Anthraquinones Tautomerism: VII.* Hydroxy-Substituted Anthraquinones

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Abstract—Tautomerism of β-mono-, β,β'-dihydroxyanthraquinones, and their anions was studied for the first time by quantum-chemical and correlation methods. 2-Hydroxyanthraquinone exists exclusively in 9,10-quinoid form, and its ionization involves a tautomeric transformation into 10-oxido-2,9-anthraquinone. β,β'-Dihydroxy-anthraquinones can exist as the corresponding 9,10-, 2,9-, 2,6-, and 2,3-quinoid tautomers, and the most character-istic forms of their anions are 2,9-quinoid structures. The considerable difference in the known spectra of the same compound is due to the shifts of the tautomeric equilibria.

We used in our previous communications correlation and quantum-chemical methods for investigation of prototropic keto-enol tautomerism of α hydroxy-substituted anthraquinones [1–5], naphthoquinones, and naphthacenequinones [5] consisting in proton transfer in a chelate cycle.
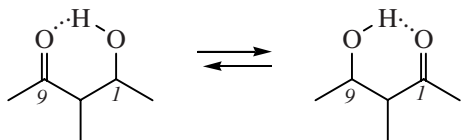

These studies established that α hydroxy-substituted quinones existed as equilibrium mixtures of isomers whose structure differed due to prototropic tautomerism and rotational isomerism. The variations in the structure of compounds (the number of benzene rings, the number and mutual position of hydroxy groups, the presence and position of other substituents) causes the shift of the mentioned equilibria that can result in considerable changes of their color. The considerable difference in the absorption spectra of the same or structurally related compounds measured by different researchers that could not be previously understood were due just to the shifts of these equilibria.

The general character of tautomeric and conformer equilibria has been demonstrated by their discovery already for a large number of hydroxyquinones. At the same time in each group of structurally related com-pounds these equilibria have certain special features.

* For Communication VI, see [1].

Consequently the study of tautomerism and rotational isomerism becomes one of the urgent problems in the quinones chemistry. The investigation of their effect on the chemical properties of compounds and the opportunities of equilibrium shift for the synthesis are yet ahead. Obviously the anthraquinones chemistry cannot develop exclusively like 9,10-anthraquinones chemistry. The same is valid for similar quinones.

For compounds containing a β-hydroxy group another tautomerism type is possible involving a proton transfer along a conjugation chain H–O–(CH=CH)$_4$–C=O from the hydroxy group in position *2* of the anthraquinone framework to the carbonyl in the position *10* [6, 7].
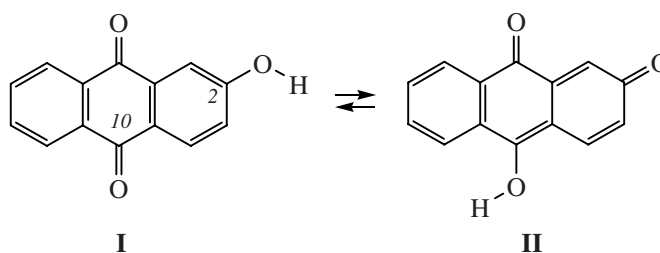
In this study the procedures we have developed are applied to the tautomerism investigation in β-hydroxy-substituted anthraquinones that yet is not understood. It is all the more important for the β-hydroxy groups are present in a large number of natural anthraquinones that found wide application in the composition of pharmaceuticals and physiologically active substances [8–10]. β Hydroxy-substituted derivatives are also

important as dyes, analytical reagents, indicators and in other applications [10].

π Electronic PPP method in Dewar version [11] applying variable β approximation [12] is still the only semiempirical quantum-chemical procedure that has been proved by many examples to be capable of adequate simulating the results of the structural transformations in hydroxyanthraquinones.

In the long-wave part of electronic spectra of β-hydroxy-substituted anthraquinones calculated by PPP method four bands may be distinguished containing a contribution from the intramolecular charge transfer [13, 14]: two π_l,π^*-bands, long-wave $\pi_l,\pi^*\alpha$ and short-wave $\pi_l,\pi^*\beta$, and also "hybrid bands" $\pi_l,\pi^*\alpha + \pi,\pi^*$ and $\pi_l,\pi^*\beta + \pi,\pi^*$ (Table 1). For the sake of simplicity in this table the values with zero or very low oscillator forces ($f < 0.08$) are omitted.

