Phytochemistry, Vol. 26, No. 10, pp. 2819–2823, 1987.
Printed in Great Britain.

0031–9422/87 $3.00 + 0.00
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CHROMONES FROM *DICTYOLOMA INCANESCENS*

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(*Revised received* 9 *February* 1987)

Key Word Index—*Dictyoloma incanescens*; Rutaceae; prenylated chromones; chroman; 5-(3-methylbut-2-enyl)allopteroxylin; 6-(3-methylbut-2-enyl) allopteroxylin methyl ether.

Abstract—Extraction of *Dictyoloma incanescens* bark gave 6-(3-methyl-but-2-enyl) allopteroxylin and 6-(3-methylbut-2-enyl) allopeteroxylin methyl ether, the structures of which were established by chemical transformations and spectroscopic means.

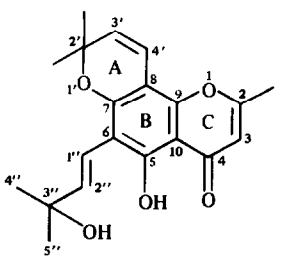
INTRODUCTION

Previously, the bark and leaves of *Dictyoloma incanescens DC.* (Rutaceae), were examined and indole alkaloids (gramine, *N,N*-dimethyl-5-methoxytryptamine) were isolated [1]. A reinvestigation of the bark of *Dictyoloma incanescens*, a Brazilian tree, led to the isolation of two additional compounds **1** and **2**.

RESULTS AND DISCUSSION

Compound **1**, $C_{20}H_{22}O_4$ was soluble in 2% aqueous potassium hydroxide and gave a green colour with alcoholic ferric chloride indicating its phenolic nature. It had IR absorption consistent with a chromone and this and other properties indicated a possible relationship with sorbifolin **3** which has been obtained from a related plant species [2–4].

The presence of 2,2-dimethylchromene (6H, *s*, δ1.45; 1H, *d*, δ6.62, J = 10 Hz and 1H, *d*, δ5.53, J = 10 Hz) and 2-methylchromone systems (3H, *s*, δ2.32) could be deduced from its H^1 NMR spectrum, which also revealed an olefinic proton singlet (δ5.95, H_3), a 3,3-dimethylallyl fragment and a chelated phenolic proton (δ13.1). Detailed analysis of the spectral data confirmed **1** to be 6-(3-methylbut-2-enyl)allopteroxylin, previously isolated from *Spathelia sorbifolia L.* (Rutaceae) [4]. This was proved by the acetic acid cyclization to a chromanderivative **4** which requires the 3,3-dimethylallyl side chain to be adjacent to the phenolic group on C-5 [4].



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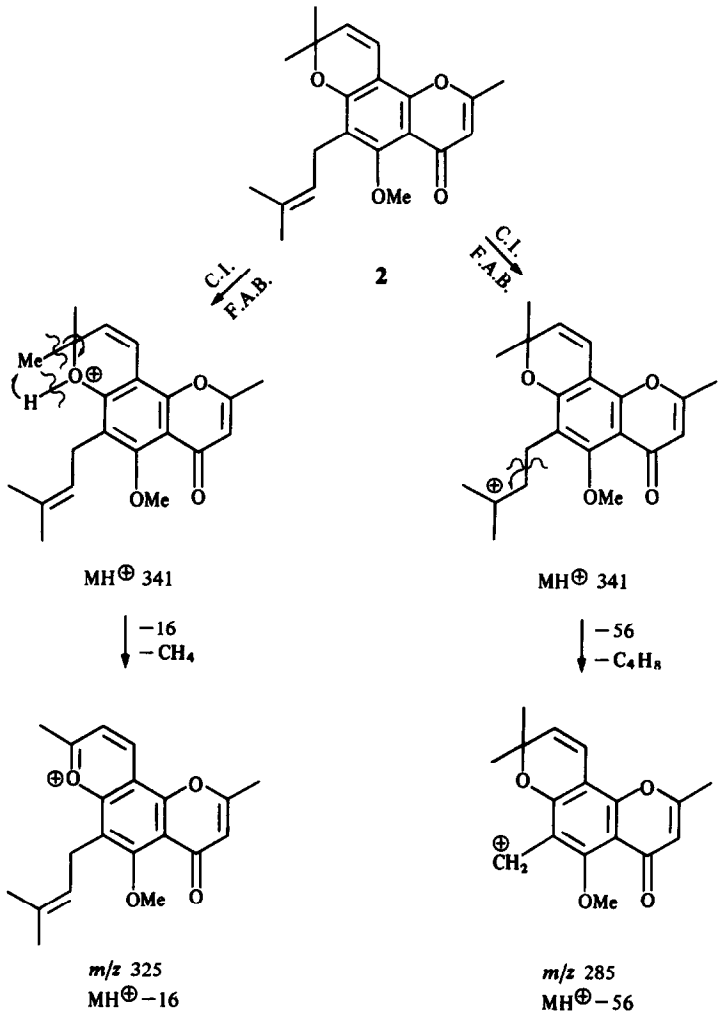
Compound **2**, $C_{21}H_{24}O_4$ was also found to be a chromone. The FAB mass spectral fragmentation pattern of **2** was very similar to that of **1** (A) and the corresponding ions of **2** differed by 14 mass units from those of **1**. The base peak was due to the protonated molecular ion at *m/z* 341. The loss of methane (CH_4) from the 2,2-dimethylpyran unit of the molecular ion afforded ion *m/z* 325. An ion due to the loss of a C_4H_8 unit $[MH-56]^+$: *m/z* 285 was also observed, showing that **2** was the methyl ether of (Scheme 1).

