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SENDANIN, A NEW LIMONOID FROM *MELIA AZEDARACH* LINN. *VAR. JAPONICA* MAKINO

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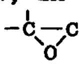
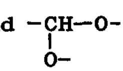
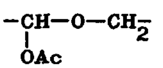
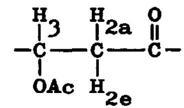
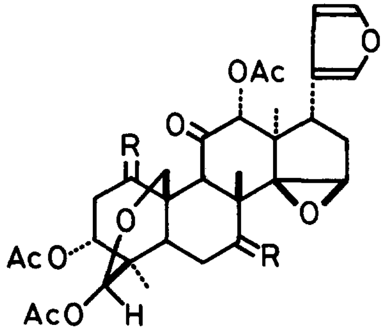
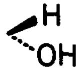
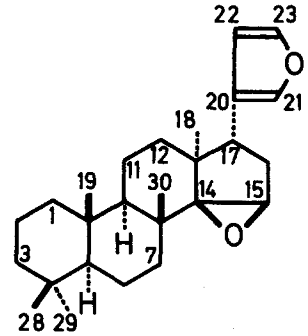
A number of limonoids have been isolated from *Melia azedarach* and *Azadirachta indica* (Meliaceae).1) The closely related species *Melia azedarach* Linn. *var. japonica* Makino is a large tree found commonly in the southwest of Japan, and has an intense bitter taste in the fruits and bark. We report herein the isolation and structure determination of a new bitter limonoid designated as sendanin from this tree.

Sendanin (1) was isolated in 0.02 % yield as colorless prisms, $C_{32}H_{40}O_{12}$, mp 251-252°, $[\alpha]_D^{16}$ +4.3° (c 0.12, $CHCl_3$), from the methanol extract of the dry bark by partitioning, acetylation, and careful silica gel column chromatography, and exhibits the following spectral data. IR (KBr): 3590, 3460, 3150, 1750, 1735, 1720, 1510, 1270, and 885 cm^{-1}; UV (EtOH): 210 nm (ε 8790); MS: m/e 556 (M^+-60), 538 (M^+-60-18), 496 (M^+-120), 478 (M^+-120-18), and 436 (M^+-180); ^1H NMR (δ_H): Table 1; ^{13}C NMR (δ_C): Table 2. These data suggest that (1) has one β-substituted furan ring,2) one ketonic, two hydroxyl, and three acetate groups. The secondary nature of two hydroxyl groups is revealed by the appearance of two doublets in the ^1H NMR spectrum at δ 6.20 and 6.61 (25°C), which shift to a higher field by warming. This was confirmed by the oxidation of (1) with Jones' reagent which afforded a triketone (2), $C_{32}H_{36}O_{12}$, mp 190-192°. ^{13}C NMR spectrum of (2) displays three ketonic carbon signals at δ 206.0, 205.5, and 201.6. The ^1H and ^{13}C NMR spectra of (1) show, in addition to the above functional groups, the presence of two groupings,  $-\overset{|}{C}\underset{O}{\diagdown\!\diagup}CH-$ [δ_H 3.91 (1H, s)3); δ_C 59.1 (d) and 73.2 (s)4)] and  $-\underset{O-}{\underset{|}{CH}}-O-$ [δ_H 6.10 (1H, s)5); δ_C 95.6 (d)6)]. The appearance of the ^1H NMR signal at δ 4.58 (2H, s) in conjunction with consideration of the number of the oxygen atoms in (1) suggests that the latter grouping constitutes the partial structure  $-\underset{OAc}{\underset{|}{CH}}-O-CH_2-$. The ^1H NMR data of (2), coupled with double resonance experiments, indicate the presence of a system  $-\underset{OAc}{\underset{|}{\overset{H_3}{\overset{|}{C}}}}-\underset{H_{2e}}{\underset{|}{\overset{H_{2a}}{\overset{|}{C}}}}-\overset{O}{\overset{\|}{C}}-$ [H_{2e}: δ 2.53 (1H, br. d, J = 16 Hz), H_{2a}: δ 3.57 (1H, dd, J = 6 and 16 Hz), H_3: δ 5.56 (1H, br. d, J = 6



(1) R =


(2) R = O



(3)

Hz)], which in turn had derived from a monoacetylated 1,3-glycol system in (1). The ^{13}C NMR spectrum of (1) assisted with off-resonance technique also shows the presence of four quaternary carbons (δ 46.5, 43.2, 42.2, and 39.8, each s), three methine carbons (δ 49.8, 39.2, and 29.0, each d), four oxygen-bearing methine carbons (δ 79.1, 74.0, 70.1, and 69.5, each d), and three methylene carbons (δ 36.6, 34.2, and 26.5, each t).

From the afore-mentioned data and the biogenetic considerations,7) it would be quite reasonable to assign for (1) the 14,15-epoxymeliacan skeleton (3).7c) The possible location of the hemiacetal ring would be C_{28}-C_{19} or C_{19}-C_{30} and the monoacetylated 1,3-glycol system must rest in A ring. The exact positions and configurations of the groupings present in (1) were determined by X-ray diffraction method.

