

## Brief Communications

### The chemistry of naphthazarine derivatives

#### 5.\* The structure of dehydroechinochrome monohydrate

G. V. Malinovskaya, A. Ya. Chizhova, V. Ph. Anufriev,\* V. P. Glazunov, and V. A. Denisenko

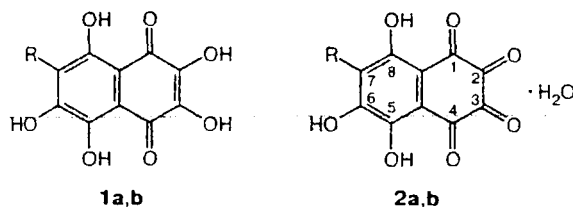
Pacific Institute of Bioorganic Chemistry, Russian Academy of Sciences,  
159 prosp. 100-letiya Vladivostoka, 690022 Vladivostok, Russian Federation.  
Fax: +7 (423 2) 31 4050. E-mail: anufriev@marine.su

Based on IR and  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectroscopic studies, the oxidation product of echinochrome with  $\text{Ag}_2\text{O}$  was assigned the structure of 2,3-epoxy-7-ethyl-2,3-dihydro-2,3,5,6,8-pentahydroxy-1,4-naphthoquinone.

**Key words:** echinochrome, 7-ethyl-2,3,6-trihydroxynaphthazarine, 7-ethyl-2,3,5,6,8-pentahydroxy-1,4-naphthoquinone, 2,3,6-trihydroxy-7-propylnaphthazarine, 2,3,5,6,8-pentahydroxy-7-propyl-1,4-naphthoquinone, dehydroechinochrome, 7-ethyl-2,3-dihydro-5,6,8-trihydroxy-2,3-dioxo-1,4-naphthoquinone, 2,3-epoxy-7-ethyl-2,3-dihydro-2,3,5,6,8-pentahydroxy-1,4-naphthoquinone, silver(I) oxide, oxidation.

It is known that di- and polycarbonyl vicinal compounds are prone to hydration, which is why they are often isolated in the form of *gem*-diols.<sup>2</sup> The study of the chemical properties of 2,3-dihydroxynaphthazarines (2,3,5,8-tetrahydroxy-1,4-naphthoquinones) showed<sup>3,4</sup> that echinochrome (7-ethyl-2,3,5,6,8-pentahydroxy-1,4-naphthoquinone, **1a**) is easily oxidized by such reagents as  $\text{HClO}$ ,  $\text{Ag}_2\text{O}$ , or  $\text{H}_2\text{O}_2$  in the presence of peroxidase to give a product that was assigned (from spectrophotometric measurements and some qualitative reactions) the structure of dehydroechinochrome or 7-ethyl-2,3-dihydro-5,6,8-trihydroxy-2,3-dioxo-1,4-naphthoquinone monohydrate (**2a**). However, these methods were not adequate to determine the exact structure of compound **2a**. The product that had been assigned structure **2a** was later obtained<sup>5</sup> by autooxidation of echinochrome (**1a**) in aqueous solutions at pH 7.2–7.4.

In recent years, echinochrome (**1a**) became the subject of extensive investigations<sup>6</sup> because of its use as a cardioprotector in clinical practice.<sup>7</sup> That is why a study of the mechanism of action of echinochrome and products of its metabolism (first of all, oxidation products) is of current interest.

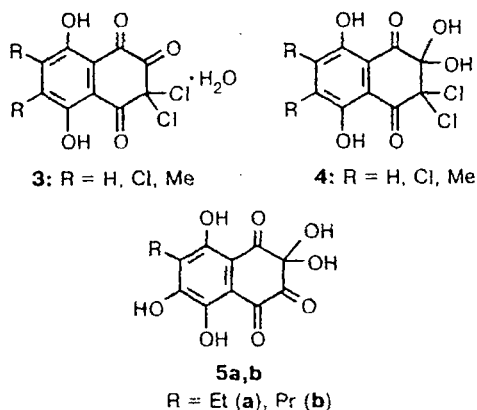


R = Et (**a**), Pr (**b**)

