PHOTOLYSIS OF 2-PIPERIDINO- AND 2-MORPHOLINO-3-METHOXY-1,4-NAPHTHOQUINONES

R. P. Shishkina, V. N. Berezhnaya, and V. I. Mamatyuk

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PMR and ^{13}C NMR spectroscopy was used to establish the structure of the primary products of the photolysis of 2-piperidino- and 2-morpholino-3-methoxy-1,4-naphthoquinones. A scheme for the subsequent dark transformations of these compounds is proposed.

Fokin and Detsina [1] have obtained the products of dehydration of the heterocyclic ring, namely, enamines of N-(1,4-naphthoquinon-2-yl)dihydro-1,4-oxazine and N-(1,4-naphthoquinon-2-yl)-1,4,5,6-tetrahydropyridine as stable compounds upon the irradiation of benzene solutions of 2-morpholino- and 2-piperidino-1,4-naphthoquinones, respectively, at 80°C. Fokin and Prudchenko [2] assigned the naphth[2,1-d]-2,3-dihydrooxazole structure to the unstable compounds isolated upon the irradiation of a series of 2-dialkylamino-1,4-naphthoquinones in hydrocarbons at 20°C. A UV spectral study of the photolysis of 2-dialkylamino-1,4-naphthoquinones and 2-morpholinonaphthoquinone showed that the primary step in the photolysis is identical in both cases [3,4]. Gritsan and Bazhin [4] proposed a scheme for the conversion of the primary product in the photolysis of 2-morpholino-1,4-naphthoquinone to an enamine involving the hydrolysis of the C–O bond of the oxazole ring as the first step in contrast to the scheme of Maruyama et al. [5], who proposed initial oxidation of the primary product to a quinoid species.

In the present work, we established the structure of the primary product of the photolysis of 1,4-naphthoquinones with a secondary alicyclic amino group and the products of its subsequent dark transformations. We studied 2-piperidino-3-methoxy- (Ia) and 2-morpholino-3-methoxy-1,4-naphthoquinones (Ib) and showed that these compounds are photolyzed with retention of isosbestic points to the end of the photolysis by analogy to 2-piperidino- and 2-morpholino-1,4-naphthoquinones not containing a methoxy group [6].

A grayish-yellow product (IIa) was obtained upon the photolysis of a hexane solution of (Ia) flushed with argon at 20°C under conditions similar to those of Fokin [2]. Elemental analysis and mass spectrometry indicated that the formula for (IIa) is $C_{16}H_{17}NO_4$, i.e., this product has one more oxygen atom than in (Ia). The IR spectrum of (IIa) has a carbonyl band at 1670 cm^{-1} in addition to the OH band at 3560 cm^{-1}. The PMR spectrum of (IIa) in $CDCl_3$ (δ, ppm) has signals at 7.99 m (1H, H^4), 7.57 m (1H, H^1), 7.44 m (2H, $H^{2,3}$), 5.23 m (1H, $H^{11a,a}$,* $J_{H^{11a},a_{H^{11a}}} = 10.0$, $J_{H^{11a},a_{H^{11e}}} = 3.5$ Hz), 4.61 m (1H, H^{8e}, $J_{H^{8e},H^{8a}} = 14.5$, $J_{H^{8e}H^{8a}} = 4.5$, $J_{H^{8e}H^{9e}} = 2.0$ Hz), 3.73 s (3H, OCH_3), 3.34 m (1H, H^{8a}, $J_{H^{8a}H^{9a}} = 11.0$, $J_{H^{8a}H^{9e}} = 4.0$ Hz), 2.29 m (1H, H^{11e}), 1.43 m (1H, H^{11a}), 1.96 m and 1.75 m (1H, 1H, $H^{9e,10e}$). The multiplets for H^{9a} and H^{10a} overlap and give a complex signal in the vicinity of 1.5 ppm, while the hydroxy group appears at 1.25 ppm. The difference in the chemical shifts of H^1 and H^4 is a result of ring formation. The most characteristic signals in the ^{13}C NMR spectra at –20°C in $CDCl_3$ with complete spin–spin coupling suppression and monoresonance conditions are a singlet at 178.80 ppm (C^5, C=O), singlet at 99.06 ppm (C^{12a}), and doublet at 90.42 ppm (C^{11a}). The $J_{^{13}C-^1H}$ coupling constant for the C^{11a}–H fragment (161 Hz) indicates that this carbon atom is bound to two heteroatoms. The structure 12a-hydroxy-6-methoxy-9,10,11,11a-tetrahydro-8H-naphth[2′,1′:4,5]oxazolo[3,2-a]pyridin-5-one was assigned to (IIa) on the basis of the analytical and spectral data presented.

