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SECO-ISOTETRANDRINE FROM *LAURELIA SEMPERVIRENS*

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Key Word Index—*Laurelia sempervirens*; Monimiaceae; *seco*-isotetrandrine; *seco-bis*benzylisoquinoline; NMR.

Abstract—*Seco*-isotetrandrine was isolated from *Laurelia sempervirens* leaves and its structure elucidated by extensive use of NMR spectroscopy.

INTRODUCTION

The evergreen tree *Laurelia sempervirens* is common in the Andean and Coastal Cordillera of Chile. Its distribution area ranges from the VI to X Regions (35–41° S) and it is known under the trivial name 'Laurel'. This species was used by the Mapuche Amerindians as a diuretic and to relieve headache [1]. Hypotensive and enzyme inhibitory activities have been reported for the leaf extract [2] and the hypotensive response was related to the alkaloid content [3]. Previous chemical studies on *L. sempervirens* reported the isolation of bisbenzylisoquinoline and monomeric aporphine alkaloids [4–6].

Following our chemical and pharmacological studies on Mapuche medicinal plants, we now report the isolation and structural elucidation of a *seco*-bisbenzylisoquinoline from *L. sempervirens* leaves.

RESULTS AND DISCUSSION

The alkaloid fraction of *L. sempervirens* leaves gave, after separation, laurotetanine [3], the bisbenzylisoquinoline alkaloid, isotetrandrine, previously obtained from this species [4], and compound **1**.

The EI mass spectrum of **1** showed a base peak at *m/z* 411. However, the [M + 1] peak at *m/z* 653 in the CI mass spectrum, along with the ^{1}H and ^{13}C NMR data (Tables 1 and 2) indicated a bis-alkaloid. The typical aldehyde signal (^{1}H: 9.89 *s* and ^{13}C: 190.8 *d*), a structural feature not present in typical bisbenzylisoquinolines, pointed to a *seco*-derivative. Decoupling experiments were in good agreement with this assumption, which was finally confirmed by long-range correlations observed in a HMBC experiment (Table 3). The NOE results were helpful for assigning all signals (Table 3). Compound **1** is a result of oxidative cleavage of the co-occurring alkaloid, isotetrandrine.

The base peak at *m/z* 411 in the EI mass spectrum is in accordance with a fragment corresponding to the *a*

Table 1. ^{1}H NMR data for compound **1**

H	$CDCl_3$	Benzene-d_6
1	3.66 *dd*	4.07 *dd*
$3_{1,2}$	3.32 *m*	3.21 *m*
	2.95–2.75 *m*	2.65 *m*
$4_{1,2}$	2.95–2.75 *m*	2.65 *m*
	2.42 *m*	2.22 *m*
6	6.51 *s*	6.27 *s*
$11_{1,2}$	2.95–2.75 *m*	3.30 *dd*
		3.05 *dd*
13	6.94 *d*	7.38 *d*
16	6.86 *d*	6.64 *d*
17	7.03 *dd*	7.30 *dd*
$3'_{1,2}$	3.47 *t*	2.75 *t*
$4'_{1,2}$	2.95–2.75 *m*	2.32 *m*
6′	6.56 *s*	6.29 *s*
9′	7.22 *s*	7.99 *s*
11′	9.89 *s*	9.67 *s*
13′/17′	7.77 *d* A_2B_2	7.54 *d* A_2B_2
14′/16′	6.92 *d*	6.88 *d*
N-2 Me	2.41 *s*	2.26 *s*
C-7 OMe	3.82 *s*	3.36 *s*
C-8 OMe	3.62 *s*	3.80 *s*
C-15 OMe	3.72 *s*	3.21 *s*
N-2′ Me	3.03 *s*	2.78 *s*
C-7′ OMe	3.81 *s*	3.50 *s*

J (Hz): $1,11_1 = 2.5$; $1,11_2 = 10$; $11_1,11_2 = 14$; $13,17 = 2$; $16,17 = 8.5$; $3',4' = 7$.
(400 MHz, δ values).

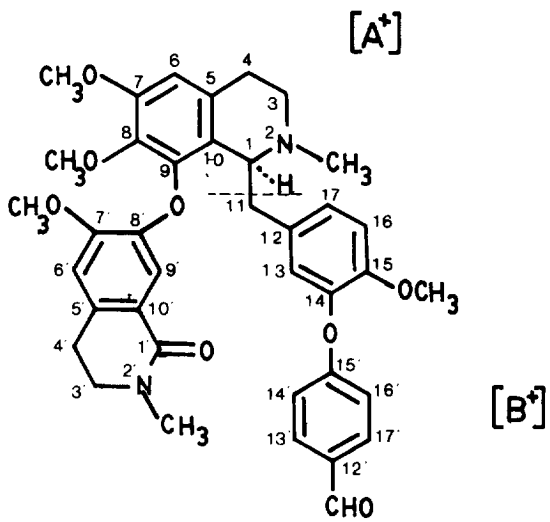
Table 2. ^{1}C NMR data for compound **1** (100 MHz, δ values)