In the context of current works on the synthesis and study of the chemical properties of polyhydroxy-

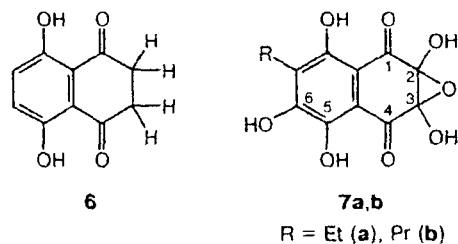
\*For part 4, see Ref. 1.

naphthazarines, in particular, their 2,3-dihydro-2-oxo derivatives, we reinvestigated the nature of echinochrome oxidation products. Recently, we showed<sup>7,8</sup> that 2,3-dihydro-2-oxonaphthazarine monohydrates of type 3 have the structure of *gem*-diols 4, which correlates well with their properties as  $\alpha$ -dicarbonyl compounds.<sup>2</sup> Taking into account that 2,3-dihydro-2-oxo- and 2,3-dihydro-2,3-dioxonaphthazarines are structurally similar, one can assume that an echinochrome oxidation product is *gem*-diol 5a (one of its possible isomers is shown).



To check this assumption, echinochrome 1a and its homolog 1b were oxidized with Ag<sub>2</sub>O under the conditions described earlier.<sup>4</sup> The pattern of the <sup>1</sup>H NMR spectra of the products does not rule out tentative structures of *gem*-diols 5a and 5b. Indeed, the signals for the  $\alpha$ -OH protons in the oxidation products are shifted upfield ( $\delta$  ~11.10 and 11.60) as compared to analogous signals for the starting 2,3-dihydroxynaphthazarines 1a<sup>9</sup> and 1b<sup>10</sup> ( $\delta$  12.10 and 12.30, respectively), which suggests that the compounds obtained have the 2,3-dihydronaphthazarine structure. In the range of signals for the *gem*-OH protons of diols of type 4 ( $\delta$  ~3.70 and ~5.30), their <sup>1</sup>H NMR spectra exhibit two broadened singlets (1 H each) at  $\delta$  4.46 and 4.53 and  $\delta$  4.35 and 4.43, respectively. However, a band at ~1750 cm<sup>-1</sup> in the medium-frequency range, which is due to absorption of the C=O group in position 2 and characteristic<sup>1</sup> of 2,3-dihydro-2-oxonaphthazarine derivatives of type 3, is absent in the IR spectra of the oxidation products. The C=O stretching vibrations manifest themselves as intense absorption bands at 1655 cm<sup>-1</sup>, suggesting that the oxidation products have the dihydronaphthazarine structure. Their integral intensity measured together with the intensity of bands of the C=C stretching vibrations (1601 and 1596 cm<sup>-1</sup>) amounts to  $(6.54 \pm 0.08) \cdot 10^4$  L mol<sup>-1</sup> cm<sup>-2</sup>, which coincides with that of dihydronaphthazarine 6. The <sup>13</sup>C NMR spectrum of the oxidation product exhibits signals only for two CO carbon atoms ( $\delta$  196.6 and 198.5), which is in full agreement with the IR spectroscopic data. In addition, this spectrum contains signals ( $\delta$  94.7 and 94.8) for two carbon atoms, each being bonded to two oxygen atoms.

Based on the data obtained, we assigned structures 7a and 7b to the oxidation products of echinochrome 1a and its homolog 1b, respectively.



It is interesting to note that in compounds 7a and 7b there is no marked intramolecular hydrogen bond between the hydroxy groups in positions 2 and 3 and the carbonyl groups at C(1) and C(4), respectively, and between the hydroxy groups in positions 5 and 6, which is evidenced by a shift of a band of the  $\beta$ -OH stretching vibrations upon replacement of weakly basic solvents by, e.g., CHCl<sub>3</sub> and CH<sub>2</sub>Cl<sub>2</sub> (see Experimental).

