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# Hydroxylation of 4-Arylimino-5-hydroxy-1,4-dihydronaphthalen-1-ones

**A. D. Bukhtoyarova and L. V. Ektova**

*Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Division, Russian Academy of Sciences, pr. Akademika Lavrent'eva 9, Novosibirsk, 630090 Russia*

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**Abstract**—Heating of 4-arylimino-5-hydroxy-1,4-dihydronaphthalen-1-ones with sodium hydroxide in the presence of $K_3Fe(CN)_6$ gives the corresponding 2,5-dihydroxy derivatives, while in the reaction with $FeCl_3 \cdot 6H_2O$ 4-arylimino-3,5-dihydroxy-1,4-dihydronaphthalen-1-ones are formed.

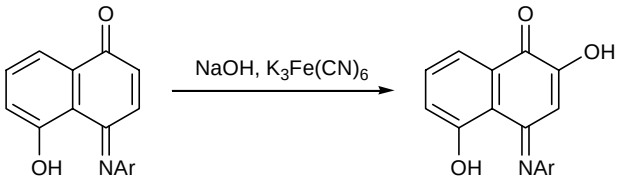
Extensive studies in the field of naphthoquinonimines originate from their high reactivity which makes them convenient starting compounds for the synthesis of various classes of organic compounds [1]. In addition, naphthoquinonimine derivatives are used as dyes for optical data storage systems [2] and color photography [3] and as anticarcinogenic agents [4]. Taking into account that some hydroxy-1,4-naphthoquinones are natural compounds possessing a high biological activity [5], we anticipated that combination of a hydroxynaphthoquinone and *N*-arylmonoquinonimine fragments in a single molecule will give rise to new useful properties. The main procedures for introduction of a hydroxy group into *N*-arylquinonimines are based on hydrolysis of the corresponding amino derivatives and oxidation of quinonimines in alkaline medium [1]. A number of 4-arylimino-2-hydroxy-1,4-dihydronaphthalen-1-ones exhibiting antituberculous activity were synthesized by reaction of 1,2-dioxo-1,2-dihydronaphthalene-4-sulfonic acid potassium salt with the corresponding arylamines [6].

In the present work we studied hydroxylation of 4-arylimino-5-hydroxy-1,4-dihydronaphthalen-1-ones **Ia**–**Ie** under different conditions. 5-Hydroxy-4-phenylimino- and 5-hydroxy-4-(2,4,6-trimethylphenylimino)-1,4-dihydronaphthalen-1-ones **Ia** and **Ib** were oxidized with $K_3Fe(CN)_6$ only in aqueous alkali, and the products were the corresponding 2,5-dihydroxy derivatives **IIa** and **IIb** (Scheme 1). Compound **IIa** was also obtained by acid hydrolysis of 5-hydroxy-4-phenyl-2-phenylamino-1,4-dihydronaphthalen-1-one (**III**) in dilute sulfuric acid.

By oxidation of naphthoquinonimine **Ia** with $FeCl_3 \cdot 6H_2O$ in DMF we obtained 3,5-dihydroxy-4-phenyl-1,4-dihydronaphthalen-1-one (**IVa**) which is isomeric to **IIa**. Compound **Ib** failed to react under analogous conditions, while *N*-(4-methylphenyl)-, *N*-(4-butoxycarbonylphenyl)-, and *N*-(4-methoxyphenyl)-4-imino-5-hydroxy-1,4-dihydronaphthalen-1-ones **Ic**–**Ie** were converted into 3,5-dihydroxy derivatives **IVc**–**IVe** (Scheme 2). It should be noted that neither 2- nor 3-hydroxy derivatives were formed in reactions of naphthoquinonimines **Ia**–**Ie** with such oxidants as $K_2S_2O_8$, $(NH_4)Ce(NO_3)_6$, or $NaIO_4$ in neutral medium.

