Chemistry of naphthazarin derivatives
7.* Determination of structures of substituted 2,6(7)-dihydroxynaphthazarins by UV and IR spectroscopy

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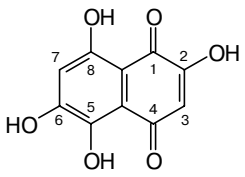
A set of substituted 2,6- and 2,7-dihydroxynaphthazarins were synthesized. The difference in the UV spectra of alkaline alcoholic solutions of 2,6- and 2,7-dihydroxynaphthazarins allows the reliable differentiation of the structures of these compounds. The IR spectra of 2,6- and 2,7-dihydroxynaphthazarins have characteristic nonoverlapping intervals of stretching vibration frequencies of the β-hydroxy groups. Based on these spectral regularities, the data on cuculoquinone, which has been isolated previously from lichen *Cetraria cucullata* and has been identified as 7,7′-bis(3-ethyl-2,5,6,8-tetrahydroxynaphthalene-1,4-dione), were revised and the structure of 6,6′-bis(3-ethyl-2,5,7,8-tetrahydroxynaphthalene-1,4-dione) was assigned to this compound.

Key words: 2,6-dihydroxynaphthazarin, 2,5,6,8-tetrahydroxy-1,4-naphthoquinone; 2,7-dihydroxynaphthazarin, 2,5,7,8-tetrahydroxy-1,4-naphthoquinone; 7,7′-bis(3-ethyl-1,4,5,8-tetrahydroxynaphthalene-2,6-dione), 7,7′-bis(3-ethyl-2,5,6,8-tetrahydroxynaphthalene-1,4-dione), 6,6′-bis(3-ethyl-2,5,7,8-tetrahydroxynaphthalene-1,4-dione); electronic absorption spectra; IR absorption spectra; cuculoquinone, *Cetraria cucullata*.

Numerous examples that illustrate difficulties encountered in determining the relative arrangement of the β-hydroxy groups in substituted 2,6(7)-dihydroxynapthazarins (2,5,6(7),8-tetrahydroxy-1,4-naphthoquinones) are surveyed in the monograph by R. H. Thomson.[2] Natural products are often available in small amounts, which hinders the use of chemical methods for the establishment of their structures, whereas the available physicochemical methods do not allow unambiguous conclusions about the arrangement of the substituents in the quinoid moiety (at the C(2) and C(3) atoms) with respect to the substituents at the C(6) and C(7) atoms. We faced an analogous problem when studying products of nucleophilic replacement of one of the chlorine atoms in naphthazarin derivatives by the alkoxy or amino groups.[3,4]

As for 2,6-dihydroxynaphthazarin (**1**), 2,7-dihydroxynaphthazarin (**2**), and their derivatives bearing identical substituents at positions 3 and 7(6), the determination of their structures by ^{1}H NMR spectroscopy presents no difficulties. Thus, the molecule of isomompain (**1**) is totally symmetrical (taking into account the peculiar tautomerism of naphthazarins involving intramolecular proton transfer from the α-OH group to the adjacent carbonyl oxygen atom) as a result of which all pairs of protons, including the protons of the α-hydroxy groups at the C(5) and C(8) atoms, are magnetically equivalent within the NMR time scale. To the contrary, the molecule of mompain (**2**) is unsymmetrical with respect to the α-hydroxy groups, resulting in the magnetic nonequivalence of their protons and, consequently, in the different chemical shifts, whereas the protons of the β-hydroxy groups (at the C(2) and C(7) atoms) and the protons at the C(3) and C(6) atoms are magnetically equivalent within the NMR time scale taking into account the tautomerism of the naphthazarin moiety. The introduction of a substituent into the nuclei of 2,6(7)-dihydroxynaphthazarins at the C(3) atom or different substituents at the C(3) and C(7) (or C(6)) atoms gives rise to unsymmetrical structures, which leads to the above-mentioned difficulties associated with the determination of the relative arrangement of the hydroxy groups in molecules of these compounds.



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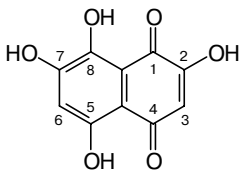

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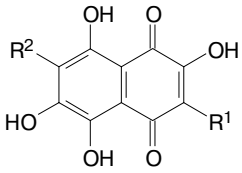
With the aim of searching for a simple and reliable procedure, which could allow one to solve the above-mentioned problem, we synthesized several pairs of substituted 2,6- and 2,7-dihydroxynaphthazarins. Thus, free-radical ethylation of 2,6-dihydroxynaphthazarin (**1**) and mompain (**2**)[5] under the action of propionyl peroxide under conditions of thermolysis afforded ethylisomompain (**3**), ethylmompain (**4**), 3,7-diethyl-2,6-dihydroxynaphthazarin (**5**), and 3,6-diethyl-2,7-dihydroxynaphthazarin (**6**).



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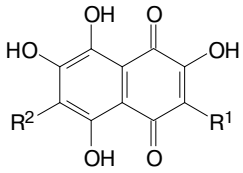


4, 6

3, 4: R^1 = Et, R^2 = H; **5, 6:** R^1 = R^2 = Et

3-Chloro-2,6-dihydroxynaphthazarin (**8**) and 3-chloro-2,7-dihydroxynaphthazarin (**12**) were prepared from 2,3-dichloronaphthazarin (**7**) according to Scheme 1.

The structure of compound **8** was established by its conversion into 2,6-dihydroxynaphthazarin.[4] The nucleophilic replacement of the chlorine atom in dichloronaphthazarin (**10**) by the methoxy group yielded predominantly product **11**. After hydrolysis of the reaction mixture, compound **8** (25%) was isolated along with the major product **12** (43%). The corresponding chloroethyl derivatives **13** and **14** were prepared by free-radical alkylation of monochloronaphthazarins **8** and **12**, respectively.

