Tetrahedron Letters, Vol.31, No.5, pp 751-754, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

NOVEL METABOLITES FROM *PLOIARIUM ALTERNIFOLIUM*: A BIXANTHONE AND TWO ANTHRAQUINONYLXANTHONES

Graham J. Bennett[†], Hiok-Huang Lee[*†] and Timothy K. Lowrey[§]
[†]Department of Chemistry and [§]Department of Botany
National University of Singapore, 10 Kent Ridge Crescent
Singapore 0511

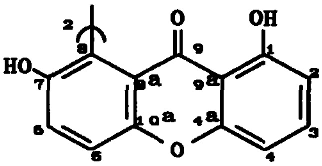
Summary: From branches of the shrub *Ploiarium alternifolium* three novel metabolites have been isolated: a C-C'-linked bixanthone, ploiarixanthone(1), and two anthraquinonylxanthones, euxanmodin A and B (2 and 3).

Ploiarium alternifolium (Vahl) Melch.[1] occurs either as a shrub or a tree depending on its habitat, and is confined to South-East Asia. From the benzene extract from branches of the shrub we have obtained several polar compounds, three of which have been identified (1-3). The red-brown bark of the tree-form also contains compounds 1 and 2. Ploiarixanthone (1) represents the first C-C'-linked bixanthone from Nature, although synthetic analogues have been reported.[2] A bixanthone with an ether linkage has been isolated from *Swertia chirata*,[3] and bis-tetrahydroxanthones are known in fungi and lichens.[4] The anthraquinonylxanthone structures proposed for **2** and **3** are also novel.

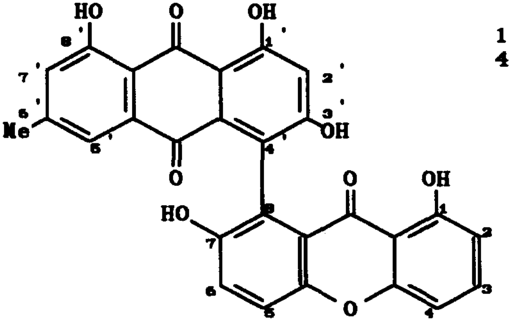
Ploiarixanthone (1) is a yellow, optically active ($[\alpha]_D^{25}$ +23°, c 0.25, MeOH), crystalline solid, mp > 360°C. Its IR spectrum shows a chelated carbonyl (1646cm^{-1}) and a non-chelated hydroxyl (3520 cm^{-1}), and its UV spectrum [λ_{max}^{EtOH} (logϵ) 243 (4.69), 262 (4.75), 324 (3.83) and 393 (4.08) nm] was found to be similar to that of 1,7-dihydroxyxanthone (euxanthone).[5] Hrms (M^+ 454.0685) gave the molecular formula $C_{26}H_{14}O_8$, which, in addition to a significant fragment at half mass (m/e 227), was suggestive of a bixanthone. A symmetrical aromatic structure is indicated by the ^{1}H NMR spectrum (Table 1) which shows six signals due to seven protons, all above δ 6.5. Three protons form an ABC system (*J* 8.2 and 1.0 Hz), and also visible are a two-proton singlet and two hydroxyl protons, one chelated. The ^{13}C NMR spectrum (Table 2) exhibits eight quaternary and five methine carbons, indicating that the two magnetically equivalent hydrogens are on different carbons. By comparison with ^{1}H NMR spectra of known xanthones,[6] the ABC system could only be assigned to the 2, 3 and 4 protons of a 1-oxygenated xanthone ring. The remaining ring therefore contained a hydroxyl in the 5, 6, or 7 positions, two protons with a similar environment, and a C-C' link to an identical xanthonyl moiety. The ^{1}H NMR spectrum of the colourless tetra-acetate (4) (mp 224°C)[7] helped to assign the position of the linkage. The acetyl protons appear upfield as two singlets at δ 1.86 and 2.08. This may be explained if the two halves of the molecule are twisted from coplanarity, and the two acetyl methyls of each xanthonyl unit lie above the π-electron cloud of the other. By analogy with bianthraquinones,[8] such shielding of 1-acetoxy protons should only occur if the C-C' link is at C-8 or C-2. As the latter position has been accounted for, the linkage is C-8 to C-8'. It follows that the second acetoxy group should be *ortho* to the C–C' link at C-7, and that ploiarixanthone is 8,8'-bieuxanthone (1). Further evidence in support of structure 1 comes from an ^{1}H NMR comparison with euxanthone (Table 1) and from the ^{13}C NMR data for 1 (Table 2) which compare well with those of the relevant rings of 1- and 2-hydroxyxanthones.[9]