*On the basis of the coupling constant, H^{11a} occupies a position close to axial.

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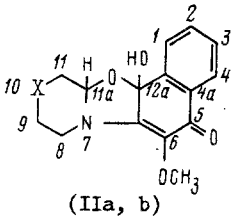
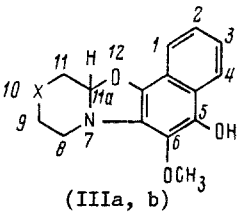


(IIa, b)



(IIIa, b)

X = CH_2 (a), O (b).

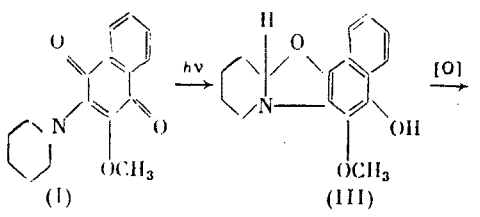
The electronic absorption spectrum of (IIa) in toluene shows an absorption maximum at 366 nm. In a UV study of the photolysis of 2-piperidino-3-methoxynaphthoquinone (Ia) in toluene or hexane at 20°C, absorption arose in the vicinity of 340 nm [6]. Thus, the spectrum of a compound different from (IIa) was recorded. This compound is apparently the product of the oxidation of the primary photolysis product (IIIa), which was detected upon photolysis at −40°C. The PMR spectrum of (IIIa) differs markedly from the PMR spectrum of (IIa) and shows a broad singlet at 5.77 ppm for the OH group and triplet at 5.02 ppm for H^{11a}. The other eight protons of the piperidine ring appear as five groups of signals.* The structure of 6-methoxy-9,10,11,11a-tetrahydro-8H-naphth[2′,1′:4,5]oxazolo[3,2-a]pyridin-5-one was assigned to (IIIa).

Naphthdihydrooxazole (IIIa) is unstable and undergoes dark transformations upon warming of the solution to 20°C, leading to a mixture of products. Thus, the PMR spectrum shows signals for (IIa) (4.60 and 5.20 ppm), aldehyde (IVa) (9.73 ppm), and, probably, enamine (Va) (5.79 and 6.09 ppm), whose ratio varies over time.

In turn, (IIa), which is relatively stable as a solid, is unstable in solution at −20°C. PMR and ^{13}C NMR spectroscopy for the solution in $CDCl_3$ showed that (IIa) is completely converted 18 h after dissolution into 5-(3-methoxy-1,4-naphthoquinon-2-yl)aminovaleraldehyde (IVa), which is the major reaction product if the irradiation of a hexane solution of (Ia) is carried out without prior flushing with argon. Product (IVa) was isolated as its 2,4-dinitrophenylhydrazone. Upon standing, the dark red solution of aldehyde (IVa) is converted to an unstable blue product, which is probably enamine (Va) similar to that described for 2-piperidinonaphthoquinone [1].

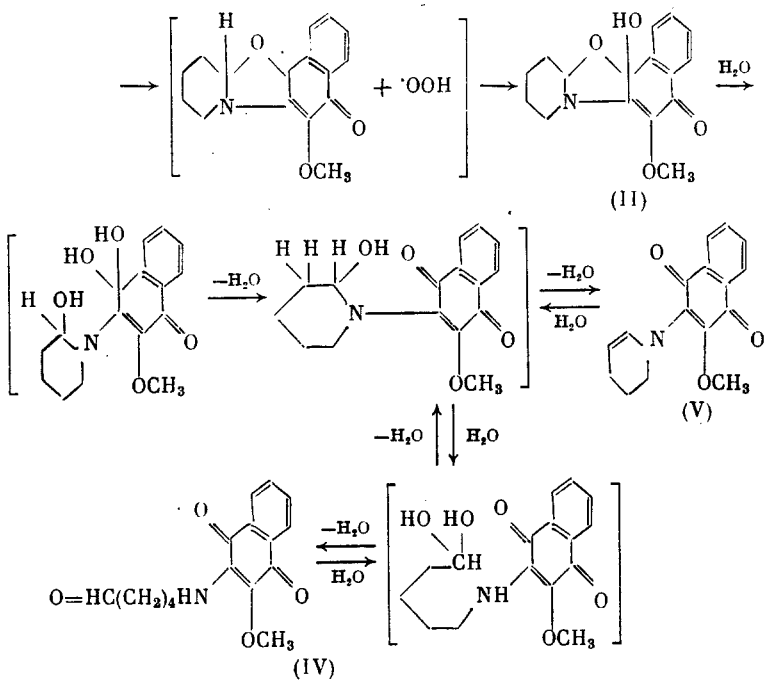
A study of the photochemical transformations of 2-morpholino-3-methoxy-1,4-naphthoquinone (Ib) showed that the replacement of the piperidino by a morpholino group does not lead to a change in the nature of the photolysis products. Thus, 6-methoxy-8,9,11,11a-tetrahydronaphth[2′,1′;4,5]oxazolo[2,3-c][1,4]oxazin-5-ol (IIIb) was detected in the low-temperature photolysis of (Ib), which like its analog (IIIa) is only stable at reduced temperature. The photolysis of (Ib) in hexane at 20°C in an argon atmosphere gave 12a-hydroxy-6-methoxy-8,9,11,11a-tetrahydronaphtho[2′,1′:4,5]oxazolo[2,3-c]oxazin-5-one (IIb), which is the product of the oxidation of the primary photolysis product. An increase in the reaction temperature and replacement of hexane by benzene lead to a product of further transformations, namely, enamine (Vb). The PMR spectrum of (Vb) has clear doublets for the methine protons at 5.79 and 6.06 ppm.

