

A CLERODANE FURANO-DITERPENE FROM *TINOSPORA CORDIFOLIA*

JAMPANI BHOGI HANUMAN, RAMA KRISHNA BHATT, and BALAKRISHNA SABATA*

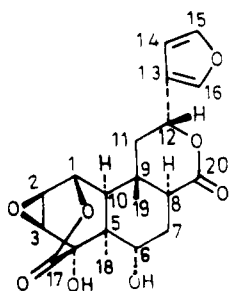
Department of Chemistry, Indian Institute of Technology, Powai, Bombay 400 076, India

ABSTRACT.—A new clerodane furano-diterpene **2** with the molecular formula $C_{20}H_{22}O_8$ has been isolated from the stems of *Tinospora cordifolia*. Its spectral characteristics are very similar to those of known clerodane furano-diterpenes and it is proposed to be an epimer of 6-hydroxyarcangelisin [**1**] on the basis of 1H - and ^{13}C -nmr spectral studies.

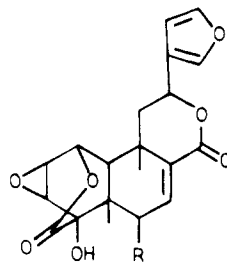
Tinospora cordifolia Miers (Menispermaceae), locally known as "guduchi," is distributed throughout India. It has long been used in Ayurvedic medicine for the treatment of jaundice, rheumatism, and urinary diseases. Several reports (1-5) are available on the isolation of various compounds from this plant. Our interest in indigenous medicinal plants led us to study this plant, and a hot $CHCl_3$ extract of the stems yielded a new clerodane furano-diterpene **2**. It is found to be an epimer of 6-hydroxyarcangelisin [**1**], and structure **2** is proposed on the basis of 1H -nmr, spin-decoupling, and ^{13}C -nmr studies along with comparison of the spectral data with data from closely related clerodane furano-diterpenes such as 6-hydroxyarcangelisin [**1**] (6), fibraurin [**3**] (7), 6-hydroxyfibraurin [**4**] (7), palmarin [**5**] (8,9), and jateorin [**6**] (9).

RESULTS AND DISCUSSION

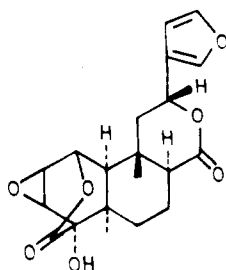
Elemental and mass spectral analysis ($[M]^+ 390$) suggested the molecular formula of the furano-diterpene as $C_{20}H_{22}O_8$. Its ir spectrum showed characteristic absorptions for hydroxy groups ($3500, 3460\text{ cm}^{-1}$), δ -lactones ($1760, 1720\text{ cm}^{-1}$), furan ring ($3160, 1510, 1030, \text{ and } 880\text{ cm}^{-1}$, positive Ehrlich test) and an epoxide (1200 cm^{-1} symmetrical stretchings, $950\text{--}850$ and $860\text{--}740\text{ cm}^{-1}$ asymmetrical stretchings), and thus all eight oxygen atoms were accounted for.



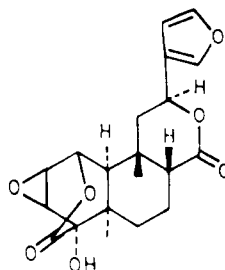
1
2 C-12, C-6 epimer of **1**



3 R=H
4 R=OH



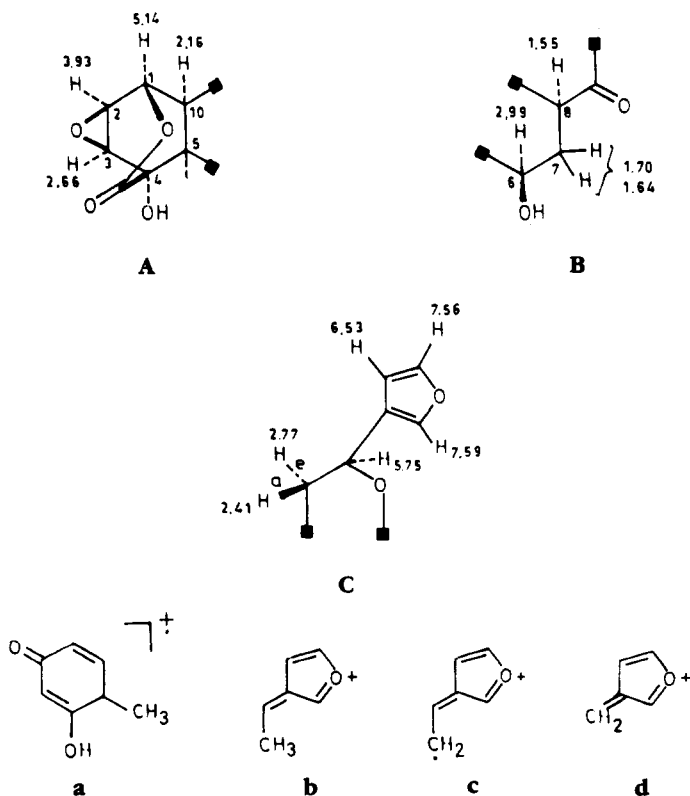
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6

