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CORDATIN, A NEW DITERPENE FROM *APARISTHMIUM CORDATUM*

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Key Word Index—*Aparisthmium cordatum*; Euphorbiaceae; *trans*-clerodane diterpene; cordatin.

Abstract—A new furano diterpene, cordatin, with a clerodane skeleton has been isolated from the bark of *Aparisthmium cordatum*. Its molecular structure has been investigated by spectroscopic means and by X-ray analysis.

INTRODUCTION

In a preceding paper, Muller *et al.* [1] reported the structure elucidation of aparisthman (2) a new diterpenoid from *Aparisthmium cordatum*. We now report the structure of cordatin (1) isolated from the benzene extract of the bark of this plant. This plant was reported [2] as causing contact dermatitis.

RESULTS AND DISCUSSION

Cordatin (1) mp 170–172°, $[\alpha]_D^{20} + 140°$ (MeOH; *c* 0.1), has the molecular formula $C_{21}H_{26}O_6$ from combustion analysis and mass spectrometry. The spectral properties indicated the presence of a β-substituted furan [λ_{max} 214 (6200); ν_{max} 1500, 880 cm^{-1}; δ6.42 (1H, *t*, *J* = 1.6 Hz), 7.42 (1H, *br*), 7.48 (1H, *t*, *J* = 1.6 Hz.)], two angular methyl groups [δ1.13 (3H, *s*), 1.34 (3H, *s*)], a methyl ester [ν_{max} 1740 cm^{-1}, δ3.80 (3H, *s*)], a tertiary hydroxyl [δ80.5 *s*, ν_{max} 3550 cm^{-1}], a δ-lactone (ν_{max} 1720 cm^{-1}) and a *cis*-disubstituted olefin [δ 5.90 (1H, *m*), 5.35 (1H, *d*, *J* = 10 Hz)]. The ^{1}H NMR spectrum (Table 1) in addition showed signals of one proton each at δ5.28 (*dd*, *J* = 3.12 Hz), 2.32 (*dd*, *J* = 5.12 Hz) and at 2.01 (*dd*, *J* = 3.12 Hz). Proton spin decoupling at 400 MHz indicated the relationship between these protons. Thus irradiation at δ5.90, removed the 10 Hz coupling from the signal at δ5.35. Irradiation at δ5.28 removed a 3 Hz coupling from the signal at δ2.01 and a 12 Hz coupling from the signal at δ1.80. The other assignments are summarized in Table 1.

These results suggested a relationship of the furan and the lactone moieties as found in salviarin (3) [3] and bacchotricuneatin A(4) [4]. The ^{13}C NMR spectrum (Table 1) contained signals arising from three methyl groups, (δ 14.6, *q*, 24.2 *q*, 53.2 *q*), four furanoid carbons (δ123.8 *s*, 108.5 *d*, 143.5 *d*, 139.5 *d*), two olefinic carbons (δ123.2 *d*, 129.9 *d*), four methylene carbons (δ17.6 *t*, 22.9 *t*, 28.3 *t*, 48.7 *t*), three methine carbons (δ44.7 *d*, 44.5 *d*, 69.7 *d*), three quaternary carbons [δ80.5 *s*, 40.4 *s*, 35.3 *s*), one lactone carbonyl group (δ175.8 *s*) and one ester carbonyl group (δ173.7 *s*).

The chemical shifts observed are also in good agreement with those observed for a part of the structures of compounds 3 and 4 [3, 4] and for fluoribundic acid (5) [5]. All these results lead to the conclusion that cordatin (1) is closely related to salviarin (3). The structure of cordatin (1) was finally confirmed by X-ray analysis. A perspective view of this new compound is showed in Fig. 1. The bond distances and angle values revealed a *trans*-relationship between the methyl group (C-20) attached to C-9 and the hydrogen borne by C-10 and the same relationship between the methyl group (C-18) attached to C-5 and the carboxyl carbon (C-19) linked to C-4. A *cis*-relationship was shown between the hydrogen borne by C-8 and the methyl group (C-20) located at C-9. These results demonstrate that cordatin has the *trans*-clerodane skeleton with a half-chair conformation for the ring A due to the location of the double bond between C-2 and C-3. However, it should be noted the absolute stereochemistry has not been determined.

EXPERIMENTAL

Mp are uncorr., ^{1}H NMR (400 MHz) and ^{13}C NMR (20.9 MHz) in $CDCl_3$ with TMS as int. standard. The plant material was collected in July 1982 in the vicinity of Belem-Para

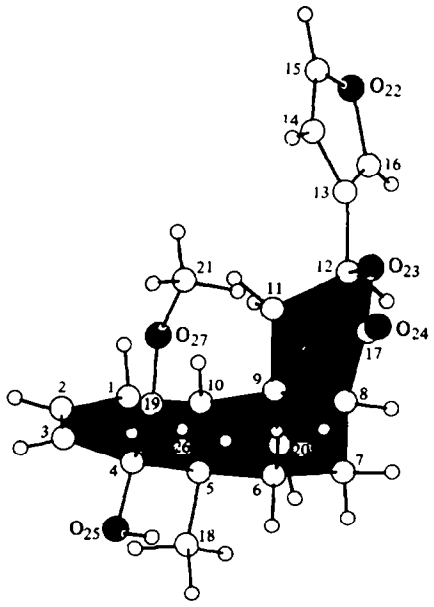

Fig. 1. A perspective view of cordatin 1.

