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TINOCORDIFOLIN, A SESQUITERPENE FROM *TINOSPORA CORDIFOLIA**

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Key Word Index—*Tinospora cordifolia*; Menispermaceae; tinocordifolin; sesquiterpene.

Abstract—A new daucane-type sesquiterpene, tinocordifolin, has been isolated from the stem of *Tinospora cordifolia* and its structure established by detailed spectroscopic studies. © 1998 Elsevier Science Ltd. All rights reserved

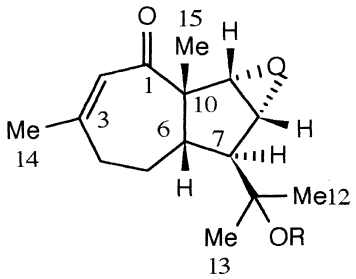
INTRODUCTION

Tinospora cordifolia Miers. occurs throughout the plains of India. It is popularly known in the Indian system of medicine as Giloe and has been in traditional use for several centuries in the treatment of jaundice, diabetes, skin diseases and anaemia [1]. This species is rich in clerodane derived diterpenes [2, 3]. Recently, we reported on the isolation and characterization of several new furanoditerpene glucosides [4, 5], two phenylpropene disaccharides [6] and a sesquiterpene glucoside [7] from *T. cordifolia*. In the present paper, we describe the structural elucidation of a new sesquiterpene (**1**) named as tinocordifolin, together with tinocordifolioside (**2**), N-*trans*-feruloyl tyramine (**4**) and 4-hydroxy-3-methoxy benzoic acid (**6**).

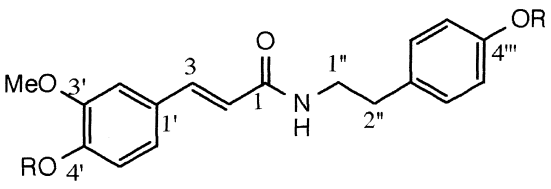
RESULTS AND DISCUSSION

Tinocordifolin (**1**) was assigned the molecular formula $C_{15}H_{22}O_3$ (FAB–MS, *m/z* 273 $[M + Na]^+$). This conclusion was supported by the ^{13}C NMR and DEPT spectra. The presence of a hydroxyl, α,β-unsaturated carbonyl and an epoxide ring was indicated by the IR absorptions at 3440, 2960, 1655, 1370 and 1230 cm^{-1}. Evidence for an α,β-unsaturated carbonyl was also provided by uv absorption at 250 nm.

Compound **1** gave rise to ^1H NMR signals (Table 1) for three methyl groups at δ 0.99, 1.14 and 1.18 (ea.*s*), a vinyl methyl at δ 2.02 (*d*, J = 1.4 Hz) coupled to an olefinic proton at δ 5.75 (*q*, J = 1.5 Hz) as deduced from the ^1H–^1H COSY experiment. Two methine groups bearing oxygen at δ 2.89 (*br s*, 1H) and 2.74 (*dd*, J = 1.3, 6.7 Hz, 1H) could be explained by an epoxide ring. This was supported by the resonances at δc 53.5 and 54.7 in the ^{13}C NMR spectrum (Table 2). The presence of a carbonyl function was supported by a resonance at δ 203.3. The DEPT experiment showed the presence of three quaternary carbons (one at δ 56.8, one olefinic carbon at δ 169.4 and one oxygenated at δ 73.3), five methines (two CH at δ 50.3, 57.2,



1 R = H
2 R = β-D-glucopyranosyl
3 R = tetra-*O*-acetyl-β-D-glucopyranosyl



4 R = H
5 R = Ac

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Table 1. ^{1}H NMR data of compounds **1**, **2** and **3** ($CDCl_3$)*

