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1,2,7-TRIHYDROXY-8-METHOXY-6-METHYLANTHRACENE, THE PUTATIVE PRECURSOR OF THE MARINE PIGMENT HALLACHROME

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Prota *et al.* (1) reported in 1972 the isolation and structure of hallachrome (**1**), the red pigment of the sea-worm *Halla parthenopeia* Delle Chiaje. Hallachrome is, to our knowledge, the unique representative of a naturally occurring 1,2-anthraquinone unsubstituted at positions 9 and 10.

We report now the occurrence in *H. parthenopeia* of 1,2,7-trihydroxy-8-methoxy-6-methylanthracene (**2**) as the main component, to be considered the biogenetic precursor of hallachrome (**1**). Compound **2** occurs also in the sea-worm *Lumbriconereis impatiens* Claparède.

$CHCl_3$ treatment of *H. parthenopeia* resulted in the isolation of nearly pure hallachrome, as previously reported (1), while extraction with Me_2CO, removal of the solvent, partitioning with *n*-BuOH of the resulting aqueous suspension, and performing LH-20 chromatography of the butanolic solubles yielded **2** as an amorphous solid. Compound **2** was isolated also from *L. impatiens* after a similar procedure.

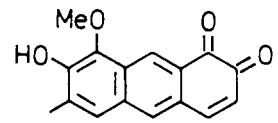
The molecular formula of **2** was established as $C_{16}H_{14}O_4$ by high resolution mass measurements on the molecular ion at *m/z* 270. The nmr spectrum of **2**, containing methyl singlets at δ 2.36 and 3.87, five aromatic protons at δ 7.09 (d, *J* 9.2 Hz), 7.55 (s), 7.73 (d, *J* 9.2 Hz), 8.26 (s) and 8.47 (s), and exchangeable protons at δ 9.40 ca., was strongly reminiscent of that of **1**, the differences observed in the chemical shift values being attributed to the reduced nature of **2**.

Acetylation of **2** yielded a triacetate (**3**) identical in all respects to the leucotriacetate of **1** prepared as previously reported (1), thus establishing the structure of **2** as 1,2,7-trihydroxy-8-methoxy-6-methylanthracene. Moreover, the substitution pattern of 3 was further supported by nOe experiments (Table 1). The reported results confirm also the structure of **1**, from which the leucotriacetate **3** is derived.

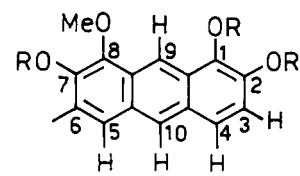
TABLE 1. Nuclear Overhauser Effects Measured on the Triacetate **3** ($CDCl_3$; Difference Spectra)

Protons irradiated (δ)	Protons enhanced (δ)
7.30 (H-3)	7.89 (H-4)
7.89 (H-4)	7.30 (H-3) 8.35 (H-10)
8.35 (H-10)	7.89 (H-4) 7.62 (H-5)
7.62 (H-5)	8.35 (H-10) 2.37 (Ar-CH_3)
2.37 (Ar-CH_3)	7.62 (H-5)
4.02 (OCH_3)	8.59 (H-9)
8.59 (H-9)	4.02 (OCH_3)

Air oxidation of **2**, catalyzed by dilute acid or base, smoothly yields the quinone **1**; however, in the worm *L. impatiens* in which a large amount of the hydroquinone **2** was found, the quinone **1** was observed only in trace amounts



1



2 R=H
3 R=Ac

suggesting that the in vivo conversion of **2** into **1** should be enzymically controlled.

EXPERIMENTAL

EQUIPMENT USED.—Mps were determined with a Kofler apparatus and are uncorrected. Uv spectra were obtained on a Shimadzu Bausch & Lomb, Spectronic 210 spectrometer. Nmr spectra were recorded on Bruker 500 and Bruker 250 instruments, using TMS as internal standard. Mass spectra were obtained on AEI MS-30 and MS-902 instruments.

