Tetrahedron Letters, Vol. 34, No. 51, pp. 8251-8254, 1993
Printed in Great Britain

0040-4039/93 $6.00 + .00
Pergamon Press Ltd

The Structure of Xanthoquinodin A1, A Novel Anticoccidial Antibiotic Having A New Xanthone-Anthraquinone Conjugate System

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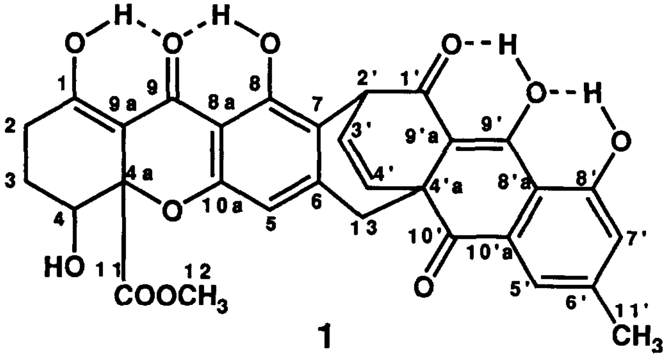
Summary: The structure of the anticoccidial antibiotic xanthoquinodin A1(1), isolated from *Humicola* sp. FO-888, was elucidated by ^{1}H- and ^{13}C-NMR experiments. It contains a new type of xanthone and anthraquinone conjugate system.

The anticoccidial antibiotics xanthoquinodins A1, A2, A3, B1 and B2 were isolated from a cultured broth of *Humicola* sp. FO-888 during the course of screening for new anticoccidial antibiotics from soil isolates[1]. In this communication, we report the structure elucidation of the main component xanthoquinodin A1 (1).

The physico-chemical properties of 1 were as follows; mp. 187~188°C, $[\alpha]_D^{25}$= +404° (c=0.1, CH3OH), UV $\lambda_{max}^{CH_3CN}$ nm (ε) : 230(20400), 273(10300), 335(21600) and 378(sh, 10900) ; IR $\upsilon_{max}^{CHCl_3}$ cm^{-1} : 1735(C=O), 1680(C=O), 1600(C=C) and 1570(C=C). The molecular formula of 1 was established to be $C_{31}H_{24}O_{11}$ by high resolution EI-MS (m/z 572.1316, calcd. 572.1317). Its acetylation gave a pentaacetyl derivative (EI-MS (m/z 782(M$^+$)), FAB-MS (m/z 783(M+H)$^+$ and 805(M+Na)$^+$), suggesting the presence of five hydroxy moieties in the structure.



1

The ^{1}H- and ^{13}C-NMR spectral data are shown in Table 1. These data confirmed the above formula. The ^{1}H-^{1}H COSY, ^{1}H-^{13}C COSY and ^{1}H-^{13}C long range COSY experiments revealed the presence of the partial structures [A], [B], [C] and [D].

In the long range selective proton decoupling (LSPD) experiments, the hydrogen-bonded phenolic proton at δ13.91 was found to be coupled to one methylene carbon at δ24.3 (C-2) and two olefinic carbons at δ179.7 (C-1) and δ100.1 (C-9a). In addition, the methine proton at δ4.26 (H-4) was coupled to an ester carbonyl carbon at δ170.9 (C-11), a quaternary oxygenated carbon at δ83.9 (C-4a) and an olefinic carbon at δ100.1 (C-9a). And the methyl protons at δ3.68 (H-12) was coupled to a carbonyl carbon at δ170.9 (C-11). These data suggest the partial structure [A']. The methine proton at δ4.78 (H-2') was correlated to a carbonyl

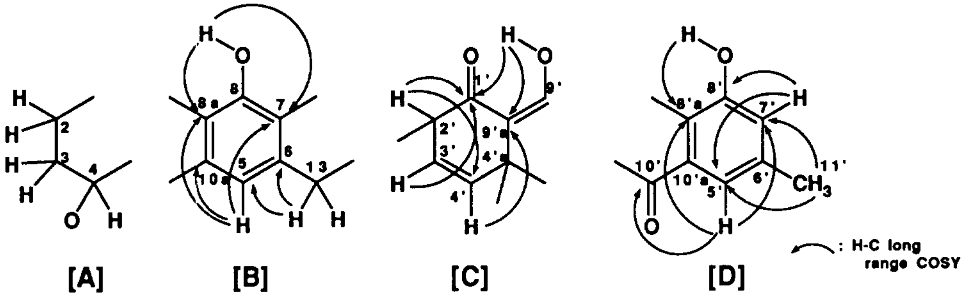
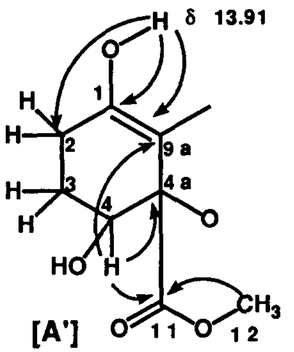


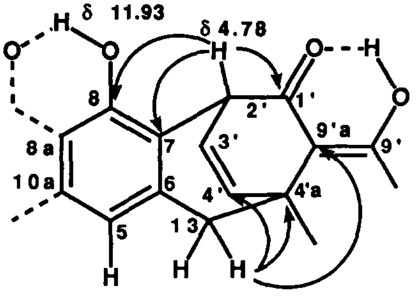
Table 1. ^{13}C and ^{1}H NMR Chemical Shifts of **1** δ = ppm in $CDCl_3$