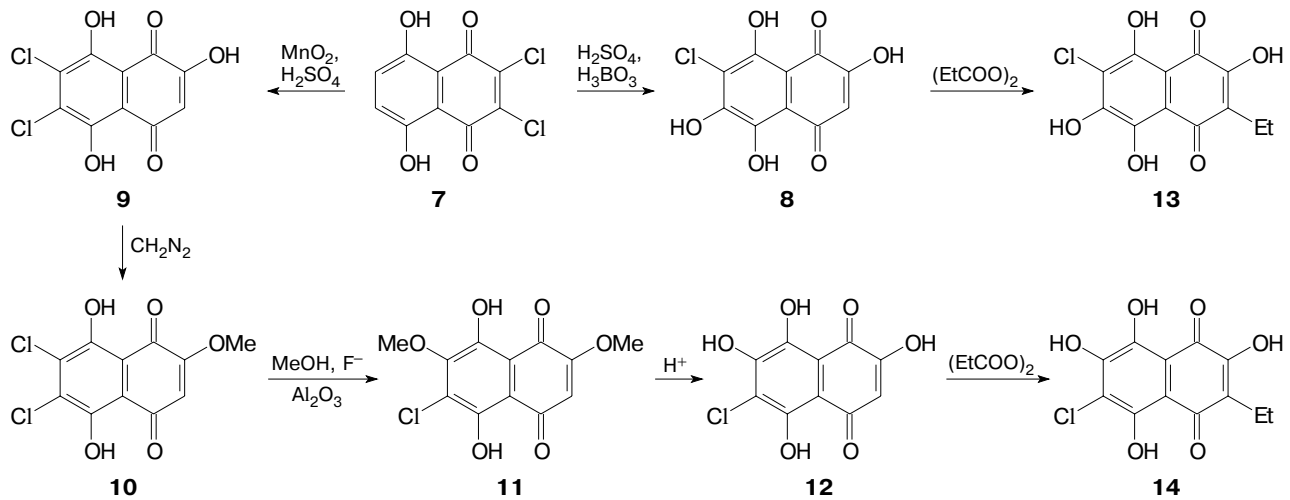
Compounds **3**, **5**, **8**, **13**, **4**, **6**, **12**, and **14**, whose structures were unambiguously established based on their directed syntheses from 2,6-dihydroxynaphthazarin (**1**), 2,7-dihydroxynaphthazarin (**2**), and 2,3-dichloronaphthazarin (**7**), were studied by UV and IR spectroscopy.

Previously, electronic absorption spectroscopy has been used for studying the structures of naphthazarins.[6,7] In the cited investigations, only absorption bands in the visible region were considered as the major criterion. However, detailed examination of the UV spectra of 2,6(7)-dihydroxy-substituted naphthazarins demonstrated that this spectral region is equally informative. Thus, the UV spectra of mompain (**2**) and its derivatives **4**, **6**, **12**, and **14** have an intense band in the region of 229—240 nm and a lower-intensity band in the region of 269—273 nm assigned to $\pi\rightarrow\pi^*$ transitions. The UV spectra of the corresponding 2,6-dihydroxynaphthazarins **1**, **3**, **5**, **8**, and **13** have a low-intensity long-wavelength band as a shoulder (Table 1).

In the UV spectra of alkaline alcoholic solutions of 2,7-dihydroxynaphthazarins **2**, **4**, **6**, **12**, and **14**, the above-mentioned bands are shifted bathochromically. The second band is shifted to 296—305 nm and its absorption increases by a factor of 1.3—1.4. The spectra of alkaline alcoholic solutions of 2,6-dihydroxynaphthazarins **1**, **3**, **5**, **8**, and **13** have no absorption bands in this region. Therefore, the presence of an intense absorption band at 296—305 nm in the UV spectra of alkaline solutions of 2,7-dihydroxynaphthazarins can serve as a simple reliable criterion, which allows one to differentiate these compounds from the corresponding 2,6-dihydroxy derivatives.

In the visible region of the electronic spectra of 2,6-dihydroxy (**1**, **3**, **5**, **8**, and **13**) and 2,7-dihydroxy derivatives (**2**, **4**, **6**, **12**, and **14**), a low-intensity band with a pronounced fine structure is observed, which is typical of the $n\rightarrow\pi^*$ transition in the naphthazarin system.[6] It should be mentioned that the absorption in the spectra of the 2,6-dihydroxy derivatives is observed at 460—529 nm, whereas the absorption of the 2,7-dihydroxy derivatives is observed in the longer-wavelength region (480—556 nm). A comparison of the visible regions of the spectra of 2,6-dihydroxy derivatives **1**, **3**,

Scheme 1



9 **7** **8** **13**

10 **11** **12** **14**

Table 1. UV spectra of compounds **1—6**, **8**, and **12—14** in methanolic and alkaline methanolic solutions

