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A BIOACTIVE BENZOINDENONE FROM *EICHHORNIA CRASSIPES* SOLMS

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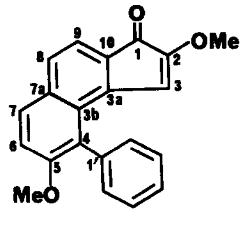
Abstract: The structure 2,5-dimethoxy-4-phenyl-benzoindenone (1) has been attributed to a metabolite from *Eichhornia crassipes* on the basis of its spectroscopic properties. The compound was proved to inhibit the growth of the fungus *Candida albicans*.

In pursuing our search for biologically active compounds from aquatic plants, we have examined *Eichhornia crassipes* Solms, a species whose extracts have been reported to have effects as growth regulators.[1] Beside new oxygenated sterols which reduced the root growth of *Raphanus sativum* L.[2] we have isolated some new aromatic compounds and in this preliminar paper we report the characterization of 2,5-dimethoxy-4-phenyl-benzoindenone (1) which represents the first example of a benzoindenonic compound isolated from a natural source.



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The molecular formula $C_{21}H_{16}O_3$ was attributed to the red oily metabolite on the basis of the molecular peak at *m/z* 316.1091 in its high resolution mass spectrum and was supported by the ^1H and ^{13}C nmr data (Table 1).

The carbonyl absorption at 1733 cm^{-1} in the IR spectrum was in good agreement with the values reported for indenones bearing electronegative groups at C-2[3] and the UV spectrum with bands at 236, 258, 302, 362 and 455 nm conforted the benzoindenonic system[4].

The ^1H nmr spectrum showed two methyl singlets at δ 3.86 and 4.08, a methine singlet at δ 6.83, four methine doublets at δ 6.90, 7.57, 7.61 and 8.63 beside five further aromatic protons in the 7.34-7.46 ppm range. The protons at δ 6.90 and 7.61 as well as those at δ 7.57 and 8.63 were *ortho* coupled and their arrangement at the C-6 - C-9 positions was deduced by a homonuclear COSY long-range showing correlations between H-6 at δ 6.90 and H-8 at δ 7.57 as well as between H-7 at δ 7.61 and H-9 at δ 8.63. The experiment evidenced two further scalar interactions between the H-6 proton and the methyl at δ 4.08 as well as between the singlet at δ 6.83 and the methyl at δ 3.86. These spatial proximities, confirmed by nOe difference experiments, located a methoxyl group at C-5 and the other one, vicinal to the singlet, on the five-member ring. The subsequent assignment of this methoxyl group at C-2 derived by the chemical shift of the vicinal H-3 proton. In fact the H-2 and H-3 proton resonances in indenone are at δ 5.83 and 7.52[5]; as a methoxyl group upfield shifts the vicinal proton (0.6-0.8 ppm), the value 6.83 ppm is undoubtedly indicative of the assigned position.

The ^{13}C nmr data, obtained by on-resonance and DEPT experiments, were accounted for by a carbonyl carbon at δ 179.8, eight quaternary, ten methine and two methyl carbons. The chemical shifts of these carbons and the one-bond and long-range 2D heterocorrelations univocally proved the structure **1**. In a long-range experiment, obtained by choosing a delay corresponding to 10 Hz C,H coupling, the three bond long-range couplings were evidenced. The H-3 proton showed connettivity with the carbonyl C-1 and significatively, the H-3, H-7 and H-8 protons were correlated to the same carbon at δ 125.7 attributed to the C-3b carbon.

Table 1. NMR Data of Benzoindenone **1** in $CDCl_3$.

Position	DEPT	$\delta\ ^{13}C$	H-C one bond $\delta\ ^{1}H$	H-C long-range $\delta\ ^{13}C$
1	C	179.8	-	-
2	C	152.1	-	-
3	CH	112.0	6.83 s	124.3,125.7,55.4,179.8
3a	C	143.0	-	-
3b	C	125.7	-	-
4	C	121.4	-	-
5	C	157.4	-	-
6	CH	104.7	6.90 d (8.4)	121.4, 126.3
7	CH	130.7	7.61 d (8.4)	125.7, 130.7
7a	C	126.3	-	-
8	CH	130.7	7.57 d (8.0)	125.7, 130.7
9	CH	128.3	8.63 d (8.0)	126.3, 143.0
10	C	124.3	-	-
2-OMe	CH_3	55.4	3.86 s	152.1
5-OMe	CH_3	55.9	4.08	157.4

The aromatic H-2' - H-6' protons in the 7.34-7.46 ppm range are correlated to the methine carbons at δ 126.9, 127.9 (x2) and 128.1 (x2). C-1' δ 148.4.
The coupling costants in Hz are reported in parentheses.
Solid lines indicate proton correlations revealed by homonuclear decoupling experiments. Broken lines indicate proton correlations revealed by homonuclear long-range COSY experiments.

The compound **1** was subjected to antimicrobial screening procedures against Gram+, Gram- and the fungus *Candida albicans* and was found active only against the fungus. The assays were performed according to the diffusion technique for the antibiotic screening[6] using as reference standards tetracycline, cephamendole and nistatine. The compound was dissolved in DMSO and 100 μl of a $2x10^{-3}$ M solution were applied on a Whatman paper disk and after four days at 22°C inhibition diameter was measured (73% related to the controls).The cup-plate technique was used to determine the minimum inhibitory concentration. 100μl of solution from $2x10^{-3}$ M to $2.5x10^{-4}$ M were transfered to 9 mm diameter holes cut into the agar plates. After four days at 22°C the inibition was still evident (20% related to the controls) with a concentration $5x10^{-4}$ M.

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