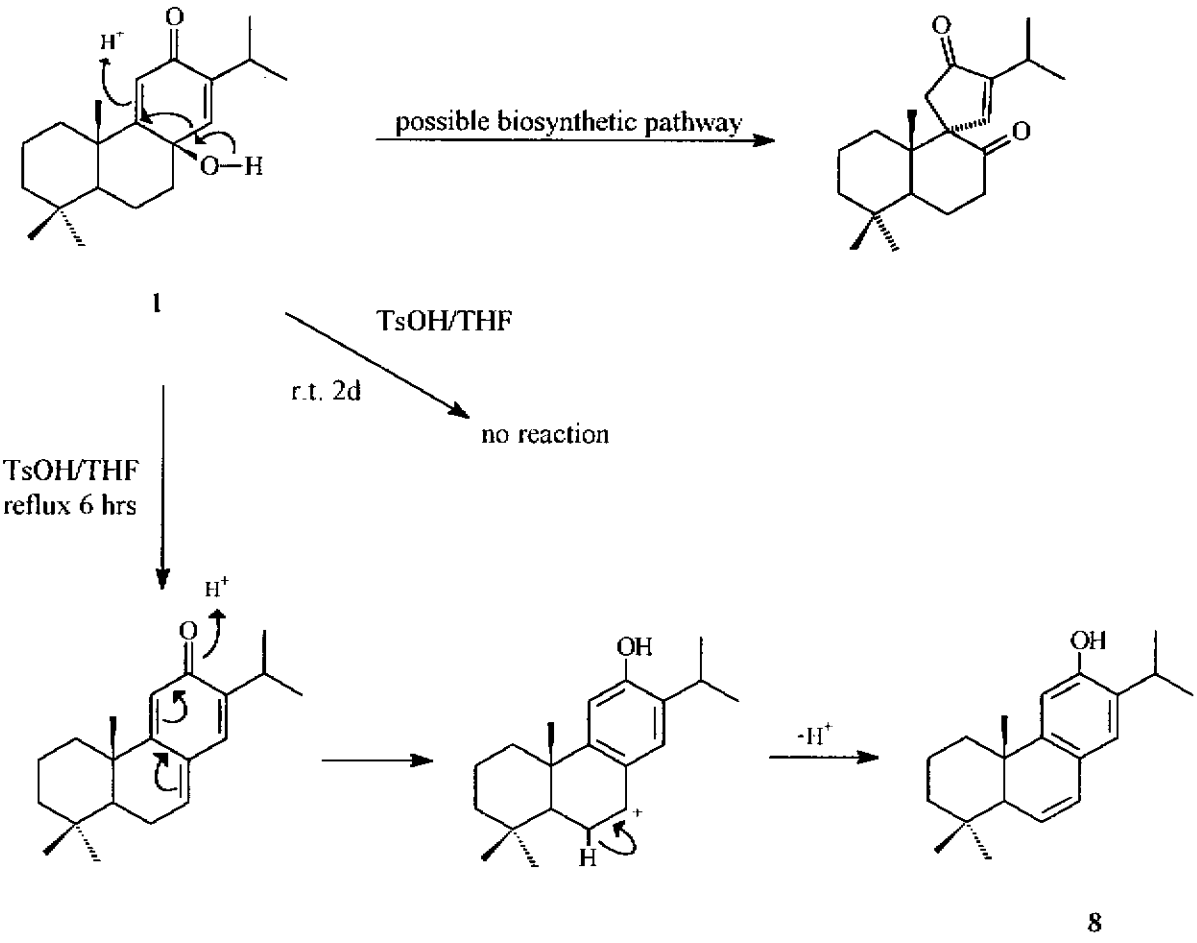


6 HMBC (→)



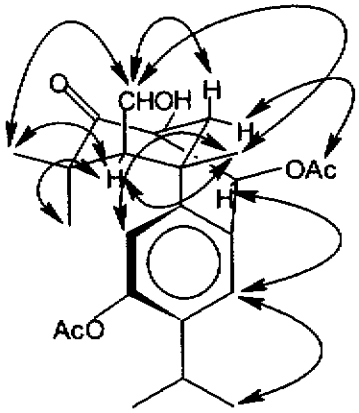
7 Major NOESY (⟷)