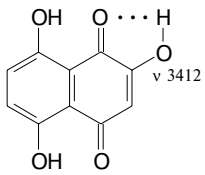
Compound	λ_{max}/nm (lg ε)	
	MeOH	MeOH+NaOH
1	229 (4.23), 315 (3.86), 461 sh (3.62), 488 (3.70), 526 sh (3.55)	206 (4.19), 223 (4.15), 255 (4.21), 357 (3.94), 433 sh (3.82), 465 (3.87), 510 sh (3.66)
2	212 (4.26), 229 (4.43), 273 (4.18), 320 (3.98), 481 sh (3.74), 515 (3.79), 549 sh (3.64)	229 (3.79), 249 (3.92), 297 (3.74), 368 (3.19), 446 sh (3.17), 476 (3.13), 540 (3.13), 575 (3.07)
3	213 (4.28), 235 (4.30), 270 sh (3.90), 317 (3.96), 461 sh (3.67), 490 (3.73), 526 sh (3.59)	205 (4.29), 224 (4.24), 260 (4.28), 368 (4.04), 385 sh (4.01), 442 sh (3.93), 463 (3.96)
4	213 (4.28), 233 (4.36), 269 (3.94), 323 (3.87), 478 sh (3.69), 510 (3.74), 546 sh (3.57)	230 (4.23), 249 (4.27), 296 (4.30), 375 (3.73), 452 (3.65), 478 (3.67), 526 sh (3.56), 565 (3.65), 606 br.sh (3.56)
5	238 (4.28), 252 sh (4.40), 328 (3.85), 431 sh (3.63), 463 (3.68), 495 (3.77), 529 (3.65)	265 (4.26), 379 (3.90), 389 (3.89), 446 sh (3.86), 469 (3.90)
6	215 (4.24), 236 (4.36), 269 (3.96), 331 (3.90), 450 sh (3.63), 481 (3.68), 514 (3.21), 549 (3.53)	202 (4.21), 231 (4.45), 255 (4.28), 298 (4.24), 385 (3.68), 463 (3.71), 490 (3.75), 568 (3.60)
8	214 (4.27), 236 (4.35), 267 sh (3.86), 326 (4.00), 467 (3.84), 495 (3.91), 529 (3.77)	216 (4.21), 260 (4.39), 365 (4.13), 382 (4.09), 437 sh (3.94), 463 (4.04), 521 (3.79)
12	216 (4.26), 235 (4.32), 274 (3.87), 329 (3.81), 455 sh (3.56), 488 (3.69), 546 (3.74), 559 (3.56)	223 (4.24), 250 (4.35), 299 (4.15), 366 (3.67), 457 (3.67), 483 (3.69), 532 sh (3.64), 565 (3.67), 633 br.sh (3.50)
13	217 (4.22), 239 (4.32), 253 sh (4.20), 333 (3.92), 467 sh (3.74), 495 (3.82), 529 (3.70)	207 (4.21), 265 (4.32), 375 (3.99), 389 (3.98), 446 sh (3.92), 467 (3.96)
14	215 (4.24), 240 (4.30), 272 (4.06), 337 (3.79), 490 (3.79), 521 (3.78), 556 (3.67)	230 (4.20), 251 (4.40), 305 (4.18), 385 (3.67), 460 (3.80), 485 (3.85), 556 (3.67), 602 br.sh (3.57)

5, **8**, and **13** in neutral and alkaline methanolic solutions revealed a hypsochromic shift accompanied by a substantial increase in the intensity of the bands (by a factor of 1.3—1.5) and by leveling down of their fine structures. To the contrary, 2,7-dihydroxy derivatives **2**, **4**, **6**, **12**, and **14** are characterized by the bathochromic shift of the absorption maximum.

The characteristic time of IR spectroscopy is smaller than the period of interconversion of the tautomeric forms of naphthazarin derivatives,[8] which opens up new opportunities for investigation of their structures. Previously, the IR spectra of naphthazarin derivatives were virtually always measured in KBr pellets or Nujol mulls[2,7] because of the low solubility of these compounds in nonpolar or weakly polar aprotic solvents, although the spectra recorded in such solvents enable one to analyze the region of stretching vibrations of the β-hydroxy groups (hereinafter ν(OH)) of hydroxynaphthazarins (3350—3550 cm^{-1}). The latter region is practically important, but it is poorly informative in the case of spectra recorded in KBr pellets.

Actually, the high-frequency region of the IR spectrum of mompain (**2**) in KBr pellets has a single absorption band (3240 cm^{-1}),[7] whereas the spectrum of **2** in chloroform has two pronounced narrow ν(OH) absorption bands of the β-hydroxy groups at 3431 and 3524 cm^{-1} with half-widths ($\Delta\nu_{1/2}$) of 46 and 37 cm^{-1}, respectively. In addition, the IR spectrum of a chloroform solution of mompain, like the spectrum of naphthazarin (5,8-dihydroxy-1,4-naphthoquinone),[9] has a low-intensity diffuse absorption band at 3400—2200 cm^{-1} with the maximum at ~3000 cm^{-1} belonging to the stretching vibration of the α-hydroxy groups.

Apparently, the difference in the positions of the ν(OH) absorption bands is associated with the difference in the strength of intramolecular hydrogen bonds in which the β-hydroxy groups of the quinoid (at the C(2) atom) and aromatic (at the C(7) atom) moieties of compound **2** can be involved. To elucidate this fact, we studied the IR spectra of model compounds, *viz.*, naphthopurpurin (**15**) and purpurin (**16**). Thus, the IR spectrum of a chloroform solution of naphthopurpurin containing the β-hydroxy group in the quinoid moiety[10] has the ν(OH) absorption band at 3412 cm^{-1} ($\Delta\nu_{1/2}$ 51 cm^{-1}). The IR spectrum (recorded in the same solvent) of purpurin containing the β-hydroxy group in the benzoid moiety has the absorption band at 3519 cm^{-1} ($\Delta\nu_{1/2}$ 40 cm^{-1}). Like the spectra of mompain (**2**) and naphthazarin,[9] the IR spectra of model compounds **15** and **16** have a broad diffuse absorption band of the stretching vibration of the α-hydroxy groups in the region of 3400—2200 cm^{-1}.



