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(−)-DIHYDROSESAMIN, A LIGNAN FROM *DAPHNE TANGUTICA*

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Key Word Index—*Daphne tangutica*, Thymelaeaceae, lignan, (−)-dihydrosesamin, (7*R*, 8*S*, 8′*S*)-9-hydroxy-7,9′-epoxy-piperolignan, X-ray analysis

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Abstract—A new naturally occurring lignan has been isolated from the roots of *Daphne tangutica* and elucidated as (−)-dihydrosesamin by NMR, mass spectroscopy and X-ray analysis

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INTRODUCTION

The roots and stems of *Daphne tangutica* Maxim (*D retusa* Hemsl) are known as 'Ai Tuotuo' in Chinese herb medicine and are used as an abortifacient and a remedy for rheumatism and toothache Chemical investigations on this drug have so far not been reported We describe herein the isolation and structure elucidation of (−)-dihydrosesamin (**1**) from the drug

RESULTS AND DISCUSSION

A dichloromethane extract of the roots of *D tangutica*, fractionated over a Si gel column, afforded a compound, which after purification by prep TLC, melted at 98–99° and gave an optical rotation of $[\alpha]_D^{25} = -15\ 9°$ (pyridine, *c* 0 67) The molecular formula $C_{20}H_{20}O_6$ of **1** was based on high resolution mass spectroscopy (M^+356 128) The UV spectrum in methanol showed maxima at 235 nm ($\epsilon = 9187$) and 286 nm ($\epsilon = 9378$), whilst in the IR spectrum a hydroxyl group at 3380 cm^{-1} was detectable The ^{1}H NMR spectrum (60 MHz) showed two methylendioxy groups at δ 5 90, six aromatic protons (δ 6.67–6 82) indicating two trisubstituted benzene rings, three nonequivalent methylene groups with signals at δ 2 72, between δ 3 53 and 3 86 and 3 98, and signals at δ 4 78 and between δ 2 18 and 2 53 integrating for three methine protons A hydroxyl group at δ 1 77 was exchangable with D_2O The ^{1}H NMR spectrum and the chromatographic behaviour of **1** resembled that of authentic (+)-dihydrosesamin, which was synthesized by Takahashi *et al* [1] from (+)-sesamin by partial hydrogenolysis The mass spectrum of **1** showed characteristic fragments at *m/z* 135 and 149, arising from the cleavage of the tetrahydrofuran ring The first fragment ion peak (3,4-methylenedioxybenzyl residue) represents the base peak, whilst in ring closed sesamin-type compounds the corresponding intensity ranges between 27 and 44% [1] The ^{13}C NMR spectrum was obtained at 20 15 MHz in $CDCl_3$, the carbon shifts of **1** are listed in Table 1

Table 1 ^{13}C NMR data for (−)-dihydrosesamin*

1	134 2	1′	137 1
2	106 2	2′	108 0†
3	147 8	3′	145 9
4	147 8	4′	145 3
5	108 2†	5′	108 9†
6	119 0	6′	121 3
7	82 8	7′	33 3
8	52 6	8′	42 3
9	60 8	9′	72 9
(3,4)-OCH$_2$O-	100 9	(3′, 4′)-OCH$_2$O-	100 8

*The δ values are in ppm downfield from TMS
†Signals may be reversed

The structure of **1** derived from NMR and mass spectral data was confirmed by X-ray structure analysis (Figs 1 and 2) The tetrahydrofuran ring exists in envelope form with the hydrogens at C-7 and C-8 in the *trans*-position. The other benzodioxalane ring is over C-7′ *cis*-connected to the tetrahydrofuran ring with respect to the CH$_2$OH groups The assignment of the absolute configuration could be made from the optical rotation This is the first time that (−)-dihydrosesamin has been isolated from a plant The other lignans, which have been found in the Thymelaeaceae belong to the bisepoxy-lignan series (pinoresinol and syringaresinol) or the monoepoxy-lignan series with an butanolid ring

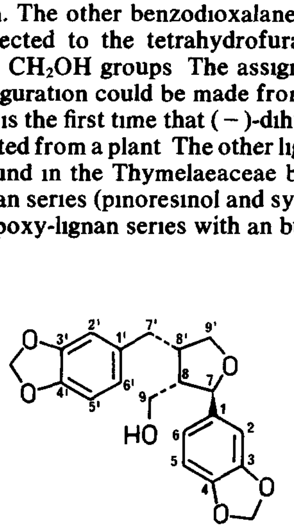

Fig 1 (−)-Dihydrosesamin (1)