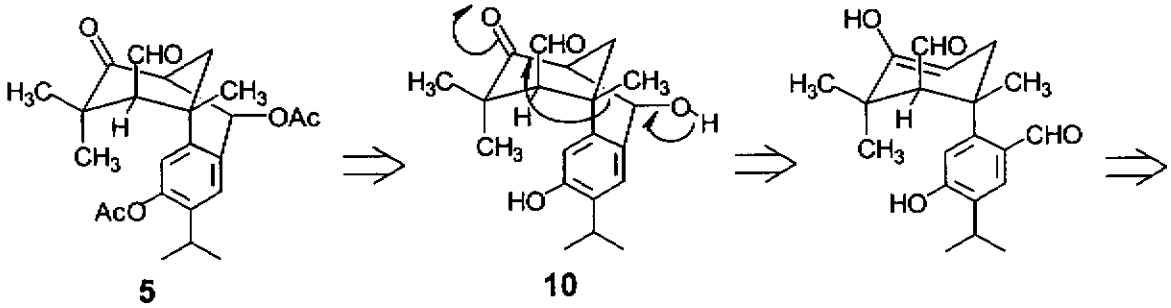
1

8

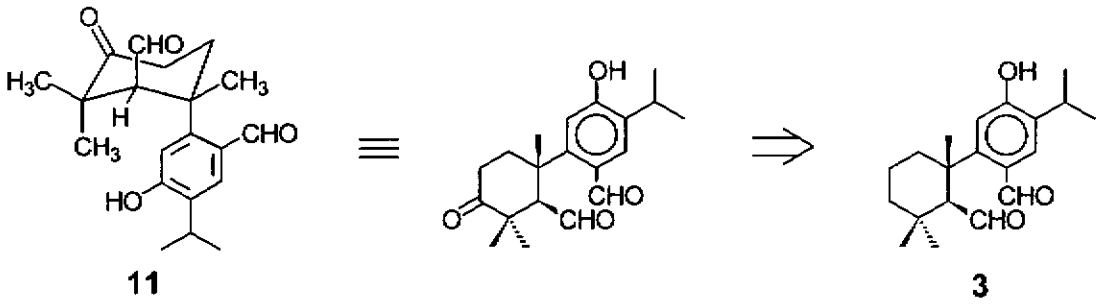
Chart 1



9 (NOESY ⟷)



5 **10**



11 **3**

Chart 2 (Retrobiotransformation of **5**)

A NOVEL BICYCLO[2. 2. 2]OCTANE SKELETON DITERPENE, OBTUNONE, FROM THE HEARTWOOD OF *CHAMAECYPARIS OBTUSA* VAR. *FORMOSANA*

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Obtunone, a novel bicyclo[2. 2. 2]octane skeleton diterpene, was isolated from the heartwood of *Chamaecyparis obtusa* var. *formosana*. Its structure was determined spectroscopically by interpretation of 2D-NMR experiments, including HMBC and NOESY.

KEY WORDS *Chamaecyparis obtusa* var. *formosana*; Cupressaceae; bicyclo[2. 2. 2]octane; diterpene; obtunone

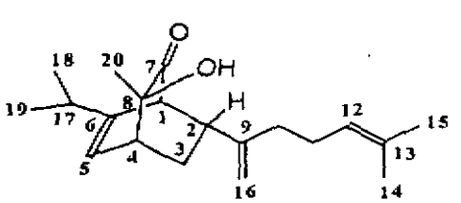
Due to its strong resistance to wood-decaying fungi, the wood of *Chamaecyparis obtusa* S. et Z. var. *formosana* Rehd. (Taiwan hinoki; Cupressaceae) is an important building material in Taiwan. Previously, Kafuku and Nozoe studied the essential oil[1] and acidic components[2] (isolated 1-rhodinic acid, carvacrol, 2-methoxy-5-isopropylphenol, and β-thujaplicine). Afterward, Lin[3] continued the component studies and found *p*-cresol, α-thujaplicine, 1-rhodinic acid, β-thujaplicine, terpine hydrate, and 4-isopropylsalicylaldehyde. We have investigated the chemical components of the bark of this plant, from which two carbamates together with steroids, diterpenes, and lignan[4] were identified. No further investigation of the components of the heartwood of this plant has been reported, which led us to undertake the present study.

The acetone extract of the heartwood of this plant was partitioned with ethyl acetate and water. After repeated purification with SiO_2 on column chromatography and HPLC, a novel diterpene obtunone (**1**) together with 3,10-dihydroxydielmentha-5,11-diene-4,9-dione (**2**)[5] were isolated. Based on the following spectral evidence (COSY, HMQC, HMBC, and NOESY), the novel diterpene was assigned as structure (**1**), a peculiar bicyclo[2. 2. 2]octane skeleton diterpene.

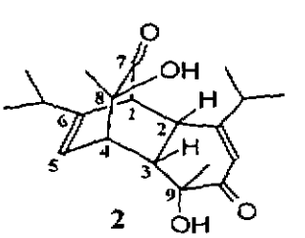
Obtunone (1), a colorless liquid, $[\alpha]^{25}_{D}$= -47.6° (c = 0.43, $CHCl_3$) was formulated as $C_{20}H_{30}O_2$ on the basis of HRMS (M^+ *m/z* 302.2249, calc. 302.2246). It contained a hydroxy group (3435 cm^{-1}), a carbonyl group (1726 cm^{-1}), and an isopropyl group attached on a double bond [1382 and 1366 cm^{-1}; 0.89 and 0.97 (3 H each, d, J = 6.9 Hz), 2.10 (1 H, sept d, J = 6.9, 1.6 Hz)], an isobutylidene moiety [1.58 and 1.65 (3 H each, br s), 5.06 (1 H, br t, J = 5.3 Hz)], one trisubstituted and 1,1-disubstituted double bond [6.03 (1 H, ddd, J = 6.9, 1.6, 1.6 Hz), 4.68 and 4.75 (1 H each, s)], an ethylene group linked between two olifinic groups [1.98-2.12 (4 H, m)], a methine proton located between the carbonyl and olefinic groups [3.07 (1 H, dd, J = 1.6, 1.6 Hz)], and a methyl group attached to a quaternary carbon bearing a hydroxy group [1.22 (3 H, s)] discernible in its spectral data. A methine proton at δ 2.81 was considered to be linked

