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DYSOXYLIN, A LIMONOID FROM *DYSOXYLUM RICHII*

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Key Word Index—*Dysoxylum richii*; Meliaceae; limonoid; dysoxylin; tetranortriterpene.

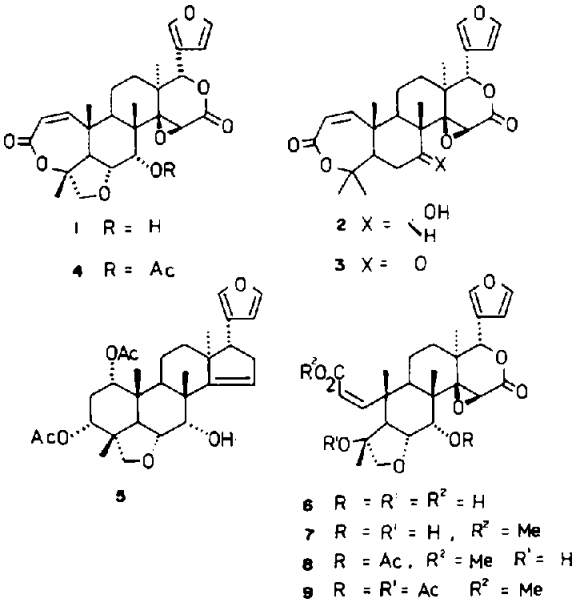
Abstract—Dysoxylin, a new limonoid, was isolated from the fresh leaves of *Dysoxylum richii* collected in Suva, Fiji. The proposed structure was based on spectral assignments and chemical interconversions.

INTRODUCTION

Limonoids are widely distributed in plants of the Meliaceae [1]. We have examined methanolic extracts of the leaves of *Dysoxylum richii* (Gray) C.DC. as part of a study of the chemical constituents of Fijian plants, and we now wish to report the structure of dysoxylin (**1**), the second limonoid from a plant in the genus *Dysoxylum* [2].

RESULTS AND DISCUSSION

The chloroform-soluble portion of the leaf extract was fractionated by silica gel flash chromatography to give dysoxylin (**1**) as an amorphous solid (yield 0.1% dry wt) that had a molecular formula of $C_{26}H_{30}O_8$ (M^+ 470.1937 dev. −0.4 mmu). Bands at 3480, 1740, and 1690 cm^{-1} in the IR spectrum of **1** could be assigned to hydroxyl, saturated lactone and unsaturated lactone functionalities respectively.



The ^1H (Table 1) and ^{13}C (Table 2) NMR spectra of dysoxylin (**1**) indicated that it was a limonoid and that it contained A, C, and D ring functionality identical to that found in obacunol (**2**) [3] and obacunone (**3**) [4]. Resonances at δ3.01 (*d*, J = 12 Hz, 1H), 4.01 (*dd*, J = 12, 2 Hz, 1H) and 3.64 (*d*, J = 2 Hz, 1H) in the ^1H NMR could be assigned to methine protons on C5, C6, and C7 of the B ring of the limonoid skeleton. Acetylation of dysoxylin (Ac_2O/DMAP/triethylamine [5]) gave a good yield of the monoacetate (**4**). The ^1H NMR of **4** showed that H-7 had undergone an acetylation shift from δ3.64 in **1** to 5.0 in **4**, and that H15 had shifted upfield from δ3.95 in **1** to 3.69 in **4**. These data were consistent with the presence of an alpha hydroxyl substituent at C7 in dysoxylin.

Only four tertiary methyl resonances were apparent in the ^1H and ^{13}C NMR spectra of **1** (Tables 1 and 2), in contrast to the five expected for the limonoid skeleton and observed in obacunol (**2**) and obacunone (**3**). A pair of geminal proton resonances at δ4.33 (*d*, J = 9 Hz) and 3.82 (*d*, J = 9 Hz) indicated that the fifth methyl residue was connected to C6 via an ether linkage identical to that found in salannin [6] and diacetylvilasinin (**5**) [7].

