Photocyclization of 2-azido-1-(4-tert-butylphenoxy)-9,10-anthraquinone in the presence of substituted phenols*

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New types of phototransformations in the quinone series, viz., photocyclizations of 1-aryloxy-2-azido-9,10-anthraquinone in the presence of phenols, were studied. The photolysis affords mainly 5H-naphtho[2,3-c]phenoxazine-8,13-diones, in which the nitrogen atom is covalently bound to the phenyl ring of the attached phenol. As a result, complex polycyclic derivatives of phenoxazines were prepared in high yields in one step.

Key words: photolysis, photocyclization, 9,10-anthraquinones, azides, 5H-naph-tho[2,3-c]phenoxazine-8,13-diones, phenols, X-ray diffraction analysis.

It is known^{1,2} that visible light irradiation of 1-aryloxy-9,10-anthraquinone derivatives causes migration of the aryl group to the *peri*-oxygen atom to form highly reactive 9-aryloxy-1,10-anthraquinones. Earlier, we have modified 1-aryloxy-9,10-anthraquinones by introducing the second photoactive (acyloxy, 3 nitroso, 4 diazo, azo, 5 or azido^{6,7}) group into the quinone molecule and studied the factors determining the reactivity and the preference of a particular reaction pathway. The photolysis and thermolysis of 2-diazo and azido derivatives proved to be a convenient general approach to the synthesis of new heterocyclic 9,10-anthraquinone derivatives annelated at positions 1 and 2 with furan, thiophene, phenoxazine, or phenothiazine heterocycles. A new photoreaction, viz., the cyclization of 2-azido-1-(4-tert-butylphenoxy)-9,10anthraquinone in the presence of excess 4-tert-butylphenol yielding 5*H*-naphtho[2,3-*c*]phenoxazine-8,13-dione substituted at the nitrogen atom, was discovered in the study.⁷ To our knowledge, data on analogous photoinitiated cyclizations of azido derivatives are lacking in the literature.

Undoubtedly, a detailed investigation of this cyclization is of theoretical interest because the mechanism of this reaction and the dependence of its efficiency on the chemical nature of the reagents remain unclear. These data can be useful also in the applied aspect because the observed photocyclization is a new one-step synthesis of various polycyclic phenoxazines and phenothiazines.

The aim of the present study was to investigate photochemical transformations of 2-azido-1-(4-*tert*-butyl-phenoxy)-9,10-anthraquinone in the presence of phenol

and its alkyl derivatives, compare the efficiency of the phototransformations, and determine the structures of photocyclization products.

Results and Discussion

2-Azido-1-(4-tert-butylphenoxy)-9,10-anthraquinone (1) was synthesized from 2-amino-1-chloro-9,10-anthraquinone by introducing the 4-tert-butylphenoxy group according to a known procedure⁸ followed by the diazotization of the amino group and the reaction of the resulting solution of the diazonium salt with NaN₃ by analogy with the study.⁹

A solution of azidoanthraquinone 1 and phenol ArOH in a ratio of 1:3 in dry benzene was irradiated at 20 °C with full light from a mercury lamp or with sunlight until azide 1 was completely consumed (Scheme 1). The photocyclization in the presence of unsubstituted phenol or *ortho*- and *para*-alkyl-substituted phenols afforded the corresponding 5*H*-naphtho[2,3-*c*]phenoxazine-8,13-diones 2a—d in high yields. In all cases, small amounts (<5%) of 1-hydroxy-2-(4-*tert*-butylphenylamino)-9,10-anthraquinone were detected in photolysates by analogy with the study.⁷

The structures of phenoxazines **2a**—**d** were determined by elemental analysis, mass spectrometry, and IR, UV, and ¹H NMR spectroscopy. When assigning the signals in the ¹H NMR spectra of compounds **2a**—**d** (see the Experimental section), we found signals for six protons of the anthraquinone moiety, *viz.*, the characteristic pairs of signals for the protons H(10), H(11) and H(9), H(12) of the unsubstituted anthraquinone ring and two signals for

^{*} Dedicated to the memory of Academician N. N. Vorozhtsov on the 100th anniversary of his birth.

