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A DITERPENOID FURANOLACTONE FROM *TINOSPORA CORDIFOLIA*

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Key Word Index—*Tinospora cordifolia*; Menispermaceae; clerodane diterpenoids.

Abstract—A new diterpenoid furnolactone having molecular formula $C_{20}H_{22}O_6$, has been isolated from the stems of *Tinospora cordifolia*. Its spectral characteristics are very similar to the clerodane diterpenoids. Its structure followed from ^{1}H NMR and ^{13}C NMR studies.

INTRODUCTION

Tinospora species (Menispermaceae) are widespread in India and *Tinospora cordifolia* Miers, which is known as 'Guduchi', has long been used in Ayurvedic medicine for the treatment of jaundice, rheumatism and urinary diseases. Several compounds [1–4] have been isolated from this plant. In the present investigation a diterpenoid furanolactone was isolated from the chloroform extract of this plant. Its structure (**1**) has been proposed mainly with the help of ^{1}H NMR, spin-decoupling and ^{13}C NMR studies along with the comparison of the spectral data with the closely related clerodane diterpenoids such as tinosporide (**2**) [4], columbin (**3**) [5], salviarin (**4**) [6], floribundic acid (**5**) [7] and fibleucin (**6**) [8].

RESULTS AND DISCUSSION

Elemental analysis and mass spectrum (M^+ 358) gave the molecular formula of the diterpene as $C_{20}H_{22}O_6$. Its IR spectrum showed characteristic absorptions for hydroxyl group (3500 cm^{-1}), a γ-lactone (1745 cm^{-1}), δ-lactone (1710 cm^{-1}) and a furan ring (1500, 1020, 870 cm^{-1}, positive Ehrlich test); thus six oxygen atoms are accounted for.

The ^{1}H NMR spectrum of this compound was very similar to that of other furano-diterpenoids and the assignments are given in Table 1. The signals at δ7.48 (1H, *m*), 7.43 (1H, *m*), 6.32 (1H, *dd*, $J_1 = 8.0$, $J_2 = 1.6$ Hz) were assigned to two α- and one β-protons of a β-substituted furan moiety. Signals for two angular methyl groups were observed as singlets at δ1.06 and δ1.25 (3H each). A D_2O exchangeable singlet at δ3.88 (1H) for a hydroxyl group was observed. The signals at δ5.41 (1H, *dd*, $J_1 = 10.9$, $J_2 = 4.5$ Hz), 1.95 (1H, *dd*, $J_1 = 14.4$, $J_2 = 10.9$ Hz) and 2.20 (1H, *dd*, $J_1 = 14.4$, $J_2 = 4.5$ Hz) were assigned to an ABX system as given in part structure 'B' (C-11, C-12) and this part of the spectrum is given in Fig. 1. A double doublet at δ5.15 (1H, $J_1 = 10.5$, $J_2 = 2.0$ Hz) was assigned to a proton α to an oxygen function (C-6) coupled with an adjacent methylene group in a ring as shown in part structure 'A' (C-6, C-7). The signal at δ2.41 (1H, *dd*, $J_1 = 11.0$, $J_2 = 2.0$ Hz) which is placed α to a carbonyl (C-8) coupled with methylene protons in a ring as shown in part structure 'A' (H-8, H-7). The two signals at δ2.64 (1H, *m*) and 2.07 (1H, *m*), were assigned to protons attached to C-7. The multiplet at δ6.41 (2H) was accounted for the *cis*-disubstituted ethylenic protons (H-2, H-3).

The presence of part structure 'A' was proposed on the basis of 250 MHz ^{1}H NMR decoupling experiments. On irradiating the signal at δ2.41 (*dd*, $J_1 = 11.0$, $J_2 = 2.0$ Hz), the multiplicity pattern at δ2.64 and 2.07 has been changed. Irradiation of the signal at δ2.64, and the signals at 2.41 (*dd*), and 5.15 (*dd*) collapsed into doublets with 10.3 Hz coupling constant and the signal at δ2.07 collapsed into a double doublet with 10.3 Hz coupling constant only. This also suggested that the non-irradiated proton at C-7 (δ2.07) has the axial–axial coupling with C-6 and C-8 protons.

