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# TAUTOMERIC AND CONFORMATIONAL ISOMERISM OF NATURAL HYDROXYANTHRAQUINONES

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*Natural 1,5-di-, 1,4,5-tri-, and 1,4,5,8-tetrahydroxyanthraquinones and their anions and metal complexes were shown to be equilibrium mixtures of tautomers and conformers using quantum-chemical and correlation analysis of elecronic absorption spectra. Solvent effects, ionization, complexation, and the introduction and substitution of substituents were accompanied by shifts of tautomeric and conformational equilibria that determine the color of the compounds.*

**Key words:** natural anthraquinones, 1,5-dihydroxyanthraquinone, 1,4,5-trihydroxyanthraquinone, 1,4,5,8-tetrahydroxy-2-methylanthraquinone, anthrarufin, ziganein, morindaparvin B, islandicin, digitopurpone, helminthosporin, erythroglaucin, xanthorin, isoxanthorin, cinnarubin, ventione A, cinodontin, electronic absorption spectra, quantum-chemical calculation, substituent $\sigma^A$-constants, correlation analysis, prototropic tautomerism, conformational isomerism, conformers, ionization, metal complexes.

We demonstrated in our previous reports [1, 2] using substituted 1,8-dihydroxyanthraquinones as examples that the chemistry of natural anthraquinones [3, 4] deviates from the traditional bounds of exclusively 9,10-quinonid structures, which cannot explain several known facts. These concepts hindered further development of this most important branch of knowledge and needed to be re-examined.

The structures of each of the hydroxyanthraquinones and their anions cannot be expressed by a single structural formula. They exist as mixtures of tautomers in dynamic equilibrium with each other. Depending on the external conditions, each compound can exist as several different mixtures of different tautomers, each of which has a single $\pi_l,\pi^*$ absorption band. Therefore, the electronic absorption spectra characterize this mixture and indicate in which tautomeric forms the compound exists under the given conditions.

These concepts first explained why the experimental absorption spectra have a complicated multi-band $\pi_l,\pi^*$ absorption whereas quantum-chemical calculations indicate the existence for each hydroxyanthraquinone of a single $\pi_l,\pi^*$ band and why the absorption spectra of the same compound measured by different researchers in the same solvents can differ substantially.

Hydroxyanthraquinones are widely distributed in nature and are used extensively in medicinal and biologically active preparations and as natural dyes [3-5]. Therefore, the study of their tautomerism is becoming an important scientific problem.

The methodology developed by us was based on a linear correlation of experimental spectrophotometric data and parameters calculated by a quantum-chemical method [6, 7], a good instrument for studying tautomerism of organic compounds. Until now the Dewar version [8] of the PPP $\pi$-electron method using an approximation in which $\beta$ is varied [9] has been the single semi-empirical quantum-chemical method for which the ability to model adequately the results of structural changes in hydroxyanthraquinones using several examples has been established.

Furthermore, the experimental $\lambda_{max}$ that characterize the $\pi_l,\pi^*$ absorption bands correlate poorly in several instances with $\lambda_{calc}$ calculated for the possible tautomers [10]. The number of $\pi_l,\pi^*$ bands for certain compounds exceeds the number of possible tautomers. The reason for this is the ability of hydroxyanthraquinones not only to tautomerize but also to change conformation to form conformers in which one or several hydroxyls are located *trans* to the carbonyl, as a result of which the intramolecular H-bonds (IHB) C=O···H–O are broken [10]. An example is cinodontin, natural 1,4,5,8-tetrahydroxyanthraquinone, to which structure **1** is assigned [3, 4, 11].