Scheme 1

Ar in ArOH	2	ОН	R	<i>t/</i> h	Yield (%)
Ph	а	4′	Н	4.5	87
4-MeC ₆ H ₄	b	2´	5´-Me	3.5	82
$2,6-Me_2C_6H_3$	С	4´	3´,5´-Me ₂	3.0	86
4-Bu ^t C ₆ H ₄	d	2′	5´-Bu ^t	4.0	79

the protons H(6) and H(7) of the substituted ring. The ¹H NMR spectra of products **2b,d** obtained by the photocyclization with para-substituted phenols show two set of signals, each set corresponding to three aromatic protons (H(1), H(3), H(4) and H(3'), H(4'), H(6')) with the splitting pattern being typical of 1,2,4-trisubstituted benzenes. 10 This is evidence for the attachment of the nitrogen atom at the ortho position with respect to the hydroxy group. In the ¹H NMR spectra of compounds **2a,c**, the signals for the protons H(2'), H(3'), H(5'), H(6') and H(2'), H(6') appear as a broad singlet and a singlet, respectively, which is indicative of the replacement of the hydrogen atom in the para position of the aromatic ring of phenol. To prove the position of the tert-butyl substituent in the aromatic ring of the phenoxazine fragment, we studied compound 2c by X-ray diffraction.

The three-dimensional structure of compound 2c is shown in Fig. 1. The pentacyclic moiety of the molecule is virtually planar (the rms deviation from the plane is 0.109 Å). However, although the phenyl rings are planar within 0.006—0.044 Å, the O(14) and N(5) atoms in the oxazine ring deviate in the same direction from the plane passing through the other four C atoms of the oxazine ring by 0.072 and 0.064 Å, respectively. The geometric parameters of molecule 2c are within 3σ of the mean values. ¹¹ It should be noted that we found no structures containing a

similar pentacyclic moiety in the Cambridge Structural Database. 12 The most similar compounds containing the phenoxazine moiety, such as 2-methyl-2-(10-phenoxazinyl)propionitrile, 13 10-piperidylacetylphenoxazine, 14 10-acetyl-1-cyanophenoxazine, 15 and 10-acetyl-3-cyanophenoxazine, 16 are nonplanar, and the oxazine ring in these compounds adopts a boat conformation. The bond lengths and bond angles in the phenoxazine fragment of molecule 2c are similar to the corresponding parameters in the above-mentioned compounds. The N(5)—C(4a)and N(5)—C(5a) bond lengths are the only exceptions. In molecule 2c, these bonds are shortened to 1.392(6) and 1.396(6) Å compared to the analogous bonds in the reference compounds (from 1.426 to 1.455 Å). Presumably, this difference is associated with a flattening of the oxazine ring in molecule 2c. The plane passing through the atoms of the phenyl ring C(1')-C(6') (the rms deviation from the plane is 0.006 Å) is virtually perpendicular to the plane of the pentacyclic moiety (the dihedral angle between these two fragments is $82.4(1)^{\circ}$).

In the crystal structure of compound 2c, the molecules are linked to each other by the O(3)—H...O(2) hydrogen bonds (O(3)...O(2), 2.864(6) Å; H...O, 1.93(6) Å; O(3)—H...O, 154(4)°) to form infinite head-to-tail chains along the b axis. The chains are linked in pairs by π -stacking arene—arene interactions (Fig. 2). The distance between the planes of the adjacent molecules involved in the π -stacking interactions is 3.56 Å; the intercenter distance between the 1,4-benzoquinone and oxazine rings is 3.568(3) Å. The pairs of chains are packed in stacks along the a axis with the distance of 3.45 Å between the planes of the adjacent molecules. The intercenter distances vary from 3.934(3) to 4.133(4) Å, which is indicative of a large shift of the π -stacking interaction.

