ISSN 1070-4280, Russian Journal of Organic Chemistry, 2013, Vol. 49, No. 5, pp. 746–749. © Pleiades Publishing, Ltd., 2013.
Original English Text © L.M. Gornostaev, A.E. Devyashina, Yu.V. Gatilov, 2013, published in Zhurnal Organicheskoi Khimii, 2013, Vol. 49, No. 5, pp. 763–766.

Cyclization of 2-Chloro-3-(1,4-oxocyclohexa-2,5-dienylideneamino)-1,4-dihydronaphthalene-1,4-diones into 6-Chloro-10,12a-dihydroxy-7*H*,12a*H*-benzo[*c*]phenoxazin-5-ones

L. M. Gornostaev[a], A. E. Devyashina[a], and Yu. V. Gatilov[b]

[a]*Astaf'ev Krasnoyarsk State Pedagogical University, Krasnoyarsk, 660049 Russia*
e-mail: gornostaev@kspu.ru
[b]*Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Branch, Russian Academy of Sciences, Novosibirsk, Russia*

Received July 10, 2012

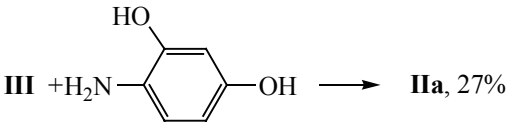
Abstract—2-Chloro-3-(4-oxocyclohexa-2,5-dienylideneamino)-1,4-dihydronaphthalene-1,4-diones maintained in the conc. sulfuric acid undergo cyclization affording in a high yield 6-chloro-10,12a-dihydroqси-7*H*,12a*H*-benzo[*c*]phenoxazin-5-ones whose structure is proved by XRD analysis.

DOI: 10.1134/S1070428013050012

In [1] an approach was described to a synthesis of 2-chloro-3-(1,4-oxocyclohexa-2,5-dienylideneamino) [1,4]-naphthoquinones **Ia, Ib**. quinoneimines **Ia, Ib** in sulfuric acid of various concentrations: in the acid of 5–80% concentration these compounds remained intact, and at a short keeping in the acid of 92–95% concentration at 0–5°C they converted into 6-chloro-10,12a-dihydroxy-7*H,*12a*H*-benzo[*c*]phenoxazine-5-oneы **IIa, IIb** in high yields (Scheme 1). The latter substances were identified by ^{1}H NMR and mass spectra and by XRD analysis.

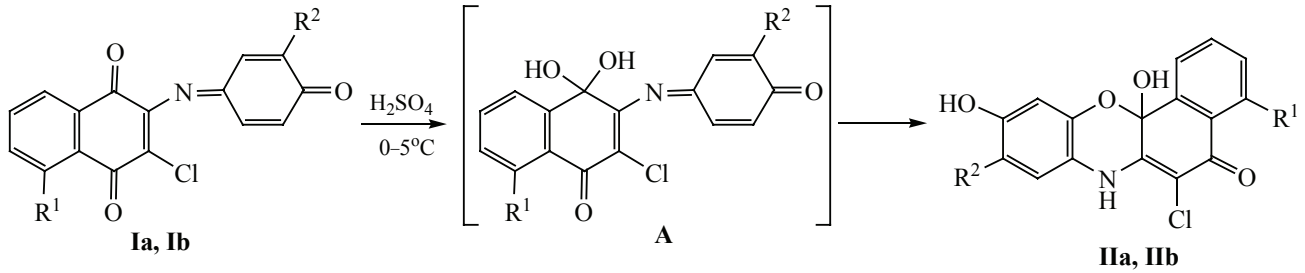
We presume that the reaction mechanism includes the preliminary hydration of initial quinoneimines **Ia, Ib** at the carbonyl group giving diol **A** followed by its cyclization into phenoxazinones **IIa, IIb**.

Similar phenoxazinones [6-chloro-12a-hydroxy-5*H*-benzo[*c*]phenoxazin-5-one (**IV**)] were obtained in [2] by the reaction of 2,3-dichloro-1,4-naphthoquinone (**III**) with *ortho*-aminophenols.