H	**1** δ (*J* in Hz)	**2** δ (*J* in Hz)	**3** δ (*J* in Hz)
2	5.75 (*q*, 1.5)	5.71 (*q*, 1.1)	5.75 (*q*, 1.5)
4a	1.80 (*m*)	1.73 (*m*)	1.76 (*m*)
4b	1.60 (*m*)	1.73 (*m*)	1.50 (*m*)
5a	1.90 (*m*)	1.94 (*m*)	1.88 (*m*)
5b	1.73 (*m*)	1.73 (*m*)	1.72 (*m*)
6	1.94 (*m*)	1.94 (*m*)	1.92 (*m*)
7	1.98 (*m*)	1.94 (*m*)	1.94 (*m*)
8	2.74 (*dd*, 1.3, 6.7)	2.76 (*dd*, 1.2, 6.3)	2.68 (*dd*, 1.6, 7.7)
9	2.89 (*br s*)	2.94 (*br s*)	2.76 (*br s*)
12	1.18 (*s*)	1.17 (*s*)	1.13 (*s*)
13	1.14 (*s*)	1.14 (*s*)	1.05 (*s*)
14	2.02 (*d*, 1.4)	2.02 (*d*, 1.1)	2.02 (*d*, 1.5)
15	0.99 (*s*)	0.95 (*s*)	0.94 (*s*)
1′	—	4.42 (*d*, 7.3)	4.64 (*d*, 7.9)
2′ to 6′	—	3.20 to 3.90	—
2′	—	—	4.93 (*dd*, 7.9, 9.5)
3′	—	—	5.20 (*t*, 9.5)
4′	—	—	5.02 (*t*, 9.8)
5′	—	—	3.65 (*m*)
6′a	—	—	4.19 (*dd*, 5.9, 12.1)
6′b	—	—	4.07 (*dd*, 2.4, 12.1)
OCOMe	—	—	2.06 (*s*)
	—	—	2.02 (*s*)
	—	—	2.01 (*s*)
	—	—	1.99 (*s*)

* Chemical shifts are in ppm from interal TMS.

two HC–O– at δ 53.5 and 54.7 and one olefinic carbon at δ 121.5), two methylenes (δ 20.6 and 36.7) and four methyls (δ 20.2, 23.5, 25.3 and 27.9). Taking into account the above data, compound **1** was deduced to be a daucane-type of sesquiterpene [8, 9]. These patterns were very similar to those of tinocordifolioside tetraacetate (**3**) previously reported [7] from the same plant. Its structure was determined with the help of 2D NMR, ^{1}H–^{1}H COSY, ^{13}C–^{1}H HMQC, HMBC and NOE and from high resolution FAB–MS.

Table 2. ^{13}C NMR data of compounds **1**, **2** and **3** ($CDCl_3$)*

C	**1**	**2**	**3**
1	203.3	204.9	203.4
2	121.5	121.3	121.4
3	169.4	170.8	169.8
4	20.6	20.1	20.1
5	36.7	36.6	36.4
6	57.2	56.9	57.0
7	50.3	48.9	49.1
8	54.7	55.1	54.5
9	53.5	54.4	53.1
10	56.8	56.9	56.9
11	73.3	80.3	81.1
12	23.5†	23.7†	22.4†
13	25.3†	23.8†	22.8†
14	27.9	24.1	23.8
15	20.2	20.2	20.1
1′	—	96.9	94.8
2′	—	75.3	71.5
3′	—	76.7	73.0
4′	—	70.4	68.8
5′	—	73.6	71.5
6′	—	62.3	62.3
OCOMe	—	—	20.7
	—	—	20.7
	—	—	20.6
	—	—	20.6
OCOMe	—	—	170.6
	—	—	170.3
	—	—	169.4
	—	—	169.1

* Chemical shifts are in ppm from interal TMS.
† Values may be interchanged within the column.

We also isolated tinocordifolioside (**2**), the ^{1}H and ^{13}C NMR (DEPT) spectral data (Tables 1 and 2) and FAB–MS of which are presented for the first time.

Thus tinocordifolin (**1**) is an aglycone of **2** and is presumed to have the same relative configuration at the chiral centres. This is the first report of its natural occurrence. Compound **1** was also isolated from the EtOAc extract prepared by cold percolation of the plant material which rules out the possibility of it being an artefact.

Compound **4** was isolated as its diacetate (**5**). The ^{1}H and ^{13}C NMR, DEPT, ^{1}H–^{1}H COSY and FAB–MS of the latter suggested its structure as N-*trans*-feruloyal tyramine diacetate [10]. 4-Hydroxy, 3-methoxy benzoic acid (**6**) was identified by comparison with the published spectroscopic data [11]. This is not an artefact as it was detected by HPLC in the MeOH extract prepared by cold percolation of the plant. Compounds **4** and **6** were isolated for the first time from *T. cordifolia*.