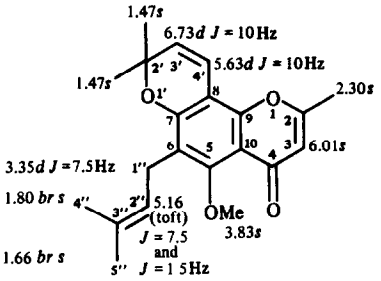
The ^1H NMR spectrum of **2** (Scheme 2) was similar to that of **1** except for the lack of a chelated phenolic proton and the presence of a three proton singlet at δ3.83 in the former substance.

Assignment of the ^1H (400 MHz) NMR spectra of **2** resulted from two dimensional NMR experiments (^1H–^{13}C chemical shift correlation), [5] especially for the assignment of H3', H4', H4" and H5". Structure **2** was confirmed by methylation of **1** to **2** (identical ^1H and ^{13}C nmr spectra); the new natural product is therefore 6-(3-methylbut-2-enyl)allopteroxylin methyl ether.

Carbon-13 NMR studies of flavonoids have been reported [6–8]. In flavones the C-6 was considered to be represented by the higher field signal and the C-8 by the lower field signal. On the other hand, a large difference (12 ppm) between the C-6 and C-8 shifts in 4,4'-dimethoxyscandenin **5**, [8] with angular fusion of the pyran ring was observed. Isomeric coumarin system **6** (4,4'-dimethoxyonchocarpic acid) was shown to display much smaller chemical shift difference (1 ppm) [8]. This slight difference (2–3 ppm) between the C-6 and C-8 chemical shifts was observed in isoflavones **7** (auriculatin), **8** (milletin) and **9** (trapezifolixanthone), possessing a linear fused pyran unit (scheme 4). [8, 9]. In order to complete the study of angular ring fusion in chromones, the ^{13}C NMR spectra of **2**, **3**, **4** and **10** were recorded. The spectra of the compounds studied are presented in Scheme 3: the large difference between the C-6 and C-8 chemical shifts in **5** is reflected in chromones **4**, **2** and **10** (9.5–13.7 ppm). A much smaller difference (7.2 ppm) is observed in tetracyclic chromone **3**. These results, which might well be general in the field of chromones, flavones and coumarins are summarized on Scheme 4.



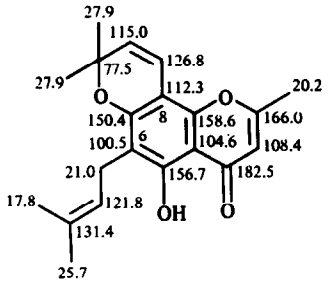
Scheme 1.



Scheme 2. ^{1}H Chemical shifts for **2** (400 MHz-^{1}H NMR).

EXPERIMENTAL

Commercial apparatus (ZAB. 2F and 70-70-VG Instruments) have been used for FAB mass spectra. Mps uncorr. IR spectra were measured in CCl_4. ^{1}H NMR spectra were recorded in $CDCl_3$ with TMS as int. standard, chemical shifts being expressed in δ units (ppm). ^{13}C NMR spectra were recorded at 25.2 MHz. ^{1}H-^{13}C shift correlation (BRUCKER WM.400): The pulse sequence was ($\pi/2$, ^{1}H)-($t_1/2$)-(π, ^{13}C)-($t_1/2$)-(τ_1)-($\pi/2$, ^{1}H; $\pi/2$, ^{13}C)-(τ_2)-(BB, ^{1}H: FID, t_2) with $\tau_1 = 0.00357$ sec and $\tau_2 = 001785$ sec. The spectral width in F_1 was 1200 Hz and in F_2, 7246 Hz, the number of data points in t_2 was 4096 and 256 increments, were recorded, before FOURIER transformation, the data were multiplied with unshifted sinebell in F_2 and exponential in F_1. Total acquisition was 20 hr. The $\pi/2$ pulse was 14 μsec for ^{13}C and the decoupler $\pi/2$ pulse was 43 μsec. Column chromatography was performed on 230–400 mesh MERCK silica gel 60. *Dictyoloma incanescens DC.* was collected in