The X-ray diffraction data provide unambiguous evidence that the cyclization under study is accompanied by a change in the position of the *tert*-butyl substituent in the phenoxazine ring. The substituent, which is in the *para* position with respect to the oxygen atom in the aryloxy group of starting azide 1, is attached at the *para* position with respect to the nitrogen atom in the reaction products. In earlier studies 17–19 on the photolysis and thermolysis of isomeric 2-aryloxy-1-azido-9,10-anthraquinones, the same change in the position of the substituent was demonstrated by the independent synthesis.

Our experimental data are not contradictory to the commonly accepted mechanism of photocyclization of aryl azides containing an arylthio or aryloxy group in the *ortho* positions with respect to the azido group^{7,17–20} (Scheme 2). According to the published data, the carbon atom of the substituent bound to the heteroatom is attacked by singlet nitrene 3 that is generated upon photodecomposition of the azido group²¹ to form intermediate

Fig. 1. Three-dimensional structure of 2-*tert*-butyl-5-(4′-hydroxy-3′,5′-dimethylphenyl)naphtho[2,3-*c*]phenoxazine-8,13-dione (**2c**) based on X-ray diffraction data.

Fig. 2. π -Stacking interactions between molecules 2c in the adjacent chains based on X-ray diffraction data (the projection along the crystallographic direction [101]).

biradical spiro complex 4. The formation of phenoxazines 2a—d upon irradiation of azide 1 in the presence of sub-

stituted phenols can be attributed to the radical substitution of the hydrogen atom in phenol derivatives by this intermediate biradical spiro complex. The experimentally observed direction of the attack (*ortho* and *para* positions) is consistent with the known features of the free-radical aromatic substitution.^{22,23}

To summarize, we studied a new type of phototransformations in the quinone series, viz., the photocyclization of 1-aryloxy-2-azido-9,10-anthraquinones in the presence of phenols. 5H-Naphtho[2,3-c]phenoxazine-8,13-diones, in which the nitrogen atom is covalently bound to the phenyl ring of the introduced reagent, were prepared in high yield. The present study demonstrated that the above-described photocyclization provides a convenient one-step procedure for the synthesis of various N-substituted polycyclic derivatives of phenoxazine.

Experimental

The IR spectra were recorded on a Vector-22 (Bruker) spectrophotometer in KBr pellets. The UV-Vis spectra were measured on a Hewlett Packard Agilent 8453 spectrophotometer in ethanol ($1 \cdot 10^{-4} \text{ mol L}^{-1}$). The ¹H NMR spectra were recorded on a Bruker WP-200SY instrument (the chemical shifts are given on the δ scale) with SiMe₄ as the internal standard. The EI mass spectra were obtained on a Finnigan MAT-8200 instrument. The TLC analysis was carried out on Silufol UV-254 plates using a 9:1 toluene—ethanol system as the eluent. The column chromatography was carried out on silica gel (140-350 µm). The solvents were dried before use. Photolysis was carried out using light from a SVD-120A lamp through an UFS-1 light filter (280—400 nm) and also with the use of the full spectrum of the mercury lamp. The synthesis and physicochemical characteristics of the starting azidoanthraquinone 1 have been described earlier.7

Preparative photolysis of azide 1 in the presence of phenols (general procedure). A solution of compound 1 (0.4 g, 1 mmol) and substituted phenol (3 mmol) in dry benzene (0.5 L) was irradiated at 20 °C for 3—4.5 h until the starting compound disappeared (TLC monitoring). The reaction solution was concentrated, and the residue was chromatographed on silica gel. 1-Hydroxy-2-(4-tert-butylphenyl)amino-9,10-anthraquinone (0.01—0.02 g) was isolated from the first violet band by elution with benzene. This product was identified by comparing with an authentic sample.⁸ Then the major violet band was eluted with chloroform. Products 2a—d were recrystallized from an ethanol—benzene mixture.