Euxanmodin A (2), $C_{28}H_{16}O_9$, is a bright red solid, mp > 360°C, $[\alpha]_D^{25}$ +7°, (c 0.15, MeOH) [M$^+$ 496.0786; IR 1665 sh, 1648 sh, 1639 and 1605 cm^{-1}; λ_{max}^{EtOH} (logϵ) 250 (4.60), 261 (4.66), 293 (4.31), 397 (3.97) and 455 (4.05) nm]. Its UV spectrum is characteristic of an anthraquinone.[10] Furthermore, with alkali, 2 gave a violet colour which was discharged to yellow on addition of dithionite.[10] The ^{1}H NMR spectrum of 2 (Table 1), like 1, showed an ABC system (*J* 8.2 and 1.0 Hz) and a two-proton singlet which, together with a m/e 227 fragment in the mass spectrum, suggested the presence of a 8-euxanthonyl moiety, and therefore that 2 was an anthraquinonylxanthone. Such molecules should be susceptible to reductive clevage[11,8] and indeed treatment of 2 with hot alkaline dithionite gave a mixture of euxanthone and 1,3,8-trihydroxy-6-methylanthraquinone (emodin), each identified by mp, UV and ^{1}H NMR. The position of the C-C' linkage was determined as follows. The ^{1}H NMR spectrum of 2 exhibits three aromatic singlets, two of which appear broadened, and may be assigned to the protons *ortho* to the methyl group (*ie.* H-5' and H-7'). The chemical shift of the third singlet is close to that observed for H-2' of emodin (Table 1), implying that the remaining C-4' is the position of the C-C' link in euxanmodin A. The yellow penta-acetate (5) (mp 232°C) exhibits three shielded acetyl groups in its ^{1}H NMR spectrum (Table 1). This is in accord with structure 2, as a molecular model shows that the 1, 3' and 7-acetyls occupy positions above an aromatic plane. For the same reason, H-5', and to a lesser extent the 6'-methyl group, appear upfield from their positions in the ^{1}H NMR spectrum of emodin. Finally comparison with 3 confirmed euxanmodin A as 2.

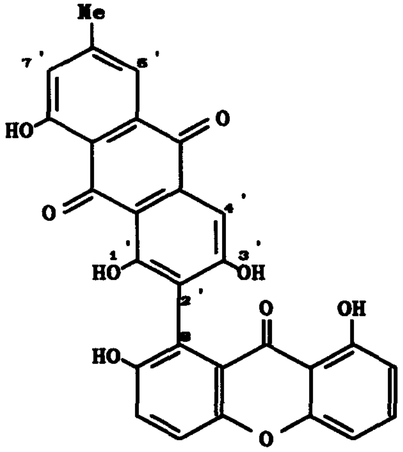
Euxanmodin B (3), $C_{28}H_{16}O_9$, is an orange solid, mp 290°C [M$^+$ 496.0791, λ_{max}^{EtOH} (logϵ) 244 (4.63), 288 (4.49), 400 (4.08) and 442 (4.12) nm]. The similarity of the UV, mass, and ^{1}H NMR (Table 1) spectra of 2 and 3 suggested that they were isomeric, differing only in the position of the C-C' link. The ^{1}H NMR spectrum of the penta-acetate (6) (mp 268°C) shows four upfield acetyls (AcO-1, 1, 3' and 7) (Table 1). Additionally, the chemical shifts of H-4', H-5' and H-7' in 3 appear close to their positions in emodin and a



1 R=H
4 R=Ac



2 R=H
5 R=Ac
7 R=Me



3 R=H
6 R=Ac
8 R=Me

Table 1: ^{1}H NMR Data*for Compounds 1-3, Euxanthone (EU) and Emodin (EM)

Proton	COMPOUND				
	1	EU	2	3	EM
2 dd	6.87	6.92	6.87	6.88	-
3 t	7.50	7.58	7.66	7.53	-
4 dd	6.59	6.74	6.61	6.65	-
5/6	7.44s	7.35m	7.42s	7.50m	-
8 dd	-	7.62	-	-	-
2'	-	-	6.83s	-	6.65d
4'	-	-	-	7.51s	7.30d
5' brs	-	-	7.30	7.59	7.58
7' brs	-	-	6.98	7.05	7.07
6-Me s	-	-	2.32	2.45	2.45
OH	12.61	12.75	12.93	12.64	12.25
	8.62	9.49	12.62	12.54	12.19
			12.22	12.19	
			10.40	10.37	
			8.62	8.84	
OAc	1.86	-	1.89	1.94	-
[of	1.86		1.90	2.01	
compounds	2.08		2.04	2.04	
4,5 & 6]	2.08		2.45	2.16	
			2.46	2.40	

