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Chemistry of naphthazarin derivatives

12.* Synthesis and investigation of prototropic tautomerism of 3-(alk-1-enyl)-2-hydroxynaphthazarins

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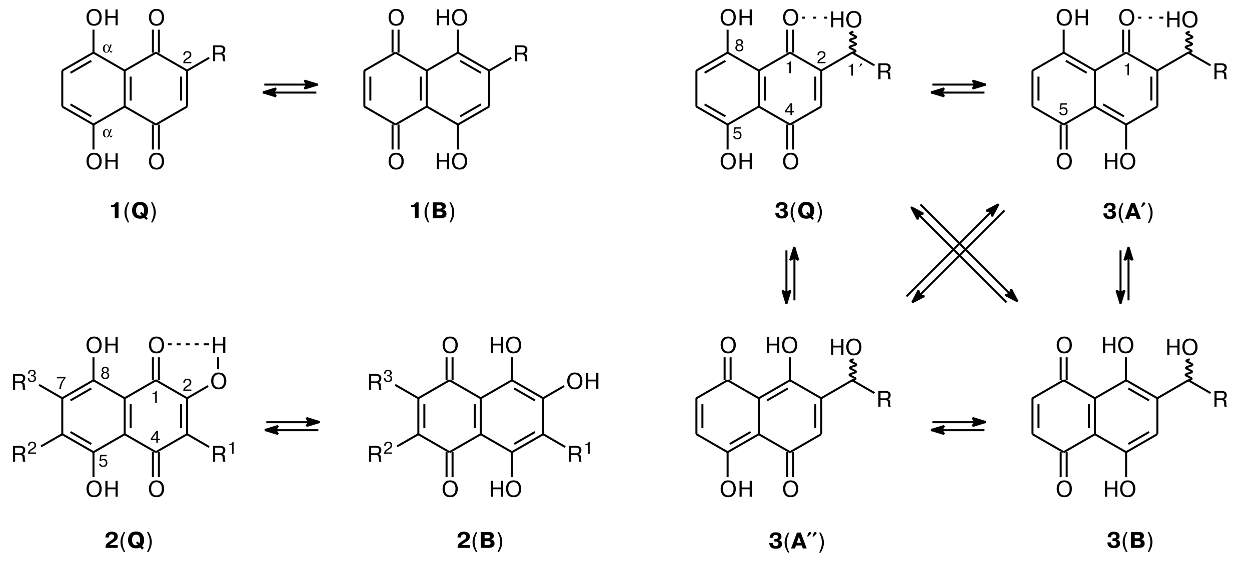
Substituted 3-(alk-1-enyl)-2-hydroxynaphthazarins were synthesized. According to data from IR spectroscopy, these compounds exist in organic aprotic solvents as mixtures of tautomeric 1,4-naphthoquinonoid forms. The compositions of tautomeric mixtures were quantitatively determined. The effects of the structure of the alkenyl substituent and the polarity of the solvent on the tautomeric equilibrium were qualitatively estimated.

Key words: 3-(alk-1-enyl)-2-hydroxynaphthazarins; prototropic tautomerism; IR spectroscopy of hydroxynaphthazarins in solutions.

Prototropic tautomerism of naphthazarin (5,8-dihydroxy-1,4-naphthoquinone) and its derivatives **1** is a little studied issue.[2—4] NMR spectroscopy is of limited application in the analysis of this phenomenon because of the averaging of the corresponding ^{1}H, ^{13}C, and ^{17}O NMR signals for the quinonoid and benzenoid moieties of these compounds due to a high rate of tautomeric exchange on the NMR time scale.[5—7] Splitting of the signals for the carbon atoms in the ^{13}C NMR spectrum of naphthazarin is observed only upon deep cooling of a sample.[6] Quantitative analysis of tautomeric mixtures of these compounds using methylation of the α-hydroxy groups followed by investigation of the reaction products by NMR spectroscopy can be performed only approxi-

Scheme 1



1: R = H, Alk, OMe, Hal, COMe, STol, SOTol, SO_2Tol
2: R^1, R^2, R^3 = H, Alk, Cl, OMe, OH
3: R = Me, $—CH_2CH=CMe_2$

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* For Part 11, see Ref. 1.

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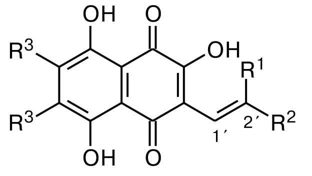
mately due to the difference in the reactivity of tautomers.[8–10]

Generally, no time averaging of the spectroscopic parameters is observed when IR spectroscopy is employed. However, this method has received little use in studies of tautomerism of naphthazarins, because the absorption bands of C—H and C=O stretching vibrations are poorly informative.[11] Recently, IR spectroscopy has been used for studying prototropic tautomerism of naphthazarin (di)hydroxy derivatives **2** [11,12] and 1´-hydroxyalkylnaphthazarins **3**.[13] The tautomeric compositions of these compounds in an aprotic medium was quantitatively determined (Scheme 1) based on the analysis of the stretching vibration frequencies of the hydroxy groups at the C(2) and C(1´) atoms in hydroxynaphthazarins **2** and **3**, respectively, and the intensities of their absorption bands. Generally, (di)hydroxynaphthazarins exist in organic aprotic solvents as mixtures of the quinonoid (**Q**) and benzenoid (**B**) forms, whereas the *ana*-quinonoid forms (**A**´ and **A**´´) are present along with the tautomers **Q** and **B** in solutions of 1´-hydroxyalkylnaphthazarins.