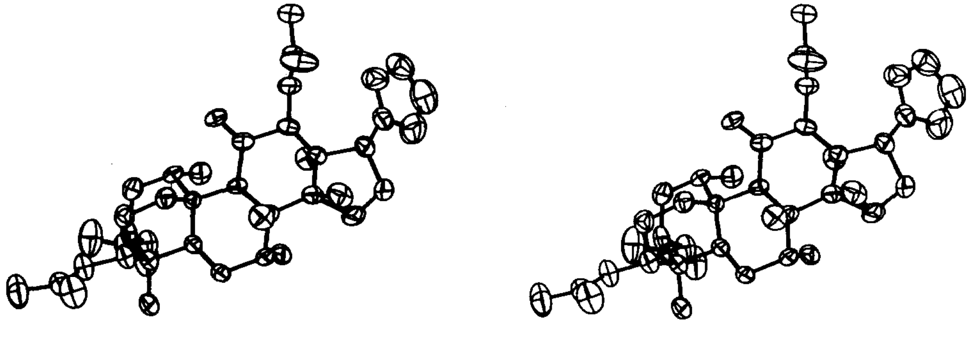


Fig. 1

Table 1 ^{1}H NMR spectra of (1) and (2)
(100 MHz, δ values)$^{a)}$

	(1)$^{b)}$		(2)$^{c)}$	
H-1	4.74 m			
H-2α			2.53 d	J = 16
H-2β			3.57 dd	J = 16 and 6
H-3	5.47 br d	J = 5	5.56 br d	J = 6
H-7	3.84 m			
H-9	5.32 s		4.20 s	
H-12	5.82 s		5.65 s	
H-15	3.91 s		3.91 s	
H-19	4.58 s		4.49 AB q 4.71	J = 14
H-21	7.24 s		7.12 s	
H-22	6.19 d	J = 2	6.08 d	J = 2
H-23	7.39 d	J = 2	7.25 d	J = 2
H-28	6.10 s		6.00 s	
Me	0.93 1.24 1.82		0.69 1.11 1.21	
OAc	1.82 1.94 1.97		1.70 1.87(×2)	
C_1-OH	6.20 d	J = 4		
C_7-OH	6.61 d	J = 4		

a) Coupling constants are expressed in Hz.
s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet.

b) Recorded in pyridine-d_5 at 25°C.

c) Recorded in $CDCl_3$ - benzene-d_6 (1:1).

Table 2 ^{13}C NMR spectra of (1) and (2)
(25 MHz, δ values, TMS as standard)

Carbon atom	(1)$^{d)}$		(2)$^{e)}$	
1	70.1^{*1}	d	205.5^{*3}	s
2	36.6	t	40.4	t
3	74.0	d	73.6	d
4	39.8^{*2}	s	45.7^{*4}	s
5	29.0	d	40.1	d
6	26.5	t	32.9	t
7	69.5^{*1}	d	201.6^{*3}	s
8	42.2^{*2}	s	50.2^{*4}	s
9	49.8	d	53.6	d
10	43.2^{*2}	s	51.4^{*4}	s
11	208.7	s	206.0^{*3}	s
12	79.1	d	77.7	d
13	46.5^{*2}	s	46.4^{*4}	s
14	73.2	s	67.9	s
15	59.1	d	57.7	d
16	34.2	t	35.6	t
17	39.2	d	45.0	d
19	66.0	t	62.3	t
20	124.0	s	122.1	s
21	143.2	d	142.7	d
22	112.8	d	111.3	d
23	141.6	d	140.6	d
28	95.6	d	93.6	d
$COCH_3$	170.9(×2)	s	169.7	s
	170.0	s	169.3	s
			169.0	s
$COCH_3$	22.8	q	21.4	q
	21.1	q	20.6(×2)	q
	20.7	q		
CCH_3	20.7	q	17.9	q
	19.2	q	15.4(×2)	q
	15.7	q		

d) Recorded in $CDCl_3$.

e) Recorded in $CDCl_3$ - benzene-d_6 (1:1).

*1-4 These values may be interchanged.

The crystals, $C_{32}H_{40}O_{12}$, are monoclinic, space group $P2_1$; a = 9.749(4), b = 13.461(5), c = 11.933(4) Å, β = 91.27°; D_x = 1.308 g·cm^{-3} (Z = 2). Intensities of 2450 reflections were collected on a Philips four-circle diffractometer by the ω/2θ scan technique with graphite-monochromated Mo-$\underline{K}\alpha$ radiation for a maximum 2θ angle of 55°. The structure was solved by multisolution tangent refinement methods[8] and has been refined by least-squares calculations to a final R of 0.057.[9,10]

The stereo view of the molecule is shown in Fig. 1. The positions and configurations of substituents are: 1α-OH, 3α-OAc, 4α-CH_3, 5α-H, 7α-OH, 8β-CH_3, 9α-H, 11-oxo, 12α-OAc, 13α-CH_3, 14β,15β-epoxy, 17α-C_4H_3O (furan ring). The hemiacetal ring is formed between C_{28}-C_{19}. The ring C has a boat form. The five-membered ring D takes an envelope form with C_{17} by 0.61 Å out of the mean plane through the other four atoms.

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