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DITERPENOIDS FROM *MICRANDROPSIS SCLEROXYLON**

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Key Word Index—*Micrandropis scleroxylon*; Euphorbiaceae; micrandrol-C; 2,6-dihydroxy-7-methyl-1-methylthiophenanthrene; micrandrol-D.

Abstract—The structure of micrandrol-C from *Micrandropsis scleroxylon* (Euphorbiaceae) is revised to 2,6-dihydroxy-7-methyl-l-methylthiophenanthrene. This and other micrandrols are probably diterpenes in view of their co-occurrence with micrandrol-D, the hemiketal of 1,2,3,4,9,10-hexahydro-6-hydroxy-4a-hydroxymethyl-1,1,7-trimethyl-2-oxophenanthrene.

In previous reports we assigned structures **1a**, **1b**, **2a**, **1c** and **1d** respectively to micrandols-A, -B, -C (from *Micrandropsis scleroxylon* [2]), -E and -F (from *Sagotia racemosa* [1]). According to these proposals, micrandrol-C is anomalous with respect to the position of one of its hydroxyls at C-8, and indeed Prof. Charles Brown, University of Kent, U.K. has kindly advised us that there are some discrepancies between his ^{1}H NMR data for synthetic 2,8-dimethoxy-7-methyl-1-methyl-thiophenanthrene (**2b**) and the analogous data which we reported for di-*O*-methylmicrandrol-C [2].

The re-examination of micrandrol-C and its derivatives [2], which thus became advisable, involved analysis of 270 MHz ^{1}H NMR spectra (Table 1). The low field region of all these spectra showed two pairs of doublets (J = 9 Hz for both) corresponding to two groups of *ortho*-related protons and two singlets corresponding to two *para*-related protons. The structure of micrandrol-C thus had to be revised to **1e**.

Indeed, upon irradiation at the frequencies assigned to H-3, H-4, H-9 and H-10, the doublets of, respectively, H-4, H-3, H-10 and H-9 collapsed into singlets. Furthermore, irradiation at the frequencies of H-4 and of H-5 produced NOE enhancements of the H-5 (14 ± 2%) and H-4 (17 ± 2%) signals. Finally, irradiation at the frequencies of H-8 and Me-7 resulted in reduction of the widths of half-height of, respectively, Me-7 (2 to 1 Hz) and H-8 (3 to 1.5 Hz) signals.

From the biosynthetic point of view, the micrandrols were tentatively classified as diterpenoids [2]. This hypothesis was firmly established with the isolation, from *Micrandropsis scleroxylon*, of micrandrol-D (**3**). Determination of the constitution of this compound involved initially HRMS, indicating the molecular formula $C_{18}H_{24}O_3$, and ^{1}H NMR spectroscopy, again pointing unmistakably to the micrandrol-type aromatic ring D. Double irradiation experiments corroborated the proximity of H-14 to both Me-13 and H-7. The presence of an oxy-function at C-3 being biosynthetically justified, nature and localization of the hemiketal bridge resulted from ^{1}H and ^{13}C NMR evidence. The OCH_2 protons are represented by doublets (δ 4.00 and 4.10, J = 9.5 Hz) and the methylene group is hence inserted in a fully substituted carbon; C-3 is represented by a singlet at δ 99.4 and this carbon must hence be fully substituted inclusively by two oxy-functions.

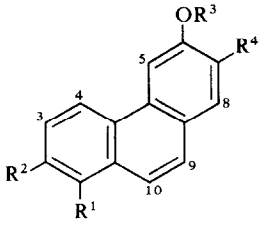
Independent corroborative evidence was derived from the study of the ketonic diacetate (ν_{max} 1715 cm^{-1}) which resulted in quantitative yield upon treatment of micrandrol-D with Ac_2O and C_5H_5N at room tempera-

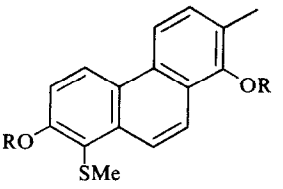
Table 1. ^{1}H NMR (270 MHz) chemical shifts of micrandrol-C (**1e**) and derivatives (**1f**, **1g**, **1h**)*

