The chemistry of naphthazarin derivatives 6.* Hydration of 2-oxo-2,3-dihydro-1,4-naphthoquinone derivatives in organic solvents

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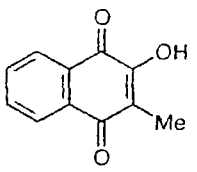
In water-containing organic solvents, 2-oxo-2,3-dihydronaphthoquinone derivatives are hydrated to give the corresponding 2,2-dihydroxy-2,3-dihydronaphthoquinones. The hydration is reversible; in some cases, a keto—*gem*-diol equilibrium is established. The susceptibility of 2-oxo-2,3-dihydronaphthoquinone derivatives for hydration depends on the donor—acceptor properties of substituents at C(3), C(6), and C(7), on whether or not hydroxy groups are present at C(5) and C(8), and on the organic solvent basicity.

Key words: 2-hydroxy-1,4-naphthoquinone; 2-oxo-2,3-dihydro-1,4-naphthoquinone; 2,2-dihydroxy-2,3-dihydro-1,4-naphthoquinone; geminal diol; keto—*gem*-diol equilibrium; chlorination, dichlorine monoxide; free radical alkylation, acetyl peroxide.

Data on the synthesis and chemical properties, in particular, in relation to water, of 2-oxo-2,3-dihydro-1,4-naphthoquinone derivatives are scarce.[2] In a study of chlorination of phthiocol (2-hydroxy-3-methyl-1,4-naphthoquinone (**1**)), it has been found[3] that 3-chloro-3-methyl-2-oxo-2,3-dihydro-1,4-naphthoquinone (**2**) formed initially in this reaction efficiently adds water to give hydrate **3**, while the reverse dehydration (**3**→**2**) proceeds only under conditions of vacuum distillation. Synthesis of 2,3-dioxo-2,3-dihydro-1,4-naphthoquinones from the corresponding 2,3-dihydroxy-1,4-naphthoquinones has been described.[4] It was shown that these compounds readily add water even during their synthesis to give the corresponding monohydrates; however, the methods used in that case[4] did not allow the researchers to draw an ultimate conclusion on the structure of the resulting compounds. In recent years, determination of the exact structure of 2-oxo-2,3-dihydro-1,4-naphthoquinone hydrates and identification of the factors influencing their formation have become topical tasks because these compounds have been found in natural objects[5] and because of the need to elucidate the mechanism of action and the routes of metabolism of pharmacologically active polyhydroxy-1,4-naphthoquinones.[6]



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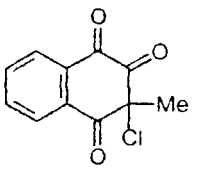

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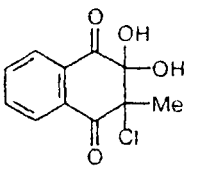
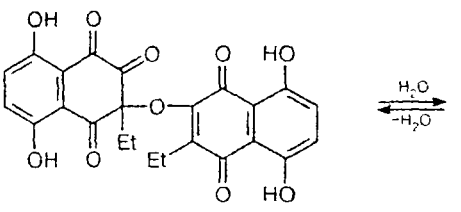


3

Recently we have shown[7] that in organic solutions containing water, the dideoxy analog of islandoquinone **4**, containing a 2-oxo-2,3-dihydro-1,4-naphthoquinone fragment, is equilibrated with the corresponding monohydrate **5**, which can be isolated and characterized under certain conditions.



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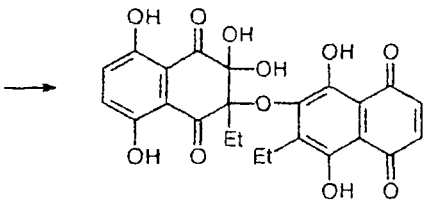

5

In this study, we consider the effect of the nature of substituents on the conversion of 2-oxo-2,3-dihydro-1,4-naphthoquinone **6** into the corresponding geminal diols **7** in organic solvents with various basicities in the presence of water.

We found that one factor stabilizing the hydrated form of the 2-oxo-2,3-dihydro-1,4-naphthoquinone derivatives is the presence of electron-withdrawing sub-

* For Part 5, see Ref. 1.

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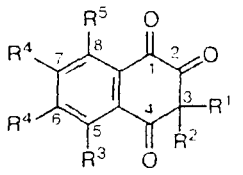
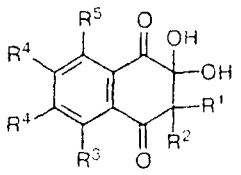


6a—n



7a—n

a—f: $R^1 = R^2 = Cl$

	R^3	R^4	R^5
a	H	H	H
b	OH	H	H
c	H	H	OH
d	OH	Cl	OH
e	OH	H	OH
f	OH	Me	OH

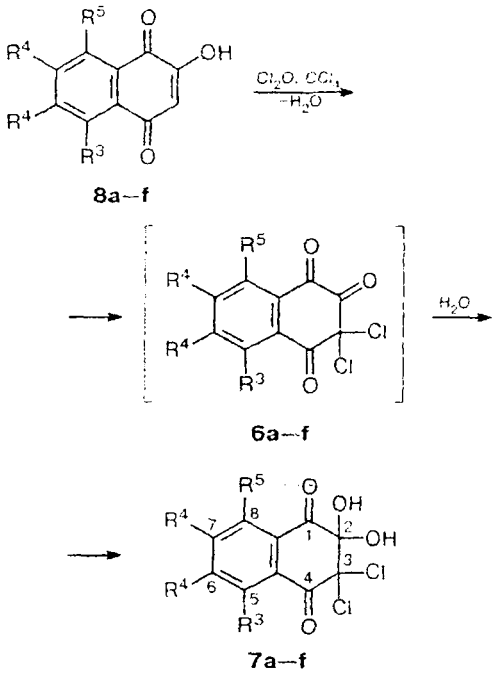
g—j: $R^1 = Cl$, $R^2 = Me$, $R^3 = R^5 = OH$