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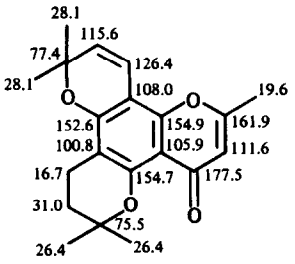

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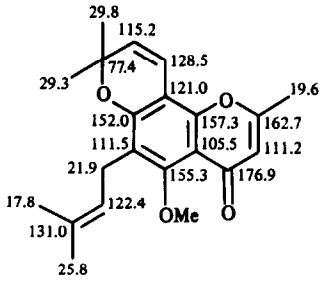

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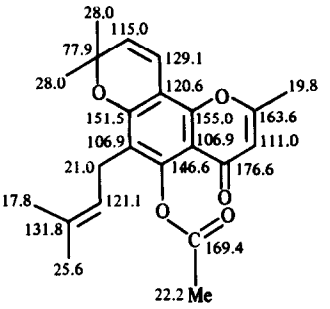

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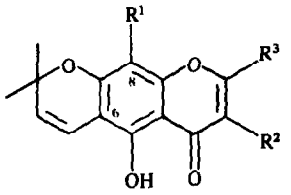
Scheme 3.

Fortaleza–Nordeste (BRASIL) and identified by Professor F. J. A. Matos (Universidade Federal do Ceara, Brasil).

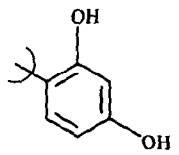
Extraction of the bark. Dried bark of *Dictyoloma incanescens* (4 kg) was milled and extracted with boiling 95% EtOH (20 l/8 hr). The mixture was filtered. The extract was sirup conc under red. pres. to a thick sirup (120 g). 10 g were extracted with 600 ml of boiling pentane for 48 hr. The pentane extract evapd to dryness left 3 g of residue which was dissolved in CH_2Cl_2 and chromatographed on a column of silica gel eluting with increasing percentages of CH_2Cl_2–ether. CH_2Cl_2 eluted 6-(3-methylbut-2-enyl) allopteroxylin **1** (560 mg). It was recrystallized twice from MeOH–H_2O to give 346 mg yellow crystals, m.p. 101–103° (lit [2] m.p. 99–101.5°). 328 $[MH]^+$, MS *m/z* 311 $(MH-CH_4)^+$, 271 $(MH-C_4H_8)^+$. Found: C, 73.85; H, 6.87, $C_{20}H_{22}O_4$ requires: C, 73.61; H, 6.75. IR ν_{max} (1665, 1635 and 1590 cm^{-1}), UV (EtOH): λ_{max}: 227, 241, 268, 301, 319 and 352 nm (ε 24.300, 19.650, 32.850, 2650, 2600 and 3100). ^1H (400 MHz) δ1.45 (6H, *s*), 1.68 *br* and 1.79 *br* (3H, each, *s*), 2.32 *br* (3H, *s*), 3.29 (2H, *d*, J 7 Hz), 5.24 (1H, *t*, J = 7 Hz), 5.53 (1H, *d*, J = 10 Hz), 5.95 *br* (1H, *s*), 6.62 (1H, *d*, J = 10 Hz) and 13.1 (1H, *s*). CH_2Cl_2–ether (9:1) eluted 6-(3-methylbut-2-enyl) allopteroxylin methyl ether **2** (400 mg). It was recrystallized twice from ether to give 280 mg crystals. Mp 102–103°. 341 $[MH]^+$, MS *m/z* 325 $[MH-CH_4]^+$ and 285 $[MH-C_4H_8]^+$. Found: C, 73.74; H, 6.78; $C_{21}H_{24}O_4$ requires C, 74; H, 7. IR ν_{max} (1665, 1635, and. 1590 cm^{-1}). ^1H (400 MHz) δ1.47 (6H, *s*), 1.66 *br* and 1.80 *br* (3H, each, *s*), 2.30 (3H, *s*), 3.35 (2H, *d*, J 7.5 Hz), 3.83 (3H, *s*), 5.16 (1H, *t* *t*, J = 7.5 and 1.5 Hz), 5.63 (1H, *d*, J = 10 Hz), 6.01 *br* (1H, *s*), 6.73 (1H, *d*, J = 10 Hz).