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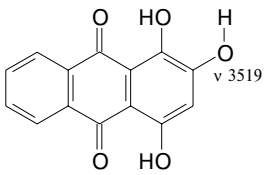

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Variations in the substituents serving as electron donors (Et) or acceptors (Cl) lead to a change in the stretching vibration frequencies of the β-hydroxy groups of the compounds under study. In the IR spectra of 2,7-dihydroxynaphthazarin derivatives **2**, **4**, **6**, **12**, and **14**, the frequencies of the OH groups at the C(2) and C(7) atoms are in the ranges of 3431—3413 and 3533—3523 cm^{-1}, respectively (Table 2).

In the IR spectra of chloroform solutions of 2,6-dihydroxynaphthazarins **1**, **3**, **5**, **8**, and **13**, the stretching vibration frequencies of both β-hydroxy groups are lower

Table 2. Stretching vibration frequencies of the OH groups in the IR spectra of the compounds synthesized

Compound	ν/cm^{-1}		
	2-OH	6-OH (7-OH)	C=O, C=C
1	3392 m	3509 m	1602 s
2	3428 m	(3530) m	1603 s
3	3391 m	3512 m	1631 sh.m, 1600 s
4	3430 m	(3531) m	1631 m, 1603 s
5	3394 m	3512 m	1599 s, 1580 sh.m
6	3427 m	(3533) m	1630 sh.m, 1602 s, 1587 s
8	3373 m	3508 m	1610 s, 1594 sh. s
12	3413 m	(3523) m	1632 m, 1609 c, 1595 m.sh
13	3377 m	3508 m	1631 sh.m, 1606 s, 1597 s
14	3417 m	(3526) m	1630 s, 1604 s, 1586 sh.m

Note. Stretching vibrations of the α-hydroxy groups in compounds **1—6**, **8**, and **12—14** are observed as a broad diffuse band in the region of 3400—2200 cm^{-1}.

than those in the spectra of the corresponding 2,7-dihydroxynaphthazarins **2**, **4**, **6**, **12**, and **14** (see Table 2). For the series of isomompain derivatives under study, the ν(OH) frequencies of the OH groups at the C(2) and C(6) atoms are observed in the ranges of 3392—3373 and 3512—3508 cm^{-1}, respectively.

A comparison of the ranges in which the ν(OH) frequencies of the compounds of the mompain (**2**, **4**, **6**, **12**, and **14**) and the isomompain series (**1**, **3**, **5**, **8**, and **13**) vary demonstrated that these intervals do not overlap (Fig. 1). For the above-mentioned series of compounds, the difference between the boundaries of the intervals in which the stretching vibration frequencies of the β-hydroxy groups at the C(2) atom vary is no less than 19 cm^{-1} and the corresponding differences for the β-hydroxy groups at the C(6) and C(7) atoms are no less than 11 cm^{-1}. Therefore, the regularity revealed for the ν(OH) frequencies in the IR spectra enables one to reliably identify substituted 2,6- and 2,7-dihydroxynaphthazarins.

Low concentrations of the compounds under study in chloroform, which are used for recording the IR spectra (see Experimental), preclude the formation of noticeable amounts of intermolecular associates. This was confirmed by our experiments on dilution of solutions and variation of the solvents. The frequency of the ν(OH) absorption band in the IR spectrum of naphthopurpurin (**15**) (3412 cm^{-1}) remained unchanged upon dilution with chloroform or when the $CHCl_3$ solvent was changed for CCl_4. The ν(OH) frequency in the spectrum of purpurin (**16**) also remained unchanged upon dilution with chloroform, but it changed from 3519 to 3525 cm^{-1} when $CHCl_3$ was changed for CCl_4. This fact indicates that the β-hydroxy group of the quinoid moiety in the naphthopurpurin molecule is linked to the carbonyl group at the C(1) atom through an intramolecular hydrogen bond, whereas the β-hydroxy group in the benzoid moiety of the purpurin molecule remains "free."

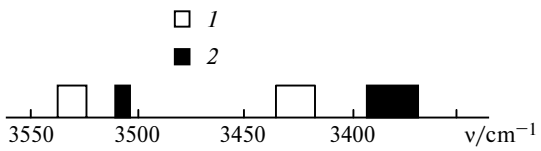
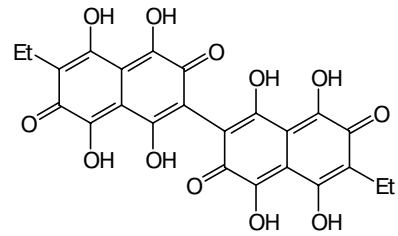


Fig. 1. Ranges of stretching vibration frequencies of the β-hydroxy group in the IR spectra of chloroform solutions of 2,7-dihydroxynaphthazarins **2**, **4**, **6**, **12**, and **14** (*1*) and 2,6-dihydroxynaphthazarins **1**, **3**, **5**, **8**, and **13** (*2*).

IR spectroscopy of solutions of 2,6(7)-dihydroxynaphthazarins in low-polarity aprotic solvents enables one to reliably identify the quinoid and aromatic β-hydroxy groups. Thus, 20-fold dilution of ethylmompain (**4**) with chloroform (from $2 \cdot 10^{-2}$ to $1 \cdot 10^{-3}$ mol L^{-1}) did not lead to changes either in the ν(OH) frequencies of the absorption bands (3430 and 3531 cm^{-1}) or in the ratio of their peak intensities. The spectrum of ethylmompain in the nonpolar solvent (CCl_4) demonstrates that the ν(OH) frequency of the first band (3430 cm^{-1}) remains unchanged (*i.e.*, the corresponding OH group is linked to the carbonyl group at the C(1) atom through an intramolecular hydrogen bond, like in the naphthopurpurin molecule), whereas the frequency of the second band increases from 3531 to 3538 cm^{-1} (*i.e.*, the OH group corresponding to this band is free, like in the purpurin molecule).