2-tert-Butyl-5-(4´-hydroxyphenyl)-5*H*-naphtho[2,3-*c*]phenoxazine-8,13-dione (2a). M.p. 236—239 °C. ¹H NMR (CDCl₃), δ: 1.23 (s, 9 H, Bu¹); 5.92 (d, 1 H, H(4), J = 8.5 Hz); 6.13 (d, 1 H, H(6), J = 8.5 Hz); 6.66 (dd, 1 H, H(3), J₁ = 8.5 Hz, J₂ = 3.0 Hz); 6.86 (br.s, 1 H, OH); 7.03 (d, 1 H, H(1), J = 3.0 Hz); 7.14 (br.s, 4 H, H(2´), H(3´), H(5´), H(6´)); 7.60 (d, 1 H, H(7), J = 8.5 Hz); 7.73 (m, 2 H, H(10), H(11)); 8.25 (m, 2 H, H(9), H(12)). IR, v/cm⁻¹: 3467 (OH); 3010, 2949, 2864 (C—H); 1666 (C=O); 1590, 1514 (C=C). UV-Vis, λ _{max}/nm (logε): 266 (4.72), 314 (3.63), 405 (3.46), 562 (4.00). High-resolution mass spectrum, found: m/z 461.1635 [M⁺]. C₃₀H₂₃NO₄. Calculated: M = 461.1627.

2-tert-Butyl-5-(2´-hydroxy-5´-methylphenyl)-5*H*-naphtho[2,3-c]phenoxazine-8,13-dione (2b). M.p. 238—241 °C. Found (%): C, 78.00; H, 5.36; N, 3.09. $C_{31}H_{25}NO_4$. Calculated (%): C, 78.32; H, 5.26; N, 2.95. ¹H NMR (CDCl₃), δ: 1.23 (s, 9 H, Bu¹); 2.30 (s, 3 H, Me); 5.97 (d, 1 H, H(3´), J = 8.5 Hz); 4.57 (br.s, 1 H, OH); 6.09 (d, 1 H, H(6), J = 8.5 Hz); 6.72 (dd, 1 H, H(4´), J_1 = 8.5 Hz, J_2 = 3.0 Hz); 6.82 (d, 1 H, H(6´), J = 3.0 Hz); 6.98 (d, 1 H, H(1), J = 3.0 Hz); 7.02 (d, 1 H, H(4), J = 8.5 Hz); 7.12 (d, 1 H, H(7), J = 8.5 Hz); 7.45 (dd, 1 H, H(3), J_1 = 8.5 Hz, J_2 = 3.0 Hz); 7.66 (m, 2 H, H(10), H(11)); 8.10 (m, 2 H, H(9), H(12)). IR, v/cm^{-1} : 3430 (OH); 3035, 2963 (C—H); 1664 (C=O); 1590, 1522 (C=C). UV-Vis, λ_{max}/nm (logε): 268 (4.70), 313 (3.64), 403 (3.48), 560 (3.98). MS, m/z: 475 [M⁺].

2-tert-Butyl-5-(4´-hydroxy-3´,5´-dimethylphenyl)-5*H***-naphtho[2,3-c]phenoxazine-8,13-dione (2c).** M.p. 325—327 °C.

¹H NMR (CDCl₃), δ : 1.23 (s, 9 H, Bu¹); 2.29 (s, 6 H, 2 Me); 5.10 (br.s, 1 H, OH); 5.92 (d, 1 H, H(4), J = 8.5 Hz); 6.17 (d, 1 H, H(6), J = 8.5 Hz); 6.66 (dd, 1 H, H(3), J_1 = 8.5 Hz, J_2 = 3.0 Hz); 6.90 (s, 2 H, H(2´), H(6´)); 7.00 (d, 1 H, H(1), J = 3.0 Hz); 7.63 (d, 1 H, H(7), J = 8.5 Hz); 7.72 (m, 2 H, H(10), H(11)); 8.25 (m, 2 H, H(9), H(12)). IR, v/cm⁻¹: 3485 (OH); 3078, 2960, 2873 (C—H); 1664 (C=O); 1597, 1516 (C=C). UV-Vis, λ_{max} /nm (logɛ): 264 (4.78), 313 (3.60), 405 (3.61), 560 (3.90). High-resolution mass spectrum, found: 489.1951 [M⁺]. $C_{32}H_{27}$ NO₄. Calculated: M = 489.1940.