The stereochemistry of dysoxylin (**1**) was determined by an analysis of spin–spin coupling constants and a series of NOE experiments. A 12 Hz vicinal coupling constant between H5 and H6 suggested that ring B was in a chair conformation and that both protons were axial, while a 2 Hz coupling between H6 and H7 implied that H7 was equatorial. Irradiation of the C19 methyl resonance in the monoacetate **4** induced NOE's into Me-30, Me-29 and H6. Irradiation of the C29 methyl resonace induced NOE's into Me-19, H-6, and H-28, β, while irradiation of the C18 methyl resonance induced an NOE into H9. These results are consistent with the stereochemistry shown for **1**.

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Table 1. ^{1}H NMR data for dysoxylin (1), obacunol (2), dysoxylin acetate (4) and 1,3-diacetylvilasinin (5) (The spectra of 1 and 4 were run in $CDCl_3$ at 400 MHz, chemical shifts are reported in ppm from internal TMS)

Compound	1	2*	4	5†
Protons on carbon no.				
1	6.33 *d* 12 Hz	6.57 *d* 12 Hz	6.31 *d* 12 Hz	
2	5.85 *d* 12 Hz	5.89 *d* 12 Hz	5.92 *d* 12 Hz	
5	3.01 *d* 12 Hz		2.82 *d* 12 Hz	2.67 *d* 12.5 Hz
6	4.01 *dd* 12 and 2 Hz		4.07 *dd* 12 and 2 Hz	4.14 *dd* 12.5 and 3 Hz
7	3.64 *d* 2 Hz	3.52 *t* 2 Hz	5.01 *d* 2 Hz	4.18 *d* 3 Hz
9	2.48 *t* 8 Hz		2.47 *t* 8 Hz	2.56 *m*
15	3.95 *s*	3.90 *s*	3.69 *s*	
17	5.58 *s*	5.64 *s*	5.58 *s*	
18	1.21 *s*	1.25 *s*‡	1.20 *s*	0.84 *s*
19	1.28 *s*	1.30 *s*‡	1.29 *s*	0.97 *s*
21	7.39 *m*	7.49 *d* 1 Hz	7.41 *m*	7.36 *m*
22	6.33 *d* 1 Hz	6.42 *t* 1 Hz	6.34 *d* 1 Hz	6.27 *m*
23	7.39 *m*	7.49 *d* 1 Hz	7.41 *m*	7.24 *m*
28	3.82 *d* 9 Hz	1.25 *s*	3.77 9 Hz	3.59 *d* 7 Hz
	4.33 *d* 9 Hz		4.24 9 Hz	3.56 *d* 7 Hz
29	1.60 *s*	1.43 *s*‡	1.55 *s*	1.18 *s*
30	1.08 *s*	1.05 *s*‡	1.17 *s*	1.11 *s*

*Data from ref. [3].
†See ref. [7] for complete data.
‡Unassigned.

Dysoxylin (1) was hydrolysed with 0.05 M NaOH in dioxane to give the dihydroxy acid 6, which was methylated with diazomethane to give the ester 7. Acetylation of ester 7 (Ac_2O/pyridine) gave a mixture of mono- and diacetates 8 and 9. The spectral data observed for all the transformation products were consistent with the proposed structures.

EXPERIMENTAL

Isolation and extraction. Fresh leaves of *Dysoxylum richii* were collected from Suva, Fiji in December 1985. A voucher specimen of this plant is deposited at the South Pacific Regional Herbarium, Institute of Natural Resources, University of the South Pacific, Suva, Fiji. The air-dried leaves (300 g) were soaked in MeOH (1.5 l) for 5 days. The MeOH extract was concd to a gum, H_2O was added and the resulting suspension was extracted successively with petrol (bp 60–80°) and $CHCl_3$. The concd $CHCl_3$ extract was dissolved in EtOAc (10 ml), soaked over alumina (10 g), filtered, and concd to give a gum (2.4 g). Fractionation of the gum by flash chromatography on silica gel using mixtures of cyclohexane–EtOAc gave crude dysoxylin (1) 0.37 g). Preparative TLC (1:1 toluene/EtOAc) of the crude material gave 1 as solid, mp 247–251°, $[\alpha]_D^{25}$ + 72.5° ($CHCl_3$; *c* 0.15); $C_{26}H_{30}O_8$ EIMS $[M]^+$ 470.1937 (dev. −0.4 mmu); ^{1}H NMR see Table 1; ^{13}C NMR see Table 2.