The revealed characteristic features of the UV and IR spectra of substituted 2,6- and 2,7-dihydroxynaphthazarins were used for investigation of the structure of hydroxylated bisnaphthazarin, *viz.*, cuculoquinone, which has been previously isolated from lichen *Cetraria cucullata*.[11] It should be mentioned that the *amphi*(2,6)-quinoid structure, *viz.*, the structure of 7,7′-bis(3-ethyl-1,4,5,8-tetrahydroxynaphthalene-2,6-dione) (**17**), has been assigned to cuculoquinone previously.[11] This structure was subjected to question in the study[2] in which this natural product was identified as 7,7′-bis(3-ethyl-2,5,6,8-tetrahydroxynaphthalene-1,4-dione) (**18**), *i.e.*, the 1,4-naphthoquinoid structure was assigned to this compound. However, based on the 1,4-naphthoquinone structure of cuculoquinone, the structure of 6,6′-bis(3-ethyl-2,5,7,8-tetrahydroxynaphthalene-1,4-dione) (**19**) may be proposed as an alternative, all the more so since the spectral methods used did not allow the authors of the cited study to unambiguously choose between this structure and structure **18**.[11]

The UV spectrum of a methanolic solution of cuculoquinone has an intense band at 239 nm and a lower-intensity band at 270 nm, which fall into the regions found for substituted 2,7-dihydroxynaphthazarins **2**, **4**, **6**, **12**, and **14** (Fig. 2). In the UV spectrum of an alkaline methanolic solution of cuculoquinone, the low-intensity long-wavelength band is shifted to 305 nm (Fig. 3) and its absorption increases by a factor of 1.4, which is typical of the spectra of 2,7-dihydroxynaphthazarin and its derivatives. In the visible region of



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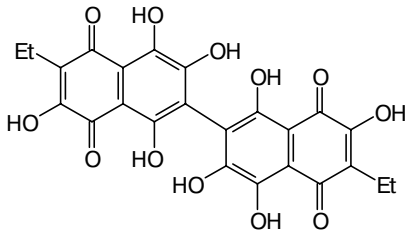

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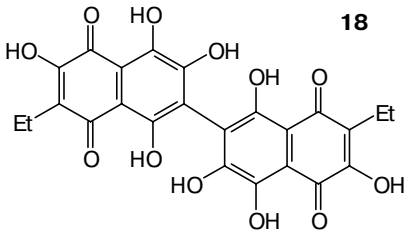

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the spectrum of cuculoquinone, the absorption band is shifted bathochromically to 571 nm on going from a neutral to alkaline methanolic solution, which is also in agreement with the above-mentioned characteristic features of the spectra of 2,7-dihydroxynaphthazarins.

The IR spectrum of a solution of cuculoquinone in chloroform has two ν(OH) absorption bands at 3527 and 3420 cm^{-1} (Fig. 4), which fall in the ranges found by us for 2,7-dihydroxynaphthazarin derivatives **2**, **4**, **6**, **12**, and **14** (see Table 2). In addition, the observed ratio of the peak intensities of the ν(OH) bands in the IR spectrum of this compound is analogous to the ratio of the corresponding intensities for 2,7-dihydroxynaphthazarins **2**, **4**, **6**, **12**, and **14**.

Therefore, the data of electronic absorption and IR spectroscopy of bisnaphthazarin isolated from lichen *Cetraria cucullata* unambiguously indicate that this compound belongs to the series of substituted 2,7-dihydroxynaphthazarins. This fact gives grounds to revise the structure of 7,7′-bis(3-ethyl-2,5,6,8-tetrahydroxynaphthalene-1,4-dione) (**18**), which has been assigned

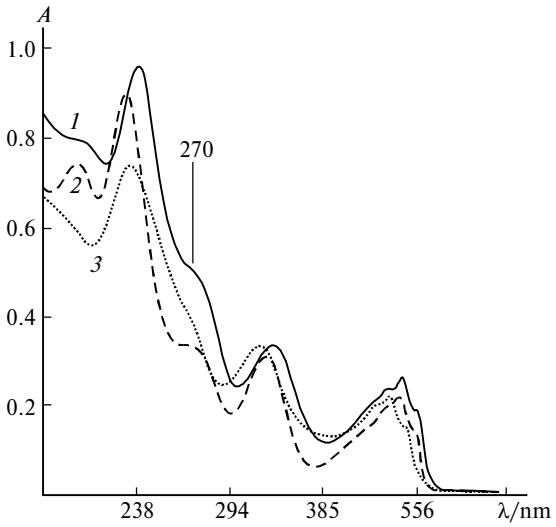

Fig. 2. Absorption spectra (*A*) of methanolic solutions of cuculoquinone (*1*), 3-ethyl-2,7-dihydroxynaphthazarin (**4**) (*2*), and 3-ethyl-2,6-dihydroxynaphthazarin (**3**) (*3*).