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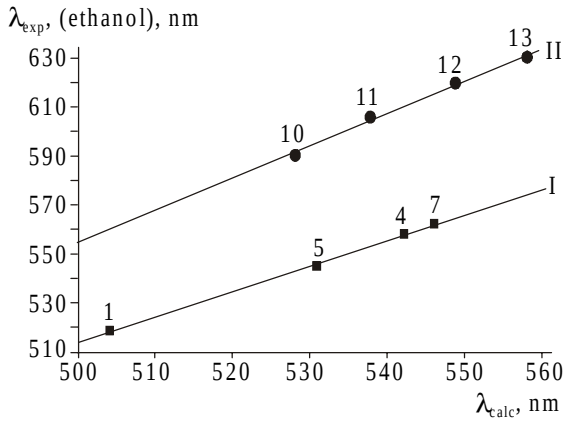



Fig. 1

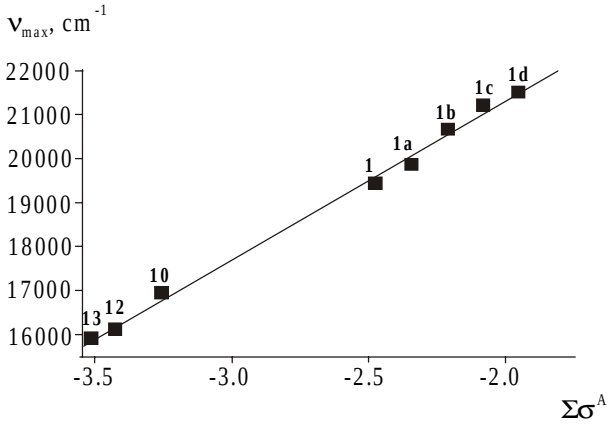
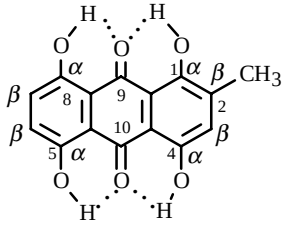



Fig. 2

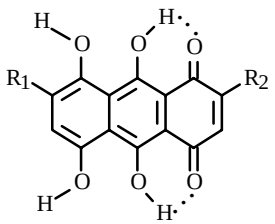
Fig. 1. Correlation of experimental $\lambda_{max}$ for cinodontin (I) and its anions and metal complexes (II) with PPP calculations. Numbering of compounds corresponds to that given in the text.

Fig. 2. Correlation of experimental $\nu_{max}$ for cinodontin and its anions and metal complexes with the sum of $\sigma^A$ constants for hydroxy and oxido groups: 1,4,5-$(OH^*)_3$-8-OH-2-$CH_3$-9,10- (1a), 1,4-$OH^*)_2$-5,8-$(OH)_2$-2-$CH_3$-9,10- (1b), 1-$OH^*$-4,5,8-$(OH)_3$-2-$CH_3$-9,10- (1c), 1,4,5,8-$(OH)_4$-2-$CH_3$-9,10-anthraquinones (1d). Numbering of the other compounds corresponds to that given in the text.

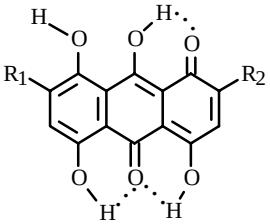


**1**

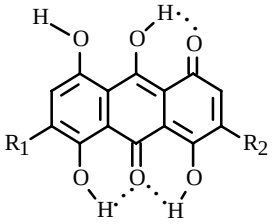
Tautomeric transformations can produce 1,4- (**2**, **3**), 1,10- (**4**-**7**), and 1,5-quinones (**8**, **9**).



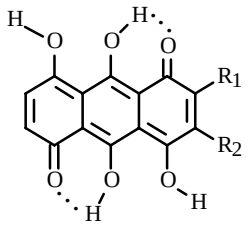
**2, 3**



**4, 7**



**5, 6**



**8, 9**

**3**, **6** - **8**: $R_1 = CH_3$, $R_2 = H$; **2**, **4**, **5**, **9**: $R_1 = H$, $R_2 = CH_3$

Each of these structures is characterized by its own $\pi_l,\pi^*$ band. The experimental $\pi_l,\pi^*$ bands were assigned to the tautomeric structures by correlation with the values calculated by a quantum-chemical method. A criterion for the correctness of the assignment was not the very close similarity of the values but their linear correlation [12].