k—n: $R^1 = R^2 = Me$

	R^3	R^4	R^5
n	H	H	H
k	OH	H	OH
g	H	Cl	
h	H	H	
j	H	Me	
l	OH	H	OH
m	OH	Me	OH

stituents at the C(3) atom. Thus 3,3-dichloro-2-oxo-2,3-dihydro-1,4-naphthoquinones (**6a—f**) add water even under the conditions of their preparation from 2-hydroxy-1,4-naphthoquinones **8a—f** to give hydrates **7a—f** in an almost quantitative yield; these products do not lose water on prolonged heating *in vacuo* (80 °C, 6 h) (Scheme 1).

Scheme 1

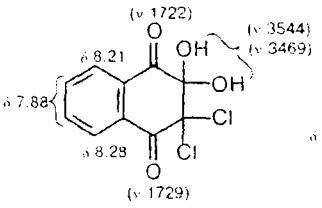


8a—f

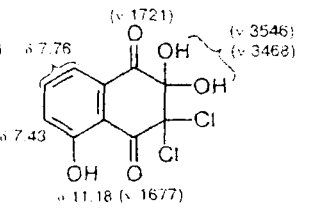
6a—f

7a—f

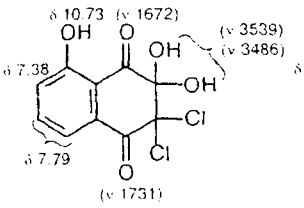
The IR spectra of compounds **7a—c** recorded in $CHCl_3$ do not exhibit the band at ~1750 cm^{-1} for carbonyl absorption, typical of 2-oxo-2,3-dihydro-1,4-naphthoquinones,[7] while the geminal OH groups are



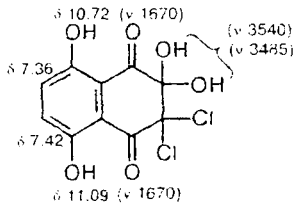
7a



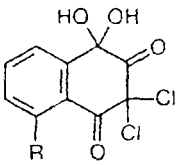
7b



7c



7e



9: R = H (**a**), R = OH (**b**)

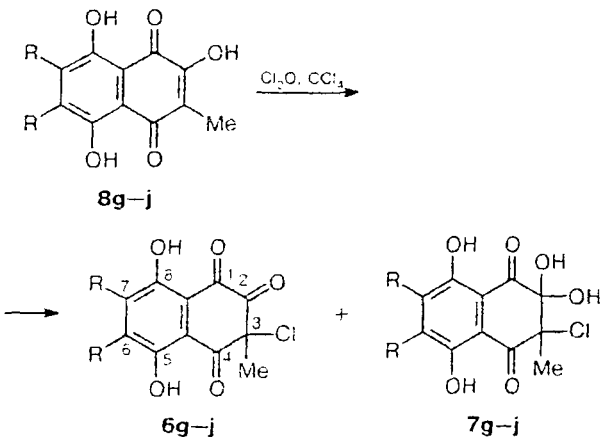
responsible for two narrow bands at about 3468—3546 cm^{-1}.* Comparison of the IR and ^1H NMR spectra of compounds **7a—c** and **7e** makes it possible to conclude unambiguously that the geminal hydroxy groups in compounds **7a** and **7b** are located at C(2) and to reject the corresponding alternative structures **9a** and **9b**.

In the case of hydrate **7c** and 2,2,5,8-tetrahydroxy-2,3-dihydro-1,4-naphthoquinones (2,2-dihydroxy-2,3-dihydronaphthazarins) **7d—f**, unlike compounds **7a,b**, the fact that the *gem*-hydroxy groups are located at C(2) follows unambiguously from the data of the ^1H NMR spectra, whose low-field region exhibits signals of the protons of α-hydroxy groups (at C(8) for **7c** and at C(5) and C(8) for **7d—f**) bound to the carbonyl groups by intramolecular hydrogen bonds (IntraHB) (see Experimental).

On passing from 2-oxo-2,3-dihydro-1,4-naphthoquinone **2**, having a chlorine atom and a methyl radical at C(3), to 2-oxo-2,3-dihydronaphthazarin (5,8-dihydroxy-2-oxo-2,3-dihydro-1,4-naphthoquinone) derivatives **6g—j**, the influence of the hydroxy groups at C(5) and C(8) hampering hydration at C(2) becomes noticeable. Whereas, as noted above, the **3**→**2** conversion proceeds under relatively harsh conditions,[3] the formation of oxo derivatives **6g—j** readily occurs even during vacuum drying of the products of their synthesis,

* The 3000—3600 cm^{-1} range in the IR spectra recorded in KBr provides little information for the assignment of absorption bands for the hydroxy groups of compounds; in particular, it did not allow the authors of Ref. 8 to make a correct choice between the structures of **6a** and **7a**.