Table 2: ^{13}C NMR Data*for Ploiarixanthone (1)

Carbon	Assignment
1	161.23
2	108.90
3	135.55
4	106.03
5	117.24
6	123.85
7	150.61†
8	119.03
9	182.68
4a	155.54
8a	121.95
9a	108.41
10a	150.18†

†: interchangeble

*: in $CDCl_3$-DMSO-d_6

signal for H-2' is clearly absent, pointing to structure 3 for euxanmodin B. Further confirmation of the positions of the C-C' links in 2 and 3 was obtained from the ^{13}C NMR spectra of their respective penta-O-methylethers (7, mp 336°C and 8, mp 288°C). In the spectrum of 7 all the methoxyl carbons resonate below δ 57, whereas in the spectrum of 8 one methoxyl carbon appears at δ 61.0, which is consistent with the expected downfield shift of the di-*ortho*-substituted 1-methoxyl in 8.[12]

A subsequent examination of the branches extract has revealed the presence of a significant quantity of emodin and a small ammount of euxanthone.

The isolation of xanthone derivatives from *Ploiarium alternifolium* is of great taxomnomic interest. *Ploiarium* is placed in the Bonnetiaceae family together with two South American genera, *Bonnetia* and *Archytaea*. The Bonnetiaceae has, in the past, been allied or merged with either the Theaceae or the Guttiferae. Our results, together with the isolation of xanthones from the other two genera,[13] support a close link between the Bonnetiaceae and the Guttiferae. Euxanthone is known in 16 genera of the Guttiferae, and anthraquinones occur widely in one Guttiferae tribe, but neither have been isolated from the Theaceae.

Biosynthetically compounds 1-3 probably arise by a stereospecific oxidative coupling of the respective monomeric halves, in a similar way to biflavonoids (which are also common in the Guttiferae). The formation of 2 and 3 would appear to involve the coupling of two monomers of different biogenetic origin, however, it is of interest to note that 1,7-dihydroxy-3-methylxanthone in *Cassia* spp. has been postulated to derive from an anthraquinone.[14]

References and Notes

1. Collected in Singapore; voucher specimen (1261 T. Lowrey) deposited at National University of Singapore Herbarium.
2. Y.G. Gaekwad and S. Sethna, *J. Indian Chem. Soc.* 1978, 55, 794.
3. S. Mandal and A. Chatterjee, *Tetrahedron Lett.*, 1987, 28, 1309.
4. B. Franck, and H. Flasch, *Fortschr. Chem. Org. Naturst.*, 1973, 30, 152; J.A. Elix, A.A. Whitton and M.V. Sargent, *ibid.*, 1984, 45, 136.
5. H.D. Locksley, I. Moore and F. Scheinmann, *J. Chem Soc.* (C), 1966, 430.
6. D. Barraclough, H.D. Locksley, F. Scheinmann, M.T. Magalhaes and O.R. Gottlieb, *J. Chem. Soc.* (*B*), 1970, 603.
7. All compounds reported gave satisfactory hrms and satisfactory microanalytical data were obtained for compounds 4 and 5
8. Y. Ogihara, N. Kobayashi and S. Shibata, *Tetrahedron Lett.*, 1968, 1881; A. Yagi, K. Makino and I. Nishioka, *Chem. Pharm. Bull.*, 1978, 26, 1111; A.G. Gonzalez, R. Freire, R. Hernandez, J.A. Salazar and E. Suarez, *Chem. Ind.* (London), 1973, 851.
9. A.W. Frahm and R.K. Chaudhuri, *Tetrahedron*, 1979, 35, 2035.
10. R.H. Thomson, *Naturally Occurring Quinones*, 2nd Ed., 1971, Academic Press, London, p 57.
11. B.H. Howard and H. Raistrick, *Biochem. J.*, 1954, 56, 56.
12. K.S. Dhami and J.B. Stothers, *Can. J. Chem.*, 1966, 44, 2855.
13. K. Kubitzki, A.A.L. Mesquita and O.R. Gottlieb, *Biochem. Syst. Ecol.* 1978, 6, 185.
14. G.R. Wader and N.A. Kudav, *Indian. J. Chem.*, *Sect. B*, 1987, 26B, 703.

(Received in UK 7 November 1989)