The reported values for the $\pi_l,\pi^*$ absorption of cinodontin in alcohols vary significantly even for the number of $\pi_l,\pi^*$ bands: 562 nm [11]; 518, 545, and 558 [13]; 471sh, 483, 503sh, 514, 539, and 552 nm [3] in ethanol and 465, 471, 484, 504, 515, 539, and 553 nm in methanol [14] (sh = shoulder). Traditional concepts of the exclusively 9,10-quinoid structure cannot explain these differences.

Correlations of the $\lambda_{max}$ values with the corresponding $\lambda_{calc}$ enabled four of the eight bands to be assigned to 9,10- and 1,10-quinoid tautomers (**1**, **4**, **5**, **7**) [line 1 in Fig. 1, eq. (1)]:

$$\lambda_{max}\ (\text{ethanol}) = (1.049\pm0.025)\lambda_{calc} - (11.2\pm13.5)\ \text{nm} \quad (1)$$

The number of forms N = 4; correlation coefficient r = 0.9994; standard deviation SD = 0.8 nm.

Because the number of experimental $\pi_l,\pi^*$ bands exceeds those assigned to the tautomers, not only tautomeric but also conformational equilibria must be characteristic of cinodontin. The $\pi_l,\pi^*$ bands were assigned to the corresponding conformers based on the correlation of the $\nu_{max}$ values with the sums of the $\sigma^A$ constants for free (OH) and bound ($OH^*$) hydroxyls and oxido groups ($O^-$) calculated for the $\alpha$- and *meso*-positions of each tautomeric anthraquinone [10]. This function [Fig. 2, Eq. (2)] showed that all known forms of cinodontin have exclusively the 9,10- and 1,10-quinoid structures. The absorption spectra did not exhibit 1,4- and 1,5-quinoid structures.

$$\nu_{max} = (3612.5\pm102.4)\Sigma\sigma^A + (28573\pm279)\ cm^{-1} \quad (2)$$

N = 8, r = 0.998, SD = 172 $cm^{-1}$.

Four short-wavelength $\pi_l,\pi^*$ bands that could not be assigned using Eq. (1) belong to conformational isomers (**1a-d**) of the 9,10-quinoid tautomer (**1**) that contain various numbers of IHB (Fig. 2).

The assignments of the $\pi_l,\pi^*$ bands to the corresponding forms was confirmed by several independent correlations. For example, $\lambda_{max}$ values of the conformers (**1a-d**) are linear functions of the number (*n*) of IHB [Eq. (3)]:

$$\lambda_{max} = (13.30\pm1.29)n + (461\pm3)\ nm \quad (3)$$

N = 5, r = 0.990, SD = 4 nm.

The $\lambda_{max}$ values of cinodontin and 1,4,5,8-tetrahydroxyanthraquinone [13] that belong to unique forms are related linearly to each other [Eq. (4)]:

$$\lambda_{max}\ (cinodontin) = (0.977\pm0.012)\lambda_{max}(1,4,5,8) + (5.3\pm6.0)\ nm \quad (4)$$

N = 6, r = 0.9997, SD = 0.8 nm.

According to generally accepted concepts [3, 11], $\beta$-hydroxyls not bound through IHB are ionized by the action of sodium acetate on hydroxyanthraquinones whereas sodium ethoxide ionizes both $\beta$- and $\alpha$-hydroxyls. This difference was used to establish the position of hydroxyls in the anthraquinone core. Thus, cinodontin, which contains only $\alpha$-hydroxyls, should be ionized by sodium ethoxide and not by sodium acetate. However, the effects of these ionizing reagents on cinodontin does not follow this scheme. Addition of sodium acetate to a solution of cinodontin in ethanol deepens the color considerably (to 620 nm), even more than adding sodium ethoxide (to 590 nm) [11].