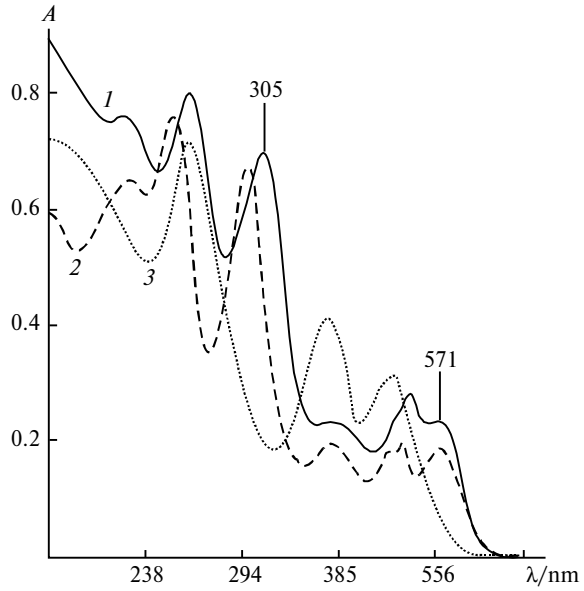

Fig. 3. Absorption spectra (*A*) of alkaline methanolic solutions of cuculoquinone (*1*), 3-ethyl-2,7-dihydroxynaphthazarin (**4**) (*2*), and 3-ethyl-2,6-dihydroxynaphthazarin (**3**) (*3*).

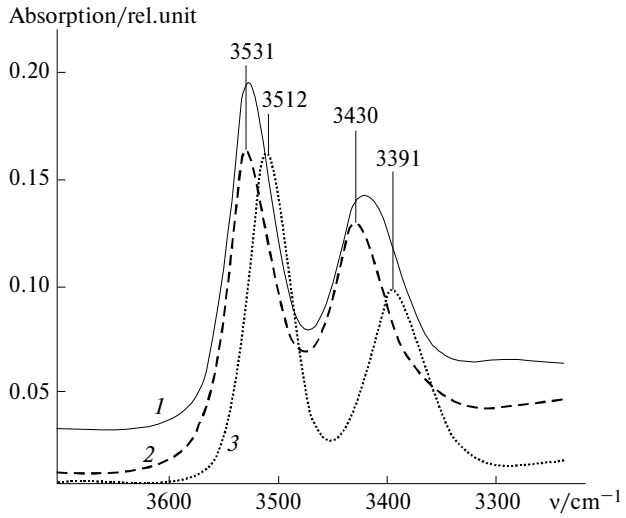

Fig. 4. Fragments of the IR spectra of chloroform solutions of cuculoquinone (*1*), 3-ethyl-2,7-dihydroxynaphthazarin (**4**) (*2*), and 3-ethyl-2,6-dihydroxynaphthazarin (**3**) (*3*).

to this compound previously, in favor of 6,6′-bis(3-ethyl-2,5,7,8-tetrahydroxynaphthalene-1,4-dione) (**19**).

In addition to cuculoquinone, its monomer was also isolated from lichen *Cetraria cucullata*. Structure **3** was assigned to this monomer based on the formal synthesis of cuculoquinone by oxidative coupling of dimethyl ether of this monomer.[11] Since structure **19** was proposed for cuculoquinone, its monomer should be identified as 3-ethyl-2,7-dihydroxynaphthazarin (**4**), which is one of the metabolites of urchins *Echinothrix* isolated previously.[12] Bisnaphthazarin **19** has been found in abyssal sea cucumbers *Psychopotes longicauda*, *Benthodytes typica*, and *B. lingua*[2] and, more recently, in lichen *Cetraria islandica*.[13] The well-studied mechanism of biosynthesis of compounds analogous to spinochromes[14] can be considered as circumstantial evidence in favor of structure **19**. The structures of all natural naphthoquinone derivatives containing the 2,7-dihydroxynaphthazarin fragment as a subgroup, which have been isolated in recent years,[13,15] are consistent with the above mechanism.

Experimental

The melting points were determined on a Boetius heating stage and were not corrected. The UV spectra were recorded on a Specord M 40 spectrophotometer in quartz tubes (the thickness of the layer was 1.0 mm). The concentrations of methanolic solutions of compounds **1—6**, **8**, and **12—14** were $(4.70—5.40) \cdot 10^{-4}$ mol L^{-1}. Alkaline methanolic solutions were prepared by the addition of a 0.3 *M* NaOH solution (50 μL) to a methanolic solution of the substrate (1.5 mL). The IR spectra were measured on a Bruker Vector 22 Fourier spectrometer (the resolution was 2.0 cm^{-1}) in $CDCl_3$ using cells with CaF_2 windows and polyethylene gaskets (the thickness of the layer was from 0.40 to 1.50 mm). The concentrations of solutions of compounds **1—6**, **8**, and **12—14** were $(2.5—5.0) \cdot 10^{-3}$ mol L^{-1}. The stretching vibration frequencies of the absorption bands of the β-hydroxy groups were measured after "smoothing" of the spectrum. The reproducibility of the results of measurements was not worse than ±0.5 cm^{-1}. The ^1H NMR spectra were recorded on a Bruker AC-250 spectrometer (250.13 MHz) in $CDCl_3$ and acetone-d_6 (Me_4Si as the internal standard). The mass spectra (EI) were obtained on an LKB-9000S instrument with direct introduction of the samples; the energies of ionizing electrons were 18 and 70 eV.

The course of the reactions and the purities of the compounds were monitored by TLC on Merck 60F-254 plates using a 2 : 1 hexane—acetone system as the eluent. The individual compounds were isolated from mixtures of the reaction products by preparative TLC on plates (20×20 cm) with a nonfixed silica gel layer (H^+ form;[5] 5—40 μm) in the 2 : 1 hexane—acetone system. The yields of the resulting compounds were not optimized. Compounds **1** and **2** were prepared according to a procedure reported previously.[5] The conditions of conversion of 2,3-dichloronaphthazarin (**7**)[16] into 6,7-dichloro-2-hydroxynaphthazarin (**9**) have been reported previously.[17]