Earlier,[14] we have studied the reactions of hydroxynaphthazarins with aliphatic aldehydes giving rise to 3-(alk-1-enyl)-2-hydroxynaphthazarins **4**. The presence of a double bond at position 1´ of the side chain is a characteristic feature of alkenylhydroxynaphthazarins **4**. The double bond is involved in conjugation with the double bond system of the naphthazarin moiety and, being an electron donor, affects the tautomeric equilibrium of these compounds. The tautomerism of 3-(alk-1-enyl)-2-hydroxynaphthazarins has attracted interest also because such compounds (for example, **5**) were found in nature.[15]



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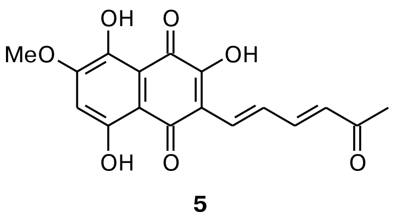
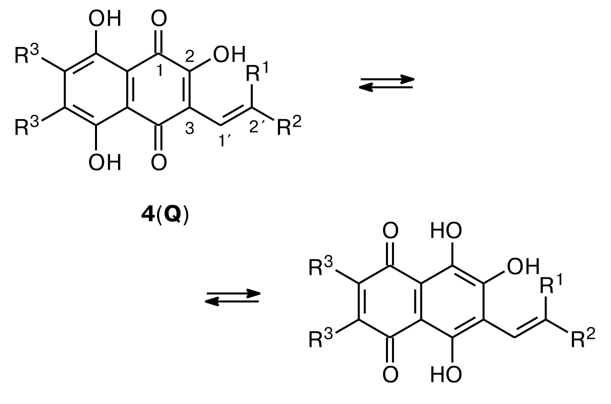


5

4: R^1 = H, Alk; R^2 = Alk; R^3 = H, Me, Cl

The present work was aimed at studying the influence of the alkenyl substituent at the C(3) atom of 2-hydroxynaphthazarin derivatives **4** on the tautomeric equilibrium of these compounds in aprotic organic solvents (Scheme 2).

Scheme 2

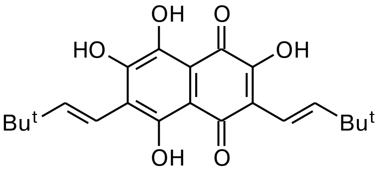


4(**Q**)

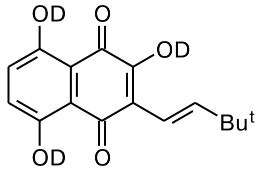
4(**B**)

4: R^1 = H, Alk; R^2 = Alk, R^3 = H, OH, OMe, Cl

To quantitatively determine the tautomeric compositions of these compounds in solutions, we chose symmetrical alkenylhydroxynaphthazarin **4a** as the reference compound. Molecule **4a** contains one hydroxy group in the quinonoid moiety and another hydroxy group in the aromatic moiety.



4a



4b(**D**)

In the IR spectrum of a hexane solution* of compound **4a**, in contrast to the spectra of alkylhydroxynaphthazarins, the benzenoid (**B**) and quinonoid (**Q**) ν(OH) bands are split into two components at 3542, 3527 and 3412, 3383 cm^{-1}, respectively (Fig. 1, *a*). Splitting of the ν(OH) bands cannot be attributable to coupling of the stretching vibration of the β-hydroxy group with the C=C stretching vibration of the alkenyl fragment or its overtone. For example, splitting of the ν(OD) bands (2519 and

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* In hexane, the largest splitting of the ν(OH) absorption bands of hydroxynaphthazarins was observed due to the effect of the polarity of the solvent on the half-widths of absorption bands, which has been found earlier.[11]

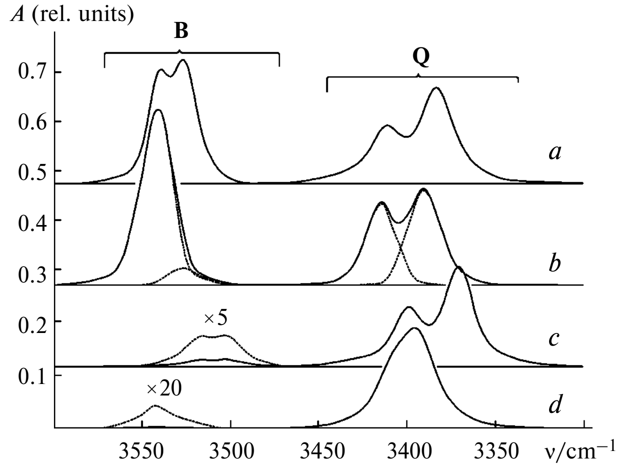
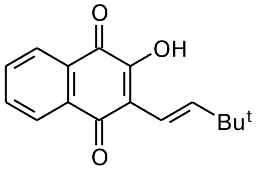
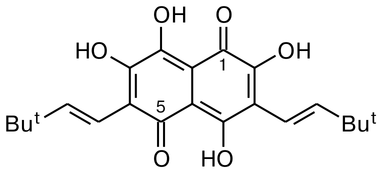


Fig. 1. High-frequency region of the IR spectra of hexane solutions of (di)alkenyldihydroxynaphthazarins **4a** (*a*) and **4c** (*b*) and of alkenylhydroxynaphthazarins **4b** (*c*) and **4d** (*d*) (the results of deconvolution of the band contours into individual components are indicated by dashed lines).