On irradiating, the signal at δ5.41 (X of ABX) the signals at δ1.95 and 2.20 (AB of ABX) collapsed into two doublets ($J_{AB} = 14.4$ Hz). On irradiation of the signal at δ2.20 (B of ABX system), the signal at δ5.41 collapsed into a doublet ($J_{AX} = 10.9$ Hz) and A of ABX collapsed into a doublet ($J = 10.9$ Hz) with fine splitting (which could be due to long range coupling of H-10) as shown in Fig. 1. The 10.9 Hz coupling constant indicated that A and X of ABX system have an axial–axial relationship. The J_{BX} value was calculated from the spectrum to be 4.5 Hz. These indicated the presence of the part structure 'B' in **1**.

The noise-decoupled and single frequency off-resonance decoupled ^{13}C NMR spectrum (Table 2) contained signals arising from two methyl carbons (*q*, δ24.3 and 28.3), three methylene carbons (*t*, δ17.3, 25.5 and 41.9), four methine carbons (*d*, δ44.4, 47.4, 70.6 and 74.1), two olefinic carbons (*d*, δ128.6 and 136.3), three furanoid carbons (*d*, δ108.3, 139.3 and 143.9), four quaternary carbon atoms (*s*, δ35.2, 37.1, 80.4 and 124.8) and two lactone carbonyl carbons (*s*, 168.8 and 173.3). These values compare well with the values reported for clerodane derivatives (Table 2).

The proposed structure **1** as a diterpenoid furanolactone clearly satisfied the above spectral data. The mass fragmentation pattern also supported structure **1**. The

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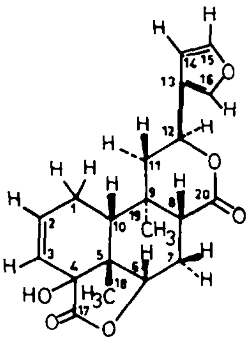
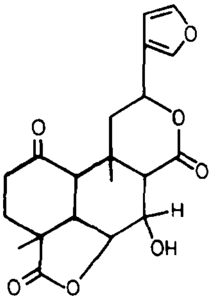


(1)



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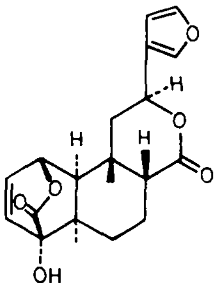

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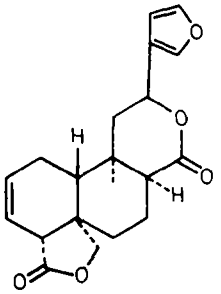

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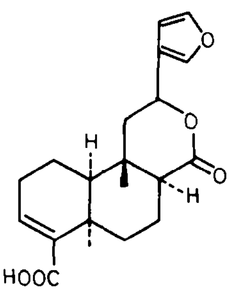

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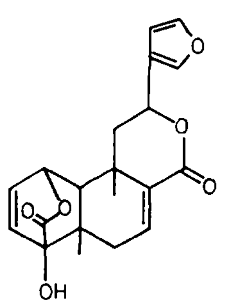


(6)

Table 1. ¹H NMR spectral data of diterpenoid furanolactones

	2	3	4	1*
H-1	—	—	—	1.74 (*m*)
H-2	—	6.38–6.58	6.00	6.41 (*m*)
H-3	—			
H-4	—	—	2.78	—
H-6	5.05	—	1.35	5.15 (*dd*, $J_1 = 10.5, J_2 = 2.0$)
H_a-7	3.90	—	1.85 and 1.99	2.07 and 2.64 (*m*)
H_e-7		—		
H-8	3.65	—	2.47	2.41 (*dd*, $J_1 = 11.0, J_2 = 2.0$)
H-10	2.18	—	2.47	1.38 (*m*)
H_a-11	—	—		1.95 (*dd*, $J_1 = 14.4, J_2 = 10.9$)
H_e-11	—	—	1.72 and 2.24	2.20 (*dd*, $J_1 = 14.4, J_2 = 4.5$)
H-12	5.75	5.1–5.3	5.36	5.41 (*dd*, $J_1 = 10.9, J_2 = 4.5$)
H-14	6.33	6.38–6.58	6.43	6.32 (*dd*, $J_1 = 7.8, J_2 = 1.6$)
H-15	7.37	7.47–7.57	7.48	7.48 (*m*)
H-16	7.27		7.43	7.43 (*m*)
C-Me	1.17 and 1.22	1.08 and 1.22	1.01	1.06 and 1.25
OH	4.80	3.50	—	3.88 (*s*)

*At 250 MHz, chemical shifts are in δ-values from TMS, coupling constants (J) in Hz, in $CDCl_3$ solution.