7-Chloro-2,5,6,8-tetrahydroxy-1,4-naphthoquinone (8). A mixture of 2,3-dichloronaphthazarin (**7**) (259 mg, 1 mmol), boric acid (280 mg), and concentrated H_2SO_4 (3 mL) was heated on a molten metal bath at 200—210 °C for 1 h. The mixture was cooled to ~20 °C, poured into ice water (25 mL), and kept for 15 h. The precipitate that formed was filtered off, washed with water (3×2 mL), and dried under reduced pressure over P_2O_5. Elution with the 2 : 1 hexane—acetone system on a column with SiO_2 (Chemapol L 40/100 μm) afforded compound **8** in a yield of 132 mg (51%), m.p. 227—230 °C (with decomp.). Found (%): C, 47.02; H, 2.02. $C_{10}H_5ClO_6$. Calculated (%): C, 46.81; H, 1.96. ^1H NMR (acetone-d_6), δ: 6.62 (s, 1 H, H(3)); 10.52 (br.s, 1 H, β-OH); 12.31 and 13.03 (both s, 1 H each, α-OH). MS (70 eV), *m/z* (I_{rel} (%)): 256/258 $[M]^+$ (100), 228/230 (42), 200 (5), 193 (12), 186 (17).

6,7-Dichloro-5,8-dihydroxy-2-methoxy-1,4-naphthoquinone (10). Compound **10** was prepared in quantitative yield by careful treatment of substrate **9** with a solution of diazomethane in diethyl ether.[18] M.p. 216—218 °C. Found (%): C, 46.02; H, 2.17. $C_{11}H_6Cl_2O_5$. Calculated (%): C, 45.70; H, 2.09. ^1H NMR ($CDCl_3$), δ: 3.98 (s, 3 H, OMe); 6.29 (s, 1 H, H(3)); 12.77 and 13.28 (both s, 1 H each, α-OH). MS (18 eV), *m/z* (I_{rel} (%)): 288/290/292 $[M]^+$ (100), 287/289/291 $[M - 1]^+$ (88), 273/275/277 (23), 272/274/276 (44), 270/272/274 (75), 269/271/273 (59), 258 (10), 256 (10), 223 (14), 222 (10).

7-Chloro-2,5,7,8-tetrahydroxy-1,4-naphthoquinone (12). A mixture of dry 6,7-dichloro-2-methoxynaphthazarin (**10**) (85 mg, 0.29 mmol), freshly calcinated CsF (400 mg, 2.6 mmol), and freshly calcinated Al_2O_3 (360 mg, 3.5 mmol) in anhydrous MeOH* (10 mL) was refluxed with stirring for 10 h. Then the reaction mixture was cooled and the precipitate was filtered off and washed successively with 5% HCl (0.5 mL) and acetone (3 mL). The combined acidic filtrates were concentrated to ~1 mL under reduced pressure, diluted with H_2O (20 mL), and extracted with chloroform (3×10 mL). The extract was worked up according to a standard procedure and the residue was refluxed in concentrated HBr (15 mL) for 15 min. The reaction mixture was diluted with H_2O (50 mL) and extracted with ethyl acetate (3×10 mL). The extract was concentrated and compound **12** was isolated in a yield of 32 mg (43%) by preparative TLC, R_f 0.28, m.p. 257—261 °C. Found (%): C, 46.60; H, 2.05. $C_{10}H_5ClO_6$. Calculated (%): C, 46.81; H, 1.96. ^1H NMR (acetone-d_6), δ: 6.65 (s, 1 H, H(3)); 10.16 (br.s, 1 H, β-OH); 12.08 and 13.00 (both s, 1 H each, α-OH). MS (18 eV), *m/z* (I_{rel} (%)): 257/259 (40), 256/258 $[M]^+$ (100), 255/257 (11), 228/230 (13), 224 (9), 223 (30), 222 (75). In addition to compound **12**, compound **8** was isolated from the reaction mixture by preparative TLC in a yield of 19 mg (25%), R_f 0.33.

Radical alkylation of 2,6(7)-dihydroxynaphthazarins 1, 2, 8, and 12 with propionyl peroxide. Propionyl peroxide[19] was added dropwise to a boiling solution of the substrate (0.5 mmol) in Bu^tOH (30 mL). The course of the reaction was monitored by TLC. The reaction was terminated when the degree of conversion reached ~60%. The reaction mixture was concentrated and the residue was chromatographed by preparative TLC.

Ethylation of mompain **2** (110 mg) afforded a fraction with R_f 0.43, *viz.*, **3,6-diethyl-2,5,7,8-tetrahydroxy-1,4-naphthoquinone (6)** in a yield of 5.2 mg (6% with respect to consumed mompain **2**), m.p. 185—187 °C. Found (%): C, 61.02; H, 4.98. $C_{14}H_{14}O_6$. Calculated (%): C, 60.43; H, 5.07. ^1H NMR ($CDCl_3$), δ: 1.19 (t, 6 H, 2 CH_3, J = 7.7 Hz); 2.72 (q, 4 H, 2 CH_2, J = 7.7 Hz); 6.73 (br.s, 2 H, 2 β-OH); 11.79 and 13.54 (both s, 1 H each, α-OH). MS (70 eV), *m/z* (I_{rel} (%)): 278 $[M]^+$ (99), 277 $[M - 1]^+$ (100), 263 (22), 262 (18), 247 (13), 235 (18).

The major product with R_f 0.36, *viz.*, **3-ethyl-2,5,7,8-tetrahydroxy-1,4-naphthoquinone (4)**, was obtained in a yield of 39.8 mg (51% with respect to consumed compound **2**), m.p. 183—186 °C (sublim.) (*cf.* lit. data:[13] m.p. 182—188 °C).