Scheme 2



in which they occur as mixtures with the corresponding *gem*-diols **7g—j** (Scheme 2).*

The IR spectra of compounds **6h** and **6j** recorded immediately after they have been dissolved in anhydrous $CHCl_3$ exhibit, in addition to intense absorption bands at 1652 and 1657 cm^{-1} corresponding to the 1- and 4-oxo groups of the dihydronaphthazarin fragment involved in an IntraHB, intense bands at 1745 and 1748 cm^{-1}, respectively, which point to the presence of oxo groups not involved in IntraHB. However, according to ^1H NMR spectroscopy, in water-containing $CHCl_3$, compounds **6g—j** are slowly converted into the corresponding *gem*-diols **7g—j**. For example, the following degrees of conversion were attained 2.5 h after dissolution: **6j→7j** (77%), **6h→7h** (82%), and **6g→7g** (90%). Some acceleration of hydration in the series of oxodihydronaphthazarins **6j**, **6h**, and **6g**, is apparently due to the increase in the electron-withdrawing properties of the substituents at the C(6) and C(7) atoms.

It should be noted that complete conversion of compounds **6g—j** into the corresponding *gem*-diols **7g—j** was not attained; 24 h after dissolution in chloroform contacting with the aqueous phase, the contents of the products were 98, 92, and 90%, respectively. This can be explained by assuming the existence of a keto—*gem*-diol equilibrium (Scheme 3).

The process of hydration of oxo derivatives **6g—j** is strongly affected by basic solvents, which stabilize the *gem*-diol form due to the formation of hydrogen bonds with the hydroxy groups at the C(2) atom. Thus according to the IR spectral data, the degree of **6j→7j** conversion for a solution of oxodihydronaphthazarin **6j** in water- and dioxane-containing $CHCl_3$ (the

* The synthesis of compounds **6g—j** from hydroxynaphthazarins **8g—j** is accompanied by evolution of 0.5 equiv. of H_2O; therefore, the content of *gem*-diols **7g—j** in the corresponding reaction mixtures does not exceed 50%.

Scheme 3

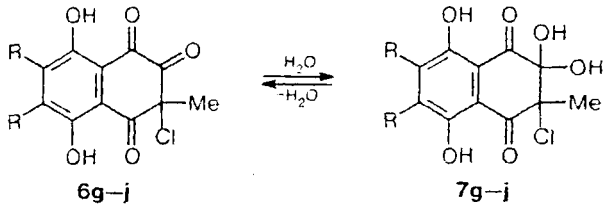


Table 1. Effect of dioxane on the degree of conversion of oxodihydronaphthazarin **6j** into *gem*-diol **7j** in a $CHCl_3$ solution

Time /h	Content of **7j** (%) at the molar ratio **6j** : H_2O : dioxane		
	1 : 1 : 3	1 : 1 : 30	1 : 2 : 30
0.25	21	48	~100
1.5	36	84	
3	48	~100	
8	52		
20	53		

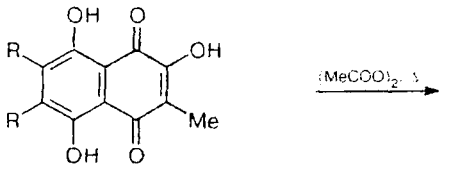
Note. The initial concentration of the chloroform solution of oxohydronaphthazarin **6j** is equal to 0.105 mol L^{-1}. The percentage of *gem*-diol **7j** was estimated from the decrease in the peak intensity of the C=O stretching band at 1745 cm^{-1}.

6j : H_2O : dioxane molar ratio was 1 : 1 : 3) reaches ~50% after 8 h. A dynamic equilibrium is established between the oxo- and *gem*-diol forms, as indicated by the data on the content of **6j** in the solution after 20 h (Table 1). In the medium IR region, the absorption intensity at 1745 cm^{-1}, due to the C=O group in the *oxo*-form, decreases with time, reaching a constant value after 8 h. A band at ~3260 cm^{-1} appears in the high-frequency region of the IR spectrum, indicating that the hydroxy groups at C(2) in *gem*-diol **7j** are bound to dioxane by strong intermolecular hydrogen bonds (InterHB).* When the amount of dioxane increases 10-fold (the ratio **6j** : H_2O : dioxane = 1 : 1 : 30), the same degree of **6j→7j** conversion (48%) was attained after 15 min, while after 3 h, oxodihydronaphthazarin **6j** has been converted almost entirely into hydrate **7j**. A twofold increase in the amount of water (the ratio **6j** : H_2O : dioxane = 1 : 2 : 30) results in rapid hydration of oxo derivative **6j** (Table 1).

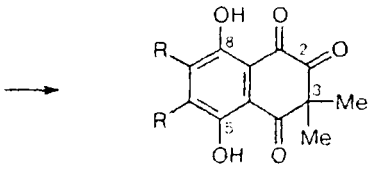
The strength of the InterHB between the *gem*-OH groups of compound **7j** and molecules of acetone is close to that between molecules of **7j** and dioxane. Thus the absorption band due to *gem*-O—H in the high-frequency region of the IR spectrum of compound **7j** in acetone is exhibited at ~3290 cm^{-1}. In acetone solutions

* The strength of the hydrogen bond estimated from the shift of the stretching frequency of the 2-hydroxy groups in *gem*-diol **7j**[9] amounts to ~5.5 kcal mol^{-1}.