In the ^{1}H NMR spectrum of compound **IIa** the proton signsld of the hemiketal hydroxy group (7.99 ppm) and of the proton linked to the nitrogen atom (10.35 ppm) appeared close to the region of the corresponding signals in the spectrum of compound **IV** (8.06, 10.54 ppm) [2].

Scheme 1.



$R^1 = R^2 = H$ (**a**); $R^1 = OH$, $R^2 = CH_3$ (**b**).

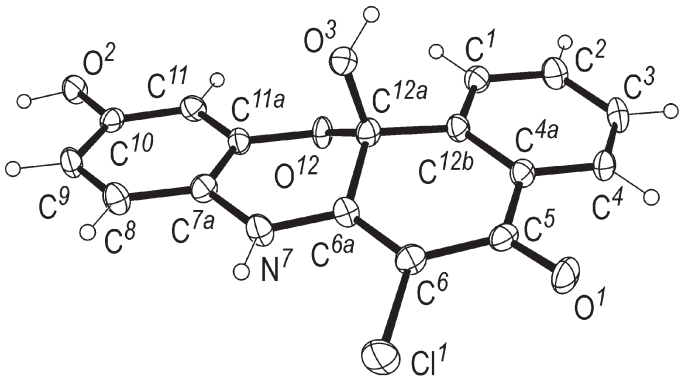
The mass spectrum of phenoxazinone **IIa** lacks the molecular ion, but contains intensive ions of *m/z* 299 (54.75%) and 297 (100%) that apparently have formed by dehydration of molecular ions (M^+ 315 and 317). The fragment ions of *m/z* 269 (31.63%) and 271 (10.21%) evidently form by decarbonylation of the preceding ions. At the same time the high resolution mass spectrum contains a peak of the protonated molecular ion $[M + H]^+$ of the mass 316.0371 corresponding to the composition of the obtained product.

Electron absorption spectra of compounds **IIa, IIb** also resemble that of phenoxazinone **IV**: λ_{max} (logε) in ethanol is 261 (4.51), 411 (4.17) (**IIa**); 255 (4.39), 390 (4.28) (**IV**).

We also obtained by the reaction of 2,3-dichloro-1,4-naphthoquinone (**III**) with 4-aminobenzene-1,3-diol phenoxazinone **IIa** identical by its parameters to that obtained from quinoneimine **Ia**, but the yield was small.

The structure of phenoxazinone **IIa** was proved by XRD analysis (see the figure).

The Cambrodge Crystallographic Database [3] has no compounds with this tetraheterocyclic scaffold. Oxazine ring is present in an *envelop* conformation with the deviation of atom C^{12} from the plane by 0.595 Å. The conformation of the dienone ring is nearly a flattened *boat* with the deviation from the plane of atoms C^6 and C^{6a} by 0.373 and 0.414 Å respectively. The molecules in the crystal are bound by the hydrogen bonds O^2–H···O^1 [H···O 1.89(4) A, O–H···O 164(4)°], and O^3–H···O^2 [1.89(4) Å, 169(4)°] into bands along the (*a*–*c*) axis. A π-stacking interaction π($C^{1–4}C^{4a}C^{12a}$)-π($C^{7a}C^{8–11}C^{11a}$) exists between the bands with intercenter distance 3.815(2)



The structure of the molecule of 6-chloro-10,12a-dihydroxy-7*H*,12a*H*-benzo-[*c*]phenoxazin-5-one (**IIa**) by XRD data.