* Reagents were prepared according to a known procedure.[3]

Found (%): C, 58.04; H, 4.25. $C_{12}H_{10}O_6$. Calculated (%): C, 57.60; H, 4.03. ^{1}H NMR ($CDCl_3$), δ: 1.19 (t, 3 H, CH_3, J = 7.7 Hz); 2.68 (q, 2 H, CH_2, J = 7.7 Hz); 6.65 and 6.90 (both br.s, 1 H each, β-OH); 11.70 and 13.11 (both s, 1 H each, α-OH). MS (70 eV), m/z (I_{rel} (%)): 250 $[M]^+$ (100), 249 $[M - 1]^+$ (48), 235 (8), 207 (29), 206 (13). The fraction with R_f 0.29 contained the initial mompain **2**, 40.7 mg (37%).

Ethylation of isomompain **1** (110 mg) afforded a fraction with R_f 0.51, *viz.*, **3,7-diethyl-2,5,6,8-tetrahydroxy-1,4-naphthoquinone (5)**, in a yield of 28 mg (29% with respect to consumed isomompain **1**), m.p. 228—232 °C. Found (%): C, 59.63; H, 5.23. $C_{14}H_{14}O_6$. Calculated (%): C, 60.43; H, 5.07. ^{1}H NMR (acetone-d_6), δ: 1.13 (t, 6 H, 2 CH_3, J = 7.9 Hz); 2.65 (q, 4 H, 2 CH_2, J = 7.9 Hz); 9.74 (br.s, 2 H, 2 β-OH); 13.11 (s, 2 H, 2 α-OH). MS (70 эВ), m/z (I_{rel} (%)): 278 $[M]^+$ (97), 277 $[M - 1]^+$ (100), 263 (22), 262 (22), 250 (64), 249 (14). **3-Ethyl-2,5,6,8-tetrahydroxy-1,4-naphthoquinone (3)** was obtained as the major product in a yield of 60.7 mg (70%), R_f 0.40, m.p. 227—229 °C. Found (%): C, 57.42; H, 4.40. $C_{12}H_{10}O_6$. Calculated (%): C, 57.60; H, 4.03. ^{1}H NMR (acetone-d_6), δ: 1.12 (t, 3 H, CH_3, J = 7.9 Hz); 2.61 (q, 2 H, CH_2, J = 7.9 Hz); 6.51 (s, 1 H, H(7)); 9.79 and 10.13 (both br.s, 1 H each, β-OH), 12.43 and 13.37 (both s, 1 H each, α-OH). MS (18 eV), m/z (I_{rel} (%)): 250 $[M]^+$ (100), 249 $[M - 1]^+$ (40), 236 (8), 235 (11), 234 (7), 222 (8), 207 (7). The fraction with R_f 0.32 contained the initial isomompain **1**, 33 mg (30%).

Ethylation of 6-chloro-2,7-dihydroxynaphthazarin (**12**) (128 mg) afforded a complex mixture of products from which the fraction with R_f 0.36, *viz.*, **6-chloro-3-ethyl-2,5,7,8-tetrahydroxy-1,4-naphthoquinone (14)**, was isolated by preparative TLC in a yield of 3 mg (2%), m.p. 218—222 °C. ^{1}H NMR ($CDCl_3$), δ: 1.18 (t, 3 H, CH_3, J = 7.5 Hz); 2.71 (q, 2 H, CH_2, J = 7.5 Hz); 11.76 (br.s, 1 H, α-OH); 13.37 (s, 1 H, α-OH). ^{1}H NMR (acetone-d_6), δ: 1.14 (t, 3 H, CH_3, J = 7.5 Hz); 2.70 (q, 2 H, CH_2, J = 7.5 Hz); 9.77 (br.s, 1 H, β-OH); 12.11 (br.s, 1 H, α-OH); 13.58 (s, 1 H, α-OH). MS (70 eV), m/z (I_{rel} (%)): 284/286 $[M]^+$ (23), 283/285 $[M - 1]^+$ (100), 249 (9), 241 (9).

Ethylation of 7-chloro-2,6-dihydroxynaphthazarin (**8**) (128 mg) afforded a complex mixture of products from which the fraction with R_f 0.42, *viz.*, **7-chloro-3-ethyl-2,5,6,8-tetrahydroxy-1,4-naphthoquinone (13)**, was isolated by preparative TLC in a yield of 5 mg (3%), m.p. 221—224 °C. ^{1}H NMR ($CDCl_3$), δ: 1.17 (t, 3 H, CH_3, J = 7.6 Hz); 2.70 (q, 2 H, CH_2, J = 7.6 Hz); 12.58 and 12.78 (both s, 1 H each, α-OH). ^{1}H NMR (acetone-d_6), δ: 1.14 (t, 3 H, CH_3, J = 7.5 Hz); 2.69 (q, 2 H, CH_2, J = 7.5 Hz); 9.97 (br.s, 1 H, β-OH); 12.92 and 12.95 (both s, 1 H each, α-OH). MS (70 eV), m/z (I_{rel} (%)): 284/286 $[M]^+$ (14), 283/285 $[M - 1]^+$ (100), 269/271 (16), 268/270 (12), 241/243 (41).

6,6′-Bis(3-ethyl-2,5,7,8-tetrahydroxynaphthalene-1,4-dione) (19). UV (MeOH), λ_{max}/nm (lg ε): 216 (4.00), 239 (4.10), 270 (3.81), 329 (3.61), 545 sh (3.39), 485 (3.45), 518 (3.51), 556 (3.34). UV (MeOH+NaOH), λ_{max}/nm (lg ε): 229 (4.00), 258 (3.99), 305 (4.18), 385 (3.45), 463 sh (3.47), 495 (3.56), 571 (3.42). IR ($CDCl_3$), ν/cm^{-1}: 3527 m, 3420 m, 1631 sh.m, 1602 s, 1586 sh.s.

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