The position of the newly introduced hydroxy group in the naphthalene ring was confirmed by the

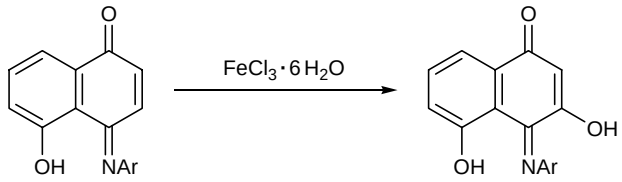
**Scheme 1.**




**Ia**, **Ib** **IIa**, **IIb**

Ar = Ph (**a**), 2,4,6-$Me_3C_6H_2$ (**b**).

**Scheme 2.**



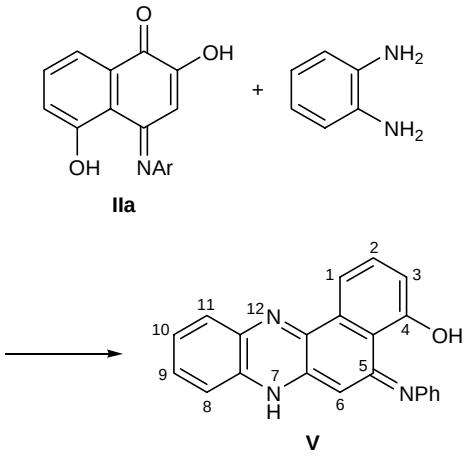

**Ia**, **Ic**–**Ie** **IVa**, **IVc**–**IVe**

Ar = Ph (**a**), 4-$MeC_6H_4$ (**c**), 4-$BuOCOC_6H_4$ (**d**), 4-$MeOC_6H_4$ (**e**).

1070-4280/04/4009-1284 

fact that the reaction of 2,5-dihydroxy derivative **IIa** with *o*-phenylenediamine afforded 5-phenylimino-5*H*-benzo[*a*]phenazin-4-ol (**V**) (Scheme 3). 3,5-Dihydroxy isomers **IVa** and **IVc**–**IVe** failed to react with *o*-phenylenediamine. Isomeric 2,5- and 3,5-dihydroxy-substituted compounds **IIa** and **IVa** can also be distinguished by spectral data. In the $^1$H NMR spectrum of 2,5-dihydroxy derivative **IIa**, the signal from the 5-OH proton is located in a weaker field ($\delta\Delta$ = 0.81 ppm) relative to the corresponding signal of initial compound **Ia** ($\delta$ 13.76 ppm [7]). By contrast, the 5-OH signal in the spectrum of 3,5-dihydroxy isomer **IVa** is displaced upfield ($\delta\Delta$ = 2.22 ppm). Analogous effect of the introduced hydroxy group on the position of the downfield signal was observed for 2- and 3-hydroxyjuglones [8]: the corresponding $\delta\Delta$ values were +0.41 and –0.83 ppm, respectively.

**Scheme 3.**




The reasons for the different directions of oxidative hydroxylation of 4-arylimino-5-hydroxy-1,4-dihydronaphthalen-1-ones are not clear so far. Presumably, 2,5-dihydroxy derivatives **IIa** and **IIb** are formed via 1,4-addition of NaOH, followed by oxidation of the adduct with $K_3Fe(CN)_6$ in a way similar to reactions of 4-imino-1,4-dihydronaphthalen-1-ones with other nucleophiles (which usually lead to 2-substituted derivatives [1]). The only example of formation of 3-*tert*-butoxy-4-phenylimino-1,4-dihydronaphthalen-1-one in the oxidation of *N*-phenyl-1-naphthylamine with *tert*-butyl hydroperoxide was reported in [9].

## EXPERIMENTAL

The IR spectra were recorded in KBr on UR-20 and Vector-22 instruments. The electron absorption spectra were measured on Specord UV-Vis, Hewlett–Packard 4853, and Beckmann DU-8 spectrophotometers from solutions in EtOH. The $^1$H NMR spectra were obtained on a Bruker WP-200SY spectrometer using $CDCl_3$ or DMSO-$d_6$ as solvent. The molecular weights and elemental compositions were determined from the precise *m*/*z* values of the molecular ions in the mass spectra which were run on Finnigan MAT-8200 and Finnigan AEI MS-900 mass spectrometers. The progress of reactions and the purity of products were monitored by thin-layer chromatography on Silufol plates using chloroform as eluent.