This fact cannot be explained by the traditional concepts of the exclusively 9,10-quinone structure for cinodontin and its anions. Furthermore, it is direct proof of the existence of tautomeric transformations and indicates that $\alpha$-hydroxyls not bound by IHB are present. Figure 1 shows that the 620 nm band should be assigned to 4,5,9-trihydroxy-2-methyl-8-oxido-1,10-anthraquinone (**12**), i.e., sodium acetate ionizes the single free 8-hydroxyl of the 1,10-quinoid tautomer (**4**). The 590 nm band belongs to 1,4-dihydroxy-2-methyl-5,8-dioxido-9,10-anthraquinone (**10**), i.e., sodium ethoxide ionizes the two hydroxyls of the 9,10-quinoid tautomer (**1**) that are bound by IHB to two different carbonyls. The $\lambda_{calc}$ (528 nm) of **10** differs markedly from the corresponding values for the three other isomeric dianions of tautomer **1** (523-524 nm). This enabled the structure of the resulting dianion to be confidently determined. The difference in the structures of the tautomeric anions is also a reason for the anomalous action of the two ionizing reagents on cinodontin.

Additions of complexing metal salts are also used in the chemistry of natural anthraquinones to determine the position of the hydroxyls in the anthraquinone core. It is commonly thought [3, 11] that $\alpha$-hydroxyls form metal complexes. This produces a bathochromic shift of the long-wavelength absorption band. The lack of a bathochromic shift indicates that the compound contains only $\beta$-hydroxyls. Furthermore, we found [15] that the formation of complexes of hydroxyanthraquinones with metals does not in and of itself lead to a bathochromic shift. Complexation is very often accompanied by tautomeric transformations that are the reason for the deepening of the color of the compounds [16, 17].

The correlation of the experimental $\lambda_{max}$ measured for an ethanol solution of cinodontin in alkaline medium or containing added complexing metal salts [11] with $\lambda_{calc}$ for cinodontin anions [line II in Fig. 1, Eq. (5)] enabled the structures of the corresponding metal complexes to be established:

$$\lambda_{max} = (1.328\pm0.074)\lambda_{calc} - (110.2\pm40.4)\ nm \quad (5)$$

N = 4, r = 0.997, SD = 1.7 nm.

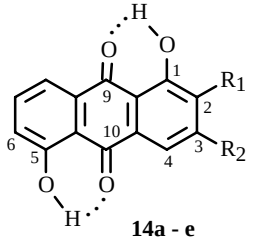
The addition of an Al(III) salt leads to the formation of a complex with $\lambda_{max}$ 630 nm in which the ligand has the structure 4,5,8-trihydroxy-6-methyl-9-oxido-1,10-anthraquinone (**13**). In the complex with Mg(II) (606 nm), cinodontin has the 4,8,9-trihydroxy-3-methyl-5-oxido-1,10-anthraquinone structure (**11**). The $\pi_l,\pi^*$ band (562 nm) does not shift in the presence of a Mg(II) salt and HCl, which indicates that Mg(II) forms a complex with the nonionized tautomer (**7**).

The methodology proposed by us enabled features of the tautomeric and conformational structures of the various groups of hydroxyanthraquinones to be established.

TABLE 1. Solvent Effects on Position of $\pi_l,\pi^*$ Bands of Anthrarufin

| Solvent | Assignment of $\pi_l,\pi^*$ bands to tautomers and conformers, nm | | | |
|---|---|---|---|---|
| | 1-OH*-5-OH-9,10 | 1,5-$(OH^*)_2$-9,10 | 5,9-$(OH)_2$-1,10 | 5-OH-9-OH*-1,10 |
| Acetone | 402 | | 418 | 432 |
| Benzene | 402 | | 422 | 437 |
| Hexane | 400 | 415 | | 433 |
| DMSO | | | 420 | |
| DMF | | 417 | | |
| Dichloromethane | | | | 428 |
| Methanol | 400 | 415 | | 430 |
| Pyridine | 405 | | 423 | 435 |
| Chloroform | 401 | | 420 | 435 |
| $CCl_4$ | 400 | 418 | | 435 |
| Ethylacetate | | 416.5 | | |
| Ethanol | 400 | 416 | | 431 |
| Ether | 400 | 415 | | 433 |