Scheme 4



8: R = Cl (**g**), H (**h**), Me (**j**)

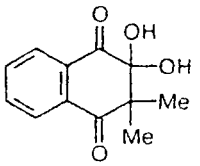


6: R = Cl (**k**), H (**l**), Me (**m**)

containing an amount of water sufficient for hydration, compounds **6g—j** are immediately converted into *gem*-diols **7g—j**.

The introduction of two methyl groups, which are electron-density donors, into position 3 of oxodihydronaphthazarin derivatives stabilizes the structure. For instance, in the organic phase of the $CHCl_3$—H_2O system, in water-containing dioxane or acetone, the products of free radical methylation of 2-hydroxy-3-methylnaphthazarins **8g—j** have the structures of **6k—m**, respectively (Scheme 4). A typical feature of the IR spectra of compounds **6k—m** is the presence of absorption bands at 1733—1737 cm^{-1} corresponding to the CO groups not involved in IntraHB and the absence of absorption bands for *gem*-hydroxy groups (~3400—3600 cm^{-1}).

As noted above in relation to compounds **6g—j**, the hydroxy groups at C(5) and C(8) stabilize the 2-oxo-2,3-dihydro-1,4-naphthoquinone structure in solutions in water-containing organic solvents. In the case of compounds **6k—m**, this feature of hydroxy groups at C(5) and C(8) is displayed especially clearly. Indeed, whereas compounds **6k—m** do not undergo hydration, the product of methylation of phthiocol (**1**) exists only as *gem*-diol **7n** under the same conditions.



7n

Thus, 2-oxo-2,3-dihydro-1,4-naphthoquinone derivatives dissolved in water-containing organic solvents are hydrated at the oxo group attached at the C(2) atom to give the corresponding geminal diols; in the general case, they are equilibrated with the initial *oxo*-form. Electron-withdrawing substituents at C(3) and, to a lesser extent, at C(6) and C(7) shift the equilibrium toward the hydrated form. In some cases, this form not only predominates in solution but can also be isolated as a stable product. An increase in the solvent basicity also stabilizes the *gem*-diol form. On the other hand, hydroxy groups at the C(5) and C(8) atoms act in the opposite direction, *i.e.*, stabilize the initial *oxo*-form.

Experimental

Melting points were determined on a Boetius hot stage and were not corrected. IR spectra were recorded on a Specord M-82 spectrophotometer and a Bruker Vector 22 FT spectrophotometer in $CHCl_3$, dioxane, and acetone. ^1H and ^{13}C NMR spectra were recorded on a Bruker WM-250 spectrometer (250.13 MHz for ^1H and 62.9 MHz for ^{13}C) in $CDCl_3$ and acetone-d_6 (with Me_4Si as the internal standard). Mass spectra (EI) were run on an LKB-9000S instrument with direct sample injection with an energy of ionizing electrons of 70 eV. The course of the reactions was monitored and the purity of the products was checked by TLC on Silufol UV-254 plates in the 3 : 1 hexane—acetone system. Individual compounds were isolated from product mixtures using PTLC on 20×20 cm plates with a nonfixed layer of 5—40 μm silica gel (H^+ form)[10] in the 3 : 1 hexane—acetone system. The product yields were not optimized. Most of the initial compounds were prepared by previously described procedures: **2,5-dihydroxy-1,4-naphthoquinone (8b)** and **3,5-dihydroxy-1,4-naphthoquinone (8c)**,[11] **6,7-dichloro-2,5,8-trihydroxy-1,4-naphthoquinone (8d)**,[12] **2,5,8-trihydroxy-1,4-naphthoquinone (8e)**,[13] **2,5,8-trihydroxy-6,7-dimethyl-1,4-naphthoquinone (8f)**,[14] **6,7-dichloro-2,5,8-trihydroxy-3-methyl-1,4-naphthoquinone (8g)**,[15] and **2,5,8-trihydroxy-3-methyl-1,4-naphthoquinone (8h)**.[13]

2,5,8-Trihydroxy-3,6,7-trimethyl-1,4-naphthoquinone (8j). A mixture of 3-methyl-2,4-dimethoxyphenol (0.74, 4.4 mmol) and dimethylmaleic anhydride (1.11 g, 8.8 mmol) were introduced with stirring at 140 °C into a melt of anhydrous $AlCl_3$ (5.34 g, 40 mmol) and NaCl (0.94 g, 16 mmol). The temperature of the mixture was increased to 190 °C and the melt was stirred for an additional 3 min. The reaction mixture was cooled and hydrolyzed with 5% HCl (75 mL). The crude product **8j** formed over a period of 12 h was separated, washed with 50 mL of hot H_2O, dried, and purified on a column with silica gel L 40/100 μm (H^+-form)[10] using the hexane—acetone gradient system, 8 : 1→6 : 1 (300 mL). Yield 0.68 g (62%), m.p. 226—229 °C. ^1H NMR ($CDCl_3$), δ: 2.09 (s, 3 H, CH_3); 2.26 (s, 3 H, CH_3); 2.29 (s, 3 H, CH_3); 7.38 (br.s, 1 H, β-OH); 12.14 (s, 1 H, α-OH); 13.55 (s, 1 H, α-OH). MS, *m/z* (I_{rel} (%)): 249 $[M + 1]^+$ (23), 248 $[M]^+$ (100), 220 (20), 219 (11), 202 (19).