**2,5-Dihydroxy-4-phenylimino-1,4-dihydronaphthalen-1-one (IIa) and 2,5-dihydroxy-4-(2,4,6-trimethylphenylimino)-1,4-dihydronaphthalen-1-one (IIb).** A mixture of 0.5 mmol of compound **Ia** or **Ib** in 10 ml of ethanol and 6 mmol of NaOH and 1 mmol of $K_3Fe(CN)_6$ in 5 ml of $H_2O$ was heated for 30 min at 70–75°C. The mixture was poured into water and neutralized with 5% hydrochloric acid, the precipitate was filtered off, the filtrate was extracted with $CHCl_3$ (3×20 ml), and the extract was dried over $CaCl_2$ and evaporated to dryness. The residue was combined with the precipitate and dissolved in $CHCl_3$, and the solution was applied to a column charged with silica gel. Traces of the initial compound were washed off with chloroform, and the subsequent elution with acetone afforded compound **IIa** or **IIb**. Yield of **IIa** 76%, mp 221–222°C (from benzene–hexane, 1:5). IR spectrum, $\nu$, cm$^{-1}$: 1620 (C=N), 1645 (C=O), 3292 (OH). $^1$H NMR spectrum ($CDCl_3$), $\delta$, ppm: 6.61 s (1H, 3-H), 7.03 d (2H, 2'-H, 6'-H, $J$ = 10 Hz), 7.27–7.57 m (6H, 3'-H, 4'-H, 5'-H, 6-H, 7-H, OH), 7.78 d.d (1H, 8-H, $J_{ortho}$ = 9.0, $J_{meta}$ = 1.5 Hz), 14.57 s (1H, OH). UV spectrum, $\lambda_{max}$, nm ($\varepsilon\times10^{-4}$ l mol$^{-1}$ cm$^{-1}$): 423 (0.75). Found: $[M]^+$ 265.07360. $C_{16}H_{11}NO_3$. Calculated: *M* 265.07389.

Yield of **IIb** 62%, mp 297–299°C (from hexane). IR spectrum, $\nu$, cm$^{-1}$: 1647 (C=N), 1664 (C=O), 3333 (OH). $^1$H NMR spectrum ($CDCl_3$), $\delta$, ppm: 2.03 s (6H, $2CH_3$), 2.30 s (3H, $CH_3$), 6.16 s (1H, 3-H), 6.92 s (2H, 3'-H, 5'-H), 7.34 d (1H, 6-H, $J$ = 8.0 Hz), 7.51 t (1H, 7-H, $J$ = 8.0 Hz), 7.74 d (1H, 8-H, $J$ = 8.0 Hz), 14.70 s (1H, OH). UV spectrum, $\lambda_{max}$, nm ($\varepsilon\times10^{-4}$ l mol$^{-1}$ cm$^{-1}$): 392 (0.47). Found: $[M]^+$ 307.12035. $C_{19}H_{17}NO_3$. Calculated: *M* 307.12083.

**Hydrolysis of 5-hydroxy-2-phenylamino-4-phenylimino-1,4-dihydronaphthalen-1-one (III).** A solution of 0.3 mmol of compound **III** in 5 ml of 50% sulfuric acid was heated for 15 min at 125°C. The

mixture was cooled and poured into water, and the precipitate was filtered off and dried. Yield of **IIa** 51%.

**Reaction of 5-hydroxy-4-arylimino-1,4-dihydronaphthalen-1-ones Ia and Ic–Ie with iron(III) chloride.** A mixture of 1 mmol of 5-hydroxy-4-arylimino-1,4-dihydronaphthalen-1-one **Ia** or **Ic**–**Ie** in 15 ml of DMF and 10 mmol of $FeCl_3 \cdot 6H_2O$ was stirred for 3 h at 80–90°C. The mixture was poured into water, 5 ml of 5% hydrochloric acid was added, and the precipitate of compound **IVa** or **IVc**–**IVe** was filtered off, dried in air, and purified by column chromatography on silica gel using chloroform as eluent.