2500 cm^{-1}) is also observed in the IR spectrum of compound **4b**(**D**) containing deuterated hydroxy groups. The IR spectrum of naphthoquinone **6**, like that of compound **4a**, also shows two quinonoid ν(OH) bands at 3390 and 3360 cm^{-1}, which indicates that the *ana*-quinonoid tautomer (**A**) is absent in a solution of compound **4a**. Dilution studies of compound **4a** ruled out the possible formation of complexes with intermolecular hydrogen bonding.



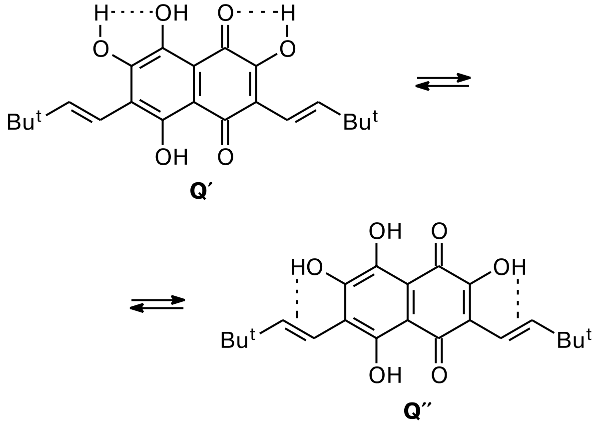
6



4a(A)

From the aforesaid it can be suggested that the observed splitting of the ν(OH) bands is associated with the involvement of the hydroxy groups of compound **4a** in intramolecular hydrogen bonding with either the C=O group[11,12] or the π electrons of the double bond of the alkenyl substituent[16,17] (Scheme 3).

Scheme 3



4a

The tautomeric equilibrium in solutions of hydroxy derivatives of naphthazarin was quantitatively estimated by IR spectroscopy based on a peak intensity ratio for the ν(OH) bands.[11,12] Taking into account the complex character of the ν(OH) absorption bands in the IR spectra of alkenylhydroxynaphthazarins, the tautomeric equilibrium (*k*) for these compounds in solutions can be estimated from the ratio of the total areas of the benzenoid and quinonoid ν(OH) bands. According to this ratio measured in the spectrum of dialkenyldihydroxynaphthazarin **4a**, k_1 is 1.15 for solutions in $CHCl_3$ and CCl_4 and k_2 is 0.94 for hexane solutions. We used the constants k_1 and k_2 for estimating the ratio between the tautomers **Q** and **B** in solutions of alkenylhydroxynaphthazarins **4b—e** according to Eqs (1) and (2):

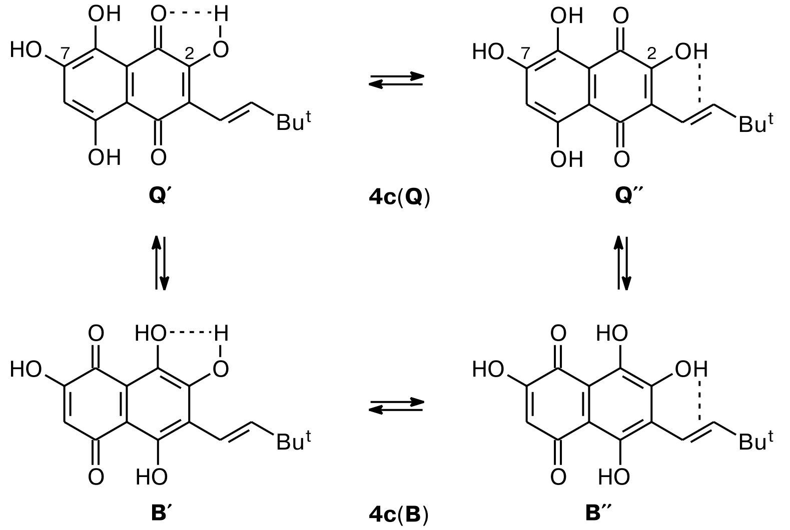
$$[\mathbf{Q}]=100/(1+R_S/k_{1,2}), \qquad (1)$$

$$[\mathbf{B}]=100-[\mathbf{Q}], \qquad (2)$$

where [**Q**] and [**B**] are the percentages of the tautomers **Q** and **B**, respectively (for example, of forms **4**(**Q**) and **4**(**B**)) and R_S is the ratio of the total areas of the benzenoid and quinonoid ν(OH) bands in the spectrum of the compound under study.