between an olifinic group and a methylene group due to the presence of a coupling pattern with ddd (J = 6.9, 2.8, 2.8 Hz). The remaining signals for the methine and methylene protons are at δ 2.69 (1 H, ddd, J = 9.6, 6.1, 1.6 Hz) and δ 1.33 (1 H, ddd, J = 13.0, 6.1, 2.8 Hz), and 2.37 (1 H, ddd, J = 13.0, 9.6, 2.8 Hz), respectively. Irradiation at δ 2.37, the signals at 1.33, 2.69, and 2.81 simplified to dd (J = 6.1, 2.8 Hz), dd (J = 6.1, 1.6 Hz), and dd (J = 6.9, 2.8 Hz), respectively. Due to the molecular formula $C_{20}H_{30}O_2$ of **1**, the index of hydrogen deficiency (IHD) of **1** is six. Therefore, obtunone (**1**) is a bicyclic compound. Due to ^{1}H-^{1}H COSY and HMQC spectra (Table 1), the NMR data and attachment of the spin-system were reasonably assigned. Its structural inferences were reinforced by the HMBC (Table 1) technique. Regarding the stereochemistry, the pronounced NOESY correlation (structure **3**) between H-5 and H-20, H-1 and H-2, and H-3 and H-4 established the formulated configuration in **1**. The unique skeleton of diterpene has not yet been observed.

Compound **2**,[5] isolated from *Callitris macleayana*, was obtained from compound **4** (unobserved in the natural state) *via* endo addition of bio-Diels-Alder self-dimerization. The absolute configuration of **2** was obtained from CD measurements and determined to be 8*R* and 9*R*. Compound **2**, isolated from *C. obtusa* var. *formosana*, expressed the specific rotation value as isolated from *Callitris macleayana*. Obtunone (**1**) was also yielded from **4** and myrcene (**5**) *via* the bio-Diels-Alder addition. The absolute configuration of C-8 in obtunone (**1**) was assigned as the *R*-configuration like that in compound **2** based on the same biological pathway. The formation of compound **2** was proceeded by endo addition from compound **4**. Obtunone (**1**) was also obtained by endo addition between compounds **4** and **5** *via* the bio-Diels-Alder reaction. Therefore, C-2 can be assigned to have the *R*-configuration. Carman [6] endeavored to carry out self-Diels-Alder dimerization of compound **4**. The resulting product **2** was not yielded probably because the desired electron-deficient dienophile and electron-rich diene place contradictory demands upon a single unit. Finally, on reflux with ethanolic sulfuric acid[6], compound **6** afforded dimerization to give **2** in low yield (30%).



1



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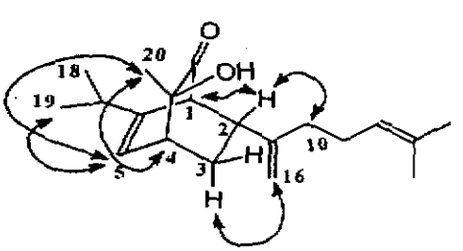
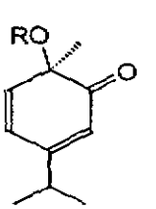


3 NOESY ⟷



4 R = H
6 R = Ac

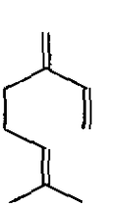


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Table 1. NMR Data, COSY, HMBC, and NOESY Correlation of 1 (500 MHz, 125 MHz in $CDCl_3$)

n°	C	DEPT	δ ^{13}C	δ ^{1}H (*J*=Hz)	COSY	HMBC	NOESY
1		CH	55.4	3.07 dd (1.6,1.6)	2, 5	2, 3, 5, 17	2, 17, 18
2		CH	39.8	2.69 ddd (9.6, 6.1, 1.6)	1, 3	1, 3, 4, 10, 16	1, 10
3		CH_2	26.1	2.37(β) ddd (13.0, 9.6, 2.8)	2, 3α, 4	1, 2, 4	2, 4
				1.33(α) ddd (13.0, 6.1, 2.8)	2, 3β, 4		4, 16
4		CH	42.8	2.81 ddd (6.9,2.8, 2.8)	3, 5	3, 5, 20	3, 5
5		CH	125.3	6.03 ddd (6.9.1.6,1.6)	1, 4, 17	1, 3, 4, 17	19, 20
6		C	144.7			1, 2, 4, 17, 18, 19	
7		C	213.2			1, 2, 4, 20	
8		C	72.2			1, 3, 4, 5, 20	
9		C	150.2			1, 2, 3, 10, 11, 16	
10		CH_2	36.3	2.04-2.10 m	11	2, 11, 16	2
11		CH_2	26.5	1.98, 2.12 m	10, 12	10, 12	12
12		CH	123.7	5.06 br t (5.3)	11	10, 11, 14, 15	15
13		C	131.8			14, 15	
14		CH_3	17.7	1.58 s		12, 15	15
15		CH_3	25.6	1.65 s		12, 14	12, 14
16		CH_2	109.8	4.68 s, 4.75 s		2, 10	3, 11
17		CH	33.1	2.10 sept d (6.9, 1.6)	5, 18, 19	1, 5, 18, 19	1
18		CH_3	21.0	0.89 d (6.9)	17	17, 19	17
19		CH_3	19.8	0.97 d (6.9)	17	17, 18	5
20		CH_3	25.9	1.22 s		4	5