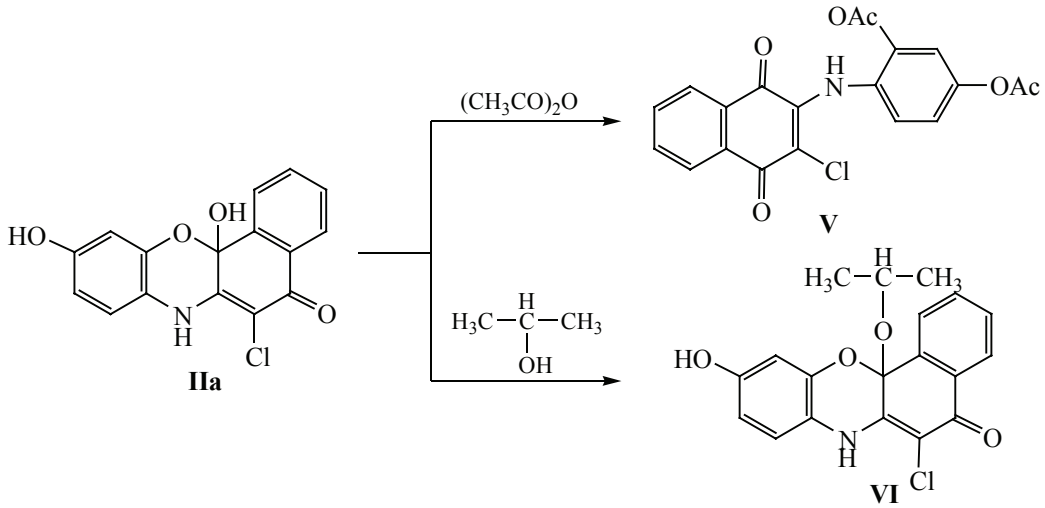
and interplanar distance 3.5 Å.

Compounds **IIa, IIb** exist in solution (according to ^{1}H NMR data) and in solid state in the hemiketal form. Compound **IIa** reacts with alcohols in this form, but at the acetylation with acetic anhydride in pyridine the phenoxazine ring suffers opening with the formation of 2-(2,4-diacetoxyphenylamino)-3-chloro-1,4-naphthoquinone (**V**) (Scheme 2).

n the ^{1}H NMR spectrum of ketal **VI** the methyl group protons appear as two doublets at 0.49 and 0.67 ppm with a ratio of integral intensities close to unity. This is apparently due to the existence of compound **VI** as two diastereomers since the carbon atom in the position *12a* is asymmetrical.

We believe that the presence in the molecules of compounds **IIa, IIb** of versatile functional groups opens opportunities to their further modification.

Scheme 2.



EXPERIMENTAL

^{1}H NMR spectra were registered on a spectrometer Bruker DRX (500 MHz), solvent DMSO-d_6, internal referenc TMS. The monitoring of the reaction progress and checking the purity of obtained compounds was performed by TLC in toluene on Silufol UV-254 plates. The melting points were measured on a Boëtius heating microblock. Mass spectra were obtained on an instrument Finnigan MAT-8200 (direct admission, EI, 70 eV), high resolution mass spectra were recorded on a GC-MS instrument Bruker micrOTOF equipped with electrospray ionization and quadrupole mass analyzer using sample solutions in acetonitrile Electron absorption spectra were taken on a spectrophotometer Evolution 300 in ethanol at the layer thickness 1 cm and the sample concentration $1\cdot10^{-4}$ mol l^{-1}. In the study were used commercially available 2,3-dichloro-1,4-naphthoquinone (Acros) and 4-aminobenzene-1,3-diol hydrochloride (Aldrich).

XRD experiment was carried out on a diffractometer Bruker Kappa APEX II [graphite monochromator, λ(MoK_α) 0.71073 Å, ω,φ-scanning, 200 K]. The correction for extinction was performed using SADABS program. The structure was solved by the direct method and refined in the anisotropic approximation for nonhydrogen atoms. The positions of hydrogen atoms of the OH and NH groups were determined from the difference synthesis ant were refined in the isotropic approximation. The other hydrogen atoms were refined in the *rider* model. All calculations were carried out applying SHELX-97 software. The data obtained are deposited in Cambrodge Crystallographic Datab Center (CCDC № 888778).

