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AN UNEXPECTED DIHYDROPHENANTHRENE FROM CLUSIA PARALYCOLA

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Abstract: An isopropenyldihydrophenanthrene, probably derived from a 2-prenylbiphenyl, has been isolated from Clusia paralycola.

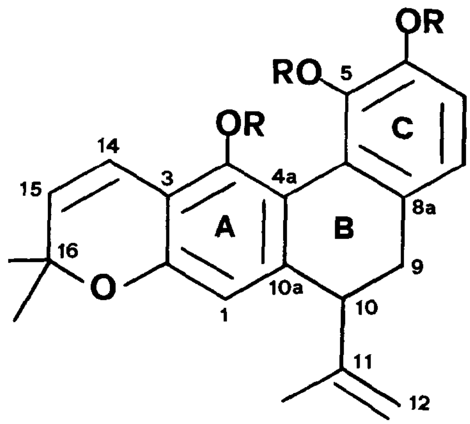
The acetone extract of the roots of Clusia paralycola (Guttiferae, subfam. Clusioideae), collected in Pernambuco State (Brazil), showed significant antimicrobial activity. From the EtOAc soluble portion of the extract, a novel prenylated phenanthrene, paralycolin A (1), which showed cytotoxic activity in vitro on KB and P388 cells (ID_{50} 3.8 and 2.6 μg/ml, respectively), has been isolated. This paper deals with structure determination of this compound. The physicochemical properties of paralycolin A were as follows : light brown microcrystalline solid (CH_2Cl_2 - heptane), mp 95-8°C, $[\alpha]_D^{20}$ -88 (c= 0.66, $CHCl_3$); HRMS, M^{+} 350.1516, calcd for $C_{22}H_{22}O_4$, 350.1518; UV λ_{max}^{MeOH} nm (log ε): 236 (4.38), 320 (4.28). The IR spectrum ($CHCl_3$) showed the absorptions due to hydroxy groups (3540, 3400 cm^{-1}), to an exo-methylene (900 cm^{-1}) and no carbonyl band. The ^1H NMR spectrum (table 1) revealed the presence of three aromatic protons (two of which are ortho coupled), a 2,2-dimethyl-2H-pyran ring, an isopropenyl group and a system $-CH_2-CH<$. To fit these data with the molecular formula the compound must contain a further ring and it was thus assumed that paralycolin A had a dihydrophenanthrene basic skeleton. Noteworthy was the chemical shift of the aromatic protons (table 1) which excluded their location on C-4 and C-5 [1]. Three phenolic hydroxyls were evidenced by the formation of a triacetylderivative, 2 (mp 155-7 °C; ν_{max}1760, 1370 cm^{-1}; M^{+} 476), with pyridine - Ac_2O and of a trimethylderivative, 3 (mp 99-100 °C; M^{+} 392), with Na_2CO_3 - dimethylsulphate. These derivatives gave also

Table 1. ^{1}H and ^{13}C NMR data for 1

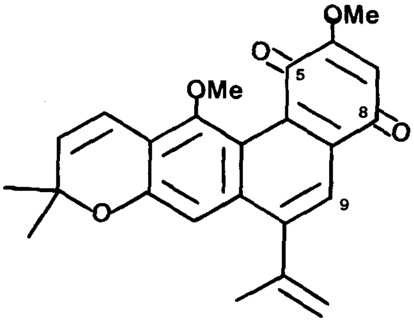
C/H Number	δ_H[a]	J values	δ_C[b]
C-1/H-1	6.90 s		104.5
C-2			152.1
C-3			109.1
C-4			148.8
C-4a			116.0
C-4b			121.8
C-5			141.2
C-6			146.6
C-7/H-7	7.13 d	8.5	113.2
C-8/H-8	6.70 d	8.5	116.3
C-8a			127.8
C-9/H_2-9	3.37 dd	16 ; 2	25.4
	2.75 dd	16 ; 6.5	
C-10/H-10	3.70 dd	6.5; 2	38.4
C-10a			135.4
C-11			142.9
C-12/H_2-12	4.70 s; 4.60 s		112.4
C-13/Me-13	1.60 s		20.4
C-14/H-14	6.70 d	10	129.1
C-15/H-15	5.60 d	10	116.6
C-16			76.1
C-17/Me-17	1.43 s		27.4
C-18/Me-18	1.34 s		27.4

[a] 60 MHz; $CDCl_3$ + D_2O

[b] 25.2 MHz; $CDCl_3$



1	H
2	Ac
3	Me
4	Me (9-10 dehydro)



5

useful information about the substitution pattern of the aromatic rings. The marked diamagnetic shift ($\Delta\delta$ 0.5 ppm) of the α chromene proton (H-14) as well as the inter-ring long range coupling between H-14 and H-1 in the ^{1}H NMR spectrum of 2, suggested a peri relationship between one phenolic OH and the chromene ring [2].Accordingly H-14 underwent a paramagnetic shift in C_5D_5N [3] in the ^{1}H NMR spectrum of paralycolin A. Furthermore in the ^{13}C NMR spectrum of 3, two OMe signals appeared at low field (δ 62.1 and 60.5), indicating that they are ortho-disubstituted [4]. The above findings established the substitution pattern of A and C rings as depicted in 1, but left undetermined the location of the isopropenyl group on C-9 or C-10. DDQ-dehydrogenation of 3 afforded two compounds, both with $M^{\rceil+}$ 390. One of these $C_{25}H_{26}O_4$, was assigned the expected phenanthrene 4 [5] while the other [$\lambda_{max}^{CHCl_3}$ 271 (4.37), 294 (4.26)sh, 438 (3.45); HRMS, $M^{\rceil+}$ 390.1458, calcd for $C_{24}H_{22}O_5$, 390.1468] exhibited in the ^{1}H NMR spectrum three aromatic proton singlets (δ 8.90, 7.70 and 6.60) and only two OMe signals (δ 3.82 and 3.58), and was assigned the structure 5. The latter quinone can be formed by demethylation of the C(5)-OMe and p-oxidation (C-8) [6]. The paramagnetic shift of one aromatic proton from 4 to 5 (δ 7.73 vs 8.90) located this proton (H-9) peri to the generated CO, and consequently the isopropenyl group on C-10, as depicted in 5. The natural occurrence of dihydrophenanthrenes is limited to few families [7] and the isolation of 1 from a Guttifera is unexpected. Paralycolin A may derive biogenetically from a 2-prenylbiphenyl, that is, attachment of the prenyl group (see 8a in 1) and subsequent cyclization onto C-10a in 1

References and footnotes

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5) Mp 148°C; λ_{max} 230, 284; ^{1}H NMR, δ 8.15 (H-8), 7.73 (H-9), 7.60 (H-1), 7.20 (H-7), 6.78 (H-14), 5.78 (H-15), 5.0 (H_2-12), 3.93 (2-OMe), 3.60 (1-OMe), 2.1 (Me-13), 1.48 (Me-17,18).

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