The calculation results show that the electron absorption spectra of β hydroxy-substituted anthraquinones possess qualitative distinctions depending on the symmetry of molecules. For instance, the spectra of symmetrical di- and tetrasubstituted 9,10- and 2,6-anthra-

quinones lacked the $,\pi^*\alpha$-band, and the most long-wave proved to be the $\pi_l,\pi^*\beta$-band. In the spectra of asymmetrical β substituted derivatives the $\pi_l,\pi^*\alpha$-band is the long-wave one. Thus the previously known difference in the spectra of 2,6- and 2,7-dihydroxy-9,10-anthraquinones originating from the symmetry of molecules [14] is a particular case of a more general rule.

The spectra of many β substituted anthraquinones are characterized by the presence of both π_l,π^*-bands (Table 1). The presence of many π_l,π^*-bands in the experimental spectra indicates the existence of tautomeri equilibria.

The calculated spectra of β hydroxy-substituted 2,6- and 2,3-anthraquinones unlike those of other tautomers contain weak absorption bands in the infrared region.

The assignment of π_l,π^*-bands to the tautomeric forms is carried out by comparison of the experimental and the calculated values. The criterion of correct assignment is not the maximum similarity but the linear correlation [15].

The correlation between experimental λ_{max} values with calculated λ_{calc} is expressed by two straight lines

Table 1. Results of calculation of β-hydroxyanthraquinones

Hydroxyanthraquinones	Absorption bands λ_{calc}, nm (f)			
	$\pi_l, \pi^*\alpha$	$\pi_l, \pi^*\beta$	$\pi_l, \pi^*\alpha + \pi, \pi^*$	$\pi_l, \pi^*\beta + \pi, \pi^*$
2-Hydroxy-9,10-	371 (0.170)	–	–	279 (0.383)
2,3-Dihydroxy-9,10-	420 (0.145)	–	309 (0.151)	287 (0.838)
2,6-Dihydroxy 9,10-	–	350 (0.359)	–	300 (0.430)
2,7-Dihydroxy-9,10-	380 (0.114)	343 (0.227)	–	297 (0.183)
2,3,6-Trihydroxy-9,10-	410 (0.083)	352 (0.089)	344 (0.236)	303 (0.230)
2,3,6,7-Tetrahydroxy-9,10-	–	357 (0.523)	–	–
10-Hydroxy-2,9-	473 (0.652)	–	327 (0.298)	305 (0.151)
3,10-Dihydroxy-2,9-	617 (0.352)	–	350 (0.557)	313 (0.175)
6,10-Dihydroxy-2,9-	463 (0.627)	372 (0.151)	326 (0.183)	315 (0.397)
7,10-Dihydroxy-2,9-	493 (0.664)	352 (0.194)	330 (0.128)	323 (0.282)
3,6,10-Trihydroxy-2,9-	594 (0.360)	386 (0.114)	–	328 (0.933)
6,7,10-Trihydroxy-2,9-	499 (0.558)	382 (0.149)	342 (0.349)	322 (0.306)
3,6,7,10-Tetrahydroxy-2,9-	617 (0.360)	394 (0.162)	–	344 (0.441)
9,10-Dihydroxy-2,6-	–	488 (1.006)	–	–
3,9,10-Trihydroxy-2,6-	504 (0.776)	–	352 (0.141)	–
3,7,9,10-Tetrahydroxy-2,6-	–	580 (0.590)	430 (0.095)	–
9,10-Dihydroxy-2,3-	457 (0.418)	453 (0.186)	–	–
6,9,10-Trihydroxy-2,3-	454 (0.515)	–	–	–
6,7,9,10-Tetrahydroxy-2,3-	–	442 (0.534)	–	–

(see the figure) corresponding to equations (1) and (2). On a separate line II points are located corresponding to 2,9-anthraquinoid tautomers of 2,3-dihydroxyanthraquinone and its anions.

$$\lambda_{max} = (0.922 \pm 0.013)\lambda_{calc} + (27 \pm 6) \text{ nm,} \qquad (1)$$

number of points N 17, correlation factor r 0.998, standard deviation s 3.3 nm.

$$\lambda_{max} = (0.916 \pm 0.083)\lambda_{calc} - (12 \pm 54) \text{ nm,} \qquad (2)$$
$$N\ 4,\ r\ 0.992,\ s\ 3.7 \text{ nm.}$$

This relationship made it possible to provide a classification of π_l,π^*-bands in the published electron absorption spectra (Table 2).