Synthesis of *gem*-diols 7a—f. A 0.1 *M* solution of Cl_2O (5 mL) in dry CCl_4 was added to a suspension of a substrate (**8a—f**) (0.3 mmol) in 10 mL of CCl_4 stirred at ~20 °C.[16] The reaction was carried out until the initial substrate **8a—f** disappeared from the mixture (TLC monitoring). The precipitate of product **7a—f** was separated by filtration and dried *in vacuo* at ~20 °C.

3,3-Dichloro-2,2-dihydroxy-2,3-dihydro-1,4-naphthoquinone (7a), 98%, m.p. 101—103 °C. Found (%): C, 46.08; H, 2.20. $C_{10}H_6Cl_2O_4$. Calculated (%): C, 46.00; H, 2.32. IR ($CHCl_3$), ν/cm^{-1}: 3544 m (*gem*-O—H), 3469 m (*gem*-O—H), 1729 sh (C=O), 1722 vs (C=O), 1595 m (C=C); IR (CCl_4), ν/cm^{-1}: 3553 m (*gem*-O—H), 3473 m (*gem*-O—H), 1733 vs (C=O), 1722 vs (C=O), 1597 m (C=C). ^1H NMR ($CDCl_3$), δ: 3.75 (br.s, 2 H, *gem*-OH); 7.88 (m, 2 H, 2 H_{arom}); 8.21 (m,

1 H, H_{arom}); 8.28 (m, 1 H, H_{arom}). MS, *m/z* (I_{rel} (%)): 242/244/246 [M − H_2O]$^+$ (4), 214/216/218 (97), 213/215/217 (100), 208/210 (14), 207/209 (11), 180/182 (22), 179/181 (20).

3,3-Dichloro-2,2,5-trihydroxy-2,3-dihydro-1,4-naphthoquinone (7b), 98%, m.p. 121—124 °C. Found (%): C, 43.12; H, 2.20. $C_{10}H_6Cl_2O_5$. Calculated (%): C, 43.35; H, 2.18. IR ($CHCl_3$), ν/cm^{-1}: 3546 m (*gem*-O—H), 3468 m (*gem*-O—H), ~3208 br (α-O—H), 1721 vs (C=O), 1677 m (C=O), 1605 m (C=C), 1576 m (C=C). ^{1}H NMR ($CDCl_3$), δ: 3.75 (br.s, 1 H, *gem*-OH); 5.48 (br.s, 1 H, *gem*-OH); 7.43 (m, 1 H, H_{arom}); 7.76 (m, 2 H, H_{arom}); 11.18 (s, 1 H, α-OH). ^{1}H (acetone-d_6), δ: 7.22 (br.s, 2 H, 2 *gem*-OH); 7.48 (br.d, 1 H, H_{arom}, J = 8.8 Hz); 7.74 (br.d, 1 H, H_{arom}, J = 8.0 Hz); 7.92 (t, 1 H, H_{arom}, J = 8.2 Hz); 11.08 (s, 1 H, α-OH). MS, *m/z* (I_{rel} (%)): 276/278/280 [M]$^+$ (4), 259/261/263 (14), 258/260/262 (12), 231/233/235 (36), 230/232/234 (42), 225/227 (95), 224/226 (100), 197/199 (43), 196/198 (42), 195/197 (15).

3,3-Dichloro-2,2,8-trihydroxy-2,3-dihydro-1,4-naphthoquinone (7c), 99%, m.p. 101—103 °C. Found (%): C, 43.52; H, 2.04. $C_{10}H_6Cl_2O_5$. Calculated (%): C, 43.35; H, 2.18. IR ($CHCl_3$), ν/cm^{-1}: 3539 m (*gem*-O—H), 3486 m (*gem*-O—H), ~3241 br (α-O—H), 1731 vs (C=O), 1672 m (C=O), 1607 m (C=C), 1576 m (C=C). NMR ^{1}H ($CDCl_3$), δ: 3.88 (br.s, 1 H, *gem*-OH); 5.36 (br.s, 1 H, *gem*-OH); 7.38 (m, 1 H, H_{arom}); 7.79 (m, 2 H, H_{arom}); 10.73 (s, 1 H, α-OH). MS, *m/z* (I_{rel} (%)): 276/278/280 [M]$^+$ (4), 258/260/262 (7), 257/259/261 (25), 230/232/234 (60), 229/231/233 (100), 224/226 (55), 223/225 (54), 196/198 (31), 195/197 (41), 194/196 (51).

3,3,6,7-Tetrachloro-2,2,5,8-tetrahydroxy-2,3-dihydro-1,4-naphthoquinone (7d), 95%, m.p. >93 °C (dec.). Found (%): C, 33.28; H, 1.16. $C_{10}H_4Cl_4O_6$. Calculated (%): C, 33.18; H, 1.11. IR ($CHCl_3$), ν/cm^{-1}: 3539 m (*gem*-O—H), 3491 m (*gem*-O—H), 3165 m.br (α-O—H), 1674 vs (C=O), 1564 m (C=C). ^{1}H NMR ($CDCl_3$), δ: 3.80 (br.s, 1 H, *gem*-OH); 5.30 (br.s, 1 H, *gem*-OH); 11.30 (s, 1 H, α-OH); 11.71 (s, 1 H, α-OH). MS, *m/z* (I_{rel} (%)): 360/362/364/366/368 [M]$^+$ (11), 308/310/312/314 (100), 307/309/311/313 (78), 280/282/284/286 (17), 279/281/283/285 (14), 273/275/277 (31), 245/247/249 (24).