The ^1H -nmr spectrum (Figure 1) of this compound was very similar to that of clerodane furano-diterpenes, and the assignments are given in Table 1. The signals at δ 7.59 (1H, br s), 7.56 (1H, br s), and 6.53 (1H, br s) were assigned to two α -protons and one β -proton of a β -substituted furan moiety. Signals for two angular methyl groups were observed as singlets at δ 1.21 and 1.29 (3H each). Two D_2O -exchangeable singlets at δ 4.91 (1H) and 5.02 (1H) for hydroxy groups were observed. The signals at δ 3.93 (1H, dd, $J_1=4.3$, $J_2=3.0$ Hz), 3.66 (1H, d, $J=4.5$ Hz), and 5.14 (1H, d, $J=2.7$ Hz) could be explained by considering an epoxide ring in the part structure **A**. The signal at δ 2.99 (1H, m) was assigned to a proton geminal to a hydroxy group (C-6) coupled with the proton at C-8 in a ring as shown in part structure **B** (C-6, C-7, and C-8). Hence, if the orientation of the epoxide is β (similar to fibraurin [**3**]) then the orientation of the C-1, C-4 lactone should also be β . The signal at 1.55 (1H, m) is due to the proton α to a carbonyl (C-8) coupled with vicinal methylene protons (C-7) and showing long-range coupling with the proton at C-6 in a ring as shown in part structure **B**. The two signals at 1.70 (1H, m) and 1.64 (1H, m) were assigned to protons attached to C-7. The signals at δ 5.75 (1H, dd, $J_1=11.2$, $J_2=5.8$ Hz), 2.41 (1H, dd, $J_1=14.5$, $J_2=11.0$ Hz), 2.27 (1H, dd, $J_1=14.5$, $J_2=5.6$ Hz) were assigned to an ABX system. A broad singlet at δ 2.16 was assigned to a proton at C-10 showing a very small coupling constant due to the vicinal axial equatorial orientation of H-10 and H-1 (10).

The presence of part structures **A**, **B**, and **C** was proposed on the basis of 500 MHz ^1H -nmr spin-decoupling experiments (Figure 1). On irradiating the signal at δ 3.93 (dd, $J_1=4.3$ Hz, $J_2=3.0$ Hz), the signals at δ 3.66 (d) and 5.14 (d) collapsed into two singlets. Irradiation of the signal at δ 2.99 (m) changed the multiplicity pattern at δ 1.55, 1.64, and 1.70, while irradiation of the signal at δ 1.55 (m) changed the multi-