The experimental electron absorption spectra of 2- hydroxyanthraquinone recorded in different environment contained a single π_l,π^*-band [17, 24], whose position as a function of solvent character was described by Kamlet–Taft and Koppel–Palm equations [15]. This band should be assigned to the 9,10-quinoid tautomer. Equation (1) provides the opportunity to calculate the value of λ_{max} for tautomer of 10-hydroxy-2,9-anthraquinone, 463 nm. In none of many known spectra of 2 hydroxyanthraquinone [17, 24] this band was detected.
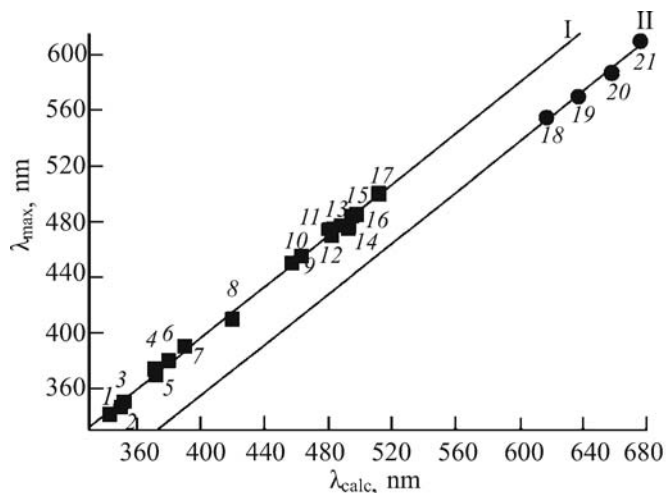
Correlation of experimental λ_{max} of mono- and dihydroxyanthraquinones and their anions with the corresponding values calculated by PPP method. (*1*) 2,7-(OH)$_2$-9,10- ($\pi_l,\pi^*\beta$); (*2*) 2,6-(OH)$_2$-9,10-; (*3*) 7,10-(OH)$_2$-2,9- ($\pi_l,\pi^*\beta$); (*4*) 6,10-(OH)$_2$-2,9- ($\pi_l,\pi^*\beta$); (*5*) 2-OH-9,10-; (*6*) 2,7-(OH)$_2$-9,10- ($\pi_l,\pi^*\alpha$); (*7*) 2,7-O$^-_2$-9,10-; (*8*) 2,3-(OH)$_2$-9,10-; (*9*) 9,10-(OH)$_2$-2,3-; (*10*) 6,10-(OH)$_2$-2,9- ($\pi_l,\pi^*\alpha$); (*11*) 6,10-O$^-_2$-2,9-; (*12*) 6-OH-10-O$^-$-2,9-; (*13*) 9,10-(OH)$_2$-2,6-; (*14*) 7,10-(OH)$_2$-2,9- ($\pi_l,\pi^*\alpha$); (*15*) 10-O$^-$-2,9-; (*16*) 9,10-O$^-_2$-2,6-; (*17*) 7,10-O$^-_2$-2,9-; (*18*) 3,10-(OH)$_2$-2,9-; (*19*) 3-OH-10-O$^-$-2,9-; (*20*) 10-OH-3-O$^-$-2,9-; (*21*) 3,10-O$^-_2$-2,9-anthraquinones.

In the spectra of its anion also appeared a single π_l,π^*-band. All the known λ_{max} values of 2-oxidoanthraquinone require assignment to 10-oxido-2,9-anthraquinone. Proceeding from the value λ_{calc} 390 nm obtained by PPP method for 2-oxido-9,10-anthraquinone we calculated by equation (1) λ_{max} for this compound of 386 nm. In none of experimental spectra of 2-hydroxyanthraquinone in alkaline media this band was observed.

Thus unlike 1-hydroxyanthraquinone [3] the tautomerism is not characteristic of these compounds, but the ionization of 2 hydroxy-9,10-anthraquinone always is accompanied by a tautomeric transformation.

Each of tautomers of the asymmetrical 2,7-dihydroxyanthraquinone is characterized by two π_l,π^*-bands of different intensity: in the spectrum of 9,10-quinoid tautomer the short-wave $\pi_l,\pi^*\beta$-band is twice as strong as the long-wave $\pi_l,\pi^*\alpha$-band, and in its 2,9-quinoid tautomer, on the contrary, the $\pi_l,\pi^*\alpha$-band nearly 3.5 times more intensive than the $\pi_l,\pi^*\beta$-band (Table 1). Each of their anions is also characterized by two π_l,π^*-bands.