The most well known compounds of the natural 1,5-dihydroxyanthraquinones (**14**) are the following:



**14a - e**

**14a:** $R_1 = R_2 = H$; **14b:** $R_1 = CH_3$, $R_2 = H$; **14c:** $R_1 = CH_2OH$, $R_2 = H$;
**14d:** $R_1 = H$, $R_2 = CH_3$; **14e:** $R_1 = H$, $R_2 = CH_2OH$

The absorption spectra of anthrarufin (**14a**) measured in ethanol exhibit three $\pi_l,\pi^*$ bands at 400, 416, and 431 nm [13]. Three tautomers are theoretically possible for anthrafurin, 9,10- (**14**), 1,10- (**15**), and 1,5-anthraquinones (**17**). Unsymmetrically substituted 1,10-anthraquinone (**15**) can exist as two tautomers, e.g., 2-*R*-1,10- (**15**) and 6-*R*-1,10-anthraquinones (**16**). Conformers in which one or both hydroxyls are *trans* to the carbonyl can exist for each tautomer.

The correlation of the $\nu_{max}$ values of **14a** and its anions with the sums of the $\sigma^A$ constants for hydroxy and oxido groups [Eq. (6)] indicates that 9,10-1,10 tautomerism is typical of them but not 1,10-1,5 quinoid tautomerism:

$$\nu_{max} = (6243\pm54)\Sigma\sigma^A + (31859\pm97)\ cm^{-1} \quad (6)$$

N = 11, r = 0.9997, SD = 62 $cm^{-1}$.

Solvent effects shift the tautomeric and conformational equilibria. Therefore, the number and position of the experimental $\pi_l,\pi^*$ bands depends on which of the possible forms anthrarufin adopts under these conditions (Table 1).

The assignments of the bands were confirmed by correlation using Eq. (7) (Table 2):

$$\lambda_{max} = \lambda_{max}(0) - k\Sigma\sigma^A\ nm \quad (7)$$

Here $\lambda_{max}(0) = \lambda_{max}$ for $\Sigma\sigma^a = 0$ and k is the sensitivity of anthrarufin to tautomeric and conformational transformations in this solvent.

The correlation revealed several nonobvious and previously unknown features of the structure of anthrarufin and its anions. 1,5-Dihydroxy-9,10-anthraquinone (**14a**) can exist as two conformers with two and one bound $OH^*$ groups. The $\pi_l,\pi^*$ band at 381 nm that corresponds to the conformer containing two free OH groups was not observed in any of numerous known spectra of anthrarufin in various solvents [13, 18]. The 1,10-quinoid tautomer **15** is known as conformers containing one or two free OH groups. Tautomer **15** with two bound hydroxyls was not observed (Table 1).

TABLE 2. Correlation Parameters of Eq. (7)

| Solvent | r | s, nm | -k | $\lambda_0$, nm |
|---|---|---|---|---|
| Acetone | 0.9990 | 0.9 | 106.76±4.68 | 283.2±5.9 |
| Benzene | 1.00000 | 0.0 | 125.0±0.00 | 263.3±0.0 |
| Hexane | 0.99994 | 0.3 | 117.9±1.3 | 269.0±1.7 |
| Methanol | 0.9992 | 0.9 | 106.96±4.41 | 281.7±5.5 |
| Pyridine | 0.9995 | 0.7 | 107.43±3.51 | 286.0±4.4 |
| $CCl_4$ | 0.998 | 1.6 | 124.32±8.19 | 261.4±10.3 |
| Chloroform | 0.99990 | 0.3 | 121.28±1.76 | 266.3±2.2 |
| Ethanol | 0.998 | 1.3 | 110.44±6.61 | 278.0±8.3 |
| Diethylether | 0.99994 | 0.3 | 117.92±1.32 | 269.0±1.7 |

Ionization of anthrarufin in alkali media also leads to shifts of tautomeric and conformational equilibria. The majority of the resulting anions have the 1,10-quinoid structure. Conformers of monoanions with free OH groups are known only for the 1,10- and not the 9,10-quinoid tautomer.