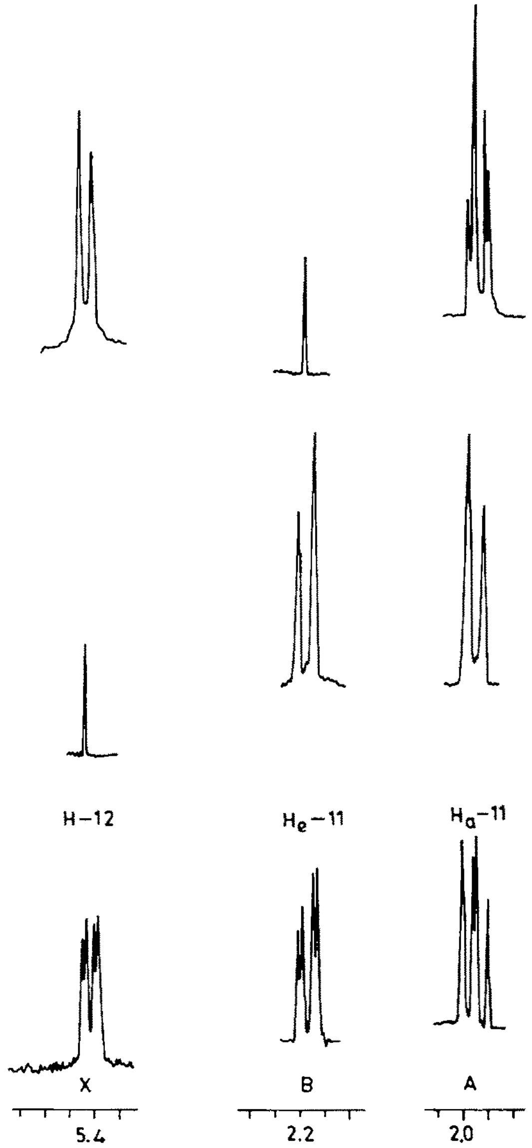
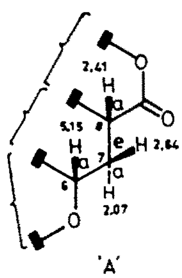


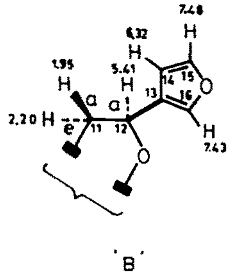
Fig. 1. The ABX part of the NMR spectrum.

mass spectrum gave peaks at m/z 358 $[M]^+$, 314 $[M-CO_2]^+$, 95, 94 and 81 which were due to the fragments 'a', 'b' and 'c' respectively in accord with similar furan lactones [9, 10]. A characteristic and base peak at m/z 107 is assigned to the ion 'd' which arose by the retro-Diels–Alder type fragmentation of ring B.

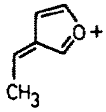
This compound belongs to the clerodane series. Columbin, belonging to this series is reported to have the *cis* A/B ring fusion [9]. Hence a *cis* A/B ring fusion is proposed for this compound. Inspection of the Drieding model clearly revealed that in 1 the hydrogen atom at C_8 has a *trans* relationship to the C-9 methyl group.



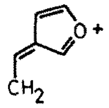
'A'



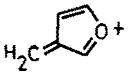
'B'



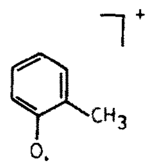
'a'



'b'



'c'



'd'

EXPERIMENTAL

Mps are uncorr. Assignments of ^{13}C NMR chemical shfits were made with the aid of off-resonance and noisedecoupled ^{13}C NMR spectra on Bruker 250 MHz instrument.