3,3-Dichloro-2,2,5,8-tetrahydroxy-2,3-dihydro-1,4-naphthoquinone (7e), 96%, m.p. 120—122 °C. Found (%): C, 41.21; H, 2.18. $C_{10}H_8Cl_2O_6$. Calculated (%): C, 40.98; H, 2.06. IR ($CHCl_3$), ν/cm^{-1}: 3542 m (*gem*-O—H), 3482 m (*gem*-O—H), ~3219 m.br (α-O—H), 1668 vs (C=O), 1596 m (C=C). ^{1}H NMR ($CDCl_3$), δ: 3.67 (br.s, 1 H, *gem*-OH); 5.36 (br.s, 1 H, *gem*-OH); 7.36 (d, 1 H, H_{arom}, J = 9.8 Hz); 7.42 (d, 1 H, H_{arom}, J = 9.8 Hz); 10.72 (s, 1 H, α-OH); 11.09 (s, 1 H, α-OH). MS, *m/z* (I_{rel} (%)): 246/248/250 (20), 241/243 (41), 240/242 (100), 212/214 (53), 211/213 (38), 205 (13).

3,3-Dichloro-2,2,5,8-tetrahydroxy-6,7-dimethyl-2,3-dihydro-1,4-naphthoquinone (7f), 98%, m.p. 124—127 °C. Found (%): C, 45.17; H, 3.22. $C_{12}H_{10}Cl_2O_6$. Calculated (%): C, 44.88; H, 3.14. IR ($CHCl_3$), ν/cm^{-1}: 3542 m (*gem*-O—H), 3475 m (*gem*-O—H), 3150 m.br (α-O—H), 1659 vs (C=O), 1585 m (C=C). ^{1}H NMR ($CDCl_3$), δ: 2.33 (s, 3 H, CH_3); 2.34 (s, 3 H, CH_3); 3.70 (br.s, 1 H, *gem*-OH); 5.33 (br.s, 1 H, *gem*-OH); 11.24 (s, 1 H, α-OH); 11.66 (s, 1 H, α-OH). ^{1}H NMR (acetone-d_6), δ: 2.33 (s, 6 H, 2 CH_3); 7.23 (br.s, 2 H, 2 *gem*-OH); 11.60 (s, 1 H, α-OH); 11.62 (s, 1 H, α-OH). ^{13}C NMR (acetone-d_6), δ: 12.45 (6-CH_3); 12.60 (7-CH_3); 89.1 (3); 95.8 (2); 108.0 (4a); 108.3 (8a); 138.8 (6); 139.2 (7); 155.5 (5); 156.3 (8); 188.4 (4); 195.0 (1). MS, *m/z* (I_{rel} (%)): 320/322/324 [M]$^+$ (2), 319/321/323 [M − H]$^+$ (9), 302/304/306 (5), 301/303/305 (36), 274/276/278 (13), 273/275/277 (32), 268/270 (77), 267/269 (74), 266/268 (37), 240/242 (28), 239/241 (100).

Synthesis of 2,3-dihydro-2-oxonaphthazarins 6g—j. Compounds **8g—j** were chlorinated by a solution of Cl_2O in CCl_4 as described above. The major fraction was isolated by PTLC and dried *in vacuo* for 6 h at 110 °C to give the corresponding 2,3-dihydro-2-oxonaphthazarins **6g—j**.

3,6,7-Trichloro-5,8-dihydroxy-3-methyl-2-oxo-2,3-dihydro-1,4-naphthoquinone (6g), m.p. > 140 °C (dec.). Found (%): C, 40.64; H, 1.63. $C_{11}H_5Cl_3O_5$. Calculated (%): C, 40.84; H, 1.56. ^{1}H NMR ($CDCl_3$), δ: 2.04 (s, 3 H, CH_3); 12.15 (s, 1 H, α-OH); 12.39 (s, 1 H, α-OH). MS, *m/z* (I_{rel} (%)): 322/324/326/328 [M]$^+$ (5), 288/290/292 (23), 287/289/291 (100), 260/262/264 (13), 259/261/263 (19), 242/244/246 (21).

3-Chloro-5,8-dihydroxy-3-methyl-2-oxo-2,3-dihydro-1,4-naphthoquinone (6h), m.p. 98—101 °C. Found (%): C, 51.65; H, 2.88. $C_{11}H_7ClO_5$. Calculated (%): C, 51.89; H, 2.77. IR ($CHCl_3$), ν/cm^{-1}: 1748 m (2-C=O), 1657 vs (1,4-C=O), 1589 m (C=C). ^{1}H NMR ($CDCl_3$), δ: 2.00 (s, 3 H, CH_3); 7.38 (d, 1 H, H_{arom}, J = 10.0 Hz); 7.46 (d, 1 H, H_{arom}, J = 10.0 Hz); 11.51 (s, 1 H, α-OH); 11.80 (s, 1 H, α-OH). MS, *m/z* (I_{rel} (%)): 254/256 [M]$^+$ (52), 226/228 (39), 220 (100), 219 (33), 192 (24), 191 (99), 174 (47), 163 (30).