	1e	**1f**	**1g**	**1h**	Multiplicity	J (Hz)	$W_{1/2}$ (Hz)
H-3	7.31	7.33	7.32	7.37	*d*	9	1.5
H-4	8.43	8.59	8.71	8.56	*d*	9	2
H-5	7.85	7.86	7.83	8.24	*s*	—	2
H-8	7.63	7.62	7.63	7.76	*s*	—	3
H-9	7.73	7.71	7.73	7.81	*d*	9	2
H-10	8.21	8.50	8.80	8.54	*d*	9	1.5
Me	2.45	2.40	2.40	2.39	*s*	—	2
SMe	2.30	2.41	3.13	2.36†	*s*	—	0.5
OAc	—	—	—	2.41†	*s*	—	0.5
OAc	—	—	—	2.44†	*s*	—	0.5
OMe	—	4.08	4.06	—	*s*	—	0.5
OMe	—	4.05	4.05	—	*s*	—	0.5

* Values (δ) in ppm from internal TMS for $CDCl_3$ solutions.
† Signals may be interchanged.

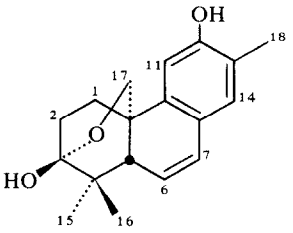
* Part 3 in the series "The Chemistry of Brazilian Euphorbiaceae". For Part 2 see ref. [1]. Based on part of the M. Sc. thesis presented by J. J. da S., CAPES Fellow, on leave of absence from Universidade Federal de Goias to Universidade de São Paulo (1980).





	R^1	R^2	R^3	R^4	9, 10
1a	Me	OH	H	Me	
1b	Me	OH	H	Me	dihydro
1c	Me	Me	H	OMe	
1d	Me	Me	H	OMe	dihydro
1e	SMe	OH	H	Me	
1f	SMe	OMe	Me	Me	
1g	SO(Me)	OMe	Me	Me	
1h	SMe	OAc	Ac	Me	

2a R = H
2b R = Me



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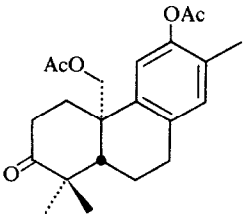

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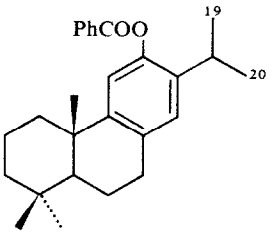

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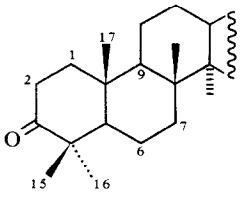

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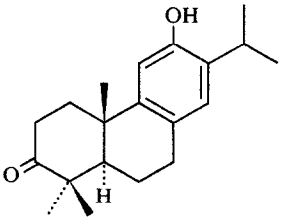

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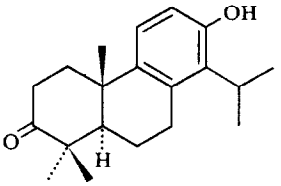

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ture. The ^1H and ^{13}C NMR spectra are fully consistent with the expected structure **4**, including an unambiguous assignment of A/B *trans* stereochemistry (cf. models **5** and **6**). Carbon chemical shifts were assigned correlating ^{13}C to ^1H signals through residual couplings in sford-spectra. Especially illuminating are the β- and γ-effects exerted by the acetoxyl at C-17 respectively on C-10 (cf. models **5** and **6**) and on C-1 (cf. **5** and **6**) and C-9 (cf. **5**) (Table 2). A further instructive difference between the spectra of **4** and **5** refers to the chemical shift values of C-13 and C-14 which reveal respectively β- and γ-effects emanating from the isopropyl group methyls of the latter compound (Table 2). An attempt to use analogous ketones [5] as models failed. In our opinion the reported chemical shift values will have to be reassigned.

The recognition of the 3*R*,3*S*,17*S* absolute stereochemistry of micrandrol-D (**3**) resulted from the fact that the derived diacetate (**4**, $[\alpha]_D$ − 105°) and the pair of model compounds hinokione (**7**, $[\alpha]_D$ + 112° [6]) and totarolone (**8**, $[\alpha]_D$ + 102° [7]) give antipodal ORD curves.

EXPERIMENTAL

Isolation of micrandrol-D. Preparation of **1a**, **1b** and **1c** by chromatographic separation of a $CHCl_3$ extract of *Micrandropsis scleroxylon* has been described [2]. All previously unused fractions were re-chromatographed on a Si gel column, $CHCl_3$–Et_2O (4:1) eluting a fraction purified by TLC (Si gel, $CHCl_3$–Et_2O, 1:1) to **3** (120 mg).