Thus, this spectral study showed that the primary products of the photolysis of 2-amino-1,4-naphthoquinones with a secondary alicyclic amino group are derivatives of naphthdihydrooxazole (III). The dark transformations of these derivatives in the case of 6-methoxy-9,10,11,11a-tetrahydro-8H-naphth[2′,1′:4,5]oxazolo[3,2-a]pyridin-5-ol (IIIa) may be represented by a scheme involving its oxidation to 12a-hydroxy-6-methoxy-9,10,11,11a-tetrahydro-8H-naphth[2′,1′:4,5]oxazolo[3,2-a]pyridin-5-one (IIa).



(I) (III)

*See the work of Fokin and Prudchenko [2].



EXPERIMENTAL

The electronic absorption spectra were taken on a Specord UV-VIS spectrometer. The IR spectra for KBr pellets and chloroform solutions were taken on a UR-20 spectrometer. The molecular mass and elemental composition were determined by determination of the precise mass number of the molecular ions on Finnigan MAT 8200 and Finnigan AEI MS-902 mass spectrometers. The PMR and ^{13}C NMR spectra were taken on Bruker WP 200 SY and Bruker AM-400 spectrometers.

2-Piperidino-3-methoxy- (Ia) and 2-morpholino-3-methoxy-1,4-naphthoquinones (Ib) were obtained and characterized according to Maruyama et al. [5].

2-Piperidino-3-methoxy-1,4-naphthoquinone (Ia). PMR spectrum in $CDCl_3$ (δ, ppm): 1.66 m (6H, CH_2), 3.38 m (4H, CH_2–N), 3.85 s (3H, OCH_3), 7.59 m (2H, $H^{6,7}$), 7.96 m (2H, $H^{5,8}$).

2-Morpholino-3-methoxy-1,4-naphthoquinone (Ib). PMR spectrum in $CDCl_3$ (δ, ppm): 3.47 t (4H, CH_2–N), 3.81 t (4H, CH_2–O), 3.90 s (3H, OCH_3), 7.63 m (2H, $H^{6,7}$), 7.99 m (2H, $H^{5,8}$).

The photoinduced forms of 2-piperidino- (IIIa) and 2-morpholino-3-methoxy-1,4-naphthoquinones (IIIb) were obtained by irradiation of a solution of 2 mg (Ia) or (Ib) in CS_2 for 3 min, flushed with argon directly in an NMR tube using a DRSh-250 lamp through a ZhS-11 light filter at –40°C. The tube was placed in a Dewar flask cooled with an acetonitrile/liquid nitrogen mixture. The thermal reaction virtually does not proceed at this temperature, permitting accumulation of the colorless oxazole form (III) in concentrations sufficient for PMR spectroscopy. After irradiation, the tube was rapidly transferred to the NMR spectrometer probe cooled to –40°C with a dry nitrogen stream.

