

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.

**Acknowledgements**—Our thanks are due to Prof. J. Shoji, School of Pharmaceutical Sciences, Showa University, Halanodai, Shinagawa-Ku, Tokyo 142, Japan, for a sample of apiin. One of us (PSM) gratefully acknowledges the CSIR for the award of a senior research fellowship.

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*Phytochemistry*, Vol 24, No 8, pp 1863–1864, 1985  
Printed in Great Britain

0031-9422/85 \$3.00 + 0.00  
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## (+)-CALOCEDRIN, A LIGNAN DIHYDROANHTRIDE FROM *CALOCEDRUS FORMOSANA*

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(Revised received 28 November 1984)

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

**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, ( $\pm$ )-hiballactone.

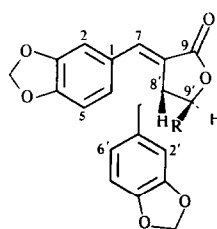
### INTRODUCTION

*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 hiballactone (savinin), have also been found.

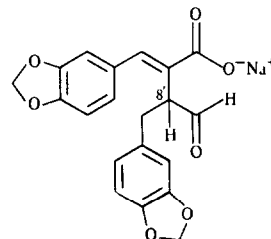
### RESULTS AND DISCUSSION

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 (–)-hiballactone **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°,  $[\alpha]_D^{25} + 6^\circ$  (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** R = H  
**2** R = OH



**3**

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 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 (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 H-8' ( $\delta 3.71$ ) did not cause any apparent effect on the signal pattern of 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 concd *in vacuo* to give 20 g of residue. Components were separated by CC on silica gel (230 g) and elution with hexane–EtOAc gradients.

(+)-Calocedrin. Crystals (105 mg)  $R_f$  0.16 (hexane– $\text{Me}_2\text{CO}$ , 7:3). Recrystallization samples from 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 (10400), 294 (9560), 330 (11 600). IR  $\nu_{\text{max}}^{\text{KBr}}$   $\text{cm}^{-1}$ : 3560 (OH), 1745 (C=O), 1640 (C=C), 1600 (aromatic). MS  $m/z$  (rel. int.): 368 (15)  $[\text{M}]^+$ , 350 (9), 316 (10), 135 (100).

**Reduction of (+)-calocedrin.** NaOH (21 mg, 0.53 mmol) was added to a soln of (+)-calocedrin (49 mg, 0.13 mmol) in 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 HCl and extracted with  $\text{CHCl}_3$ . The combined extracts were dried over  $\text{Na}_2\text{SO}_4$ , filtered, concd 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 (10800), 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).

**Acknowledgement**—The authors thank the National Science Council (ROC) for financial support.

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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)
OCH <sub>2</sub> 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> )
OCH <sub>2</sub> O	101.7 ( <i>t</i> ), 102.6 ( <i>t</i> )	101.6 ( <i>t</i> ), 102.5 ( <i>t</i> )			