

Acetate: mp 80°; Found: C, 54.31; H, 5.15;  $C_{32}H_{36}O_{18}$  requires C, 54.2; H, 5.15;  $^1H$  NMR ( $CDCl_3$ ):  $\delta$  6.26 (1H, *d*,  $J$  = 10 Hz, H-3), 7.65 (1H, *d*,  $J$  = 10 Hz, H-4), 7.40 (1H, *d*,  $J$  = 9 Hz, H-5), 6.90 (1H, *dd*,  $J$  = 9 and 2 Hz, H-6), 6.90 (1H, *d*,  $J$  = 2 Hz, H-8), coumarin protons 5.2 (4H, *m*), 4.92 (1H, *s*), 4.64 (1H, *q*,  $J$  = 12, 6 Hz), 4.13 (2H, *d*,  $J$  = 1.8 Hz); sugar protons and acetoxyl chemical shifts given in the text.

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(+)-CALOCEDRIN, A LIGNAN DIHYDROANHYDRIDE FROM *CALOCEDRUS FORMOSANA*

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**Key Word Index**—*Calocedrus formosana*; Cupressaceae; calocedrin; lignan dihydroanhydride; hubalactone.

**Abstract**—A novel lignan dihydroanhydride, (+)-calocedrin, was isolated from the wood of *Calocedrus formosana*. Its structure was determined to be *trans*- $\alpha$ -(3,4-methylenedioxybenzylidene)- $\beta$ -(3,4-methylenedioxybenzyl)- $\gamma$ -hydroxybutanolide by spectroscopic methods. Reduction of (+)-calocedrin resulted in an optically inactive lignan lactone, ( $\pm$ )-hibalactone.

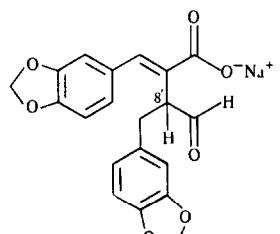
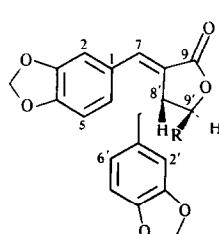
## INTRODUCTION

*Calocedrus formosana*, a member of the Cupressaceae, is an economically important tree indigenous to Taiwan [1]. Previous investigations [2, 3] on the heartwood have shown that it contains essential oil and a large quantity of terpenoid acids, such as shonanic, thujic and chaminic. Lignan components, such as hinokinin and hibalactone (savinin), have also been found.

## RESULTS AND DISCUSSION

On continuing a study of the chemical constituents, the wood of *C. formosana* was collected in our campus and subjected to extraction with acetone. The combined extracts were concentrated and the residual contents separated on a silica gel column eluting with hexane-ethyl acetate gradients. After  $(-)$ -hibalactone 1 ( $R_f$ , 0.30, hexane-acetone, 7:3) [4, 5], a novel lignan, namely  $(+)$ -calocedrin, was eluted ( $R_f$ , 0.16). Calocedrin was recrystallized from ethanol, mp 187–188°,  $[\alpha]^{25}_D + 6^\circ$  ( $c$  0.9; acetone). The mass spectrum displayed the parent peak at

*m/z* 368 and the base peak at *m/z* 135, ascribable to the 3,4-methylenedioxybenzyl fragment. The IR spectrum showed the presence of hydroxyl ( $3560\text{ cm}^{-1}$ ), lactone ( $1745\text{ cm}^{-1}$ ) and olefin ( $1640\text{ cm}^{-1}$ ) groups. Analyses of



$$1 \leq R \leq H$$

2 R  $\equiv$  OH

the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra (Tables 1 and 2) revealed that the structure of (+)-calocedrin (2) was related to that of hibalactone. Calocedrin contained an unusual hemiacetal lactone ( $-\text{CO}_2-\text{CHOH}-$ ) moiety as characterized in the  $^1\text{H}$  NMR spectrum [6]. The hydroxyl proton, coupled by  $\text{H}-9'$ , exhibited as a doublet ( $J = 5.5$  Hz) at  $\delta$  6.49 that was shifted by change of concentration or temperature. Similarly, the hemiacetal proton ( $\text{H}-9'$ ) was coupled by the hydroxyl proton, displaying as a doublet ( $J = 5.5$  Hz) at  $\delta$  5.67. Since irradiation at the resonance of  $\text{H}-8'$  ( $\delta$  3.71) did not cause any apparent effect on the signal pattern of  $\text{H}-9'$ , these two protons should orient nearly orthogonally (*trans* configuration) according to the Karplus empirical rule.

The structures of calocedrin and hibalactone are chemi-

cally correlated. (+)-Calocedrin was reduced by sodium borohydride in the presence of sodium hydroxide [7]. The product (66% yield) exhibited compatible physical and spectroscopic properties (mp, mmp, HPLC, UV, IR and  $^1\text{H}$  NMR) with those of (-)-hibalactone, except optical activity. An intermediate aldehyde 3, obtained from hemiacetal opening, was presumed to undergo epimerization prior to reduction under the alkaline conditions.

## EXPERIMENTAL

*Plant material.* *Calocedrus formosana* (Florin) Florin was collected in the campus of the National Taiwan University. The skinned and air-dried wood (600 g) from branches 6–8 cm in diam. was selected for study. After extraction  $\times 3$  with  $\text{Me}_2\text{CO}$ , the combined extracts were concentrated *in vacuo* to give 20 g of residue. Components were separated by CC on silica gel (230 g) and elution with hexane– $\text{EtOAc}$  gradients.