In the IR spectrum of alkenyldihydroxynaphthazarin **4c** (see Fig. 1, *b*), the quinonoid ν(OH) band is split into two components, whereas the benzenoid band appears as a singlet. This suggests that compound **4c** in a hexane solution exists predominantly or completely in the tautomeric form **Q**, which, in turn, is a mixture of two conformers **Q**′ and **Q**′′ (Scheme 4). In this case, the benzenoid ν(OH) band belonging to the hydroxy group at the C(7) atom of tautomer **4c**(**Q**) should appear as a singlet. A comparison of the ratios of the area of the low-frequency component to the area of the high-frequency component, which were determined from the deconvolution of the quinonoid ν(OH) bands, in the spectra of compounds **4a** and **4c** provides evidence for the presence of the tautomeric form **B** (~9%) in a solution of com-

Scheme 4



pound **4c**. This percentage of tautomer **4c**(**B**) causes no noticeable splitting of the benzenoid ν(OH) band. Actually, analysis of the band belonging to the tautomer **B** in the IR spectrum of compound **4c** demonstrated that its contour is not described by a single component and gives the second weak component at 3526 cm^{-1} (Scheme 4, Fig. 1, *b*).

The IR spectrum of compound **4b** shows an intense ν(OH) band corresponding to the quinonoid tautomer **Q** along with a higher-frequency ν(OH) band belonging to the benzenoid tautomer **B** (Fig. 1, *c*). The relative intensity of the latter increases substantially on going from hexane to more polar chloroform. Calculations by Eqs (1) and (2) demonstrated that the percentage of tautomeric form **4b**(**B**) increases from 5.9% in hexane to 11.1 and 10.6% in CCl_4 and $CHCl_3$, respectively (Table 1).

Earlier,[11,12] it has been demonstrated that in a chloroform solution, ethylhydroxynaphthazarin **7** exists exclusively in the tautomeric form **Q**. Hence it follows that, being an electron donor and being involved in conjuga-

Table 1. Frequencies, half-widths of the ν(OH) absorption bands, and tautomeric compositions of compounds **4a—f** in various solvents

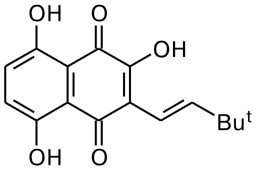
Compound	Solvent	ν(OH) $(\Delta_{1/2})$/cm^{-1}	[**Q**] : [**B**] (%)
4a	Hexane	3542 (13), 3527 (12), 3412 (20), 3383 (24)[a]	—[b]
	CCl_4	3527 (34), 3515 (35), 3418 (40), 3384 (46)[a]	—[b]
	$CHCl_3$	3517 (42), 3389 (58)	—[b]
4b	Hexane	3518, 3503, 3400 (20), 3370 (22)[a]	94.1 : 5.9
	CCl_4	3537, 3501, 3400 (36), 3370 (42)[a]	88.9 : 11.1
	$CHCl_3$	3502 (45), 3379 (65)	89.4 : 10.6
4c	Hexane	3546 (20), 3526 (20), 3423 (22), 3393 (23)[a]	91.0 : 9.0[c]
	CCl_4	3538 (26), 3524 (29), 3419 (34), 3390 (36)[a]	89.0 : 11.0[c]
	$CHCl_3$	3528 (42), 3398 (58)	—
4d	Hexane	3543 (15), 3396 (33) [3410 (26), 3394 (28)[a]][d]	99.8 : 0.2
	CCl_4	3533 (15), 3395 (43) [3411 (44), 3395 (44)[a]][d]	99.2 : 0.8
	$CHCl_3$	3506 (42), 3396 (57)	98.8 : 1.2
4e	Hexane	3543, 3409 (19), 3381 (22)[a]	98.3 : 1.7
	CCl_4	3529, 3411 (40), 3380 (45)[a]	98.6 : 1.4
	$CHCl_3$	3519, 3390 (64)	97.0 : 3.0
4f	$CHCl_3$	3519 (55), 3395 (71)	84.5 : 15.5

[a] According to the results of deconvolution of the band contour.

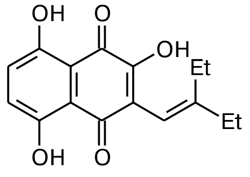
[b] For compound **4a**, [**Q**] = [**B**].

[c] For the β-hydroxy group in the *ortho* position with respect to the alkenyl substituent.

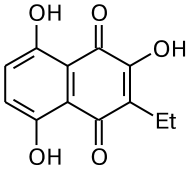
[d] The quinonoid band.