Table 2. NMR chemical shifts of micrandrol-D (3), its diacetate (4) and two model compounds (5, 6)*

	^{1}H (270 MHz)		^{13}C (22.6 MHz)			
	3	4	3	4	5	6
1	(a)	(a)	29.2	32.7	38.7	39.7
2	2.2–2.5 *m*	2.8–3.1 *m*	34.8	34.3	19.0†	33.9
3	—	—	99.6	215.4	41.6	218.3
4	—	—	35.8	47.0	33.3	47.1
5	(a)	(a)	48.3	49.9	50.0	54.8
6	(a)	(a)	20.8	19.7	19.1†	19.6
7	*ca* 2.7 *m*	2.5–2.7 *m*	30.8	29.5	29.9	33.9
8	—	—	128.7	133.4	132.8	40.4
9	—	—	136.7	140.8	146.1	50.3
10	—	—	40.3	40.0	37.5	36.8
11	6.69 *s*	6.90 *s*	112.7	120.6	117.9	—
12	—	—	152.9	147.1	148.6	—
13	—	—	123.2	128.6	136.5	—
14	6.82 *br. s*	6.95 *br. s*	131.3	131.6	126.6	—
15	1.04 *s*	1.17 *s*	17.9	21.3	21.5	20.9
16	1.11 *s*	1.13 *s*	26.8	27.2	33.2	26.8
17	4.00 *d* (b)	4.24 *d* (b)	72.4	66.1	24.7	15.8
	4.10 *dd* (c)	4.42 *d* (b)	—	—	—	—
18	2.17 *br. s*	2.11 *br. s*	15.5	15.8	27.2	—
19	—	—	—	—	23.0	—
20	—	—	—	—	22.9	—
12-OAc	—	2.29 *s*	—	20.9	—	—
	—	—	—	169.5	—	—
17-OAc	—	1.97 *s*	—	20.9	—	—
	—	—	—	171.0	—	—

*, † See Table 1.

(a) Included in a five proton multiplet δ 1.6–1.9 (3) and 1.8–2.1 (4). (b) J = 9.5 (3) and 11.5 (4) Hz. (c) J = 9.5 and 2.5 Hz; small coupling due to *W*-arrangement with H-1.

Micrandrol-D (3), mp 110–120° (CCl_4–$CHCl_3$). [M found: 288.1719; $C_{18}H_{24}O_3$ requires: 288.1725). ν_{max}^{KBr} cm^{-1}: 3425, 1621, 1504, 1465, 1269, 1100, 1037, 998, 890. λ_{max}^{MeOH} nm: 230 inf., 287; $\lambda_{max}^{MeOH+NaOH}$ nm: 242, 300. MS (*m/z*): 288 (49%) M$^+$, 258 (43), 232 (100), 215 (41), 201 (17), 187 (21), 185 (17), 174 (35), 173 (53), 172 (34), 171 (39), 159 (81). $[\phi]_D^{25}$ (1.7 mg/10 ml MeOH) −108°. ORD (1.7 mg/10 ml MeOH): $[\phi]_{350}$ − 1450, $[\phi]_{290}^{tr}$ − 4300, $[\phi]_{270}^{*}$ − 3050. CD (1.7 mg/10 ml MeOH): $[\theta]_{283}^{min}$ − 550.

Acetylation of 3 (54 mg) in Ac_2O (1 ml) and C_5H_5N (1 ml) (30 min, room temp.) gave 4 (78 mg), mp 121–123°. ν_{max}^{KBr} cm^{-1}: 1764 (ArOAc), 1742 (ROAc), 1715 (R_2CO), 1502, 1462, 1368, 1252, 1208, 1179, 1048, 929. MS (*m/z*): 372 (1%) M$^+$, 330 (10), 312 (32), 299 (17), 270 (39), 257 (100), 215 (35), 171 (30). $[\alpha]_D^{25}$ (1.5 mg/10 ml MeOH) −105°. ORD (1.5 mg/10 ml MeOH): $[\phi]_{350}$ − 1750, $[\phi]_{300}^{tr}$ − 4050, $[\phi]_{261}^{*}$ − 950. CD (1.5 mg/10 ml MeOH): $[\theta]_{280}^{min}$ − 1200. ORD 7 and 8 respectively $[\phi]_{302}^{*}$ + 1430 and $[\phi]_{312}^{*}$ + 1130 [6].

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