2-tert-Butyl-5-(5´-tert-butyl-2´-hydroxyphenyl)-5*H*-naphtho[2,3-c]phenoxazine-8,13-dione (2d). M.p. 192—195 °C.

¹H NMR (500 MHz, CDCl₃), δ: 1.22 and 1.29 (both s, 9 H each, 2 Bu^t); 5.94 (d, 1 H, H(3´), J = 8.5); 5.99 (d, 1 H, H(6), J = 8.5 Hz); 6.68 (dd, 1 H, H(4´), $J_1 = 8.5$ Hz, $J_2 = 3.0$ Hz); 6.70 (d, 1 H, H(6´), J = 3.0 Hz); 7.14 (d, 1 H, H(1), J = 3.0 Hz); 7.18 (d, 1 H, H(4), J = 8.5 Hz); 7.31 (d, 1 H, H(7), J = 8.5 Hz); 7.44 (dd, 1 H, H(3), $J_1 = 8.5$ Hz, $J_2 = 3.0$ Hz); 7.59 (td, 1 H, H(10), $J_1 = 8.0$ Hz, $J_2 = 2.0$ Hz); 7.66 (td, 1 H, H(11), $J_1 = 8.0$ Hz, $J_2 = 2.0$ Hz); 7.75 (br.s, 1 H, OH); 8.00 (dd, 1 H, H(9), $J_1 = 8.0$ Hz, $J_2 = 2.0$ Hz); 8.05 (dd, 1 H, H(12), $J_1 = 8.0$ Hz, $J_2 = 2.0$ Hz). IR, v/cm^{-1} : 3400 (OH); 2960 (C—H); 1660 (C=O), 1590, 1522 (C=C). UV-Vis, $λ_{max}/nm$ (loge): 266 (4.78), 313 (3.63), 410 (3.46), 560 (4.02). High-resolution mass spectrum, found: 517.2241 [M⁺]. C₃₄H₃₂NO₄. Calculated: M = 517.2253.

X-ray diffraction study of compound 2c. X-ray diffraction data were collected on a Bruker P4 diffractometer (Mo-K\alpha radiation, graphite monochromator, $2\theta/\theta$ -scanning technique in the range $2\theta < 50^{\circ}$). A crystal of compound 2c of dimensions 0.60×0.36×0.03 mm was selected. The crystals are monoclinic: a = 10.095(2) Å, b = 20.326(5) Å, c = 12.952(4) Å, $\beta = 110.32(2)^{\circ}$, $V = 2492(1) \text{ Å}^3$, space group $P2_1/c$, Z = 4, $C_{32}H_{27}NO_4$, $d_{calc} = 1.305 \text{ g cm}^{-3}$, $\mu = 0.086 \text{ mm}^{-1}$. The intensities of 4370 independent reflections were measured. The empirical absorption correction was applied based on azimuthal scans (the transmission was 0.79-0.98). The structure was solved by direct methods using the SHELXS-97 program package¹⁶ and refined by the full-matrix least-squares method with anisotropic displacement parameters for nonhydrogen atoms and isotropic displacement parameters for H atoms using the SHELXL-97 program package. 16 The parameters of other H atoms (except for OH) were calculated in each refinement cycle from the coordinates of the corresponding carbon atoms. The hydrogen atom of the hydroxy group at the O(3) atom was located in a difference electron density map. The final refinement was carried out based on all F^2 to $wR_2 = 0.1926$, S = 0.905, 339 variables

 $(R=0.0734 \text{ for } 1490 \text{ reflections with } F>4\sigma)$. The structure of **2c** was deposited at the Cambridge Crystallographic Data Centre (CCDC, refcode 626170). The X-ray diffraction data can be obtained free of charge *via* http://www.ccdc.cam.ac.uk/data request/cif deposit.

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Received January 19, 2007