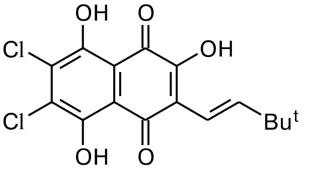
4b(**Q**)



4d(**Q**)



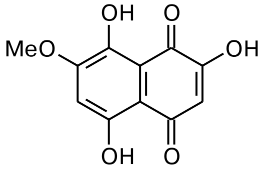
7(**Q**)



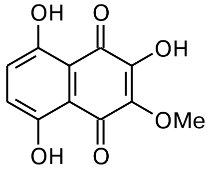
4e(**Q**)

tion with the π-bond system of the naphthazarin moiety, the double bond in the side chain of compounds **4b** and **4c** is responsible for a noticeable electron density redistribution, which, in turn, is reflected in the tautomeric equilibrium between the forms **Q** and **B**. In alkenylhydroxynaphthazarin **4d**, the degree of conjugation of the double bond of the side chain with the π-bond system of the naphthazarin unit decreases due to steric hindrance and, as can be seen from the IR spectrum of this compound (Fig. 1, *d*), the tautomeric equilibrium between forms **4d**(**Q**) and **4d**(**B**) is virtually completely shifted to the tautomer **Q** (see Table 1). An analogous situation was observed for compound **4e** where the donor effect of the double bond of a nonbranched alkenyl substituent is compensated by the influence of the chlorine atoms (electron acceptors) at positions 6 and 7.

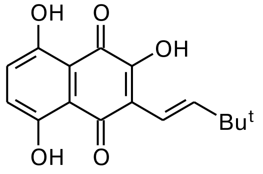
It should be noted that the effect of the substituents on the tautomeric equilibrium of naphthazarin derivatives as a strongly conjugated system is not governed by simple additive schemes and is difficult to estimate. Earlier, we have demonstrated[11] that the methoxy substituent located in different moieties of the molecule (compounds **8** and **9**) exerts different effects on the tautomeric equilibrium (the ratio of the tautomeric forms [**Q**] : [**B**] in $CDCl_3$ is given in parentheses).



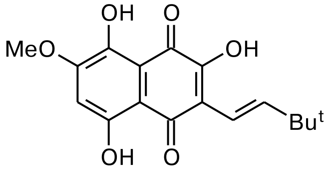
8 (70.0 : 30.0)



9 (89.0 : 11.0)



4b (89.4 : 10.6)

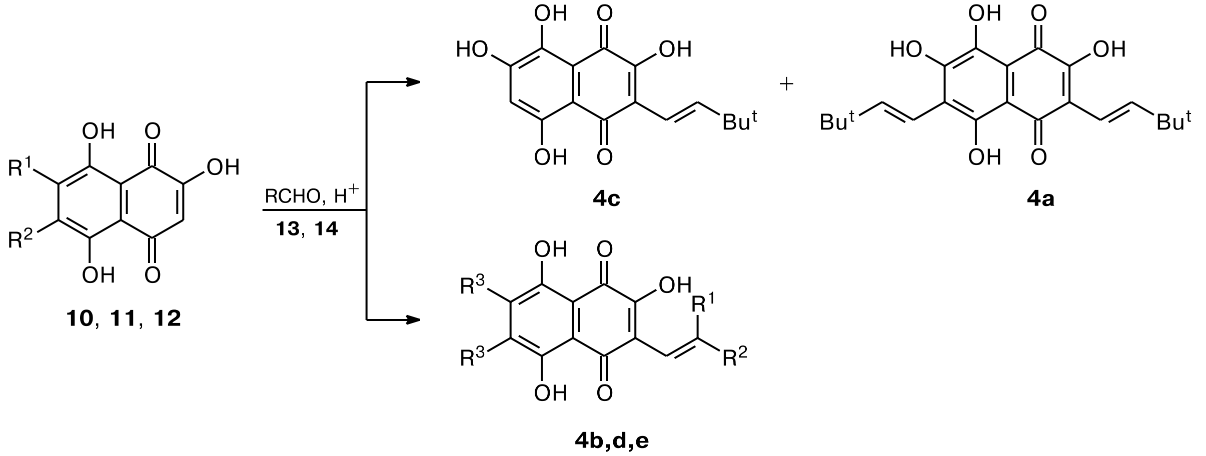


4f (84.5 : 15.5)

Measurements demonstrated that the methoxy or alkenyl substituents in compounds **4b** and **9** lead to the same shift of the tautomeric equilibrium toward the less stable tautomers **B**. However, if these substituents are located in different moieties of the molecule (compound **4f**), their effects on the shift of the tautomeric equilibrium are subtracted rather than added. The subtraction is not additive (30 – 11 = 19%), but, on the whole, gives a correct quantitative prediction of the amount of the benzenoid tautomers (the measurements gave 15.5%).

Alkenylhydroxynaphthazarins **4a–c,e** were prepared in satisfactory yields by the acid-catalyzed reactions[14] of mompain (**10**), naphthopurpurin (**11**), and 6,7-dichloro-

Scheme 5



4: $R^1 = R^3 = H$, $R^2 = Bu^t$ (**b**); $R^1 = R^2 = Et$, $R^3 = H$ (**d**); $R^1 = H$, $R^2 = Bu^t$, $R^3 = Cl$ (**e**)
10: $R^1 = OH$, $R^2 = H$; **11:** $R^1 = R^2 = H$; **12**: $R^1 = R^2 = Cl$; **13**: $R = CH_2Bu^t$; **14**: $R = CHEt_2$

2-hydroxynaphthazarin (**12**), respectively, with 3,3-dimethylbutanal (**13**) (Scheme 5).