**3,5-Dihydroxy-4-phenylimino-1,4-dihydronaphthalen-1-one (IVa).** Yield 74%, mp 229–230°C (from benzene). IR spectrum, ν, $cm^{-1}$: 1627 (C=N), 1645 (C=O), 3280 (OH). $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 6.35 s (1H, 2-H), 7.10–7.70 m (9H, 2'-H, 3'-H, 4'-H, 5'-H, 6-H, 6-H, 7-H, 8-H, OH), 11.54 s (1H, OH). UV spectrum, $\lambda_{max}$, nm ($\varepsilon \times 10^{-4}$ l $mol^{-1}$ $cm^{-1}$): 415 (0.65), 486 (0.44). Found: $[M]^+$ 265.07360. $C_{16}H_{11}NO_3$. Calculated: *M* 265.073889.

**3,5-Dihydroxy-4-(4-methylphenylimino)-1,4-dihydronaphthalen-1-one (IVc).** Yield 78%, mp 203–205°C (from benzene–hexane, 1:5). IR spectrum, ν, $cm^{-1}$: 1627 (C=N), 1635 (C=O), 3289 (OH). $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 2.33 s (3H, $CH_3$), 6.27 s (1H, 2-H), 7.09–7.21 m (4H, 2'-H, 3'-H, 5'-H, 6'-H), 7.47 br.s (1H, OH), 7.57–7.61 m (3H, 6-H, 7-H, 8-H), 11.53 s (1H, OH). UV spectrum, $\lambda_{max}$, nm ($\varepsilon \times 10^{-4}$ l $mol^{-1}$ $cm^{-1}$): 414 (0.75), 500 (0.53). Found: $[M]^+$ 279.09020. $C_{17}H_{13}NO_3$. Calculated: *M* 279.08954.

**Butyl 4-[2,8-dihydroxy-4-oxonaphthalen-1(4*H*)-ylideneamino]benzoate (IVd).** Yield 84%, mp 159–160°C (from benzene–hexane, 1:5). IR spectrum, ν, $cm^{-1}$: 1613 (C=N), 1634 (C=O), 1699 ($COO^-$), 3317 (OH). $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 0.96 t (3H, $CH_3$, *J* = 7.0 Hz), 1.48 m (2H, $CH_2$), 1.75 m (2H, $CH_2$), 4.31 t (2H, $CH_2$, *J* = 7.0 Hz), 6.50 s (1H, 2-H), 7.18 d.d (1H, 6-H, $J_{ortho}$ = 8.0, $J_{meta}$ = 2.0 Hz), 7.28 d (2H, 2'-H, 6'-H, *J* = 8.0 Hz), 7.60–7.65 m (2H, 7-H, 8-H), 7.67 br.s (1H, OH), 8.07 d (2H, 3'-H, 5'-H, *J* = 8.0 Hz), 11.48 s (1H, OH). UV spectrum, $\lambda_{max}$, nm ($\varepsilon \times 10^{-4}$ l $mol^{-1}$ $cm^{-1}$): 423 (0.76), 500 (0.46). Found: $[M]^+$ 365.12585. $C_{21}H_{19}NO_5$. Calculated: *M* 365.12631.

**3,5-Dihydroxy-4-(4-methoxyphenylimino)-1,4-dihydronaphthalen-1-one (IVe).** Yield 61%, mp 215–217°C (from $CHCl_3$–hexane, 1:10). IR spectrum, ν, $cm^{-1}$: 1626 (C=N), 1641 (C=O), 3274 (OH). $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 3.81 s (3H, $OCH_3$), 6.15 s (1H, 2-H), 6.92 d.d (2H, 2'-H, 6'-H, $J_{ortho}$ = 8.0, $J_{meta}$ = 2.0 Hz), 7.13–7.19 m (3H, 3'-H, 5'-H, 6-H), 7.39 br.s (1H, OH), 7.59–7.62 m (2H, 7-H, 8-H), 11.55 s (1H, OH). UV spectrum, $\lambda_{max}$, nm ($\varepsilon \times 10^{-4}$ l $mol^{-1}$ $cm^{-1}$): 414 (0.66), 503 (0.46). Found: $[M]^+$ 295.08486. $C_{17}H_{13}NO_4$. Calculated: *M* 295.08443.