($J_{1,2}=J_{1,3}=J_{5,17}=1.6$ Hz, $J_{2,3\alpha}=6.1$ Hz, $J_{2,3\beta}=9.6$ Hz, $J_{3\alpha,\beta}=13$ Hz, $J_{3\alpha,4}=J_{3\beta,4}=2.8$ Hz, $J_{4,5}=J_{17,18}=J_{17,19}=6.9$ Hz, $J_{11,12}=5.3$ Hz)

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New Dimeric Monoterpenes and Dimeric Diterpenes from the heartwood of *Chamaecyparis obtusa* var. *formosana*

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Two dimeric monoterpenes, obtusals A and B, and two dimeric diterpenes, obtusanols A and B, along with (*S*)-(-)-citronellol, (S)-(-)-citronellic acid, (+)-borneol, (+)-sugiol, and (-)-6,12-dihydroxyabieta-5,8,11,13-tetraen-7-one, were isolated from the heartwood of *Chamaecyparis obtusa* var. *formosana* and were characterized by spectroscopic experiments, including 2D-NMR techniques, and chemical methods. Total synthesis of optical pure of obtusals A and B were carried out from (-)-citronellol and (-)-citronellic acid, respectively.

1.Introduction. ---- Among of seven species, only two species of Chamaecyparis (Cupressaceae) are indigenous to Taiwan. C. formosensis and C. obtuse var. formosana (Taiwan hinoki) are important building materials and found in the central mountains of Taiwan at 1300–2800 m above sea level. The C. obtuse var. formosana has strong resistant to white-ant and wood-decaying characters, it also can live over one thousand years. Its timber is yellow-red with a distinguished purple-pink streak together with huge body, based on the above reasons, the value of C. obtuse var. formosana is more than C. formosensis. The previous paper, we have completed the structural elucidation of new and novel diterpenes and lignans [1– 4]. Further detailed reinvestigation of the same extract from the heartwood of C. obtuse var. formosana has yielded two new dimeric monoterpenes, obtusals A (**1**) and B (**2**), and two new dimeric diterpenes, obtusanols A (**3**) and B (**4**), together with (-)-citronellol (**5**) [5], (-)-citronellic acid (**6**) [6], (+)- borneol (**7**) [7], (+)-sugiol (**8**) [8], and (-)-6,12-dihydroxyabieta-5,8,11,13-tetraen-7-one (**9**) [8]. The structures of these new dimeric compounds were elucidated based on the following spectral evidence and chemical methods. Optical pure of obtusals A (**1**) and B (**2**) were synthesized from (-)-citronellol (**5**) and (-)-citronellic acid (**6**).

2. Results and Discussion. – Compound **1**, called obtusal A, was isolated as a liquid. HR-EI-MS revealed 1 to be a formula $C_{20}H_{32}O_4$. The IR spectrum suggested the presence of ester (1734, 1248, and 1073 cm^{-1}) and conjugated aldehyde (2716 and 1690 cm^{-1}), and olefinic (1674 cm^{-1}) groups. The UV absorption band at λ_{Max}^{MeOH} 229 nm confirmed the conjugated system. By the observation of ^{1}H- and ^{13}C-NMR (Table 1) analysis and aide from two dimensional techniques (including HMQC, HMBC, COSY, and NOSEY methods), the structure of obtusal A (**1**) was judged as a dimeric monoterpene with ester linkage not a diterpene.

The alcohol moiety exhibited two methyl signals at δ 0.94 (d, *J*=6.7 Hz) and 1.72 (s, attached on double bond), an olefinic proton at δ 6.44 (t, *J*=7.3 Hz), and an aldehyde proton at δ 9.37 (s). The olefinic proton and aldehyde proton have NOESY correlation, it gave a E-form conclusion. A multiple methylene signal at δ 4.10 (2H, H-(C1')) was considered as attaching on *O*-terminal of ester function. Because H-C(3') is a chiral center causing two protons of H-1' to be nonequivalent. The COSY correlation [H-C(2') (δ 1.58, 1.38)/H-C(3') (δ 1.57); H-C(3')/H-C(10'), H-C(4') (δ 1.51, 1.67), H-5' (δ 2.36)/H-C(4', -6')] confirmed the proton sequence. ^{1}H- and ^{13}C-NMR data of this moiety are similar to 2,6-dimethyl-8-hydroxy-2-octenal (**10**) [5] except the data of C(1') and H-C(1') (δ_H 4.10, m, in **1** and 3.72, m, in **10**; δ_C 62.5 in **1** and 60.8 in **10**). The acid moiety also contained a secondary methyl [δ 0.96 (d, *J*=6.7)], a vinyl methyl [δ 1.72 (s)], an aldehyde [δ 9.37 (s)], and an olefinic proton [δ 6.44 (t, J=7.3 Hz)]. Two methylene protons vicinal to carbonyl of ester presented at δ 2.29 (1H, dd,