To the contrary, the reaction of naphthopurpurin (**11**) with 2-ethylbutanal (**14**) in the presence of $CH_3NH_2 \cdot HCl$ or TsOH[14] did not produce the target alkenylnaphthazarin **4d**. The reaction with $NH_2CH_2CH_2COOH \cdot AcOH$ as the catalyst[18] afforded product **4d** in a yield of no higher than 5%. Compound **4d** was prepared in satisfactory yield (31%) by the reaction of substrate **11** with aldehyde **14** in the presence of an equimolar mixture of methylamine hydrochloride and *para*-toluenesulfonic acid. It should be noted that the use of the mixed catalyst allowed us also to essentially decrease the reaction time and increase the yields of the condensation products of other hydroxynaphthazarins with aldehydes, including those considered in the present study. Thus the condensation of 6,7-dichloro-2-hydroxynaphthazarin (**12**) with 3,3-dimethylbutanal (**13**) in the presence of $MeNH_2 \cdot HCl$—TsOH (1 : 1) was completed in 4 h and afforded alkenylnaphthazarin **4e** in 82% yield, whereas the reaction performed under the conditions described in the study[14] for 8 h gave this product in only 63% yield (see Experimental). Methyl ether **4f** was prepared by methylation of mompain derivative **4c** with diazomethane according to a known procedure.[19]

The structures of the compounds synthesized were established based on the data from NMR spectroscopy and mass spectrometry. In the ^1H NMR spectra of compounds **4a—c**, **4e—f**, and **6**, the coupling constants of the vinyl protons are 16.6—16.7 Hz, which unambiguously indicates the *trans* configuration of the double bond.

To summarize, the results of the present study show that the effect of the double bond of the alkenyl substituent on the tautomeric equilibrium of 3-(alk-1-enyl)-2-hydroxynaphthazarins in organic aprotic solvents (hexane, CCl_4, or $CHCl_3$) directly depends on the degree of conjugation of this bond with the π bonds of naphthazarin. If the naphthazarin fragment is coplanar with the double bond of the alkenyl substituent, solutions contain the major tautomer, *viz.*, the 3-(alk-1-enyl)-2,5,8-trihydroxy-1,4-naphthoquinone derivative, along with the second tautomer, *viz.*, 7-(alk-1-enyl)-5,6,8-trihydroxy-1,4-naphthoquinone. If the double bond of the alkenyl substituent is not involved in conjugation with naphthazarin due to steric hindrance, the influence of this double bond is comparable with that of the saturated alkyl substituent. The contributions of the substituents to the tautomeric equilibrium of alkenylhydroxynaphthazarin derivatives are not additive.

Experimental

The melting points of the newly synthesized compounds were determined on a Boetius hot-stage apparatus and were not corrected. The IR spectra were recorded on a Bruker Vector 22 Fourier-transform spectrophotometer at 2.0 cm^{-1} resolution in $CHCl_3$, CCl_4, and hexane using cells with CaF_2 windows; the layer thickness was 0.40—2.50 mm. The frequencies and areas were measured and the band contours of the stretching vibrations of the β-hydroxy groups were deconvolved after smoothing of the spectrum using the OPUS/IR 02 program package (version 3.0.2). The reproducibility of measurements of the frequencies was no lower than 0.5 cm^{-1}. The concentrations of the compounds in solutions was 5—20 mmol L^{-1}. The ^1H NMR spectra were recorded on a Bruker AC-250 spectrometer in $CDCl_3$ with Me_4Si as the internal standard. The mass spectra (EI) were obtained on an LKB-9000S instrument with direct inlet of the samples into the ion source; the energy of ionizing electrons was 70 eV. The course of the reactions and the purity of the compounds synthesized were monitored by TLC on Merck 60F-254 plates in a 3 : 1 hexane—acetone solvent system. Individual compounds were isolated from mixtures of the reaction products by PTLC on plates (20×20 cm) with a nonfixed 5—40 μm silica gel layer (H^+ form).[20] The yields of the compounds were not optimized. Mompain (**10**),[20] naphthopurpurin (**11**),[21] 6,7-dichloro-2-hydroxynaphthazarin (**12**),[22] 2-hydroxy-7-methoxynaphthazarin **8**,[23] and 2-hydroxy-3-methoxynaphthazarin **9** [24] were synthesized according to procedures described earlier.

Condensation of 2-hydroxynaphthazarins 10—12 with 3,3-dimethylbutanal. A solution of the substrate (1 mmol), 3,3-dimethylbutanal (**13**) (5 mmol), and $MeNH_2 \cdot HCl$ (1.2 mmol) in ethanol (40 mL) was refluxed, the course of the reaction being monitored by TLC. The reaction mixture was concentrated to 2—3 mL, water (40 mL) was added, and the mixture was extracted with diethyl ether (3×10 mL). The combined extracts were washed with water (2×10 mL) and dried with anhydrous Na_2SO_4. The solvent was removed *in vacuo*. The individual compounds were isolated by column chromatography using a hexane—acetone gradient, 50 : 1—10 : 1, followed by preparative TLC in a 3 : 1 hexane—acetone mixture.