2,6- and 2,7-dihydroxyanthraquinones differ in symmetry and in possible tautomerism, and therefore their experimental absorption spectra are quite dissimilar [14]. 2,6-Dihydroxy-anthraquinone can exist in three tautomeric forms: 9,10- (**I**), 2,9- (**II**), and 2,6-anthraquinones (**III**), and 2,7 dihydroxyanthraquinone , only in two former ones.

In the absorption spectra of symmetrical 2,6-dihydroxy-9,10- and 9,10-dihydroxy-2,6-anthraquinones and their dianions appeared the only $\pi_l,\pi^*\beta$-band, and in the spectra of asymmetrical 6,10-dihydroxy-2,9-anthraquinone and its anions, both π_l,π^*-bands.

III   **IV**
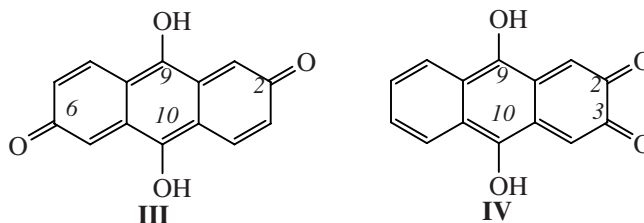
The known absorption spectra of 2,6- and 2,7-dihydroxy-anthraquinones in alkaline media show that the anions of the former exist in 2,9- and 2,6-, but not in 9,10-quinoid forms, whereas the anions of the latter compound are present in both 9,10- and 2,9-tautomeric forms (Table 2). For 6-hydroxy-10-oxido-2,9-anthraquinone of two π_l,π^*-band was found only $\pi_l,\pi^*\alpha$-band at 470 nm, but in the majority of reports mentioned in

Table 2. Classification of π_l,π^* absorption bands in the electronic spectra of β-hydroxy-substituted anthraquinones and their anions

Substituted anthra-quinones	Solvent	9,10-AQ[a]			2,9-AQ[a]						2,3-AQ[a]	2,6-AQ[a]		Refer-ences
		$\pi_l,\pi^*\beta$		$\pi_l,\pi^*\alpha$	$\pi_l,\pi^*\beta$		$\pi_l,\pi^*\alpha$				$\pi_l,\pi^*\alpha$	$\pi_l,\pi^*\beta$		
		OH	O⁻	OH	OH	O⁻	OH	OH, O⁻[b]	O⁻, OH[c]	O⁻	OH	OH	O⁻	
2-X[d]	Calculation by PPP			371			473			495				
Hydroxy-	Ethanol			374										[14]
Anion	Ethanol alkaline									484				[16]
2,6-X₂[d]	Calculation by PPP	350	362		372	483	463	463	482	480		488	498	
Dihydroxy-	Ethanol	346			370		455 п					477		[17], [18]
Monoanion	Water, pH 12.74								470					[18]
Dianion	Aqueous NaOH 1 N									475				[18]
Dianion	Aqueous NaOH concn.												485	[18]
2,7-X₂[d]	Calculation by PPP	343	390	380	352	359	493	502	506	512				
Dihydroxy-	Ethanol	341		380	350									[17]
Dihydroxy-	Water						475							[18]
Dianion	Water alkaline		390							500				[18]
2,3-X₂[d]	Calculation by PPP			420			617	658	637	676	457			
Dihydroxy-	Ethanol			410										[19]
Dihydroxy-	Ethanol			410			555							[17]
Dihydroxy-	Ethanol 16%, pH 1.0										450			[20]
Monoanion	Ethanol aqueous, pH <14						570							[20]
Mono-+dianion	Ethanol 16%, pH 13.2						578			618				[21]
Mono-+dianion	Aqueous NaOH, diluted								587	620				[20]
Dianion	Aqueous alkali, 4%									610				[22]
Dianion	Ethanol 50%, strongly alkaline									610				[23]

[a] AQ – anthraquinone.
[b] β-Oxido-substituted.
[c] *meso*-Oxido-substituted.
[d] X = OH or O⁻.

[18] only the most long-wave band was measured. The correlation by equation (1) permitted the prediction of this $\pi_l,\pi^*\beta$-band position for the anion (366 nm).

The published absorption spectra of 2,3-dihydroxy-anthraquinone [17, 20] essentially differ both in the number and the position of π_l,π^*-bands (Table 2). This fact may be understood only from the viewpoint of the existence of tautomeric equilibria. The known π_l,π^*-bands should be assigned to all three possible tautomers of the compound, including seemingly hardly possible 9,10-dihydroxy-2,3-anthraquinone (**IV**) (Table 2).