6-Chloro-10,12a-dihydroxy-7*H*,12a*H*-benzo[*c*]-phenoxazin-5-one (IIa). To 20 ml of 92–95% sulfuric acid cooled to 0–5°C was added gradually within 15 min 2 g (7 mmol) of 2-chloro-3-(1,4-oxocyclohexa-2,5-dienylideneamino)-1,4-dihydronaphthalene-1,4-dione (**Ia**), and the reaction mixture was stirred for 10 min, poured on ice, the brown precipitate was filtered off and recrystallized from a mixture DMF–H_2O, 1 : 2. Yield 1.85 g (92%), mp >300°C. EAS, λ_{max}, nm (logε): 261 (4.51), 411 (4.17). ^{1}H NMR spectrum, δ, ppm: 6.50 d.d (1H, H^{9}, *J* 8.6, 2.5 Hz), 6.60 d (1H, H^{11}, *J* 2.5 Hz), 7.30 d (1H, H^{8}, *J* 8.6 Hz), 7.60 t (1H, H$^{2(3)}$, *J* 7.5 Hz), 7.73 t (1H, H$^{3(2)}$, *J* 7.5 Hz), 7.97 d (1H, H^{1}, *J* 6.6 Hz), 7.99 s (1H, OH^{12a}), 8.00 d (1H, H^{4}, *J* 6.6 Hz), 9.45 s (1H, OH^{10}), 10.35 s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 299 (54.75), 297 (100), 271 (10.21), 269 (31.63), 63 (30.63). Found, %: C 60.40; H 3.46; Cl 11.40; N 4.14. $[M + H]^+$ 316.0371. $C_{16}H_{10}ClNO_4$. Calculated, %: C 60.85; H 3.16; Cl 11.25; N 4.43. *M* + H 316.0371. Crystallographic data**:** triclinic crystal system *P*-1, *a* 7.5379(6), *b* 8.6464(8), *c* 11.3916(11) Å, α 72.417(3), β 76.542(3), γ 66.240(3)°, *V* 642.5(1) Å^3, *Z* 2, d_{calc} 1.632 g/cm^3, μ 0.317 cm^{-1}. The intensities of 8325 reflections were measured in the range $2\theta < 51°$, 2338 among them independent (R_{int} 0.0414). Refinement parameters: wR_2 0.1110, *S* 1.040 (for all reflections), R_1 0.0399 [1671 $I \geq 2\sigma(I)$].

Authentic synthesis of compound IIa. To 0.45 g (2 mmol) of 2,3-dichloro-1,4-naphthoquinone (**III**) in 15 ml of dioxane first 0.24 g (1.5 mmol) of 4-aminobenzene-1,3-diol hydrochloride, then 0.2 g (1.4 mmol) of potassium carbonate dissolved in 10 ml of water was added, and the mixture was stirred at 25°C for 20 min. The brown precipitate was filtered off and chromatographed on silica gel. Yield 0.12 g (27%).

6-Chloro-4,10,12a-trihydroxy-9-methyl-7*H*,12a*H*-benzo[*c*]phenoxazin-5-one (IIb). To 20 ml of 92–95% sulfuric acid cooled to 0–5°C was added gradually within 15 min 0.3 g (0.9 mmol) of 2-chloro-3-(3-methyl-4-oxocyclohexa-2,5-dienylideneamino)-8-hydroxy-1,4-dihydronaphthalene-1,4-dione **(Ib),** and the reaction mixture was stirred for 15 min, poured on ice, the brown precipitate was filtered off and subjected to column chromatography on silica gel eluting with a mixture hexane–ethyl acetate, 1 : 1. Yield 0.13 g (43%), mp 297°C. ^{1}H NMR spectrum, δ, ppm: 2.10 s (3H, CH_3), 6.62 s (1H, H^{11}), 6.99 d (1H, H^{1}, *J* 8.2 Hz), 7.20 s (1H, H^{8}), 7.44 d (1H, H^{3}, *J* 7.8 Hz), 7.57 t (1H, H^{2}, *J* 7.8 Hz), 7.96 s (1H, OH^{12a}), 9.50 s (1H, OH^{10}), 10.65 s (1H, NH), 13.15 s (1H, OH^{4}). Mass spectrum, *m/z* (I_{rel}, %): 345 (1.60) [*M*]$^+$, 43(100), 36 (85.19), 29 (69.57). Found, %: C 59.29; H 4.12; Cl 10.11; N 4.02. $C_{17}H_{12}ClNO_5$. Calculated, %: C 59.04; H 3.47; Cl 10.27; N 4.05.