6-Methoxy-9,10,11,11a-tetrahydro-8H-naphth[2′,1′:4,5]oxazolo[3,2-a]pyridin-5-ol (IIIa). PMR spectrum in CS_2 (δ, ppm, J, Hz) (CH_2Cl_2 standard): 1.69 m (3H, $H^{9,9,10}$), 1.84 m (1H, H^{10}), 2.09 m (2H, $H^{11a,11e}$), 2.99 m (1H, H^{8a}, $J_{H^{8a}H^{8e}}$ = 13.0), 3.32 m (1H, H^{8e}), 3.86 s (3H, OCH_3), 5.02 t (1H, H^{11a}), 5.77 br.s (1H, OH), 7.09 m (2H, $H^{2,3}$), 7.42 m (1H, H^1), 7.77 m (1H, H^4).

6-Methoxy-8,9,11,11a-tetrahydro-8H-naphth[2′,1′:4,5]oxazolo[2,3-c][1,4]oxazin-5-ol (IIIb). PMR spectrum in CS_2 (δ, ppm, J, Hz, CH_2Cl_2): 2.98 m (1H, H^{8a}, $J_{H^{8a}H^{8e}}$ = 12.0, $J_{H^{8a}H^{9a}}$ = 9.0, $J_{H^{8a}H^{9e}}$ = 3.5), 3.03 m (1H, H^{8e}, $J_{H^{8e}H^{9a}}$ = 3.8), 3.76 m (1H, H^{9a}, $J_{H^{9a}H^{9e}}$ = 12.0), 3.91 m (1H, H^{9e}), 4.05 d.d (1H, H^{11a}, $J_{H^{11a}H^{11e}}$ = 13.0, $J_{H^{11a}H^{11a}}$ = 2.5), 4.31 s (3H, OCH_3), 4.40 d.d (1H, H^{11e}), 5.21 t (1H, H^{11a}), 5.84 s (1H, OH), 7.33 m (2H, $H^{2,3}$), 7.40 m (1H, H^1), 7.98 m (1H, H^4).

12a-Hydroxy-6-methoxy-9,10,11,11a-tetrahydro-8H-naphth[2′,1′:4,5]oxazolo[3,2-a]pyridin-5-one (IIa). A solution of 140 mg (Ia) in 500 ml hexane was poured into a cylindrical glass jacket surrounding an LB-40 daylight lamp. An argon stream was introduced for 30 min and irradiation was carried out for 3 h. The grayish-yellow precipitate formed was filtered off and washed with hexane to give 50 mg (35%) (IIa), mp 88-90°C. IR spectrum (ν, cm^{-1}): 3560 (OH), 1670 (C=O). UV spectrum in toluene (λ_{max}, nm (log ε)): 366 (3.90). Found: C, 66.51; H, 6.05; N, 4.68; O, 22.66%; molecular mass, 287.1162. Calculated for $C_{16}H_{17}NO_4$: C, 66.89; H, 5.96; N, 4.87; O, 22.27%; molecular mass, 287.1158. ^{13}C NMR spectrum in $CDCl_3$ at –20°C (δ,

ppm, $J_{^{13}C-^{1}H}$, Hz): 20.89 t (C^9, J = 128), 24.78 t (C^{10}, J = 128), 31.37 t (C^{11}, J = 133), 44.14 t (C^8, J = 142), 60.19 q (OCH_3, J = 145), 90.42 d (C^{11a}, J = 161), 99.06 s (C^{12a}), 122.35 d (C^1), 125.29 s (C^{4a}), 125.71 d, 128.92 d, 130.67 d ($C^{2,3,4}$), 130.70 s (C^{1a}), 136.00 s (C^{6a}), 150.10 s (C^6), 178.80 s (C^5).

5-(3-Methoxy-1,4-naphthoquinon-2-yl)aminovaleraldehyde (IVa). A sample of 2 mg (IIa) was dissolved in $CDCl_3$ in an ampule and left at 20°C for 18 h. Spectra of this compound were then recorded.

PMR spectrum (δ, ppm): 1.68 m (4H, β,γ-CH_2), 2.50 m (4H, α,δ-CH_2), 3.87 s (3H, OCH_3), 5.54 br.s (1H, NH), 7.60 m (2H, $H^{6,7}$), 7.98 m (2H, $H^{5,8}$), 9.76 t (1H, CH=O).

^{13}C NMR spectrum (δ, ppm): 19.16 t (γ-CH_2), 30.19 t (β-CH_2), 43.31 t (α-CH_2), 44.11 t (δ-CH_2), 61.21 q (OCH_3), 125.84 d, 125.93 d ($C^{5,8}$), 130.03 s (C^2), 132.61 s, 136.75 s ($C^{9,10}$), 138.51 s (C^3), 178.88 s (C^1), 183.12 s (C^4), 201.46 d (CH=O).