Isolation of 1. Dried and finely powdered stem of *Tinospora cordifolia* (5 kg) was extracted with $CHCl_3$ in a Soxhlet for 48 hr. Repeated chromatography over silica gel with 3% MeOH–$CHCl_3$ afforded 1 which crystallized as needles from EtOH (50 mg), mp 178°, $[\alpha]_D^{20}$ −18.1 ($CHCl_3$; c 0.55); IR ν_{max}^{nujol} cm^{-1}: 3500 (OH), 1745 (γ-lactone), 1710 (δ-lactone),

Table 2. ^{13}C NMR chemical shifts of diterpenoid furanolactones

C	4	5	6	1*
1	18.9 *t*	17.4 *t*	73.8 *d*	17.3 *t*
2	128.8 *d*	23.4 *t*	130.6 *d*	128.6 *d*
3	121.2 *d*	138.8 *d*	137.0 *d*	136.3 *d*
4	52.1 *d*	137.5 *s*	80.3 *s*	80.4 *s*
5	41.4 *s*	38.1 *s*	35.6 *s*	35.2 *s*
6	32.4 *t*	35.5 *t*	37.1 *t*	74.1 *d*
7	21.9 *t*	20.0 *t*	142.1 *d*	25.5 *t*
8	49.0 *d*	49.0 *d*	134.3 *s*	47.7 *d*
9	35.1 *s*	36.1 *s*	42.4 *s*	37.1 *s*
10	38.2 *d*	52.3 *d*	55.9 *d*	44.4 *d*
11	40.8 *t*	45.7 *t*	42.1 *t*	41.9 *t*
12	70.5 *d*	70.2 *d*	69.7 *d*	70.6 *d*
13	124.7 *s*	124.5 *s*	125.0 *s*	124.8 *s*
14	108.3 *d*	108.6 *d*	109.1 *d*	108.3 *d*
15	143.8 *d*	139.5 *d*	140.4 *d*	139.6 *d*
16	139.6 *d*	143.6 *d*	143.8 *d*	143.9 *d*
17	175.4 *s*	21.9 *q*	163.2 *s*	168.8 *s*
18	171.4 *s*	167.9 *s*	26.4 *q*	28.3 *q*
19	70.0 *t*	32.8 *q*	20.4 *q*	24.3 *q*
20	23.7 *q*	174.5 *q*	174.6 *s*	173.3 *s*

*Chemical shifts are in δ-values from TMS at 65.2 MHz, in $CDCl_3$ solution.

1500, 870 (furan ring), 1590, 1550, 1280, 1150, 1120, 1020, 980, 910, 830; UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm (log ε): 208 (3900); ^{1}H NMR (250 MHz, $CDCl_3$); ^{13}C NMR (65.2 MHz, $CDCl_3$) (given in Tables 1 and 2 respectively); MS (70 eV) *m/z* (rel. int.): 358 $[M]^+$ (5), 314 $[M - CO_2]^+$ (15), 246 (20), 220 (8), 204 (25), 152 (70), 121 (50), 107 (100), 95 (80), 94 (75), 81 (60); (Found: C, 66.97, H, 6.01. $C_{20}H_{22}O_6$ requires: C, 67.03, H, 6.14%).

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REFERENCES

1. Qudrat-i-Khuda, M., Khaleque, A., Abul Bashar, Kh., Rouf Khan, M. A. and Roy, N. (1966) *Sci. Res. Pak.* **3**, 9.
2. Khaleque, A., Wahed Miah, M. A., Sayeedul Hug, M. and Abul Bashar, Kh. (1970) *Sci. Res.* **7**, 61.
3. Qudrat-i-Khuda, M., Khaleque, A. and Roy, N. (1964) *Pak. J. Sci. Ind. Res.* **1**, 177.
4. Ahmad, M., Khaleque, A. and Wahed Miah, M. A. (1978) *Indian J. Chem.* **16B**, 317.
5. Gilbert, J. N. T., Mathieson, D. W. and Patel, M. B. (1967) *Phytochemistry* **6**, 135.
6. Savona, G., Paternostro, M. P., Piozzi, F., Hanson, J. R., Hitchcock, P. B. and Thomas, S. A. (1978) *J. Chem. Soc. Perkin Trans.* 1, 643.
7. Billet, B., Durgeat, M., Heitz, S. and Ahond, A. (1975) *Tetrahedron Letters* 3825.
8. Kumi, T., Kagei, K., Kawa Kami, Y., Gai, Y., Nezu, Y. and Sato, T.(1985) *Chem. Pharm. Bull.* **33**, 479.
9. Ramstad, E., Powell, J. W. and Wilson, B. J. (1975) *Phytochemistry* **14**, 2719.
10. Hori, T., Nakanishi, A. K., Sasaki, S. and Wood, M. C. (1967) *Tetrahedron* **23**, 2649.