C	$CDCl_3$	Benzene-d_6	C	$CDCl_3$	Benzene-d_6
1	60.6 *d*	61.6	1′	163.9 *s*	164.0
3	44.3 *t*	45.0	3′	48.1 *t*	47.8
4	22.8 *t*	23.3	4′	27.5 *t*	27.6
5	130.1 *s*	130.4	5′	132.6 *s*	132.8
6	109.4 *d*	110.1	6′	109.9 *d*	110.4
7	152.0 *s*	152.7	7′	151.3 *s*	151.7
8	140.0 *s*	141.0	8′	146.5 *s*	147.3
9	145.2 *s*	145.8	9′	113.3 *d*	113.9
10	123.9 *s*	124.4	10′	121.9 *s*	123.1
11	40.0 *t*	40.4	11′	190.8 *d*	189.8
12	134.9 *s*	135.4	12′	130.5 *s*	131.2
13	123.3 *d*	124.4	13′/17′	131.8 *d*	131.8
14	141.9 *s*	142.5	14′/16′	115.9 *d*	116.0
15	149.5 *s*	150.3	15′	164.3 *s*	164.2
16	112.4 *d*	112.8	N-2′ Me	34.9 *q*	34.7
17	127.2 *d*	127.9	C-7′ OMe	55.9 *q*	55.5
N-2 Me	42.2 *q*	42.3			
C-7 OMe	55.9 *q*	55.6			
C-8 OMe	60.7 *q*	60.6			
C-15 OMe	55.8 *q*	55.3			

Table 3. NOE and long-range correlation data for compound **1**

H	NOE	HMBC
1	H-9′, H-13, H-17, N-2 Me	C-11, N-2 Me, C-3, C-10, C-5, C-12
6	7-OMe, H-4_1, H-4_2	C-4, C-8, C-10
$11_{1,2}$	H-13	C-10, C-17, C-12
13		C-15, C-17
16		C-12, C-14
17		C-13, C-15
$3'_{1,2}$		C-4′, C-5′, C-1′
$4'_{1,2}$		C-3′, C-5′, C-10′
6′	7′-OMe, H-$4_{1,2}$	C-4′, C-8′, C-10′
9′	H-1, 8-OMe	C-5′, C-8′, C-7′, C-1′
11′		C-12′
13′/17′		C-15′
14′/16′		C-12′
N-2 Me	H-1, H-3_2, H-9′	C-1, C-3
C-7 OMe	H-6, 8-OMe	C-7
C-8 OMe	H-9′, 7-OMe	C-8
C-15 OMe	H-16, H-14′/16′	C-15
N-2′ Me		C-3′
C-7′ OMe	H-6′, H-13, H-14′/16′	C-7′

(400 MHz, benzene-d_6).



1

portion of the molecule; identical fragments are observed in the spectra of the *seco*-bisbenzylisoquinoline, curacautine, osornine [7], (−)-revolutinone [8] and (+)-sindamine [9]. The ^{1}H NMR data agree well with those reported for the oxidation product of isotetrandrine [10].

In vitro oxidation of isoquinoline alkaloids to *seco*-compounds has been reported. Cleavage occurs at the benzylic bond of the isoquinoline moiety, which is unsubstituted at C-1′ or C-1 [10]. *seco*-Isotetrandrine is structurally related to (−)-curacautine and (−)-talcamine, isolated from *Berberis buxifolia* [7], and to (+)-baluchistine, isolated from *B. baluchistanica* [11].

EXPERIMENTAL

Laurelia sempervirens R. et P. was collected in Pitreño, Lago Ranco, X Región, Chile, in February 1992. Voucher herbarium specimens were identified at the Botany Department, Universidad de Talca, Chile, and have been deposited at the Herbarium of that institution. Leaves

were dried at 40° and ground plant material (3 kg) extracted with EtOH (3 × 5 l). After evapn of solvent, the extract was treated with 5% citric acid and the acid-soluble fr. partitioned with $CHCl_3$ (3 × 1 l), basified to pH 11 and then extracted with $CHCl_3$ (4 × 1 l), yielding the crude alkaloid fr. After CC on basic alumina, laurotetanine (15 mg, 0.0005%), isotetrandrine (2 mg, 0.000066%) and **1** were isolated. Compound **1** (20 mg, 0.00066%) was purified by HPLC (RP-8, MeOH: H_2O + 1% NH_3, flow rate 3 ml min^{-1}, R_t 17.4 min). MS: 70 eV. ^1H NMR: 400 MHz; ^{13}C NMR: 100.6 MHz; $CDCl_3$ or benzene-d_6 as solvent.

seco-*Isotetrandrine* (**1**). HRMS *m/z* (rel. int.) 411.192 $[A]^+$ (100) (calc. for $C_{23}H_{27}N_2O_5$: 411.192) [M − $C_{15}H_{13}O_3$], 403 (18), 291 (20), 241.086 $[B]^+$ (4) (calc. for $C_{15}H_{13}O_3$: 241.086), 179 (20), 153 (6), 114 (6), 99 (44). CIMS *m/z* (isobutane) (rel. int.) 653 (12) [M + 1], 223 (100), 186 (48), 161 (28), 163 (30), 149 (35), 147 (35), 123 (26), 100 (74), 98 (32). $[\alpha]_D^{20}$ + 2.727 ($CHCl_3$, *c* 1.1).

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