An analysis of the literature data<sup>3-5</sup> and our results suggests that epoxide 7a is one of the intermediates in the chain of transformations of echinochrome 1a under the action of oxidants, including oxygen, at physiological pH values of the medium.

## Experimental

Melting points were determined on a Boettius hot microstage and are uncorrected. IR spectra were recorded on a Specord M-82 spectrophotometer in dioxane and on a Vector-22 Fourier-spectrophotometer in CHCl<sub>3</sub> and CH<sub>2</sub>Cl<sub>2</sub>. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a Bruker WM-250 spectrometer (250.13 and 62.9 MHz, respectively) in CDCl<sub>3</sub>, acetone-d<sub>6</sub>, and CD<sub>3</sub>CN with Me<sub>4</sub>Si as the internal standard. Mass spectra were obtained with an LKB-9000S instrument (direct inlet, 70 eV). The starting compounds 1a and 1b were prepared according to the known procedure.<sup>10</sup>

**Oxidation of hydroxynaphthazarines 1a and 1b with silver(i) oxide.** Ag<sub>2</sub>O (350 mg, 1.5 mmol) was added to a solution of substrate 1a (1b) (0.5 mmol) in 150 mL of anhydrous diethyl ether. The reaction mixture was stirred at -20 °C for 2 to 3 h (the course of the reaction was monitored by TLC with a 1 : 1 hexane-acetone solvent system) and filtered. The filtrate was concentrated, and the precipitate that formed was filtered off and dried.

**2,3-Epoxy-7-ethyl-2,3-dihydro-2,3,5,6,8-pentahydroxy-1,4-naphthoquinone (7a)**, m.p. 168–170 °C (decomp.). IR (dioxane),  $\nu$ /cm<sup>-1</sup>: 3280 b (O—H); 1666 sh.s, 1655 v.s (C=O); 1601 s, 1596 s (C=C). IR (CHCl<sub>3</sub>),  $\nu$ /cm<sup>-1</sup>: 3520 m (O—H); 3165 w ( $\alpha$ -OH); 1662 sh.s, 1651 v.s (C=O); 1604 s, 1589 s (C=C). IR (CH<sub>2</sub>Cl<sub>2</sub>),  $\nu$ /cm<sup>-1</sup>: 3507 m (O—H); 3165 w ( $\alpha$ -OH); 1662 s, 1651 v.s (C=O); 1605 m, 1590 s (C=C). <sup>1</sup>H NMR (CDCl<sub>3</sub>),  $\delta$ : 1.20 (t, 3 H, CH<sub>3</sub>,  $J$  = 7.5 Hz); 2.80 (q, 2 H, CH<sub>2</sub>,  $J$  = 7.5 Hz); 4.46 (br.s, 1 H, OH); 4.53 (br.s, 1 H, OH); 6.77 (br.s, 1 H,  $\beta$ -OH); 11.08 (s, 1 H,  $\alpha$ -OH); 11.59 (s, 1 H,  $\alpha$ -OH). <sup>1</sup>H NMR (acetone-d<sub>6</sub>),  $\delta$ : 1.17 (t, 3 H, CH<sub>3</sub>,  $J$  = 7.5 Hz); 2.78 (q, 2 H, CH<sub>2</sub>,  $J$  = 7.5 Hz); 5.94 (br.s, 1 H, OH); 6.00 (br.s, 1 H, OH); 9.58 (br.s, 1 H,  $\beta$ -OH); 11.29 and 11.89 (both s, 1 H,  $\alpha$ -OH). <sup>13</sup>C NMR (acetone-d<sub>6</sub>),  $\delta$ : 12.9, 17.3.

94.7, 94.8, 105.6, 111.5, 127.3, 145.5, 152.8, 157.8, 196.6, 198.5. MS,  $m/z$  ( $I_{\text{rel}}$  (%)): 266 (92), 265 (100), 223 (52).