J=14.8, 6.3 Hz) and 2.15 (1H, dd, J=14.8, 7.7 Hz). COSY correlation, δ 2.29/δ 1.98; δ 1.98/δ 1.57, 1.61; δ 1.61/δ 2.36, and δ 2.36/δ 6.44, identified the contiguous proton. *E*-form configuration of double bond was revealed from the NOSEY correlation between δ 6.44 and δ 9.37. The above evidence established the structure of obtusal A (1) to be an ester which was condensed from **10** and **11**. HMBC (Structure **1**) and ^{13}C data also confirmed the structure. The specific rotation of **1** is $[\alpha]_D^{20}$ –8.2, therefore the biosynthetic pathway was proposed from the condensation of (*S*)-(-)-10 and (*S*)-(-)-11, these came from (*S*)-(-)-**5**, and (*S*)-(-)-**6**. The total synthesis of **1** was carried out as follows. The oxidization of (-)-citronellol (5) in reflux ethanol with SeO_2 yielded (-)-**10** [9]. (-)-**11** was obtained from (-)-citronellic acid using the same condition. By using Mitsunobu reaction [10], the condensed product from (-)-**10** and (-)-**11** identified with obtusal A (**1**), and it showed the specific rotation $[\alpha]_D^{25}$ –5.8°.

Compound **2**, obtusal B, was isolated as an oil and showed the molecular formula $C_{20}H_{32}O_3$ from its exact mass and ^{13}C-NMR spectrum (Table 1). As compound 1, obtusal B (**2**) contained ester and conjugated aldehyde attributable to the IR absorption bands at 2710, 1735, 1695, and 1630 cm^{-1} and UV absorption band at λ_{max} 229 nm. By the analysis of ^1H- and ^{13}C-NMR spectra, it was not a diterpene and was a dimeric monoterpene linked by ester group. The following ^1H-NMR data, δ 0.98 (3H, d, J=6.6 Hz), 1.72 (3H, d, J=1.1Hz), 2.30 [1H,dd, J=14.7, 6.5 Hz, H-C(2a)], 2.18 [1H, dd, J=14.7, 7.5 Hz, H-C(2b)], 6.44 (1H, tq, J=7.3, 1.1 Hz), and 9.37 (1H, s), are almost same as acid moiety of compound 1. The alcohol moiety exhibited three singlet methyl groups at δ 0.80, 0.84, and 0.88, and a methane proton attached with ester at δ 4.87 (ddd, J=10.0, 3.4, 2.2 Hz). Comparison of ^1H- and ^{13}C-NMR data between alcohol moiety of 2 and (+)-borneol (**7**), the only difference is H-2' in 2 located at lower field than that in 7. The coupling constant of H-2' with 10 Hz as 7 revealed the hydroxy group is position at *endo*-orientation. Compound 2 exhibited specific rotation $[\alpha]_D^{25}$ +26.5°, so that the structure of **2** was proposed from the condensation of (+)-borneol (**7**) [1R, 2S] and (-)-11. In order to prove the proposal, the following reaction was achieved. Oxidation of (-)-citronellic acid with selenium dioxide yields compound 11. Acid halide (12), obtained from 11 by treament with thionyl chloride, reacted with (+)-borneol (**7**) in CH_2Cl_2 and yielded a product **2** with similar specific rotation $[\alpha]_D^{25}$ +27.3° obtusanol A (**3**) had the molecular formular $C_{40}H_{56}O_4$ on the basic of exact mass (HR-EI-MS) at *m/z* 600.4178. It showed hydroxyl (3373 cm^{-1}), aromatic (3051, 1598, 1490 cm^{-1}), and conjugated carbonyl (1654 cm^{-1}) absorption in its IR spectrum. The UV spectrum indicated a benzoyl group (224 and 278 nm). The ^1H-NMR spectrum showed two set of dehydroabietane signals as follows: 1.10, 1.12 [each 3H, d, J=6.9 Hz, H-C(16, 17), 2.22 (1H, br d, J=13.6, H_β-1, characteristic signal for dehydroabietane)] [10, 11], 3.01 (1H, sep,