2-(2,4-Diacetoxyphenylamino)-3-chloro-1,4-naphthoquinone (V). To a solution of 0.58 g (1.4 mmol) of compound **IIa** in 10 ml of pyridine was added 4 ml of acetic anhydride, and the reaction mixture was stirred at 25°C for 10 min, poured on ice, the yellow-orange precipitate was filtered off and recrystallized from toluene. Yield 0.45 g (78%), mp 163°C**.** ^{1}H NMR spectrum, δ, ppm: 2.00 s (3H, CH_3), 2.25 s (3H, CH_3), 7.04 d (1H, H$^{5'}$,*J* 7.0 Hz), 7.07 s (1H, H$^{3'}$), 7.32 d (1H, H$^{6'}$, *J* 7.0 Hz), 7.82 t (1H, H$^{7(6)}$, *J* 8.0 Hz), 7.87 t (1H, H$^{6(7)}$, *J* 8.0 Hz), 8.02 d (1H, H$^{8(5)}$, *J* 8.0 Hz), 8.04 br.d (1H, H$^{5(8)}$, *J* 8.0 Hz), 8.90 s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 399

(13.01) $[M]^+$, 357 (27.03), 315 (52.55), 280 (56.76), 279 (100), 43 (45.25). Found, %: C 59.62; H 3.51; N 3.52. $C_{20}H_{14}ClNO_6$. Calculated, %: C 60.07; H 3.50; N 3.50.

6-Chloro-10-hydroxy-12a-isopropoxy-7*H*,12a*H*-benzo[*c*]phenoxazine-5-one (VI). In 10 ml of 2-propanol was dissolved 0.22 **r** (0.7 mmol) of compound **IIa**, and the mixture was stirred at 83–85°C for 40 min. Then 7 ml of water was added dropwise, the reaction mixture was cooled, the yellow-brown precipitate was filtered off and subjected to column chromatography on silica gel eluting with chloroform. Yield 0.19 g (76%), mp 128°C. ^{1}H NMR spectrum, δ, ppm: 0.49 d (3H, CH_3, *J* 6.1 Hz), 0.67 d (3H, CH_3, *J* 6.1 Hz), 4.04 m (1H, CH), 6.54 d.d (1H, H^9, *J* 8.6 Hz), 6.69 d (1H, H^{11}, *J* 2.5 Hz), 7.32 d. (1H, H^8, *J* 8.6 Hz), 7.67 t (1H, H$^{2(3)}$, *J* 7.5 Hz), 7.75 t (1H, H$^{3(2)}$, *J* 7.5 Hz), 8.03 d (1H, H^1, *J* 7.5 Hz), 8.13 d (1H, H^4, *J* 7.5 Hz), 9.55 s (1H, NH), 10.50 s (1H, OH). Mass spectrum, *m/z* (I_{rel}, %): 299 (7.61), 297 (34.83), 63 (100), 62 (21.92), 32 (47.05). Found, %: C 63.66; H 5.79; Cl 8.59; N 3.20. $C_{19}H_{16}ClNO_4$. Calculated, %: C 63.77; H 4.47; Cl 9.93; N 3.91.

ACKNOWLEDGMENTS

The study was carried out under the financial support of the Astaf'ev Krasnoyarsk State Pedagogical University (grant no. 01-12-1/NP).

REFERENCES

1. Devyashina, A.E., Gornostaev, L.M. and Gatilov, Yu.V., *Zh. Org. Khim*., 2012, vol. 48, p. 245.
2. Agarwal, N.L. and Shafer, W., *J. Org. Chem*., 1980, vol. 45, p. 2155.
3. Allen, F.H., *Acta Cryst.,* 2002, vol. B58, p. 380 (Version, 5.33).