Dinitrophenylhydrazone (IVa). A solution of 140 mg (Ia) in 500 ml hexane was irradiated using an LB-40 lamp for 3 h without prior flushing with argon. The precipitate of 14 mg (10%) (IIa) was filtered off and washed with hexane. Then, 100 ml saturated ethanolic 2,4-ditnirophenylhydrazine and three drops of concentrated hydrochloric acid were added to the red filtrate. The precipitate was filtered off and washed with ethanol to give 110 mg (48%) (IVa), mp 177-178°C (from $CHCl_3$). IR spectrum (ν, cm^{-1}): 3340, 3290 (NH), 2940, 2865, 2835 (CH_2, CH_3), 1660, 1620 (C=O), 1570, 1335 (NO_2). UV spectrum in ethanol (λ_{max}, nm (log ε)): 232 (4.44), 278 (4.49), 360 (4.30), 500 (3.30). Found: C, 55.87; H, 4.37; N, 14.89%. Calculated for $C_{22}H_{21}N_5O_7$: C, 56.53; H, 4.53; N, 14.98%.

12a-Hydroxy-6-methoxy-8,9,11,11a-tetrahydronaphth[2′,1′:4,5]oxazolo[2,3-c]oxazin-5-one (IIb). A sample of 140 mg (Ib) in hexane was irradiated for 4 h by analogy to the procedure for (Ia) to give 40 mg (28%) (IIb),* mp 83-84°C. IR spectrum (ν, cm^{-1}): 3565 (OH), 1670 (C=O). UV spectrum in chloroform (λ_{max}, nm (log ε)): 277 sh (3.87), 369 (3.86). PMR spectrum in $CDCl_3$ (δ, ppm, J, Hz): 3.17 d.d (1H, H^{11a}, $J_{H^{11a}H^{11e}}$ = 12.0, $J_{H^{11a}H^{11a}}$ = 10.0), 3.49 t.d (1H, H^{8a}, $J_{H^{8a}H^{8e}}$ = 12.0, $J_{H^{8a}H^{9a}}$ = 12.0, $J_{H^{8a}H^{9e}}$ = 3.0), 3.70 m (1H, H^{9a}), 3.74 s (3H, OCH_3), 3.94 d.d (1H, H^{8e}, $J_{H^{8e}H^{9a}}$ = 4.0), 4.15 s (1H, OH), 4.27 d.d (1H, H^{11e}, $J_{H^{11e}H^{11a}}$ = 4.0), 4.51 d.d (1H, H^{9e}, $J_{H^{9e}H^{9a}}$ = 14.0, 5.35 d.d (1H, H^{11a}), 7.44 m (2H, $H^{2,3}$), 7.57 d.d (1H, H^1), 7.99 d.d (1H, H^4). Found: C, 62.10; H, 5.31; N, 4.71%, molecular mass 289. Calculated for $C_{15}H_{15}NO_5$: C, 62.28; H, 5.23; N, 4.84%, molecular mass, 289.

2-(2,3-Dihydro-1,4-oxazin-4-yl)-3-methoxy-1,4-naphthoquinone (Vb). A solution of 140 mg (Ib) in 500 ml benzene was irradiated for 1.5 h at 80°C using a 300-W incandescent lamp. Benzene was distilled off and subjected to chromatography on grade-II alumina with benzene as the eluent. The major blue fraction was separated and 30-50 mg (20-35%) (Vb) was obtained, mp 83-85°C. IR spectrum (ν, cm^{-1}): 1670, 1635 (C=O). UV spectrum in ethanol (λ_{max}, nm (log ε)): 243 (4.20), 248 sh (4.16), 280 (4.25), 310 sh (4.08), 581 (3.64). Found: C, 66.42; H, 4.80; N, 5.09%, molecular mass 271.0812. Calculated for $C_{15}H_{13}NO_4$: C, 66.51; H, 4.94; N, 5.17%, molecular mass 271.0844. PMR spectrum in $CDCl_3$ (δ, ppm): 3.83 m (2H, $H^{3'}$), 3.89 s (3H, OCH_3, 4.18 t (2H, $H^{2'}$), 5.79 d (1H, $H^{5'}$, $J_{H^{5'}H^{6'}}$ = 5.0 Hz), 6.06 d (1H, $H^{6'}$), 7.64 m (2H, $H^{6,7}$), 7.91 m (2H, $H^{5,8}$).

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*Thin-layer chromatography on Silufol plates with benzene as the eluent indicated a mixture of products was found in the filtrate. The major component was enamine (Vb).