

ACID-CATALYZED ISOMERIZATION OF HALLACHROME, THE RED PIGMENT OF THE MARINE WORM *HALLA PARTHENOPEIA*

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Hallachrome (**1**) (1), the red pigment of the sea-worm *Halla parthenopeia*, is a unique representative of naturally occurring 1,2-anthraquinones unsubstituted at positions 9 and 10. It is an acid-sensitive molecule, inasmuch as earlier extraction (2) of *H. parthenopeia* with HOAc afforded, instead of **1**, a violet

enches in the chemical shift values indicating the isomeric nature of **2**. On reductive acetylation, **2** gave a leucotriacetate (**3**) exhibiting an anthracene-type absorption spectrum.

To establish the substitution pattern of **2**, nOe difference ¹H-nmr spectra were recorded; the results (Table 2) indi-

TABLE 1. ¹H-nmr Data for Compounds **1**, **2**, and **4** (DMSO-*d*₆)

Proton	Chemical shift (multiplicity; <i>J</i> , Hz)		
	1	2	4
H-3	6.38 (d, 10.0)	7.56 (d, 9.1)	7.36 (d, 8.6)
H-4	7.75 (d, 10.0)	7.48 (d, 9.1)	7.30 (d, 8.6)
H-5	7.59 (s)	7.57 (s)	7.55 (s)
H-9	8.47 (s)	8.69 (s)	8.67 (s)
H-10	7.90 (s)	7.81 (s)	7.76 (s)
6-Me	2.36 (s)	1.97 (s)	1.96 (s)
OMe	3.87 (s)	3.94 (s)	—
OH	9.90 (s)	9.66 (s)	9.69 (s) and 10.0 (s)

pigment that was not further investigated.

We have now found that treatment of hallachrome (**1**) with HCl or BF₃ in MeOH affords a compound isomeric with **1** for which the 1-hydroxy-2-methoxy-6-methyl-7,8-anthraquinone structure (**2**) has been established. Compound **2**, collected as violet crystals insoluble in MeOH, was pure by tlc (EtOAc; CHCl₃-MeOH, 95:5) and has a molecular formula of C₁₆H₁₂O₄ established by hrms. Its ¹H-nmr spectrum (Table 1) contains the same signals found in the spectrum of **1**, the differ-

enced the 1-hydroxy-2-methoxy-6-methyl-7,8-anthraquinone structure for **2**.

The possibility of an intramolecular methyl shift leading from **1** to **2**, unlikely on structural grounds, was ruled

TABLE 2. Nuclear Overhauser Effects Measured on Compound **2** (DMSO-*d*₆; difference spectra)

Proton irradiated	Proton enhanced
7.56 (H-3)	3.94 (OCH ₃)
7.48 (H-4)	7.81 (H-10)
7.57 (H-5)	7.81 (H-10)
	1.97 (6-CH ₃)
1.97 (6-CH ₃)	7.57 (H-5)

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out by carrying out the reaction in EtOH; in this case, a mixture of two ethoxy derivatives (see below) resistant to several attempts at separation was obtained.

On the other hand, treatment of **1** in HCl containing dioxane afforded a non-methyl-derivative (**4**), collected as a precipitate after dilution of the reaction mixture with H₂O and shown to be pure by tlc (CHCl₃-MeOH, 9:1). The comparison of the ¹H nmr spectra of **4** with those of **1** and **2** (Table 1) indicated its structure as 1,2-dihydroxy-6-methyl-7,8-anthraquinone. Particularly diagnostic for this purpose was the chemical shift value of the 6-methyl group.

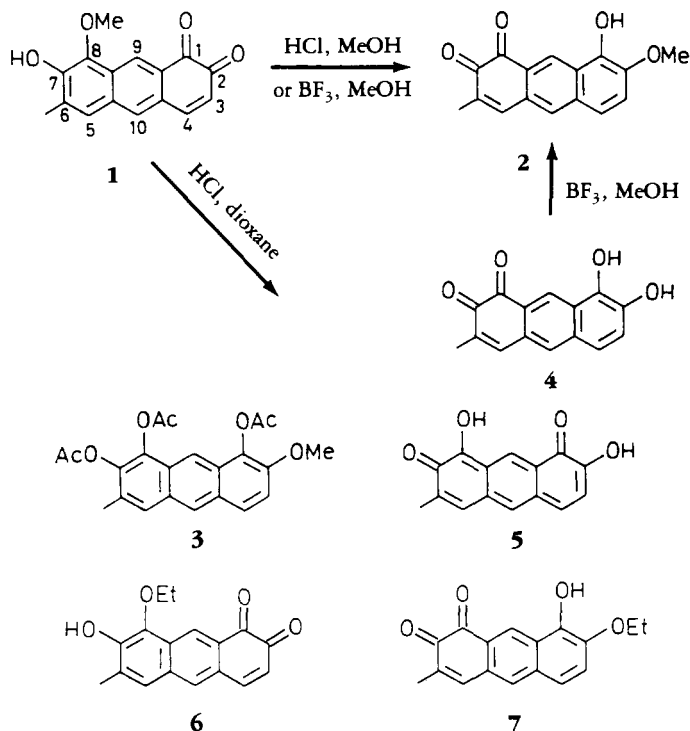
When **4** was dissolved in MeOH containing BF₃, **2** was obtained in good yield.