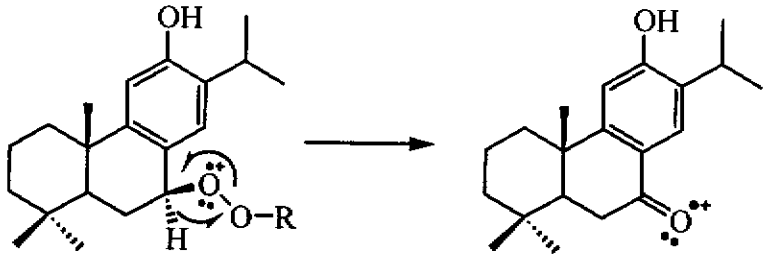
J=6.9 Hz, H-15), 4.58 (1H, br s, exchangeable, Ph-OH), 5.38 (1H, dd, *J*=9.1, 2.6 Hz, H-7), 6.68, 7.03 [each 1H, s, H-C(11, 14)]; the second set signals are δ 0.98, 1.02, 1.37 (each 3H, s, H-18, -19, -20), 1.19, 1.21 (each 3H, d, *J*=6.8 Hz), 2.32 (1H, br d, *J*=13.8 Hz, H_β-C(1), 3.29 (1H, sep, *J*=6.8 Hz), 6.76, 7.93 (each 1H, s, H-C(11'), H-C(14'). The signal at δ 5.38 was assigned as H-C(7) due to having HMBC correlation to C(6), C(8), and C(14). The ^{1}H-NMR data of former set is similar to that of 7β-hydroxyferrugiol (**13**) [13], the only difference is that chemical shift of H-C(7) and C(7) (δ_C 102.5) are lower field than the corresponded position in **13**. The second set signal of **3** is like sugiol (**8**), H-C(14) presented at lower field due to deshielding from C(7) carbonyl group. On account of *O* atom number from formula $C_{40}H_{56}O_4$, the remained two *O* atom presented peroxide form. It links C(7) and C(12') to form structure of **3**, the evidence is compatible with lower field of H-C(7) and C(7). The base peak at *m/z*300 from the mass fragmentation pattern of **3** is consistent with peroxide structure. Catalytic hydrogenolysis of **3** with 10% Pd-C in MeOH yield two products (+)-sugiol (**8**) and (+)-7β-hydroxyferrugiol (**13**). The IR spectrum of **4** suggested the presence of hydroxyl (3382 cm^{-1}), aromatic (3062, 1598, 1493 cm^{-1}), and conjugated carbonyl (1646 cm^{-1}) groups. The molecular of $C_{40}H_{54}O_5$ was established by HR-EI-MS. By the analysis of ^{1}H- and ^{13}C-NMR data together with two dimensional NMR technique, compound **4**, obtusanol B, was considered as dimeric of two dehydroabietane diterpene with peroxide linkage not a tetraterpene. A semi-moiety is a 7-oxygenated ferrugiol which was revealed from its ^{1}H- and ^{13}C-NMR data [Table 1] [It contains three singlet methyl groups, an exchangeable phenolic proton, an isopropyl attached on phenyl, two *para*-phenyl protons, a typical H_β-C(1) proton of dehydroabietane and a methane proton located on benzyl and carried a peroxide functional group (δ_H 5.4) (1 H, dd, *J*=9.0, 2.5 Hz), δ_C 102.4]. The data are almost near to the semi-moiety of compound **3**. The other semi-moiety also presents three singlet methyl group signal, a typical H_β-C(1) proton of dehydroabietane, an isopropyl group attached on a phenyl group, two *para*-phenyl protons (one at δ 8.03 is received deshielding from C(7) carbonyl, one exchangeable proton (δ 7.15, HO-C(6) strong hydrogen bond with C(7') carbonyl group. This semi-moiety is like 6,12-dihydroxyabieta-5,8,11,13-tetraen-7-one (**9**) by comparison of their ^{1}H- and ^{13}C-NMR data. Therefore, the structure of obtusanol (**4**) was suggested that C(7) position of ferrugiol and C(12') position of 6-hydroxyabieta-5,8,11,13-tetraen-7-one was connected with peroxide function. On the same mentioned above catalytic hydrogenolysis condition, (-)-**9** and (-)-**13** were isolation from compound **4**. Base peak of mass fragment of **4** is also *m/z* 300. Hydroperoxide and endoperoxide in natural occurring are very general, but dialkyl peroxide is very unique.

Table 1. *^{1}H-NMR Data* (CDCl3) *of Compounds* 1 ~ 4. δ in ppm, *J* in Hz

	1	2		3	4
Ha-C(2)	2.15 (dd, *J*=14.8, 6.3)	2.18 (dd, *J*=14.7, 7.5)	Hβ-C(1)	2.22 (br d, *J*=13.6)	2.24 (br d, *J*=13.4)
Hb-C(2)	2.19 (dd, *J*=14.8, 7.7)	2.30 (dd, *J*=14.7, 6.5)	Hα-C(7)	5.38 (dd, *J*=9.1, 2.6)	5.41 (dd, *J*=9.0, 2.5)
H-C(3)	1.98 (m)	2.01 (m)	H-C(11)	6.68 (s)	6.68 (s)
CH_2(4)	1.57 (m), 1.61(m)	1.38 (m), 1.53 (m)	H-C(14)	7.03 (s)	7.18 (s)
CH_2(5)	2.36 (m)	2.36 (m)	H-C(15)	3.01 (sep, *J*=6.9)	3.00 (sep, *J*=6.9)
H-C(6)	6.44 (t, *J*=7.3)	6.44 (tq, *J*=7.3, 1.1)	Me(16)	1.10 (d, *J*=6.9)	1.11 (d, *J*=6.9)
H-C(8)	9.37 (s)	9.37 (s)	Me(17)	1.12 (d, *J*=6.9)	1.16 (d, *J*=6.9)
Me(9)	1.72 (s)	1.72 (d, *J*=1.1)	Me(18)	0.96 (s)	1.02 (s)
Me(10)	0.96 (d, *J*=6.7)	0.98 (d, *J*=6.6)	Me(19)	0.93 (s)	0.98 (s)
CH_2(1')	4.10 (m)		Me(20)	1.21 (s)	1.27 (s)
Ha-C(2')	1.38 (m)	4.87 (dd, *J*=10.0, 3.4, 2.2	HO-C(12)	4.58 (br s)	4.60 (br s)
Hb-C(2')	1.53 (m)		Hβ-C(1')	2.32 (br d, *J*=13.8)	2.40 (br d, *J*=13.6)
Ha-C(3')	1.57 (m)	0.92 (dd, *J*=13.7, 10.0)	H-C(5')	1.92 (dd, *J*=13.2, 4.3)	
Hb-C(3')		2.34 (m)	Ha-C(6')	2.58 (dd, *J*=18.1, 4.3)	
Ha-C(4')	1.51 (m)	1.65 (br t, *J*=4.5)	Hb-C(6')	2.67 (dd, *J*=18.1, 4.3)	
Hb-C(4')	1.67 (m)		H-C(11')	6.76 (s)	6.77 (s)
Ha-C(5')	2.36 (m)	1.20 (m)	H-C(14')	7.93 (s)	8.03 (s)
Hb-C(5')	2.36 (m)	1.72 (m)	H-C(15')	3.29 (sep, *J*=6.8)	3.33 (sep, *J*=6.9)
Ha-C(6')	6.44 (t, *J*=7.3)	1.29 (m)	Me(16')	1.19 (d, *J*=6.8)	1.20 (d, *J*=6.9)
Hb-C(6')		1.89 (m)	Me(17')	1.21 (d, *J*=6.8)	1.25 (d, *J*=6.9)
H-C(8')	9.37 (s)		Me(18')	0.98 (s)	1.46 (s)
CH_3(8')		0.88 (s)	Me(19')	1.02 (s)	1.42 (s)
CH_3(9')	1.72 (s)	0.84 (s)	Me(20')	1.37 (s)	1.48 (s)
CH_3(10')	0.94 (d, *J*=6.7)	0.80 (s)	HO-C(6')		7.15 (s)

