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Cedrelanolide I, a New Limonoid From *Cedrela salvadorensis*

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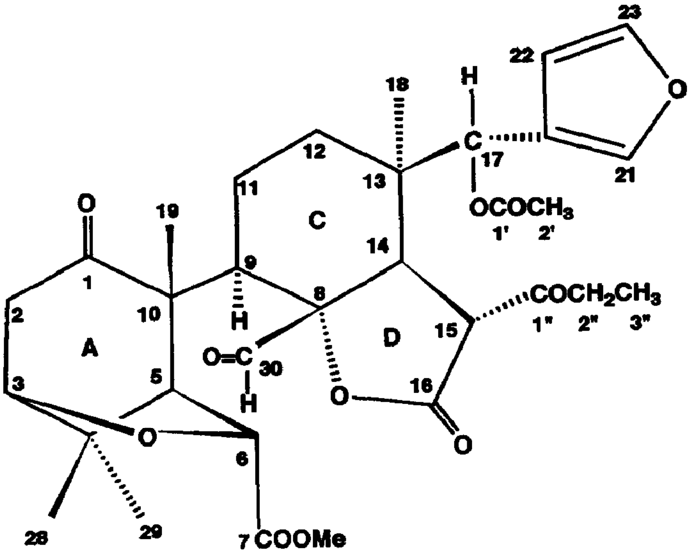
Abstract: A new limonoid, cedrelanolide I (1), has been isolated from the stem bark of *Cedrela salvadorensis* (Meliaceae). The structure was established by spectroscopic methods and X-ray diffraction analysis.

Cedrela salvadorensis Standley is a small tree of the dry Pacific slope ranging from the state of Jalisco to Chiapas in México, through Central America to the north of Pánama. No chemical studies have been described on *C. salvadorensis*, but several species of the genus have been reported to contain limonoids.[1-3] As a part of an ongoing investigation into the chemistry of the Meliaceae we have studied the $CHCl_3$ extract of the stem bark of this species and isolated a new rearranged limonoid,[4] cedrelanolide I (1).

Cedrelanolide I (1)[5] was obtained as colorless crystals. The molecular formula $C_{32}H_{40}O_{11}$ was established by HRFABMS. The IR spectrum displayed in addition to the furan absorptions (1502 and 874 cm^{-1}), strong carbonyl bands at 1790 (γ lactone), 1747 (ester), 1727 (aldehyde) and 1701 cm^{-1} (ketone). The NMR properties (Table 1) of (1) indicated the presence of an acetate, a carboxymethyl ester, a propionyl group, an aldehyde, a β-substituted furan ring, four tert-methyl groups, two oxygen-bearing methines (including the proton geminal to an acyloxy functionality), two ketones and a γ lactone group.

Analysis of the ^1H-^1H COSY spectrum indicated six separated spin systems: one is the system linking C-9 through C-12, a second links C-2 and C-3, and the others include the fragments C-14-C-15, C-21 through C-23, C-2"-C-3" and C-2. When these partial structures were compared with the two- and -three-bond connectivity data obtained from the long range heteronuclear ^1H-^{13}C COSY experiment (Table 1), the structure 1 could be assembled. The important correlations which defined ring A were those about C-1, C-3, C-4 and C-5. Moreover the cross peaks between the signal at 172.73 (C-7) and the ^1H resonances at δ 2.91 (H-5), 4.60 (H-6) and 3.75 (-OMe) defined the sequence C-5 through C-7. The correlations observed for C-8, C-14, C-16, C-18 and C-2" revealed the partial structure near the C/D ring junction as well as the placement of the propionyl grouping at C-15. The C-9/C-10 linkage was postulated on the basis of the observed ^{13}C-^{1}H long range couplings between C-5 and H-9 and C-10 and H-9. Finally, the furan ring signals at δ 140.78 (C-21) and 109.53 (C-22) showed a significant longe range correlation with the ^{1}H resonace at δ 5.51 (H-17). Proof of the limonoid structure and its relative stereochemistry was obtained by single-crystal X-ray analysis. A computer generated drawing of cedrelanolide I (1) is given in Figure 1.[6]



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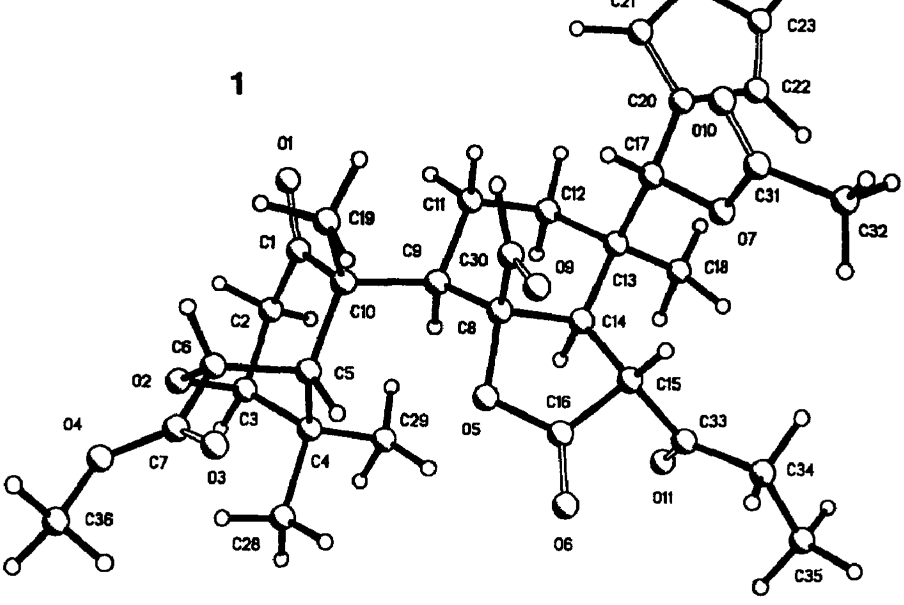

Figure 1. Stereoscopic View of Cedrelanolide I (1)

Table 1. ^{13}C and ^{1}H -NMR Spectral Data for Cedrelanolide I (1).