Considering the traditional concepts of exclusively 9,10-quinoid structures for substituted anthrarufin, the contradiction of the known data about their absorption spectra cannot be explained. For example, it is not clear why the spectrum of ziganein (**14d**) in ethanol that was measured by Imre et al. [19] contains a single $\pi_l,\pi^*$ band at 433 nm whereas that of Kazmi et al. [20] has three $\pi_l,\pi^*$ bands at 400, 430, and 470 nm whereas the spectrum of $\omega$-hydroxyziganein (**14e**) in methanol has two $\pi_l,\pi^*$ bands at 418 and 428 nm [21]. It is also not clear why the spectrum of **14b** in ethanol according to some [22] contains one $\pi_l,\pi^*$ band at 436 nm and to others [23], three (396, 420, 442 nm) whereas the spectrum of morindaparvin B (**14c**) has two (420 and 430 nm) [23].

These differences are explained by correlations with the sum of the $\sigma^A$ constants of the hydroxy and oxido groups. Equation (8) enabled the three $\pi_l,\pi^*$ bands of ziganein (**14d**) to be assigned to 1,5-$(OH)_2$-3-methyl-9,10-, 5-OH-9-$OH^*$-3-methyl-1,10-, and 9,10-$(OH^*)_2$-3-methyl-1,5-anthraquinones. According to Eq. (9), the absorption bands of its 2-methyl isomer (**14b**) correspond to 1-$OH^*$-5-OH-2-methyl-9,10-, 1,5-$(OH^*)_2$-2-methyl-9,10-, and 5-OH-9-$OH^*$-2-methyl-1,10-anthraquinones whereas the anion band (506 nm) corresponds to 5-$OH^*$-2-methyl-9-$O^-$-1,10-anthraquinone:

$$\lambda_{max} = (315.7\pm4.0) - (85.37\pm2.82)\Sigma\sigma^A \text{ nm} \quad (8)$$

N = 3, r = 0.9995, SD = 1.6 nm;

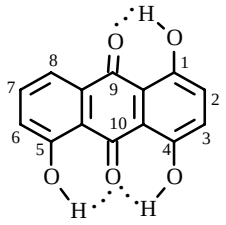
$$\lambda_{max} = (231.3\pm6.6) - (150.61\pm4.62)\Sigma\sigma^A \text{ nm} \quad (9)$$

N = 4, r = 0.9991, SD = 2.5 nm.

Therefore, shifting a methyl from one position in the anthraquinone core to another causes shifts in the tautomeric and conformational equilibria. In contrast with these compounds (**14a**, **b**, **c**, and **e**), ziganein can exist as a 1,5-anthraquinone.

Adding hydroxyls to the methyl of ziganein also causes shifts in the equilibria. The band at 418 nm in **14e**, which is absent in the spectrum of ziganein, should be assigned to 1,5-$(OH^*)_2$-3-hydroxymethyl-9,10-anthraquinone. The position of the $\pi_l,\pi^*$ bands of morindaparvin B argues in favor of its existence as a mixture of 1,5-$(OH^*)_2$-2-hydroxymethyl-9,10- and 5-OH-9-$OH^*$-2-hydroxymethyl-1,10-anthraquinones.