The reaction of mompain (**10**) with 3,3-dimethylbutanal performed for 10 h afforded 88 mg (29%) of **3-(3,3-dimethylbut-1-enyl)-2,5,7,8-tetrahydroxy-1,4-naphthoquinone (4c)**, R_f 0.41, m.p. 191—198 °C. IR ($CHCl_3$), ν/cm^{-1}: 3528 m, 3398 m (β-OH); 1651 w, 1614 s, 1591 s (C=O); ~1575 sh. m (C=C). ^1H NMR, δ: 1.15 (s, 9 H, 3 Me); 6.62 (d, 1 H, CH, J = 16.6 Hz); 6.71 (s, 1 H, H(6)); 7.18 (d, 1 H, CH, J = 16.6 Hz); 7.49 (s, 2 H, β-OH); 11.78 and 13.21 (both s, 1 H each, α-OH). MS, m/z (I_{rel} (%)): 305 $[M + 1]^+$(11), 304 $[M]^+$ (59), 303 (15), 289 (18), 261 (20), 249 (14), 248 (100), 247 (61). In addition to product **4c**, 41 mg (11%) of **2,5,7,8-tetrahydroxy-3,6-bis(3,3-dimethylbut-1-enyl)-1,4-naphthoquinone (4a)** was isolated from the reaction mixture, R_f 0.54, m.p. 175—185 °C. IR ($CHCl_3$), ν/cm^{-1}: 3517 m, 3389 m (β-OH); ~1635 sh. w, 1612 s, 1599 s (C=O); ~1575 sh. s (C=C). ^1H NMR, δ: 1.16 (s, 18 H, 6 Me); 6.61 and 7.14 (both d, 2 H each, CH, J = 16.6 Hz); 7.15 (s, 2 H, β-OH); 11.94 and 14.11 (both s, 1 H each, α-OH). MS, m/z (I_{rel} (%)): 387 $[M + 1]^+$ (26), 386 $[M]^+$ (46), 331 (57), 330 (95), 329 (100), 328 (19), 327 (21), 287 (13), 274 (38), 273 (69), 272 (17), 260 (38), 259 (76), 231 (13).

The reaction of naphthopurpurin (**11**) with 3,3-dimethylbutanal performed for 10 h afforded 115 mg (40%) of **(3,3-dimethylbut-1-enyl)-2,5,8-trihydroxy-3-1,4-naphthoquinone (4b)**, R_f 0.74, m.p. 169—175 °C. IR ($CHCl_3$), ν/cm^{-1}: 3502 w, 3379 m (β-OH); 1635 sh. w, 1616 s, 1595 s (C=O); 1572 s (C=C).

^{1}H NMR, δ: 1.15 (s, 9 H, 3 Me); 6.55 and 7.15 (both d, 1 H each, CH, J = 16.6 Hz); 7.20 (d, 1 H, H(7), J = 9.3 Hz); 7.28 (d, 1 H, H(6), J = 9.3 Hz); 7.83 (s, 1 H, β-OH); 11.56 and 12.89 (both s, 1 H each, α-OH). MS, *m/z* (I_{rel} (%)): 289 [M + 1]$^+$ (13), 288 [M]$^+$ (69), 273 (23), 233 (15), 232 (100), 231 (34).

The reaction of 6,7-dichloro-2,5,8-trihydroxy-1,4-naphthoquinone (**12**) with 3,3-dimethylbutanal performed for 8 h afforded 225 mg (63%) of **6,7-dichloro-3-(3,3-dimethylbut-1-enyl)-2,5,8-trihydroxy-1,4-naphthoquinone (4e)**, R_f 0.69, m.p. 198—202 °C. IR ($CHCl_3$), ν/cm^{-1}: 3519 v.w, 3390 m (β-OH); ~1635 sh.w, 1616 s, 1598 s (C=O); 1557 w (C=C). ^{1}H NMR, δ: 1.16 (s, 9 H, 3 Me); 6.54 and 7.19 (both d, 1 H each, CH, J = 16.6 Hz); 7.80 (s, 1 H, β-OH); 12.12 and 13.58 (both s, 1 H each, α-OH). ^{1}H NMR ($CDCl_3$ + CD_3OD), δ: 1.13 (s, 9 H, 3 Me); 6.54 and 7.17 (both d, 1 H each, CH, J = 16.6 Hz). MS, *m/z* (I_{rel} (%)): 357/359/361 [M + 1]$^+$ (12), 356/358/360 [M]$^+$ (25), 341/343/345 (16), 313/315/317 (12), 301/303/305 (50), 300/302/304 (100), 299/301/303 (55), 284 (18), 256 (27).