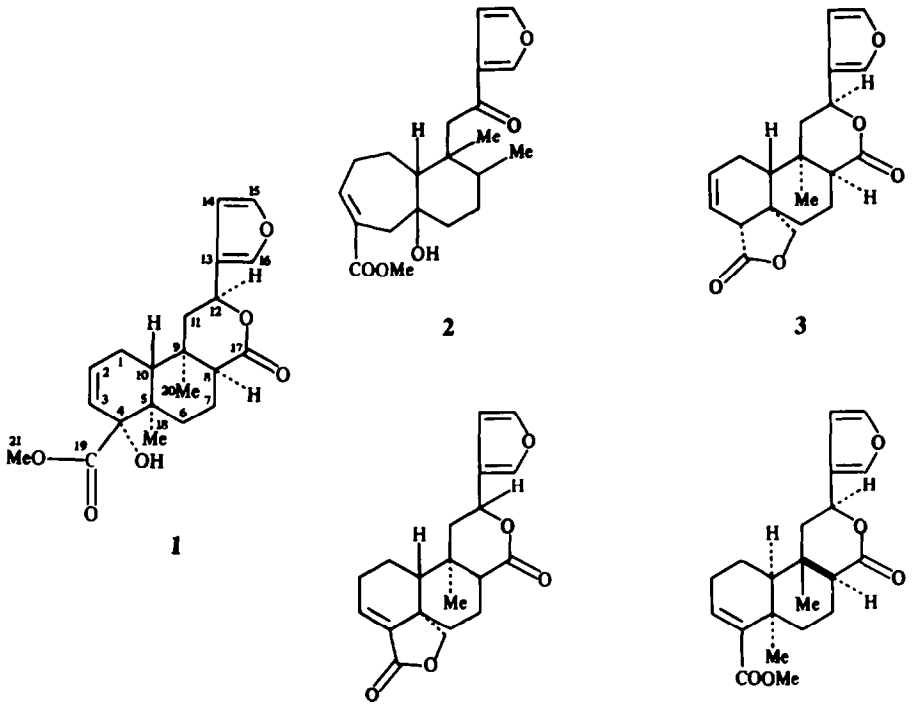

Table 1. ^{1}H NMR and ^{13}C NMR signals for cordatin (δ in ppm; TMS as int. standard)

C number	^{1}H signal (402 MHz)	Multiplicity J (Hz)	^{13}C signal (20.9 MHz)	SFORD multiplicity
1	2.14	*m*	17.6*	*t*
	2.06	*m*		
2	5.90	*m*	123.2	*d*
3	5.35	*d* (10)	129.9	*d*
4	—	—	80.5	*s*
5	—	—	40.4	*s*
6	1.44	*m*	28.3	*t*
	‡	*m*		
7	1.83	*m*	22.9*	*t*
	2.10	*m*		
8	2.32	*dd* (5, 12)	44.7†	*d*
9	—	—	35.3	*s*
10	2.49	*m*	44.5†	*d*
11	1.80	*dd* (5,12)	48.7	*t*
	2.01	*dd* (3,12)		
12	5.28	*dd* (3,12)	69.7	*d*
13	—	—	123.8	*s*
14	6.42	*t* (1,6)	108.5	*d*
15	7.48	*s*, *br*	143.5	*d*
16	7.42	*t* (1,6)	139.5	*d*
17	—	—	175.8	*s*
18	1.34	*s*	24.2	*q*
19	—	—	173.7	*s*
20	1.01	*s*	14.6	*q*
21	3.70	*s*	53.2	*q*

*,†Signals may be interchanged.
‡The signal for only one of these protons was identified.

(Brazil) and identified by Dr Paulo B. Cavalcante (Museu Paraense E. Goeldi-Belem-Brazil).