**Reaction of 5-hydroxy-4-(2,4,6-trimethylphenylimino)-1,4-dihydronaphthalen-1-one (Ib) with $FeCl_3 \cdot 6H_2O$.** A mixture of 1 mmol of compound **Ib**, 10 mmol of $FeCl_3 \cdot 6H_2O$, and 15 ml of DMF was heated for 5 h at 85–90°C. The mixture was treated as described above to isolate 69% of initial compound **Ib**. A zone containing tarry products remained in the chromatographic column.

**Reaction of 2,5-dihydroxy-4-phenylimino-1,4-dihydronaphthalen-1-one (IIa) with *o*-phenylenediamine.** A mixture of 1.3 mmol of 2,5-dihydroxy-4-phenylimino-1,4-dihydronaphthalen-1-one (**IIa**), 2.8 mmol of *o*-phenylenediamine, and 30 ml of acetic acid was stirred for 30 min at 80°C. The mixture was cooled, poured into water, and neutralized with aqueous potassium hydroxide, and the precipitate was filtered off, washed with water, and dried. The product was 5-phenylimino-5*H*-benzo[*a*]phenazin-4-ol (**V**). Yield quantitative. The product was purified by reprecipitation with benzene from acetone, mp 260°C (decomp.). IR spectrum, ν, $cm^{-1}$: 1624 (C=N), 3334 (NH). $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm: 6.97 s (1H, 6-H), 7.10–7.82 m (9H, 2-H, 3-H, 9-H, 10-H, $C_6H_5$), 7.90 d (1H, 8-H, *J* = 8.0 Hz), 8.12 d (1H, 11-H, *J* = 8.0 Hz), 8.76 d (1H, 1-H, 8.0 Hz) (signals from the NH and OH protons were not observed due to exchange with water present in the solvent). UV spectrum, $\lambda_{max}$, nm ($\varepsilon \times 10^{-4}$ l $mol^{-1}$ $cm^{-1}$): 507 (1.07). Found: $[M]^+$ 337.12140. $C_{22}H_{15}N_3O$. Calculated: *M* 337.12150.

**Reaction of 3,5-dihydroxy-4-arylimino-1,4-dihydronaphthalen-1-ones IVa and IVc–IVe with *o*-phenylenediamine.** A mixture of 1.3 mmol of compound **IVa** or **IVc**–**IVe**, 2.8 mmol of *o*-phenylenediamine, and 30 ml of acetic acid was stirred for 30 min at 80°C. The mixture was treated as described above to isolate ~90% of the initial compound.

## REFERENCES

1. *Methoden der organischen Chemie (Houben–Weyl)*, Stuttgart: Georg Thieme, 1979, vol. 7/3b, p. 235.

2. Ono, Sh., Adachi, R., Ukai, T., and Mihara, Y., JPN Patent appl. no. 62-181381, 1986; *Chem. Abstr*., 1988, vol. 108, no. 122066v.

3. Baley D. and Williams, L.A. *The Chemistry of Synthetic Dyes*, Venkataraman, K., Ed., New York: Wiley, 1972, vol. 6. Translated under the title *Khimiya sinteticheskikh krasitelei*, Leningrad: Khimiya, 1975, vol. 4, p. 320.

4. Benedetti-Doctorovich, V., Burges, E.M., Lambropoulous, J., Lednicer, D., van Deveer, D., and Zalkow, L., *J. Med. Chem*., 1994, vol. 37, p. 710.

5. Zhungietu, G.I. and Vlad, L.A., *Yuglon i rodstvennye 1,4-naftokhinony* (Juglone and Related 1,4-Naphthoquinones), Kishinev: Shtiintsa, 1978.

6. Oeriu, I. and Krecha, M., *Zh. Obshch. Khim*., 1963, vol. 33, p. 1127.

7. Ektova, L.V. and Fokin, E.P., *Zh. Org. Khim*., 1984, vol. 20, p. 805.

8. Lillie, T.J. and Musgrave, O.C., *J. Chem. Soc., Perkin Trans. 1*, 1977, p. 355.

9. Forrester, A.R., Fullerton, J.D., and McConnachie, G., *J. Chem. Soc., Perkin Trans. 1*, 1983, p. 2711.