Assignment	${}^{\delta}$C	${}^{\delta}$H	mult.	(J, Hz)	COLOC
1	212.18				3, 2β, 5, 19
2	45.38	2.66 α	dd	(19.9, 2.1)	
		2.58 β	dd	(19.9, 3.3)	
3	82.78	4.05	dd	(3.3, 2.1)	5, 2β, 28, 29
4	54.05				6, 5, 28
5	54.52	2.91	brs		3, 6, 9, 28, 29
6	77.55	4.60	brs		
7	172.73				5, 6, -OMe
8	88.50				9, 14, 11α
9	52.33	2.83	dd	(13.0, 3.3)	14, 19, 12β
10	42.43				2β, 6, 9, 19, 29
11	23.18	2.07 α	m*		
	2.36 β	dddd		(14.2, 13.0, 13.0, 3.3)	
12	37.45	1.27 α	m*		18
	1.86 β	ddd		(14.2, 3.3, 3.3)	
13	39.39				12β, 14, 18
14	61.99	3.11	d	(13.2)	18, 12β
15	51.29	3.99	d	(13.2)	14
16	170.51				15
17	73.74	5.51	brs		12α, 14, 18
18	23.06	0.83	s		12α, 12β,17
19	22.78	1.28	s		
20	121.65				17, 23
21	140.78	7.36	t	(1.76)	17, 22, 23
22	109.53	6.24	dd	(1.76, 0.9)	
23	142.81	7.33	brs		21, 22
28	22.56	1.27	s		29
29	25.98	1.15	s		28
30	196.53	10.38	s		9, 14
1'	168.73				2', 17
2'	21.12	2.08			
1"	204.92				15
2" **	38.71	3.02	dq	(18.8, 7.2)	
		2.66	dq	(18.8, 7.2)	
3"	7.25	1.18	t	(7.2)	
OMe	52.36	3.75	s		

CDCl$_3$, ^{13}C, 75 MHz, ^{1}H, 300 MHz. *Signals overlapped. **These two hydrogens are not equivalent and each make up an AB doublet further split by additional coupling with the 3" methyl-hydrogens.

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4. Cedrelanolide I (**1**) might be biogenetically derived from a methyl angolensate type of precursor. The unusual C-15 acyl group could be produced by an acyl transference from a suitable ester (probably at C-30).[9] A second modification would be the opening of the δ lactone ring to give a free acid functionality at C-16 and the acyloxy group at C-17. Finally, the C-16 acid could relactonize with a free hydroxyl group at C-8 to yield the γ lactone portion.
5. Colorless crystals (CH_2CCl_2-MeOH), mp= 280°, $[\alpha]_D^{20}$ -10.24° (c 2.56, $CHCl_3$). UV (EtOH) nm 208. IR ($CHCl_3$) cm^{-1}:1790, 1747, 1727, 1701, 1502, 1458, 1370, 1183, 1162, 1088, 1028, 990, 874. EIMS, *m/z* (relative intensity) 541 (M^+-59, 1), 511 (1.4), 455 (25), 431 (20), 370 (50), 137 (100), 95 (41), 57 (37). HRFABMS, *m/z* 601.2626 [M^+ +1] ($C_{32}H_{41}O_{11}$, Δ-2.3 mmu of calcd.).
6. Crystal data $C_{32}H_{40}O_{11}$, crystal dimensions 0.34x0.36x0.70, orthorombic, a=7.537 (2), b=16.733 (3), c=24.478 (5)Å, U=3087 (2)Å^3, space group $P2_12_12_1$, Z= 4, F000= 1280. Using ω:2θ scans at variable scan rate 2054 unique reflections were collected at 298 K on a Nicolet P3F diffractometer using Ni-filtered CuKα radiation. Data corrected by LP effects. The structure was solved by direct methods using the program SIR92.[7] Hydrogen atoms at calculated positions with a common U=0.06 Å^2. The non hydrogen atoms were refined (SHELXTL)[8] with anisotropic thermal parameter and refinement converged with R= 0.05, wR= 0.078. The function minimized was $\Sigma w(|Fo|-|Fc|)^2$, where $w= (\sigma^2(Fo) + 0.0033Fo^2)^{-1}$. The final difference map showed no features greater than ± 0.21 eÅ^{-3}. Atomic coordinates, bond lengths, bond angles, thermal parameters and structure factors have been entered into the Cambridge Crystalographic Data Centre.
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10. Thanks are due to Quim. Luis Velasco (Instituto de Química, UNAM) and Professor Teresa Germán (Instituto de Biología, UNAM) for recording the HRFAB spectrum of (**1**) and for identifying the plant material, respectively. R. Segura, visiting scientist from Universidad Nacional de Colombia, Bogotá, Colombia, acknowledges Departamento de Química, Universidad Nacional de Colombia for the opportunity to carry out this investigation.

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