Thus, it appears that the conversion of **1** into **2** involves two stages: hydrolysis of **1** with formation of a non-derivative, which exists as the 7,8-anthraquinone **4**, and subsequent methylation affording the regio-isomer **2**. The methylation step could involve an extended quinone

(**5**), whose presence in the solution could account for the ease of methylation since **5** is a vinylogous carboxylic acid.

The reaction of **1** in EtOH deserves some comments. The product of this reaction was apparently homogeneous on tlc (EtOAc; CHCl₃-MeOH, 97:3), and its molecular ion in the mass spectrum (*m/z* 282) corresponded to an ethoxy derivative homologous to **1** or **2**. The ¹H-nmr spectrum (Experimental) showed signals attributable to a mixture of two ethoxy derivatives in an approximate ratio of 1:1, as judged by the relative intensity of the ethoxy signals. The comparison of the chemical shift values of the aromatic methyls and aromatic protons with those of **1** and **2** (Table 1) suggested that the EtOH/HCl treatment of **1** afforded a mixture of two products which should be formulated as **6** and **7**.

The difference in behavior in passing from MeOH to EtOH could be explained in different ways. One possible explanation is that when the reaction was carried out in MeOH, the product



precipitated from the solution, driving the equilibrium in the direction of **2**; on the other hand, when EtOH was used, the solubility properties of the products favor the setting up of an equilibrium between **6** and **7** through the intermediate **5**. Lack of material prevented a more detailed investigation of this reaction.

Apart from some work of Boldt (3, 4), knowledge of the 1,2-anthraquinone system is still limited since few compounds of this type are known.

EXPERIMENTAL

Mps was determined with a Kofler apparatus and are uncorrected. Uv spectra were obtained on a Perkin-Elmer 402 spectrometer. ¹H-nmr spectra were recorded on Bruker 500 and Bruker 270 instruments. Mass spectra were obtained on AEI MS-30 and MS-902 instruments.

1-HYDROXY-2-METHOXY-6-METHYL-7,8-ANTHRAQUINONE (2).—Hallachrome (**1**; 20 mg) was dissolved in MeOH (50 ml) and 6 N HCl (1 ml) was added under N₂. N₂ bubbling was maintained until the reaction product precipitated from the violet solution (*ca.* 1 h). Of **2**, 18 mg was collected by filtration, mp 226-229° (dec.). Ms *m/z* 268.0755 (M⁺; C₁₆H₁₂O₄ requires 268.0732) 240, 225 (base peak), 197, 169, 139. Uv λ max (CH₃OH) 540 (log ε 3.87), 327 (4.09), 309 (4.44), 300 (4.34), 259 (4.51); λ max (MeOH-NaOH) 710, 370, 312, 286; ¹H-nmr (Table 1).

Compound **2** was also prepared by dissolving 50 mg of **1** in 50 ml of BF₃/MeOH and collecting the precipitate by filtration (90% yield).

1,7,8-TRIACETOXY-6-METHYL-2-METHOXY-ANTHRACENE (3).—To a solution of **2** (26 mg) in Ac₂O (10 ml), zinc dust (300 mg) was added, and the mixture was heated on a water bath for 1 h. After addition of EtOAc, the mixture was filtered, washed with H₂O, and taken to dryness. The crude product (33 mg) was crystallized from 95% EtOH, mp 228-230°; ms *m/z* 396 (M⁺), 354, 312, 270 (base peak), 255; uv λ max (CH₃OH) 410, 389, 358, 339, 322, 262; ¹H

nmr δ (CDCl₃) 2.38 (6H, s), 2.49 (3H, s), 2.50 (3H, s), 4.03 (3H, s), 7.42 (1H, d, *J*=9.3 Hz), 7.73 (1H, s), 7.91 (1H, d, *J*=9.3 Hz), 8.17 (1H, s), 8.34 (1H, s).

1,2-DIHYDROXY-6-METHYL-7,8-ANTHRAQUINONE (4).—To a solution of **1** (60 mg) in dioxane (15 ml), 6 N HCl (7 ml) was added under N₂. After 30 min, the solution was cooled in ice, H₂O was added and the precipitate collected by filtration (66% yield). Mp 270° (dec.); ms *m/z* 254 (M⁺), 226, 197, 169, 139; uv λ max (CH₃OH) 570 (log ε 3.77), 332 (4.11), 316 (4.39), 265 (4.53); ¹H nmr (Table 1). Treatment of **4** with BF₃/MeOH as above afforded **2**.

TREATMENT OF HALLACHROME (1) WITH EtOH-HCl.—Hallachrome (**1**, 10 mg) was dissolved in 95% EtOH (20 ml), and 6 N HCl (0.5 ml) was added under N₂. N₂ bubbling was maintained for 1 h, and then the volume of the violet solution was reduced under vacuum. The solution was diluted with H₂O, extracted with EtOAc, and taken to dryness to afford a product apparently pure by tlc. Ms *m/z* 282 (M⁺), 254, 225 (base peak), 197, 170; ¹H nmr δ (DMSO-*d*₆) 1.39 (t), 1.43 (t), 1.97 (s), 2.37 (s), 4.05 (q), 4.19 (q), 6.38 (d), 7.45 (d), 7.53 (d), 7.57 (s), 7.60 (s), 7.76 (d), 7.80 (s), 7.90 (s), 8.48 (s), 8.69 (s).

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