3-Chloro-5,8-dihydroxy-3,6,7-trimethyl-2-oxo-2,3-dihydro-1,4-naphthoquinone (6j), m.p. 79—82 °C. Found (%): C, 55.05; H, 3.98. $C_{13}H_{11}ClO_5$. Calculated (%): C, 55.23; H, 3.92. IR ($CHCl_3$), ν/cm^{-1}: 1745 m (2-C=O), 1652 vs (1,4-C=O), 1583 m (C=C). ^{1}H NMR ($CDCl_3$), δ: 1.99 (s, 3 H, CH_3); 2.36 (br.s, 6 H, 2 CH_3); 12.16 (s, 1 H, α-OH); 12.48 (s, 1 H, α-OH). MS, *m/z* (I_{rel} (%)): 282/284 [M]$^+$ (17), 254/256 (15), 248 (100), 247 (15), 220 (22), 219 (50), 191 (17).

Synthesis of 2,2-dihydroxy-2,3-dihydronaphthazarins 7g—j. 2-Oxo-2,3-dihydronaphthazarin **6g—j** (0.1 mmol) was dissolved in 5 mL of acetone containing 1% H_2O. After 1 h, the solvent was removed *in vacuo* at ~20 °C to give products **7g—j**.*

3,6,7-Trichloro-2,2,5,8-tetrahydroxy-3-methyl-2,3-dihydro-1,4-naphthoquinone (7g). IR ($CHCl_3$), ν/cm^{-1}: 3567 m (*gem*-O—H), 3490 m (*gem*-O—H), ~3150 m.br (α-O—H), 1665 vs (C=O). ^{1}H NMR ($CDCl_3$), δ: 1.95 (s, 3 H, CH_3); 3.39 (br.s, 1 H, *gem*-OH); 5.05 (br.s, 1 H, *gem*-OH); 11.29 (s, 1 H, α-OH); 12.01 (s, 1 H, α-OH). ^{1}H NMR (acetone-d_6), δ: 1.93 (s, 3 H, CH_3); 6.92 (br.s, 1 H, *gem*-OH); 7.16 (br.s, 1 H, *gem*-OH); 11.64 (s, 1 H, α-OH). 11.89 (s, 1 H, α-OH). MS, *m/z* (I_{rel} (%)): 321/323/325/327 (8), 288/290/292 (17), 287/289/291 (100).

3-Chloro-2,2,5,8-tetrahydroxy-3-methyl-2,3-dihydro-1,4-naphthoquinone (7h). IR ($CHCl_3$), ν/cm^{-1}: 3568 m (*gem*-O—H), 3482 m (*gem*-O—H), ~3210 m.br (α-O—H), 1661 vs (C=O), 1593 m (C=C). ^{1}H NMR ($CDCl_3$), δ: 1.95 (s, 3 H, CH_3); 3.47 (br.s, 1 H, *gem*-OH); 5.05 (br.s, 1 H, *gem*-OH); 7.29 (d, 1 H, H_{arom}, J = 9.7 Hz); 7.37 (d, 1 H, H_{arom}, J = 9.7 Hz); 10.74 (s, 1 H, α-OH); 11.40 (s, 1 H, α-OH). ^{1}H NMR (acetone-d_6), δ: 1.91 (s, 3 H, CH_3); 6.67 (br.s, 1 H, *gem*-OH); 6.93 (br.s, 1 H, *gem*-OH); 7.39 (d, 1 H, H_{arom}, J = 9.5 Hz); 7.43 (d, 1 H, H_{arom}, J = 9.5 Hz); 11.00 (s, 1 H, α-OH); 11.26 (s, 1 H, α-OH). MS, *m/z* (I_{rel} (%)): 272/274 [M]$^+$ (9), 255/257 (78), 254/256 (11), 227/229 (47), 226/228 (32), 223 (14), 222 (72), 221 (99), 220 (100).

3-Chloro-2,2,5,8-tetrahydroxy-3,6,7-trimethyl-2,3-dihydro-1,4-naphthoquinone (7j). IR ($CHCl_3$), ν/cm^{-1}: 3568 m (*gem*-O—H), 3480 m (*gem*-O—H), 1653 vs (C=O), 1585 m (C=C). ^{1}H NMR ($CDCl_3$), δ: 1.90 (s, 3 H, CH_3); 2.31 (s,

* Due to the thermal instability of compounds **7g—j**, we were unable to obtain satisfactory data of elemental analysis or to determine their melting points.

3 H, CH_3); 2.32 (s, 3 H, CH_3); 3.49 (br.s, 1 H, *gem*-OH); 4.99 (br.s, 1 H, *gem*-OH); 11.26 (s, 1 H, α-OH); 11.96 (s, 1 H, α-OH). ^{1}H NMR (acetone-d_6), δ: 1.90 (s, 3 H, CH_3); 2.31 (s, 6 H, 2 CH_3); 6.58 (br.s, 1 H, *gem*-OH); 6.82 (br.s, 1 H, *gem*-OH); 11.59 (s, 1 H, α-OH); 11.89 (s, 1 H, α-OH). MS, *m/z* (I_{rel} (%)): 300/302 (7), 282/284 (29), 281/283 (13), 254/256 (21), 249 (63), 248 (100), 247 (35), 246 (12).