(+)-*Calocedrin*. Crystals (105 mg)  $R_f$  0.16 (hexane– $\text{Me}_2\text{CO}$ , 7:3). Recrystallization samples from  $\text{EtOH}$  exhibited mp 187–188°;  $[\alpha]_D^{25} + 6^\circ$  ( $c$  0.9;  $\text{Me}_2\text{CO}$ ). UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm ( $\epsilon$ ): 237 (10 400), 294 (9560), 330 (11 600). IR  $\nu_{\text{max}}^{\text{KBr}}$   $\text{cm}^{-1}$ : 3560 (OH), 1745 ( $\text{C}=\text{O}$ ), 1640 ( $\text{C}=\text{C}$ ), 1600 (aromatic). MS  $m/z$  (rel. int.): 368 (15) [ $\text{M}]^+$ , 350 (9), 316 (10), 135 (100).

*Reduction of (+)-calocedrin.*  $\text{NaOH}$  (21 mg, 0.53 mmol) was added to a soln of (+)-calocedrin (49 mg, 0.13 mmol) in  $\text{MeOH}$ . After stirring for 10 min,  $\text{NaBH}_4$  (6.5 mg, 0.17 mmol) was added and the mixture refluxed (80°) for 1 hr under  $\text{N}_2$ . The mixture was cooled, acidified (pH 2) with  $\text{HCl}$  and extracted with  $\text{CHCl}_3$ . The combined extracts were dried over  $\text{Na}_2\text{SO}_4$ , filtered, concentrated and purified by TLC ( $R_f$  0.30, hexane– $\text{Me}_2\text{CO}$ , 7:3) to afford a 66% yield of ( $\pm$ )-hibalactone (30 mg, 0.085 mmol); mp 141.5–143° (authentic (–)-hibalactone, 142–143°, lit. [5] 147°), mmp 139–142°. The synthetic and authentic samples had the same  $R_f$  on HPLC ( $\mu$ -Porasil column). UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm ( $\epsilon$ ): 237 (12 100), 294 (10 800), 332 (14 140). IR  $\nu_{\text{max}}^{\text{KBr}}$   $\text{cm}^{-1}$ : 1740, 1640, 1601. MS  $m/z$  (rel. int.): 352 (12) [ $\text{M}]^+$ , 217 (18), 135 (100).

Table 1.  $^1\text{H}$  NMR spectral data of (–)-hibalactone 1 and (+)-calocedrin 2 ( $\text{Me}_2\text{CO}-d_6$ , 90 MHz, TMS,  $\delta$ )

	1	2
H-7	7.49 ( <i>d</i> , 1.5)*	7.43 ( <i>d</i> , 1.5)
H-7'	2.56 ( <i>dd</i> , 15, 10), 3.00 ( <i>dd</i> , 15, 5)	2.65 ( <i>dd</i> , 15, 10), 2.94 ( <i>dd</i> , 15, 5)
H-8'	3.75 ( <i>m</i> )	3.71 ( <i>ddd</i> , 10, 5, 1.5)
H-9'	4.25 ( <i>d</i> , 5)	5.67 ( <i>d</i> , 5.5)
$\text{OCH}_2\text{O}$	5.92 ( <i>s</i> ), 6.02 ( <i>s</i> )	5.93 ( <i>s</i> ), 6.07 ( <i>s</i> )
OH		6.49 ( <i>d</i> , 5.5)
Aromatic	6.60–7.14 ( <i>m</i> )	6.75–7.29 ( <i>m</i> )

\*Numbers in parentheses indicate coupling constants (Hz).

Table 2.  $^{13}\text{C}$  NMR spectral data of (–)-hibalactone 1 and (+)-calocedrin 2 ( $\text{Me}_2\text{CO}-d_6$ , 25.2 MHz,  $\delta$ )

C	1	2	C	1	2
1	129.2 ( <i>s</i> )	128.8 ( <i>s</i> )	1'	132.7 ( <i>s</i> )	132.2 ( <i>s</i> )
2	108.8 ( <i>d</i> )	108.7 ( <i>d</i> )	2'	109.3 ( <i>d</i> )	109.2 ( <i>d</i> )
3	149.7 ( <i>s</i> )	149.7 ( <i>s</i> )	3'	149.1 ( <i>s</i> )	148.9 ( <i>s</i> )
4	148.6 ( <i>s</i> )	148.4 ( <i>s</i> )	4'	146.9 ( <i>s</i> )	146.7 ( <i>s</i> )
5	110.0 ( <i>d</i> )	109.8 ( <i>d</i> )	5'	109.5 ( <i>d</i> )	109.4 ( <i>d</i> )
6	122.9 ( <i>d</i> )	122.7 ( <i>d</i> )	6'	126.3 ( <i>d</i> )	126.3 ( <i>d</i> )
7	136.7 ( <i>d</i> )	137.4 ( <i>d</i> )	7'	38.2 ( <i>t</i> )	36.2 ( <i>t</i> )
8	127.8 ( <i>s</i> )	126.9 ( <i>s</i> )	8'	40.1 ( <i>d</i> )	48.2 ( <i>d</i> )
9	172.0 ( <i>s</i> )	171.3 ( <i>s</i> )	9'	70.1 ( <i>t</i> )	99.8 ( <i>d</i> )
$\text{OCH}_2\text{O}$	101.7 ( <i>t</i> ), 102.6 ( <i>t</i> )	101.6 ( <i>t</i> ), 102.5 ( <i>t</i> )			

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