Dysoxylin acetate (4). To a stirred mixture of 1 (20 mg) and NEt_3 (0.5 ml) was added 4-(*N*,*N*-dimethylamino)pyridine (DMAP) (3 mg). The reaction mixture was heated to 60° for 3 hr. After cooling, the reaction mixture was diluted with water (5 ml), then extracted wtih $CHCl_3$. The organic layer was washed sequentially with aq. HCl (5%) and aq. $NaHCO_3$ (5%) before drying and concentration *in vacuo* to give dysoxylin acetate (4) as a solid, mp 235–245°; $C_{28}H_{32}O_9$ EIMS M^+ 512.2050 (dev. +0.3 mmu); ^{1}H NMR see Table 1; ^{13}C NMR see Table 2.

Dihydroxy acid. To a solution of 1 (3 mg) in dioxane (0.5 ml) was added 0.05 M NaOH (0.5 ml). The solution was refluxed for 30 min, then warmed at 50° for 90 min. Work-up gave the dihydroxyacid 6. ^{1}H NMR($CDCl_3$) 1.05 (3H, *s*, Me-30), 1.27 (3H, *s*, Me-18), 1.34 (3H, *s*, Me-19), 1.45 (3H, *s*, Me-29).

Methyl ester. Dihydroxyacid 6 was methylated with diazomethane to give the methyl ester 7. $C_{27}H_{34}O_9$ EIMS $[M]^+$ 502.2110 (dev. 0.7 mmu); ^{1}H NMR ($CDCl_3$) 1.07 (3H, *s*, Me-30), 1.22 (3H, *s*, Me-18), 1.35 (3H, *s*, Me-19), 1.45 (3H, *s*, Me-29), 3.75 (3H, *s*, COOMe).

Monoacetate and diacetate. Acetylation of 7 using Ac_2O–pyr. (room temp. for 24 hr) gave the monoacetate 8 and the diacetate 9 as gums. 8: ^{1}H NMR ($CDCl_3$) 1.11, 1.21, 1.32 and 1.45 (3H each, *s*, Me-30, Me-18, Me-19 and Me-29) 2.20 (3H, *s*, COMe), 3.73 (3H, *s*, COOMe), 5.00 ppm (1H, *d*, *J* = 2 Hz, H-7); 9: ^{1}H NMR ($CDCl_3$) 1.12, 1.23, 1.33 and 1.5 (+ H_2O) (3H each, *s*, Me-30, Me-18, Me-19 and Me-29), 1.93 and 2.20 (3H each, *s*, COMe), 3.70 ppm (3H, *s*, COOMe).

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Table 2. ^{13}C NMR data. All spectra were run in $CDCl_3$ (Chemical shifts are in ppm from internal TMS)

Carbon	1*	3†	4	5‡
1	149.8	156.8	149.3	72.28
2	119.4	122.7	119.9	27.66
3	167.7§	166.7	166.8§	71.76
4	84.9	84.0	84.4	42.32
5	52.4	53.3¶	54.3	39.62
6	77.5	39.0	76.0	72.90
7	69.6	207.5	71.0	74.01
8	43.3	52.9	43.3	45.80
9	40.4	49.1	42.0	33.62
10	44.8	43.1	44.5	39.20
11	15.4	17.0	15.4	15.21
12	26.0	32.6	26.0	33.02
13	38.5	37.3	38.8	47.36
14	69.6	65.1	69.5	159.88
15	58.1	57.2¶	56.1	120.75
16	165.6§	166.9	165.5§	34.35
17	78.1	77.9	78.0	51.58
18	17.5	16.4‖	17.7§	21.16
19	17.2	19.4‖	17.3§	26.20
20	120.5	120.0	120.2	124.52
21	143.0	143.1	143.1	139.76
22	109.9	109.7	109.8	111.06
23	141.2	140.9	141.2	142.62
28	81.3	21.0‖	81.3	77.88
29	23.5	26.7‖	23.4§	15.37
30	17.9	32.0‖	18.5§	19.47
MeCO	—	—	21.0	21.16, 21.09
MeCO	—	—	170.0	169.97, 170.28

*Assignments were based on comparison to literature values for model compounds, APT and one bond HETCOR.

†Data from ref. [4] (see also [8]).

‡Data from ref. [7].

§Values in same vertical column may be reversed.

‖Unassigned.

¶Assignements are reversed in ref. [4].

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