Synthesis of 3,3-dimethyl-2,3-dihydronaphthoquinones 6k—m and 7n. A solution of freshly prepared acetyl peroxide in Bu^{t}OH was slowly added dropwise to a boiling solution of the corresponding hydroxynaphthoquinone (**8g—j**, **1**) (0.3 mmol) in Bu^{t}OH (15 mL).[17] The course of the reaction was monitored by TLC. When the reaction had been completed, the solvent was removed. Product (**6k—m**, **7n**) was isolated by PTLC*.

6,7-Dichloro-5,8-dihydroxy-3,3-dimethyl-2-oxo-2,3-dihydro-1,4-naphthoquinone (6k), 16%, m.p. 179—183 °C, R_f 0.32. Found (%): C, 47.34; H, 2.77. $C_{12}H_8Cl_2O_5$. Calculated (%): C, 47.55; H, 2.66. IR ($CHCl_3$), ν/cm^{-1}: 1737 m (2-C=O), 1652 vs (1,4-C=O), 1558 m (C=C). ^{1}H NMR ($CDCl_3$), δ: 1.58 (s, 6 H, 2 CH_3); 12.48 (s, 1 H, α-OH); 12.78 (s, 1 H, α-OH). ^{1}H NMR (acetone-d_6), δ: 1.52 (s, 6 H, 2 CH_3); 12.41 (s, 1 H, α-OH); 12.62 (s, 1 H, α-OH). MS, *m/z* (I_{rel} (%)): 302/304/306 $[M]^+$ (22), 301/303/305 $[M - 1]^+$ (100), 274/276/278 (49), 273/275/277 (37) 259/261/263 (48), 258/260/262 (22).

5,8-Dihydroxy-3,3-dimethyl-2-oxo-2,3-dihydro-1,4-naphthoquinone (6l), 18%, m.p. 126—130 °C, R_f 0.33. Found (%): C, 61.23; H, 4.38. $C_{12}H_{10}O_5$. Calculated (%): C, 61.54; H, 4.30. IR ($CHCl_3$), ν/cm^{-1}: 3100 m,br (α-O—H), 1735 m (2-C=O), 1641 vs (1,4-C=O), 1585 m (C=C). ^{1}H NMR ($CDCl_3$), δ: 1.57 (s, 6 H, 2 CH_3); 7.36 (d, 1 H, H_{arom}, J = 9.9 Hz); 7.45 (d, 1 H, H_{arom}, J = 9.9 Hz); 11.91 (s, 1 H, α-OH); 12.08 (s, 1 H, α-OH). ^{1}H NMR (acetone-d_6), δ: 1.54 (s, 6 H, 2 CH_3); 7.42 (d, 1 H, H_{arom}, J = 9.9 Hz); 7.51 (d, 1 H, H_{arom}, J = 9.9 Hz); 11.90 (s, 1 H, α-OH); 12.01 (s, 1 H, α-OH). MS, *m/z* (I_{rel} (%)): 234 $[M]^+$ (100), 233 (86), 218 (10), 206 (30), 205 (25), 191 (61), 190 (67), 178 (15), 177 (15).

5,8-Dihydroxy-3,3,6,7-tetramethyl-2-oxo-2,3-dihydro-1,4-naphthoquinone (6m), 43%, m.p. 136—139 °C, R_f 0.34. Found (%): C, 63.76; H, 5.47. $C_{14}H_{14}O_5$. Calculated (%): C, 64.11; H, 5.38. IR ($CHCl_3$), ν/cm^{-1}: 1733 m (2-C=O), 1639 vs (1,4-C=O), 1580 m (C=C). ^{1}H NMR ($CDCl_3$), δ: 1.55 (s, 6 H, 2 CH_3); 2.35 (s, 3 H, CH_3); 2.36 (s, 3 H, CH_3); 12.59 (s, 1 H, α-OH); 12.70 (s, 1 H, α-OH). MS, *m/z* (I_{rel} (%)): 262 $[M]^+$ (100), 261 (93), 247 (16), 246 (14), 234 (53), 233 (54), 219 (42), 218 (17), 206 (15), 205 (20), 191 (25), 190 (21).

2,2-Dihydroxy-3,3-dimethyl-2,3-dihydro-1,4-naphthoquinone (7n), 9%. IR ($CHCl_3$), ν/cm^{-1}: 3504 m (*gem*-O—H), 1690 vs (C=O), 1601 m (C=C). ^{1}H NMR ($CDCl_3$), δ: 1.57 (s, 3 H, CH_3); 1.58 (s, 3 H, CH_3); 4.10 (br.s, 2 H, *gem*-OH); 7.46 (ddd, 1 H, H_{arom}, ^1J = 8.0 Hz, ^2J = 8.0 Hz, ^3J = 1.5 Hz); 7.67 (ddd, 1 H, H_{arom}, ^1J = 8.0 Hz, ^2J = 8.0 Hz, ^3J = 1.5 Hz); 7.81 (dd, 1 H, H_{arom}, ^1J = 8.0 Hz, ^2J = 1.5 Hz); 7.88 (dd, 1 H, H_{arom}, ^1J = 8.0 Hz, ^2J = 1.5 Hz).

* In the methylation of phthiocol (**1**), the formation of product **7n** is observed upon UV irradiation of the chromatographic plates.

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