The following compounds are most significant among natural 1,4,5-trihydroxyanthraquinones (**18**):




**18a - i**

**18a:** 2-$CH_3$; **18b:** 3-$CH_3$; **18c:** 7-$CH_3$; **18d:** 2-$CH_3$-7-$OCH_3$;
**18e:** 7-$CH_3$-2-$OCH_3$; **18f:** 7-$CH_3$-3-$OCH_3$; **18g:** 7-$CH_3$-2,3-$OCH_3$;
**18h:** 2-$CH_3$-7-$OCH_3$-3-COOH; **18i:** 2,3-$CH_3$-7-$OCH_3$

TABLE 3. Position of $\pi_l,\pi^*$ Absorption Bands of Certain Natural 1,4,5-Trihydroxyanthraquinones

| Compound | Solvent | Assignment of $\pi_l,\pi^*$ bands to tautomers and conformers, nm | | | | | | | | | | | Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | $18^a$ | | | $19^a$ | $18^a$ | $22^a$ | | | $21^a$ | $20^a$ | | |
| | | $3^b$ | $2^b$ | $1^b$ | $3^b$ | $0^b$ | $3^b$ | $2^b$ | $1^b$ | $0^b$ | $2^b$ | $1^b$ | |
| **18** | $-\Sigma\sigma^A$ | 1.47 | 1.60 | 1.73 | 1.82 | 1.86 | 1.94 | 2.06 | 2.20 | 2.34 | 2.52 | 2.65 | |
| **18** | PPP calc. | | | | | 483 | | | 523 | 513 | | 568 | |
| **18** | Cyclohexane | 455p | 465p | 483 | | 495 | 505p | 517 | 530 | | 562 | | 24,25 |
| **18** | Methanol | 457p | | | | 490 | | 510p | 525p | | | | 13 |
| **18a** | Ethanol | | | | | 490 | | | 530 | | | 580 | 13 |
| **18a** | Ethanol | | 460p | 479.5p | | 491 | | 513 | 527 | | | | 3 |
| **18a** | Ethanol | | | 479 | | | | 510 | 532 | 550 | | | 26 |
| **18b** | Ethanol | | 465p | 473p | | 494 | | 515p | 539p | | | | 3 |
| **18b** | Ethanol | | 462p | 476p | | 490 | | 508p | 522 | | | | 27 |
| **18c** | Methanol | | 460 | 476 | | 489 | | 507 | 522 | | | 567 | 28 |
| **18c** | Ethanol | | | 480 | | 490 | | 510 | 525 | | | | 3 |
| **18d** | Ethanol | | 460p | 475p | | 489 | | 511p | 523 | | | | 3 |
| **18d** | Ethanol | | 460p | 476p | | 488 | | 508p | 520 | | | | 27 |
| **18d** | Chloroform | | | | | 495 | | | | | | | 29 |
| **18e** | Ethanol | | 462.5 | | 485 | 489.5 | | 511 | 525 | | | | 30 |
| **18e** | Ethanol | 452 | | | 485 | 490 | | 511 | 525 | | | | 31 |
| **18f** | Methanol | | 458 | | | 486 | | | 519 | | | 560 | 28 |
| **18j** | Methanol | | | | | 490 | | | | | | | 32 |
| **18h** | Ethanol | | | 480 | | | | | 527 | | | | 33 |

Note. sh, shoulder; [a], tautomer number; [b], number of free hydroxyls in conformers.

Six prototropic tautomers are possible for **18**. These are a single 9,10- (**18**), 1,4- (**19**), and 1,5-anthraquinone (**20**) and three 1,10-anthraquinones (4,5,9-, 4,8,9-, and 5,8,9-trihydroxysubstituted, **21**-**23**).

Correlations of experimental $\lambda_{max}$ with $\lambda_{calc}$ are illustrated using islandicin (**18a**) as an example [Eq. (10)]:

$$\lambda_{max} = (1.060\pm0.032)\lambda_{calc} - (22.8\pm16.8) \text{ nm} \quad (10)$$

N = 3, r = 0.9996, SD = 1.9 nm.