Isolation of cordatin (1). Dried trunk bark (0.75 kg) was extracted with benzene (3 l) (soxhlet). The benzene extract was distilled under vacuum and the residue (49 g) subjected to CC over silica gel (1.5 kg; Merck G-60); elution with a C_6H_6–$CHCl_3$ gradient yielded after crystallization from Me_2CO, cordatin (1) (0.4 g). Mp 170–172°; $[\alpha]_D^{20}$ + 140° (MeOH; *c* 0.1); IR ν_{max}^{KBr} cm^{-1}: 3550, 3130, 1740, 1720, 1460, 1500, 1380, 1250, 1200, 1150, 1100, 1050, 1020, 1000, 880, 830; UV λ_{max}^{EtOH} 214(6200); for ^{1}H NMR and ^{13}C NMR data see Table 1. EIMS, 70 eV *m/z* (rel. int.): 374 $[M]^+$ (2.9), 315 $[M-CH_3COO]^+$ (100), 203 $[M-171]^+$ (48), 175 (17.6) 153(20.5), 133(14.5), 107(31.8), 95(15.2), 94(11.7), 81(16.6). (Found: C 67.57; H 6.94; O 25.15. $C_{21}H_{26}O_6$ requires C 67.36; H 7.00; O 25.64%). High resolution MS: 374.17149 $C_{21}H_{26}O_6$.

X-ray crystallography. A colourless prismatic crystal of 0.4 × 0.4 × 0.7 mm in dimensions was used for the X-ray analysis. Crystal data: $C_{21}H_{26}O_6$, orthorhombic, a = 17.354(10), b = 12.159(9), c = 9.147(7) Å; Vol. = 1929.7 Å^3, Z = 4, D_c = 1.29, Space group $P2_12_12_1$, CuK_α radiation, λ = 1.5418 Å.

The experimental data were collected with a Philips-4 circle diffractometer using graphite monochromated CuK_α radiation. From 2007 measured independent reflections, 1901 were significant [$I > 3\sigma(I)$]. The structure was solved by direct methods [6] and the atomic coordinates and anisotropic thermal parameters were refined to R = 3.17% by least squares refinement [7]. All hydrogen atoms were found on difference Fourier's synthesis and their atomic coordinates and isotropic thermal parameters were refined.

The atomic coordinates, anisotropic thermal parameters, bond distances and bond angles for this work are available on request to the Director of the Cambridge Crystallographic Data Centre University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW U.K. The list of observed and calculated structure

factors is available from the authors at the Institut de Chimie des Substances Naturelles.

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C-12 STEREOCHEMISTRY OF TEUPOLIN I AND RELATED DITERPENOIDS FROM *TEUCRIUM* SPECIES

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Key Word Index—*Teucrium* sp.; Labiatae; neo-clerodane diterpenoids; C-12 configuration.

Abstract—By ^{1}H NOE techniques, the configurations at the C-12 chiral centre have been assigned for 13 neo-clerodane diterpenoids isolated from *Teucrium* species. Contrary to recent suggestions in the literature, the experimental results indicate the C-12(S) stereochemistry for teupolin I.

INTRODUCTION

Earlier, the absolute stereochemistry at the C-12 chiral centre of neo-clerodane diterpenoids isolated from *Teucrium* species was generally assumed to be *S*. This view was maintained by the fact that the few X-ray analyses and chemical correlations with compounds of known absolute stereochemistry were invariably made on *Teucrium* diterpenoids with the C-12(*S*) configuration. More recent studies employing ^{1}H NOE difference techniques [1, 2], however, have shown that the *S* configuration at C-12 is by no means a common stereochemical property in this class of natural products and, eventually, a revision of earlier assignments might be called for. In one of these works [1], the authors have found the C-12(*R*) configuration for a new neo-clerodane diterpenoid they had isolated from *T. scorodonia* [3] and *T. lanigerum* [4] and which, on the basis of some physical data (mp. $[\alpha]_D$, low frequency ^{1}H NMR), the authors claimed was identical to teupolin I (**13**), a diterpenoid from *T. polium*, isolated and described by us some years ago [5]. Since the physical data considered by the authors of ref. [1] are not necessarily distinctive for members of C-12 epimeric pairs, we have undertaken a detailed high-field ^{1}H NOE study on teupolin I and related diterpenoids from *Teucrium* species (**1**–**12**) also isolated by us previously [6–14]. In this respect it may be pointed out that the teupolin I sample used in the present study was of the same batch as the ones reported in refs [5] and [10].

RESULTS AND DISCUSSION

Stereochemical considerations show that *Teucrium* diterpenoids with the C-12(*R*) configuration have their Me-17 group and H-12 proton in a nearly parallel (*syn*) steric disposition on the same side of the lactone ring. The resulting spatial proximity can be easily monitored in selective DNOE experiments by irradiating either of the two pertinent resonances and observing the net enhancement of the other signal [15]. Performing these experiments on compounds **1**–**13** we have detected significant, 5–8%, enhancements with molecules **9** and **10** only, which suggested that the remaining diterpenoids belonged to the C-12(*S*) series.

While in ref. [1] the lack of enhancements in the aforementioned experiments was considered as a conclusive evidence for the C-12(*S*) stereochemistry, we have found that the spatial proximity arising from the altered configuration at C-12 (as well as from the concomitant changes in the lactone ring stereochemistry) can be readily