ANIMAL MATERIAL.—Specimens of *H. parthenopeia* and *L. impatiens* were purchased from fishermen in the Naples area, and kindly identified by Dr. E. Fresi, Stazione Zoologica, Naples, Italy. Voucher specimens are available for inspection at the Istituto per la Chimica di Molecole di Interesse Biologico, Arco Felice, Naples, Italy.

ISOLATION OF COMPOUNDS **1** AND **2**.—From *H. parthenopeia*.—Fresh material (10 specimens; length ca. 60 cm each) was dipped into Me_2CO (500 ml) at room temperature. After 3 h the extract was decanted, and the animals were re-extracted two times with Me_2CO. The combined extracts were concentrated under vacuum, and the resulting aqueous suspension was sequentially extracted with Et_2O and *n*-BuOH.

The Et_2O extract was taken to dryness and chromatographed on a silica gel column (1.5×100 cm; $CHCl_3$ as eluent). The red band eluted (75 mg) contained hallachrome (**1**) accompanied by some cholesterol. The solution was taken to dryness, washed with 3×2-ml portions of Et_2O, and the insoluble hallachrome collected by filtration [45 mg; mp 225-230°; lit (1) 224-226°]; ms *m/z* M^+ 268; nmr δ ($CDCl_3$) 2.47 (3H, s), 4.01 (3H, s), 6.19 (1H, bs; exchangeable with D_2O), 6.47 (1H, d, *J* 10.0 Hz), 7.46 (1H, s), 7.55 (1H, d, *J* 10.0 Hz), 7.64 (1H, s), 8.73 (1H, s); δ (DMSO-d_6), 2.36 (3H, s), 3.87 (3H, s), 6.38 (1H, d, *J* 10.0 Hz), 7.59 (1H, s), 7.75 (1H, d, *J* 10.0 Hz), 7.90 (1H, s), 8.47 (1H, s).

The *n*-BuOH extract was taken to dryness, dissolved in MeOH, and chromatographed on LH-20 column (2×100 cm; MeOH as eluent). The appropriate fractions, monitored by tlc on silica (eluent: $CHCl_3$-MeOH, 7:3), were pooled and taken to dryness to yield 180 mg of pure **2**. Ms *m/z* 270.0886 (M^+, 53%; for $C_{16}H_{14}O_4$ calcd. 270.0892), 268 (35%), 255 (79%), 254 (76%), 240 (88%), 239 (100%), 225 (98%); uv λ max (CH_3OH) 406 (ε=1,700), 385 (ε=2,300), 374 (ε=2,300), 363 (ε=2,250), 265 (ε=43,000); nmr δ (DMSO-d_6) 2.36 (3H, s), 3.87 (3H, s), 7.09 (1H, d, *J* 9.2 Hz), 7.55 (1H, s), 7.73 (1H, d, *J* 9.2 Hz), 8.26 (1H, s), 8.47 (1H, s), 9.36 and 9.40 (ca. 2H, exchangeable with D_2O).

FROM *L. IMPATIENS*.—From 60 specimens of *L. impatiens* (length ca. 10 cm each) following a similar procedure, 130 mg of **2** was isolated.

1,2,7-Triacetoxy-8-methoxy-6-methylanthracene (**3**).—A solution of **2** (170 mg) in Ac_2O (1 ml) and pyridine (2 drops) was heated for 1 h to reflux. Solvents were removed under vacuum and the residue was chromatographed on a silica gel column (1×70 cm; eluent: $CHCl_3$-MeOH, 99:1) to afford 170 mg of **3**; mp 147-149° [from EtOH; lit (1) mp 148-149°]; ms *m/z* M^+ 396; uv λ max 386 (ε=4,500), 366 (ε=5,400), 348 (ε=4,450), 334 (ε=2,750), 316 (ε=1,150), 260 (ε=173,500), 254 (s; ε=101,000); nmr δ ($CDCl_3$) 2.36 (3H, s), 2.37 (3H, bs), 2.44 (3H, s), 2.52 (3H, s), 4.02 (3H, s), 7.30 (1H, d, *J* 9.1 Hz), 7.62 (1H, s), 7.89 (1H, d, *J* 9.1 Hz), 8.35 (1H, s), 8.59 (1H, s).

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