The values of $\lambda_{calc}$ for tautomers **19** and **21** in addition to **22** and **23** are identical. Therefore, the tautomers in these pairs are spectrophotometically indistinguishable. Under otherwise equal conditions, formation of the more stable tautomer is most probable. The stability of a compound in the vapor phase is characterized by the energy of atomization $\Delta H$; in solution, by the solvation coefficient M. Quantum-chemical calculations showed that the tautomers are ordered according to stability in pairs as 9,10 > 1,10 ≈ 1,4 > 1,5. However, their stability in solution has almost the opposite order 1,5 > 1,10 > 1,4 > 9,10. Tautomeric anthraquinones in the vapor phase are energetically less favorable than 9,10-anthraquinones. However, solvation increases the probability of tautomeric transformations. The M values indicate that formation of **21** is more probable for the two spectrophotometrically indistinguishable tautomers **19** and **21**; structure **22**, for **22** and **23**. Because the calculated value 523 nm, which belongs to structure **22**, enters into the correlation given above, the corresponding experimental value should be assigned to tautomer **22**.

Table 3 lists the correlation analysis for absorption spectra of **18**.

The $\pi_l,\pi^*$ bands of helminthosporin (**18c**) and its anions were assigned to tautomeric quinoid structures and their conformers based on the correlation of the $\nu_{max}$ values and the sums of $\sigma^A$ constants [Eq. (11)]:

$$\nu_{max} = (3480.9\pm74.2)\Sigma\sigma^A + (268910\pm176) \text{ cm}^{-1} \quad (11)$$

N = 14, r = 0.997, SD = 125 $cm^{-1}$.

Analogous equations were obtained for other substituted **18**, e.g., for isoxanthorin (**18f**):

$$\lambda_{max} = (0.871\pm0.025)\lambda_{calc} + (64.5\pm13.0) \text{ nm} \quad (12)$$

N = 3, r = 0.9996, SD = 1.5 nm;

$$\nu_{max} = (28590\pm242) - (4256.7\pm116.8)\Sigma\sigma^{A}\ cm^{-1} \quad (13)$$

N = 6, r = 0.9993, SD = 81 $cm^{-1}$.

The $\lambda_{max}$ values for the conformers of one tautomer depend linearly on the number *n* of free OH groups. For example, for the conformers of **18c**:

$$\lambda_{max} = (489.5\pm1.1) - (14.500\pm0.866)n\ nm \quad (14)$$

N = 3, r = 0.998, SD = 1.2 nm.

The given assignments were confirmed by several independent correlations, e.g., the proportional response to tautomeric transformations of experimental $\lambda_{max}$ of **18c** and isoxanthorin (**18f**) in methanol [Eq. (15)] and islandicin (**18a**) and erythroglaucin (**18d**) in ethanol [Eq. (16)]:

$$\lambda_{max}\ (\mathbf{18f}) = (0.956\pm0.014)\lambda_{max}\ (\mathbf{18c}) + (18.7\pm7.1)\ nm \quad (15)$$

N = 4, r = 0.9998, SD = 1.1 nm;

$$\lambda_{max}\ (\mathbf{18d}) = (0.965\pm0.034)\lambda_{max}\ (\mathbf{18a}) + (14.6\pm16.7)\ nm \quad (16)$$

N = 5, r = 0.998, SD = 1.8 nm.

The regular nature of similar trends, the very high r values, and the low SDs leave no doubt that they are reliable despite the objectively small number of points.

Table 3 shows that adding substituents such as alkyl, methoxy, and carboxylic acid to the *β*-position has only a small effect on the $\lambda_{max}$ values of individual tautomers but can shift the tautomeric and conformational equilibria. Significant differences in the color of structurally similar compounds are caused by just such transformations.

Correlation analysis established several nonobvious structural features of substituted **18**. The 9,10- and 1,10-quinoid tautomers are most typical of them. The $\pi_l,\pi^*$ bands corresponding to 1,4-quinoid structures **19** were identified only for xanthorin (**18e**). The existence of 1,5-quinoid tautomers (**20**) is rather unexpected. It is commonly thought that neighboring carbonyl and hydroxyl form invariably an IHB. However, Table 3 shows that this is absolutely not so. Conformers with broken IHBs are very common.

Data on tautomeric and conformational equilibria in hydroxyanthraquinones are not limited to those mentioned herein. They indicate that significant corrections should be made to the chemistry of natural anthraquinones.

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