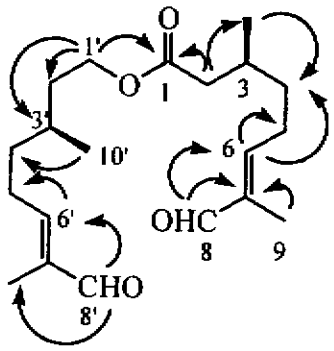
Table 2. *^{13}C-NMR Data* ($CDCl_3$) *of Compounds* 1 - 4. δ in ppm

	1	2		3	4		3	4
C(1)	172.8	173.1	C(1)	41.1	41.1	C(1')	38.2	33.7
C(2)	41.6	41.9	C(2)	18.7	18.8	C(2')	18.8	17.6
C(3)	30.0	30.2	C(3)	42.5	42.4	C(3')	41.3	37.7
C(4)	35.3	35.0	C(4)	33.3	37.7	C(4')	34.8	35.9
C(5)	26.4	26.5	C(5)	47.4	47.3	C(5')	49.7	141.1
C(6)	154.4	154.1	C(6)	34.3	34.2	C(6')	36.0	143.8
C(7)	139.4	139.5	C(7)	102.5	102.4	C(7')	198.8	179.8
C(8)	195.2	195.2	C(8)	142.7	142.6	C(8')	125.2	120.9
C(9)	9.2	9.2	C(9)	146.2	146.1	C(9')	156.0	154.2
C(10)	19.5	19.5	C(10)	41.2	41.4	C(10')	38.3	40.7
C(1')	62.5	48.7	C(11)	114.0	114.1	C(11')	108.4	109.8
C(2')	35.0	79.9	C(12)	149.4	149.4	C(12')	159.0	158.5
C(3')	29.6	36.9	C(13)	133.0	133.1	C(13')	136.3	137.2
C(4')	35.3	44.9	C(14)	120.9	120.8	C(14')	126.1	125.1
C(5')	26.4	28.0	C(15)	26.8	26.9	C(15')	27.5	27.4
C(6')	154.0	27.1	C(16)	21.7	21.7	C(16')	22.5	22.6
C(7')	139.5	47.8	C(17)	21.8	21.8	C(17')	22.5	22.6
C(8')	195.2	18.8	C(18)	33.7	33.7	C(18')	32.6	27.6
C(9')	9.2	19.7	C(19)	22.6	22.5	C(19')	21.4	28.0
C(10')	19.2	13.5	C(20)	23.4	23.2	C(20')	23.2	35.0

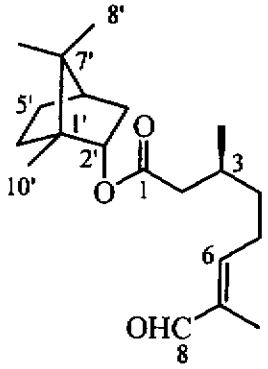


3 *m/z* 600 (3%) **8** *m/z* 300 (100%)

Chart 1



1 (→ HMBC)



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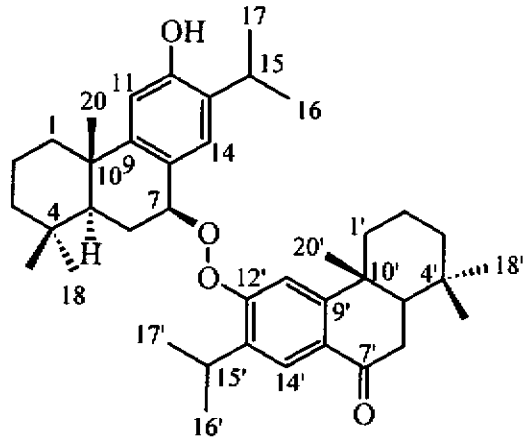