**2,3-Epoxy-2,3-dihydro-2,3,5,6,8-pentahydroxy-7-propyl-1,4-naphthoquinone (7b)**, m.p. 152–156 °C (decomp.). IR (dioxane),  $\nu/\text{cm}^{-1}$ : 3298 b (O–H); 1666 sh.s, 1656 v.s (C=O); 1602 s, 1598 s (C=C).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ),  $\delta$ : 0.99 (t, 3 H,  $\text{CH}_3$ ,  $J = 7.5$  Hz); 1.63 (m, 2 H,  $\text{CH}_2$ ); 2.77 (t, 2 H,  $\text{CH}_2$ ,  $J = 7.5$  Hz); 4.35 and 4.43 (both br.s, 1 H, OH); 6.59 (br.s, 1 H,  $\beta$ -OH); 11.09 and 11.60 (both s, 1 H,  $\alpha$ -OH).  $^1\text{H}$  NMR ( $\text{CD}_3\text{CN}$ ),  $\delta$ : 1.03 (t, 3 H,  $\text{CH}_3$ ,  $J = 7.5$  Hz); 1.64 (m, 2 H,  $\text{CH}_2$ ); 2.75 (t, 2 H,  $\text{CH}_2$ ,  $J = 7.5$  Hz); 5.07 (br.s, 2 H, 2 OH); 7.98 (br.s, 1 H,  $\beta$ -OH); 11.13 and 11.77 (both s, 1 H,  $\alpha$ -OH). MS,  $m/z$  ( $I_{\text{rel}}$  (%)): 280 (63), 279 (100), 252 (15), 251 (28), 250 (22), 224 (18), 223 (77), 222 (67).

This work was supported in part by the Russian Foundation for Basic Research (Project No. 96-15-97316).

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Received December 28, 1998;  
in revised form March 19, 1999

## Laser study of photooxidation of chloranyl-sensitized 1,2,3,4-tetrachlorodibenzo-*p*-dioxine

P. P. Levin,<sup>a\*</sup> V. A. Kuz'min,<sup>a</sup> N. A. Klyuev,<sup>b</sup> V. S. Soifer,<sup>b</sup> and A. V. Kuz'min<sup>a</sup>

<sup>a</sup>N. M. Emanuel' Institute of Biochemical Physics, Russian Academy of Sciences,  
4 ul. Kosygina, 117977 Moscow, Russian Federation.

Fax: +7 (095) 137 4101. E-mail: chembio@glas.apc.org

<sup>b</sup>A. N. Severtsov Institute of Problems of Ecology and Evolution, Russian Academy of Sciences,  
33 Leninsky prosp., 117071 Moscow, Russian Federation.

The kinetics of quenching of the triplet state of chloranyl (CA) by 1,2,3,4-tetrachlorodibenzo-*p*-dioxine (TCD) in benzene and acetonitrile was studied by nanosecond laser flash photolysis. The reaction proceeds via electron transfer (ET) with the rate constants of  $1.5 \cdot 10^9$  and  $3.7 \cdot 10^9$  L mol<sup>-1</sup> s<sup>-1</sup>, respectively. In benzene ET results in the formation of short-lived triplet radical ion pairs (lifetime 100 ns). In acetonitrile relatively long-lived (lifetime  $\geq 10$   $\mu$ s) radical anion CA<sup>•-</sup> and radical cation TCD<sup>•+</sup> are formed and decay due to bimolecular reactions in the bulk of the solvent accompanied by the consumption of TCD.

**Key words:** laser photolysis, *p*-chloranyl, 1,2,3,4-tetrachlorodibenzo-*p*-dioxine, electron transfer, radical ion, triplet radical ion pair.

Investigation of the kinetics and mechanism of photochemical reactions involving polychlorinated dibenzo-*p*-dioxines is urgent because of the high toxicity of these organic compounds formed as admixtures in several

important industrial processes.<sup>1,2</sup> Dye-sensitized photo-destruction of dioxines can be a promising method for their demolition because it allows one to perform the process under irradiation with visible light. In this work,

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 8, pp. 1610–1612, August, 1999.

1066-5285/99/4808-1589 \$22.00 © 1999 Kluwer Academic/Plenum Publishers