The anions of 2,3-dihydroxyanthraquinone were found to exist only in 2,9 quinoid form, and therewith in the same solution could be present anions of different degree of ionization. 2 Hydroxy-3-oxido-9,10-anthra-quinone stabilized by an intramolecular hydrogen bond O–H···O⁻ might exist, but 2,3-dioxido-9,10-anthra-quinone is energetically unfavorable due to two contiguous negatively charged oxido groups.

The performed assignments of π_l,π^*-bands in the known absorption spectra of anions made it possible to establish the ionization sequence of the hydroxy groups in the isomeric disubstituted 2,9-anthraquinones. In the 6,10-dihydroxy-2,9-anthraquinone first the *meso*-hydroxy group underwent ionization, in the 3,10-di-hydroxy-substituted substance each of the monoanions was found, and in the 7,10 dihydroxy-2,9-anthraquinone both hydroxy groups equally readily suffered ionization.

The complex of 2,3-dihydroxyanthraquinone with indium(III) formed in a neutral environment in the presence of boric acid [25] is the only reported complex of β,β' dihydroxyanthraquinones [14]. Evidently it

should possess 2,9 quinoid structure for it is the only one fitting to the requirement of contiguous 2-carbonyl and 3-hydroxy groups necessary for the complex formation. At the same time the measured λ_{max} value 530 nm of this complex [25] disagrees with the λ_{max} values known for the tautomeric 2,3-dihydroxy-anthraquinones and their anions (Table 2), neither it resembles any λ_{calc} value obtained for these compounds. The reason of this deviation is yet unclear, and the 2,3-dihydroxyanthraquinone complexes require further investigation.

The assignments performed were confirmed by a number of independent correlations, for instance, by proportional response to the tautomerization of 2 mono- and 2,6-disubstituted [equation (3)], 2,6- and 2,7-di-substituted [equation (4)], 2,3- and 2,6-disubstituted anthraquinones [equation (5)], 2,6-dihydroxyanthra-quinone and its anions [equation (6)].

$$\lambda_{max}(2,6-) = (0.970 \pm 0.040)\lambda_{max}(2-) + (7 \pm 18) \text{ nm,} \quad (3)$$
$$N\ 3,\ r\ 0.9992,\ s\ 3.5 \text{ nm.}$$

$$\lambda_{max}(2,7-) = (0.912 \pm 0.030)\lambda_{max}(2,6-) + (64 \pm 12) \text{ nm,}$$
$$N\ 4,\ r\ 0.9989,\ s\ 3.4 \text{ nm.} \quad (4)$$

$$\lambda_{max}(2,3-) = (1.305 \pm 0.034)\lambda_{max}(2,6-) - (41 \pm 15) \text{ nm,}$$
$$N\ 3,\ r\ 0.9997,\ s\ 3.3 \text{ nm.} \quad (5)$$

$$\lambda_{max}(O^-) = (0.988 \pm 0.049)\lambda_{max}(OH) + (17 \pm 21) \text{ nm,} \quad (6)$$
$$N\ 3,\ r\ 0.9988,\ s\ 4.8 \text{ nm.}$$

Regularity confirmed by a large number of examples and very high r values show the nonrandom character of these relations, notwithstanding the actually minimal number of points.

2,3,6-Tri- and 2,3,6,7-tetrahydroxyanthraquinones are yet unknown. The calculations by PPP method demonstrated that the effect on the successive ionization of hydroxy groups on the position of π_l, π^*-bands can be described by the linear dependence on the number n of oxido groups, for instance, for the 2,3,6,7-tetrahydroxy-9,10-anthraquinone in keeping with equation (7).

$$\lambda_{calc} = (5.125 \pm 0.124)n + (357.1 \pm 0.3) \text{ nm,} \quad (7)$$
$$N\ 14,\ r\ 0.997,\ s\ 0.5 \text{ nm.}$$

Among the isomeric anions the only point deviat-ing from this linear dependence belongs to 2,3-dihy-droxy-6,7-dioxido-9,10-anthraquinone. It is energetical-ly unfavorable due to two contiguous negatively charg-ed oxido groups, and its actual existence is hardly probable.

Thus in this study was demonstrated for the first time that tautomeric transformations are characteristic not only of α-, but also of β hydroxyanthraquinones and their anions. Just the tautomerism is the reason of essential distinctions in the absorption spectra of the same compound measured by different researchers. The ionization and variation of solvent character generate the shifts of tautomeric equilibria. The traditional concept of the 9,10-quinoid structure of β-hydroxy-substituted anthraquinones anions is wrong, thir most characteristic forms are 2,9-quinoid ones.

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