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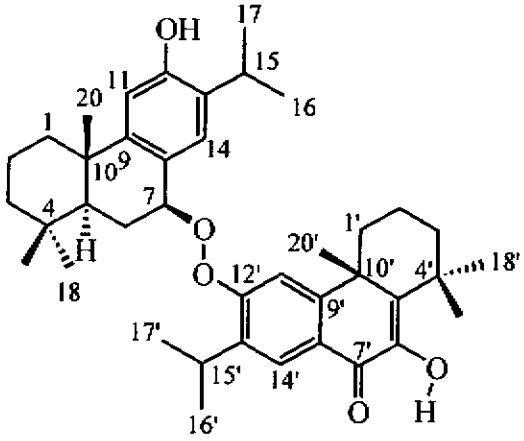

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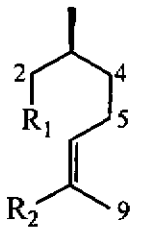
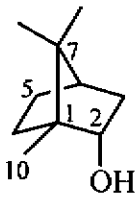
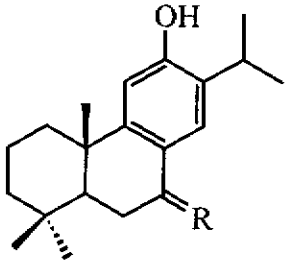


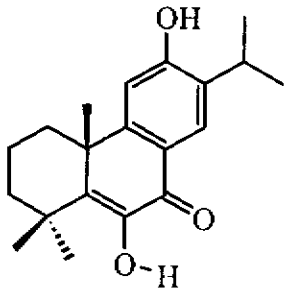
5 R_1=CH_2OH, R_2=CH_3
6 R_1=CO_2H, R_2=CH_3
10 R_1= CH_2OH, R_2=CHO
11 R_1=CO_2H, R_2=CHO
12 R_1=COCl, R_2=CHO



7



8 R=O
13 R=β-OH, α–H



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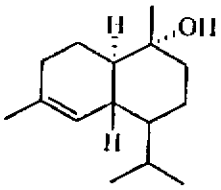
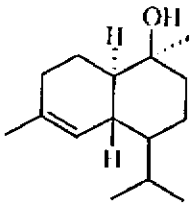
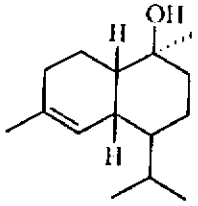
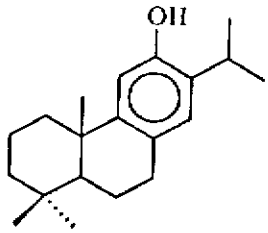
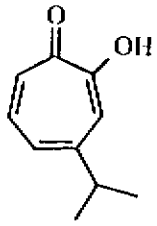
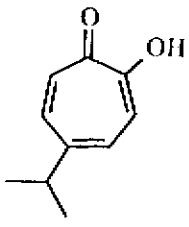
[13] Compound **13** is a new compound, which was prepared from sugiol by reduction with $NaBH_4$ in MeOH solution. (See experimental part)

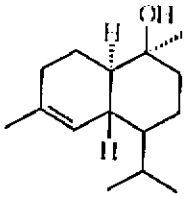
Antifungus Activity

	Fungus	conc (ppm)	Antifugal Index
 α-Cadinol	*Coriolus versicolor*	10	52.2
		50	79.4
		100	100
	Laetiporus sulphureus	50	52.9
		100	100
 T-Cadinol	*C. versicolor*	100	56.9
	L. sulphureus	100	100
 T-muurolol	*C. versicolor*	100	66.3
	L. sulphureus	100	82
 Ferruginol	*L. sulphureus*	100	51.3
 β-thujaplicine	*C. versicolor*	25	42.4
		50	100
	L. sulphureus	25	100
 γ-thujaplicine	*C. versicolor*	25	17.6
		50	100
	L. sulphureus	25	100

Biological Activities

Cytotoxicity to HL-60

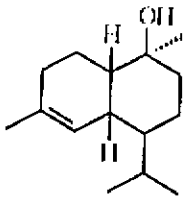
IC_{50} (μ g/ml)



8.4

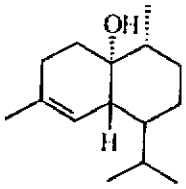
T-cadinol

IC_{50} (μ g/ml)



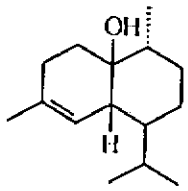
6.4

T-murrolol



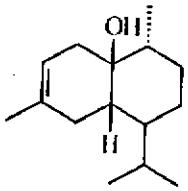
2.9

Cubenol



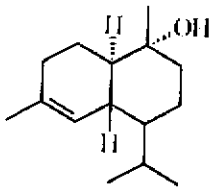
>20

epi-Cubenol



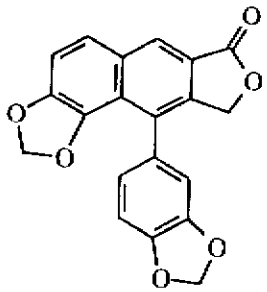
3.7

iso-epicubenol



0.1 to HeLa cell

α -Cadinol



Hep A2 (0.25 μ g/ml) (HBsAg)

Hep 3B/T2 (0.025 μ g/ml)

Helioxanthin