EXPERIMENTAL

General procedure

Mps: uncorr.; IR; KBr pellets; ^{1}H and ^{13}C NMR: 400 MHz and 100 MHz, respectively; Flash chromatography: silica gel (230–400 mesh); TLC: precoated silica gel plates.

Plant material

The plant material was collected from Palampur (H.P.) and its identity as *T. cordifolia* was confirmed by comparison with the herbarium specimen kept at the herbarium of our institute.

Extraction and isolation

The powdered stem of *T. cordifolia* (500 g) was soxhlet extracted successively with hexane and EtOAc. The concentrated EtOAc extract was subjected to CC over silica gel eluting with hexane-EtOAc (17:3). This fraction on repeated chromatography using hexane-EtOAc (9:1) yielded compound **1** (15 mg). Further elution of the column with EtOAc gave a mixture, which on acetylation with Ac_2O in pyridine, gave compound **5**. Isolation of compound **2** from the n-BuOH extract was carried out by following the experimental procedure reported earlier [7]. Careful flash chromatography using $CHCl_3$ allowed the isolation of compound **2** and further elution with $CHCl_3$-MeOH (99:1) gave **6**. Enzymatic hydrolysis of tinocordifolioside (**2**) with β-glucosidase by the usual procedure yielded an aglycone found to be identical with tinocordifolin (**1**) (TLC, co-TLC).

Tinocordifolin (**1**)

Recrystallized from hexane-EtOAc, mp 67–69°, $[\alpha]_D^{22}$ +55.80° ($CHCl_3$; c 0.50). FAB–MS *m/z*: 273 $[M + Na]^+$, 235, 217, 176, 107, 69, 59; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3440, 2960, 1655, 1370, 1230; UV $\lambda_{max}^{CHCl_3}$ nm: 250; ^1H and ^{13}C NMR: Tables 1 and 2.

Tinocordifolioside (**2**)

Recrystallized $CHCl_3$-MeOH, mp 107–109°, $[\alpha]_D^{22}$ −16.6° ($CHCl_3$; c 0.50). FAB–MS *m/z*: 435$[M + Na]^+$, 412, 397, 327, 281, 235, 221, 217, 191, 189, 59; IR $\nu_{max}^{KBr_3}$ cm^{-1}: 3400, 2920, 1645, 1370, 1250, 1230, 1065, 1020; UV $\lambda_{max}^{CHCl_3}$ nm: 250; ^1H and ^{13}C NMR: Tables 1 and 2.

N-trans-feruloyl tyramine diacetate (**5**)

Recrystallized from hexane-EtOAc, mp 157–158°. FAB–MS: 397 $[M + 1]^+$, 355, 219, 192, 177, 154, 121, 91, 43; ^1H NMR ($CDCl_3$): δ 2.30 (*s*, 3H), 2.31 (*s*, 3H), 2.87 (*t*, *J* = 6.0 Hz, 2H), 3.64 (*q*, *J* = 6.0 Hz, 2H), 3.84 (*s*, 3H), 5.76 (*br s*, 1H), 6.27 (*d*, *J* = 15.0 Hz, 1H), 7.05 (*m*, 5H), 7.23 (*m*, 2H), 7.56 (*d*, *J* = 15.0 Hz, 1H); ^{13}C NMR ($CDCl_3$); Feruloyl part δ: 165.7 (C-1), 111.2 (C-2), 140.3 (C-3), 149.3 (C-1′), 121.7 (C-2′), 133.8 (C-3′), 140.9 (C-4′), 120.6 (C-5′), 123.1 (C-6′), 55.9 (OMe), Tyramine part δ: 40.7 (C-1″), 34.9 (C-2″), 136.5 (C-1‴), 129.7 (C-2‴, 6‴), 120.8 (C-3‴, 5‴), 151.3 (C-4‴), 20.6 (OCOMe), 21.1 (OCOMe), 168.8 (OCOMe), 169.7 (OCOMe).

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