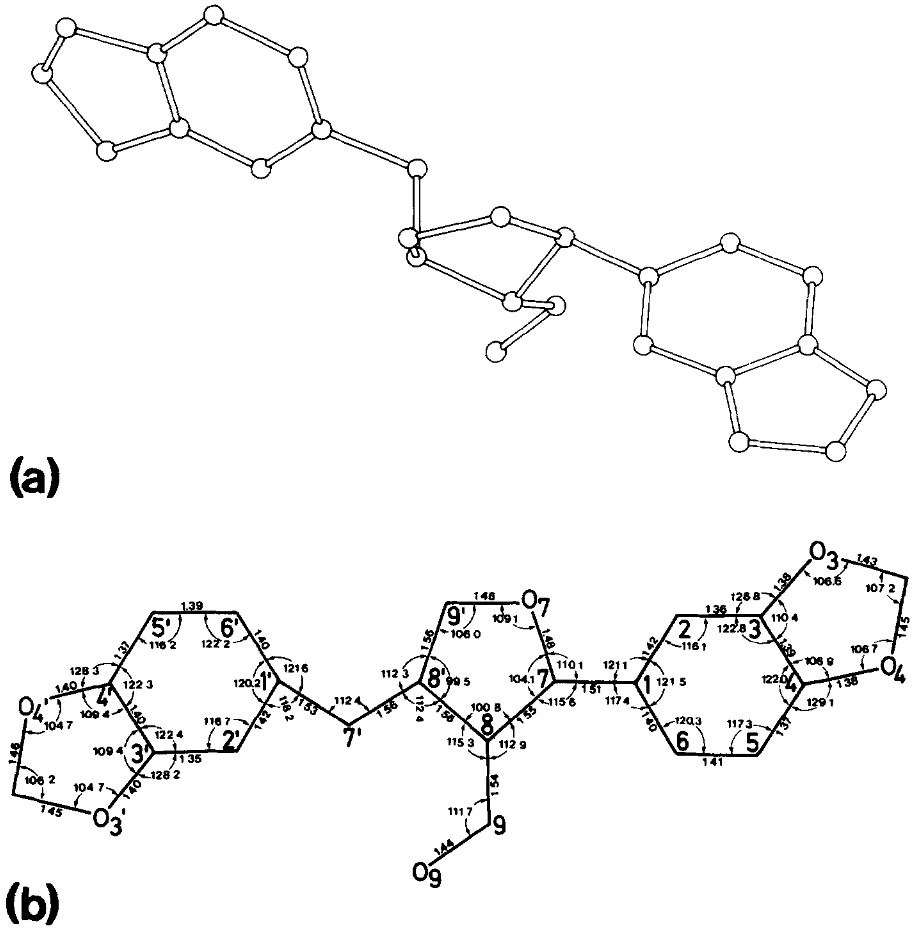

Fig 2 Crystal structure, bond distances and angles of (−)-dihydrosesamin The compound crystallized from methanol–chloroform in space group $P2_1$, $a = 9\ 841$ Å, $b = 6\ 776$ Å, $c = 13\ 459$ Å, $z = 2$ The intensities of 1344 independent reflexions were collected on a Nicolet-R 3m four circle diffractometer (Cu $K\alpha$, Ω scan, $2\delta \leq 114°$) The structure was solved by direct methods using ref [8] and refined (all H except the hydroxy group included) to a final R value of 7 4% for 1239 reflexions with $I > 2\ \sigma\ (I)$ *

(wikstromol, arctigenin, matairesinol) [2, 3] (−)-Dihydrosesamin is the first monoepoxy-lignan in the Thymelaeaceae with a 3-hydroxymethyl-2-phenyl-4-benzyl substituted tetrahydrofuran ring Lignans of the same type found in nature are lariciresinol [4], its glucoside [5], sanshodiol [6] and lariciresinol-4-methyl ether [7]

EXPERIMENTAL

Mps are uncorr TLC and prep TLC were carried out on Si gel F-254 (Merck) and CC on Si gel 60 (0 063 mm Merck No 7729)

Isolation of (−)-*dihydrosesamin* Air dried and powdered roots of *Daphne tangutica* (700 g) (collected in June 1980 in Yunnan province P R China) were extracted with CH_2Cl_2 in a Soxhlet The CH_2Cl_2 extract was evapd to a syrup The residue (20 g) was applied to a Si gel column (7 cm, height 70 cm) and eluted with toluene–Me_2CO (75 27) The fractionation was monitored by TLC The fraction containing a compound with $R_f = 0\ 47$ on TLC (toluene–Me_2CO (3 1) and H_2SO_4 reagent) was rechromatographed by CC with $CHCl_3$–Me_2CO (20 1) and then purified by prep TLC From MeOH, 0 05 g colourless crystals, mp = 98–99°, $[\alpha]_D^{25} = -15\ 9°$ (pyridine, c 0 67), UV λ_{max}^{MeOH} nm (log ε) 235 (9187), 286 (9378), IR ν_{max}^{KBr} cm^{-1} 3380, 2875, 2780, 1610, 1500, 1485, 1440, 1260, 1240, 1030, 919, 800, MS m/z 356 128 (M^+, calc for $C_{20}H_{20}O_6$ 356 126), 356 $[M]^+$ (50), 192 (14), 178 (14), 151 (26), 149 (29), 148 (18), 136 (23), 135 (100), ^1H NMR ($CDCl_3$) δ 1 77 (1H, *s*, OH), 2 18–2 53 (2H, *m*, H-8, H-8'), 2 72 (2H, *m*, H_2-7'), 3 64 (1H, *m*, H_a-9'), 3 72 (2H, *m*, CH_2OH), 3 98 (1H, *m*, H_e-9'), 4 78 (1H, *d*, $J = 5\ 5$ Hz, H-7), 5 90 (4H, *s*, $-OCH_2O- \times 2$), 6 67–6 82 (6H, arom H)

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