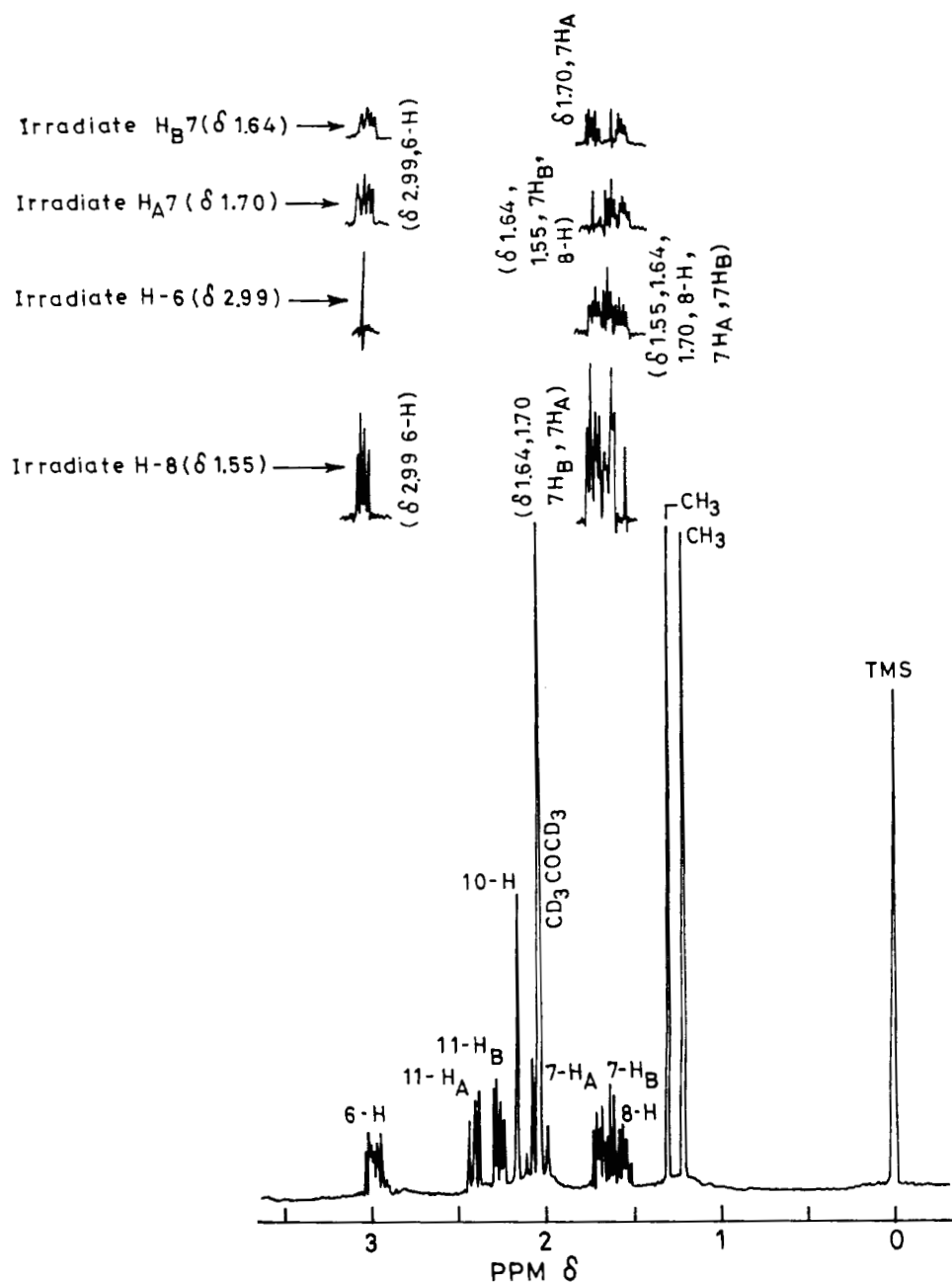


FIGURE 1. 500 MHz ^1H -nmr part spectrum ($\text{Me}_2\text{CO}-d_6 + \text{D}_2\text{O}$) and spin-decoupled spectra of **2**.

plets at δ 2.99, 1.70, and 1.64. These experiments indicated the presence of part structures **A** and **B** in the present compound.

The noise decoupled and single frequency off-resonance decoupled ^{13}C -nmr spectra (Table 2) contained signals arising from two methyl carbons (q, δ 21.4, 23.4), two methylene carbons (t, δ 27.6, 37.4), seven methine carbons (d, δ 27.2, 48.3, 50.5, 51.8, 71.5, 71.7, 73.8), three furanoid carbons (d, δ 109.6, 140.7, 144.7), four quaternary carbon atoms (s, 40.2, 41.7, 79.1, 127.2), and two lactone carbonyl carbons (s,

TABLE 1. ¹H-nmr Data^a of Clerodane Furano-Diterpenes.

Proton	Compound			
	2 ^b	1	3	4
H-1	5.14 d, $J=2.7$	5.00	5.08	5.10
H-2	3.93 dd, $J_1=4.3, J_2=3.0$	3.88	3.87	3.91
H-3	3.66 d, $J=4.5$	3.67	3.65	3.74
H-6	2.99 m	3.92	1.70–2.30	4.33
H _A -7	1.70 m	1.65, 2.07	7.25	6.86
H _B -7	1.64 m	—	—	—
H-8	1.55 m	2.97	—	—
H-9	—	—	—	—
H-10	2.16 brs	1.78	1.74	1.90
H _a -11	2.41 dd, $J_1=14.5, J_2=11.0$	1.88, 2.31	1.97	2.04, 2.29
H _c -11	2.27 dd, $J_1=14.5, J_2=5.6$	—	2.30	—
H _a -12	5.75 dd, $J_1=11.2, J_2=5.8$	5.46	5.60	5.68
H-13	—	—	—	—
H-14	6.53 brs	6.65	6.64	6.64
H-15	7.56 brs	7.68	7.67	7.69
H-16	7.59 brs	7.75	7.76	7.76
H-18	1.29 s	1.26	1.06, 1.15	1.16
H-19	1.21 s	1.05	—	1.18
4-OH	5.02 s	6.06	6.50	6.34
6-OH	4.91 brs	5.54d, 3.3	—	5.15

^a¹H-nmr data were recorded on a Bruker 500 MHz instrument in Me₂CO-*d*₆ and TMS as internal standard.