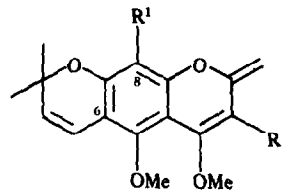
Acid catalysed cyclisation of 6-(3-*methylbut-2-enyl*) *allopteroxylin.* To a solution of **1** (30 mg) in HOAc (0.5 ml) was added conc HCl (1 drop). The solution was refluxed during 1 hr then evapd to dryness and the product was isolated by extraction with $CHCl_3$. The chroman **4** (30 mg) purified by prep. TLC (MERCK silica gel 60 PF. 254) in CH_2Cl_2–ether 10% elution, has m.p. 168–170° (recrystallized twice from petrol). IR ν_{max} 1650, 1615, 1587 and 1575 cm^{-1}. ^1H (200 MHz) δ1.39 and 1.46 (6H, each, *s*), 1.79 (2H, *t*, J = 7 Hz), 2.28 *br* (3H, *s*), 2.63 (2H, *t*, J = 7 Hz), 5.56 (1H, *d*, J = 10 Hz), 5.96 *br* (1H, *s*), 6.74 (1H, *d*, J = 10 Hz). lit. [4]

6-(3-*methylbut-2-enyl*) *allopetroxylin acetate* **10** A solution of **1** (90 mg) in pyridine (1 ml) and Ac_2O (2 ml) refluxed over night, followed by the usual work-up, gave 90 mg of a yellow-brown oil

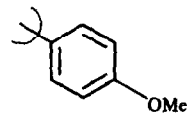


7 R^1 = 3,3 - dimethylallyl
R^3 = H
R^2 =

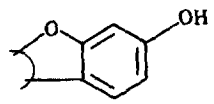




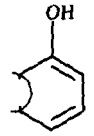
6 R^1 = 3,3 - dimethylallyl
R^2 =



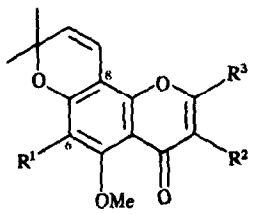
8 R^1 = 3,3 - dimethylallyl
$R^2 + R^3$ =

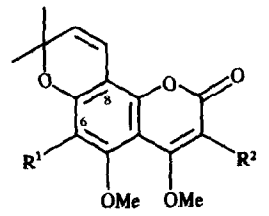


9 R^1 = 3,3 - dimethylallyl
$R^2 + R^3$ =

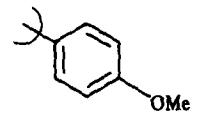


Linear compounds $\delta_{C_8} - \delta_{C_6} \simeq 1-3$ ppm





5 R^1 = 3,3 - dimethylallyl
R^2 =



Angular compounds $\delta_{C_8} - \delta_{C_6} \simeq 8-13$ ppm

Scheme 4.

which was chromatographed on CC eluting with pentane–ethyl acetate 9:1, giving 80 mg of acetate **10**. The acetate **10** crystallized from petrol m.p. 103–105°C. IR ν_{max} 1775, 1665, 1635, and 1600 cm^{-1}. ^1H (200 MHz) δ1.45 (6H, *s*), 1.65 *br* (3H, *s*), 1.78 *br* (3H, *s*), 2.27 *br* (3H, *s*), 2.41 (3H, *s*, OAc), 3.23 *br* (2H, *d*, $J \simeq 7$ Hz), 5.08 (1H, *t*, $J \simeq 7$ Hz), 5.67 (1H, *d*, $J = 10$ Hz), 5.95 *br* (1H, *s*), 6.76 (1H, *d*, $J \simeq 10$ Hz).

Methylation of **1**. A solution of **1** (50 mg) in Me_2CO (2.5 ml) dry K_2CO_3 (500 mg) and MeI (0.5 ml) was stirred at room temp. for 24 hr. The mixture was filtered and the filtrate was poured into H_2O. (10 ml). The product was isolated by extraction with $CHCl_3$ and purified by prep. TLC in CH_2Cl_2–ether (4:1) to yield **2** (40 mg) identical with the natural product.

Acknowledgements—We thank Dr S. KAN (Université Parissud), Mme C. Pasquier (C. N. R. S., Gif-suryvette) and Dr J. C. Beloeil for recording ^1H (400 MHz), ^1H (200 MHz), ^{13}C NMR spectra and ^1H–^{13}C shift correlation. We also thank Professor J. C. Tabet for recording FAB-MS and Professor F. J. A. Matos (Universidade Federal do Ceara, Brazil) for plant collecting and classification.

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