	^{13}C	^{1}H		^{13}C	^{1}H
1	179.7 s		1'	189.0 s	
2	24.3 t	2.79 1H m	2'	37.8 d	4.78 1H dd J=6.5, 1.0Hz
		2.37 1H m	3'	131.4 d	6.46 1H dd J=8.5, 6.5Hz
3	22.9 t	2.11 1H m	4'	132.7 d	6.65 1H dd J=8.5, 1.0Hz
		1.91 1H m	4'a	49.9 s	
4	66.8 d	4.26 1H dd J=4.0, 1.5Hz	5'	120.9 d	7.55 1H s
4a	83.9 s		6'	147.4 s	
5	110.3 d	6.06 1H s	7'	124.2 d	7.06 1H s
6	146.4 s		8'	161.3 s	
7	116.4 s		8'a	115.0 s	
8	158.6 s		9'	182.7 s	
8a	105.0 s		9'a	106.4 s	
9	186.6 s		10'	195.5 s	
9a	100.1 s		10'a	132.1 s	
10a	156.1 s		11'	22.0 q	2.43 3H s
11	170.9 s		1-OH		13.91 1H s
12	53.4 q	3.68 3H s	8-OH		11.93 1H s
13	38.8 t	2.87 1H d J=17.5Hz	8'-OH		11.69 1H s
		3.03 1H d J=17.5Hz	9'-OH		14.80 1H s

carbon at δ189.0 (C-1') as well as two aromatic carbons at δ116.4 (C-7) and δ158.6 (C-8). The isolated methylene protons at δ2.87 and δ3.03 (H-13) were coupled to a quarternary carbon at δ49.9 (C-4'a) and two olefinic carbons at δ132.7 (C-4') and δ106.4 (C-9'a). These results enable to connect the partial structures [B] and [C] at the two sites, namely the methine carbon (C-13) to the quaternary carbon (C-4'a) and the aromatic carbon (C-7) to the methine carbon (C-2'), constructing the partial structure [B'].

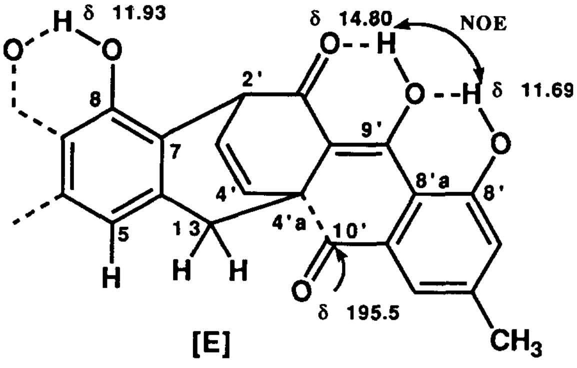


[A']



[B']

From the molecular modeling, only the connections are possible between C-9' in [B'] and C-8'a in [D], and between C-4'a in [B'] and C-10' in [D], leading to the anthraquinone structure shown in [E]. This is supported by the following evidences; 1) The carbonyl carbon C-10' should not be contained in an aromatic ring since the chemical shift of δ195.5 showed a lower field shift than those of the other carbonyl groups, 2) the phenolic protons at δ11.69 and δ14.80 could be hydrogen-bonded to the oxygen as shown in [E], 3) NOE was, in fact, observed between the two phenolic protons, and 4) an intact acetate unit was incorporated into the C-10' and C-4'a unit in a [$^{13}C_2$-1,2] sodium acetate feeding experiment (data not shown).



[E]

Considering the molecular formula of **1**, the partial structures [A'] and [E] should be connected by the remaining units, C=O and -O-. The observation of two hydrogen-bonded phenolic protons at δ13.91 in [A'] and δ11.93 in [E] suggests that [A'] and [E] must be connected through a carbonyl group at δ186.6. In addition, the quaternary carbon at δ83.9 (C-4a) in [A'] and the aromatic carbon at δ156.1 (C-10a) in [E] should be bonded through an oxygen atom, because the chemical shifts of both carbons showed lower field shifts. From the above results, the structure of xanthoquinodin A1 was elucidated to be **1**. It has an unusual connection of xanthone and anthraquinone moieties.

Recently, the structures of beticolins[2] and cebetins[3], isolated from *Cercospora beticola* which is the causal agent of sugar beet leaf disease, were reported to comprise xanthone and anthraquinone moieties connected in a different fashion from that in **1**, and to contain an epoxide function and a chlorine atom. Both xanthone and anthraquinone units of the above compounds including **1** are estimated to be biosynthesized *via* octaketide from acetate. The acetate primers in **1** are considered to be the C-13 and -6 unit for the xanthone moiety and the C-11' and -6' unit for the anthraquinone moiety. However, the methyl head of the acetate primer for the anthraquinone unit in beticolins and cebetins extended at C-3' position instead of the C-6' in **1**. It suggests that the direction of xanthone-anthraquinone connection is symmetric in beticolins and cebetins but asymmetric in **1**. Therefore, **1** is a new type of xanthone and anthraquinone conjugate containing no epoxide function and chlorine atom.

References

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(Received in Japan 22 March 1993; accepted 17 June 1993)