^bCoupling constants (J) in Hz.

TABLE 2. ¹³C-nmr Data^a of Clerodane Furano-Diterpenes.

Carbon	Compound			
	2	1	3	4
C-1	71.5 d	69.2 d	69.7 d	69.9 d
C-2	50.5 d	48.1 d	49.3 d	49.4 d
C-3	51.8 d	50.5 d	51.6 d	51.1 d
C-4	79.1 s	82.7 s	80.0 s	82.0 s
C-5	40.2 s	34.8 s	35.2 s	35.2 s
C-6	73.8 d	69.3 d	31.2 t	70.2 d
C-7	27.6 t	27.3 t	142.1 d	145.8 d
C-8	27.2 d	43.1 d	133.3 s	131.1 s
C-9	41.7 s	43.4 s	44.8 s	48.7 s
C-10	48.3 d	55.5 d	54.0 d	55.1 d
C-11	37.4 t	43.2 t	42.0 t	42.0 t
C-12	71.7 d	71.3 d	70.6 d	71.0 d
C-13	127.2 s	125.2 s	125.0 s	124.8 s
C-14	109.6 d	109.1 d	109.1 d	109.0 d
C-15	140.7 d	140.4 d	140.4 d	140.4 d
C-16	144.7 d	143.8 d	143.9 d	143.9 d
C-17	173.0 s	171.4 s	163.2 s	168.4 s
C-18	21.4 q	17.2 q	25.0 q	21.3 q
C-19	23.4 q	18.4 q	20.7 q	18.4 q
C-20	177.0 s	171.7 s	171.5 s	171.1 s

^a¹³C-nmr data were recorded on a Bruker 62.5 MHz instrument in Me₂CO-*d*₆.

δ 173.0, 177.0). These values compare well with the data reported for clerodane derivatives as given in Table 2.

The proposed structure [2] for the furano-diterpene clearly satisfied the above spectral data. The mass fragmentation pattern also supported the structure. The mass spectrum gave peaks at m/z $[M]^+$ 390, $[M - CO_2]^+$ 346, $[M - 138 (44 + 94)]^+$ 252, and 123 (100), 95, 94, and 81 that are due to the ions **a**, **b**, **c**, and **d**, respectively, in accord with similar lactones (11).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points are uncorrected. Assignments of ^{13}C -nmr chemical shifts were made with the aid of off-resonance and noise-decoupled ^{13}C -nmr spectra. The 1H -nmr spectrum was recorded on a Bruker 500 MHz instrument. *T. cordifolia* stems were collected from Surathkal, South Kanara (District), Karnataka, India (where a voucher specimen is located), and identified by Mr. R.D. Shinde, Blatter Herbarium, St. Xavier's College, Bombay. Dried and finely powdered stems of *T. cordifolia* (5 kg) were extracted with $CHCl_3$ in a Soxhlet apparatus for 48 h. Repeated cc on Si gel with 3% MeOH/ $CHCl_3$ afforded **2**, which crystallized from EtOH as colorless crystals (40 mg), mp 258–260° $[\alpha]^{22D} + 10.0^\circ$ (Me₂CO, $c=0.50$); ir ν max (nujol) cm^{-1} 3500, 3460 (-OH), 3160, 1760, 1720 (δ -lactones), 1510, 1330, 1220, 1170, 1140, 1080, 1030, 980, 970, 950, 920, 900, 880, 800, 780; uv λ max (MeOH) nm (ϵ) 210 (5628); 1H nmr (500 MHz, CD_3COCD_3) and ^{13}C nmr (62.5 MHz, CD_3COCD_3) see Tables 1 and 2, respectively; ms m/z (rel. int.) $[M]^+$ 390 (3), 346 (10), 319 (15), 291 (20), 252 (50), 207 (4), 151 (7), 123 (100), 95 (25), 94 (20), 81 (10); Anal. found: C 61.48, H 5.51, calcd. for $C_{20}H_{22}O_8$, C 61.53, H 5.64.

ACKNOWLEDGMENTS

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