Condensation of 2-hydroxy-1,4-naphthoquinone with 3,3-dimethylbutanal. A solution of 3,3-dimethylbutanal (400 mg, 4 mmol) in benzene (5 mL) was added dropwise to a boiling solution of 2-hydroxy-1,4-naphthoquinone (150 mg, 0.8 mmol), TsOH (85 mg, 0.5 mmol), and $MeNH_2 \cdot HCl$ (34 mg, 0.5 mmol) in benzene (40 mL) for 2 h. The reaction mixture was refluxed for 2 h, the course of the reaction being monitored by TLC. Then the reaction mixture was worked up as described above, and **3-(3,3-dimethylbut-1-enyl)-2-hydroxy-1,4-naphthoquinone** (**6**) was isolated in a yield of 192 mg (87%), R_f 0.82, m.p. 129—132 °C. IR ($CHCl_3$), ν/cm^{-1}: 3374 m (β-OH); 1656 s (C=O); 1638 m, 1624 w, 1610 m, 1596 m, 1582 w (C=C). ^{1}H NMR, δ: 1.15 (s, 9 H, 3 Me); 6.57 and 7.14 (both d, 1 H each, CH, J = 16.7 Hz); 7.68 and 7.76 (both td, 1 H each, H(6) and H(7), J_1 = 7.5 Hz, J_2 = 1.5 Hz); 7.77 (s, 1 H, β-OH); 8.07 and 8.13 (both ddd, 1 H each, H(5) and H(8), J_1 = 7.5 Hz, J_2 = 1.5 Hz, J_3 = 0.5 Hz). MS, *m/z* (I_{rel} (%)): 256 [M]$^+$ (20), 241 (76), 227 (6), 226 (2), 214 (10), 213 (37), 200 (100), 199 (17).

Condensation of naphthopurpurin (11) with 2-ethylbutanal. A solution of naphthopurpurin (**11**) (205 mg, 1 mmol), 2-ethylbutanal (**14**) (500 mg, 5 mmol), TsOH (102 mg, 0.6 mmol), and $MeNH_2 \cdot HCl$ (40 mg, 0.6 mmol) in benzene (40 mL) was refluxed for 5 h, the course of the reaction being monitored by TLC. The reaction mixture was worked up as described above, and **3-(2-ethylbut-1-enyl)-2,5,8-trihydroxy-1,4-naphthoquinone (4d)** was isolated in a yield of 89 mg (31%), R_f 0.70, m.p. 120—124 °C. IR ($CHCl_3$), ν/cm^{-1}: 3506 v.w, 3396 m (β-OH); ~1635 sh.w, 1616 s, 1598 s (C=O); 1554 w (C=C). ^{1}H NMR, δ: 1.02 (t, 3 H, Me, J = 7.6 Hz); 1.17 (t, 3 H, Me, J = 7.6 Hz); 2.05 (q, 2 H, CH_2, J = 7.6 Hz); 2.31 (dq, 2 H, CH_2, J_1 = 7.6 Hz, J_2 = 1.5 Hz); 5.85 (s, 1 H, CH); 7.20 (d, 1 H, H(7), J = 9.5 Hz); 7.28 (d, 1 H, H(6), J = 9.5 Hz); 11.53 and 12.84 (both s, 1 H each, α-OH). MS, *m/z* (I_{rel}(%)): 289 [M + 1]$^+$ (19), 288 [M]$^+$ (100), 273 (8), 260 (13), 259 (33), 256 (16), 234 (8), 228 (6), 218 (8).

3-(3,3-Dimethylbut-1-enyl)-2,5,8-trihydroxy-7-methoxy-1,4-naphthoquinone (4f). The reaction of an ethereal solution of 3-(3,3-dimethylbut-1-enyl)-2,5,7,8-tetrahydroxy-1,4-naphthoquinone (**4c**) (60 mg, 0.2 mmol) with a solution of diazomethane in diethyl ether[19] afforded product **4f** in a yield of 15 mg (24%), R_f 0.54, m.p. 115—120 °C. IR ($CHCl_3$), ν/cm^{-1}: 3519 w, 3395 m (β-OH); ~1612 sh.s, ~1600 sh.s, 1590 s (C=O); ~1575 sh.m (C=C). ^{1}H NMR, δ: 1.16 (s, 9 H, 3 Me); 3.97 (s, 3 H, OMe); 6.57 (d, 1 H, CH, J = 16.6 Hz), 6.61 (s, 1 H, H_{arom}), 7.17 (d, 1 H, CH, J = 16.6 Hz), 7.65 (s, 1 H, β-OH); 12.06 and 13.41 (both s, 1 H each, α-OH). MS, *m/z* (I_{rel} (%)): 319 [M + 1]$^+$ (13), 318 [M]$^+$ (63), 306 (15), 303 (14), 278 (9), 275 (24), 263 (15), 262 (88), 261 (100). In addition to product **4f**, **3-(3,3-dimethylbut-1-enyl)-5,8-dihydroxy-2,7-dimethoxy-1,4-naphthoquinone** was isolated from the reaction mixture in a yield of 50 mg (76%), R_f 0.61, m.p. 133—135 °C. ^{1}H NMR, δ: 1.16 (s, 9 H, 3 Me); 3.94 and 4.01 (both s, 3 H each, 2 OMe); 6.31 (s, 1 H, H_{arom}), 6.54 and 7.16 (both d, 1 H each, CH, J = 16.5 Hz); 12.86 and 13.73 (both s,1 H each, α-OH). MS, *m/z* (I_{rel} (%)): 333 [M + 1]$^+$ (34), 332 [M]$^+$ (63), 289 (17), 277 (14), 276 (63), 275 (100).

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