INVESTIGATION OF QUINONES

XXVIII.* REACTION OF NAPHTHO[2,3-f]QUINOXALINE-7,12-DIONES WITH BENZENESULFURIC ACID

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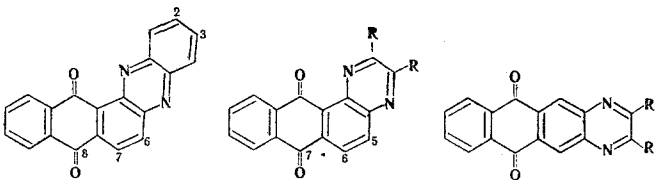
Naphtho[2,3-f]quinoxaline-7,12-diones add a molecule of benzenesulfinic acid to give 5-phenylsulfonyl-7,12-dihydroxynaphtho[2,3-f]quinoxalines. The latter are oxidized to 5-phenylsulfonyl-substituted quinones, which add a molecule of benzenesulfinic acid to the oxygen atoms of the quinone grouping to give the O^7-benzenesulfonate of 5-phenylsulfonyl-7,12-dihydroxynaphtho[2,3-f]quinoxaline. The protonated form of naphtho[2,3-f]quinoxaline-7,12-dione, which is stabilized by an intramolecular hydrogen bond, as confirmed by the anomalously high basicity of angular naphtho[2,3-f]quinoxaline-7,12-dione as compared with its linear isomer, which is inert in reactions with benzenesulfinic acid, undergoes reaction.

It has been established [2, 3] that naphtho[2,3-*a*]phenazine-8,13-diones (I) add nucleophilic agents to the carbon atoms in the 2- and 6-positions, but also add benzenesulfinic acid to the oxygen atom of the carbonyl group in the 8-position. Nucleophilic addition to the simplest anthraquinone derivative containing an angular condensed pyrazine ring – naphtho[2,3-f]quinoxaline-7,12-diones (II) – should be studied.



I II a-c III a,b

II a R=H; b R=$COOC_2H_5$; c R=C_6H_5; III a R=H; b R=CH_3

The only known compound of this series is the 2,3-dicarbethoxy derivative (IIb) [4]. We also obtained IIa and IIc by reaction of 1,2-diaminonanthraquinone with glyoxal and benzil. For comparison, we also synthesized linear naptho[2,3-g]quinoxaline-7,12-diones (III).

As a rule, anthraquinone derivatives do not undergo nucleophilic addition. However, anthraquinone pyrazines II are converted to 5-phenylsulfonyl-substituted hydroquinones IV when they are heated with benzenesulfinic acid in acetic acid or dioxane for several minutes. The absorption band of a quinone carbonyl group at 1670-1690 cm^{-1} is absent in the IR spectra of these compounds, and a band of vibrations of a hydroxyl group appears at 3200-3500 cm^{-1}. Oxidation of hydroquinones IV with ferric chloride gives 5-phenylsulfonyl-substituted quinones (V), the position of the substituent in which is proved by alternative synthesis from 3-phenylsulfonyl-1,2-diaminoanthraquinone [5] and the appropriate α-dicarbonyl compound.

* See [1] for communication XXVII.

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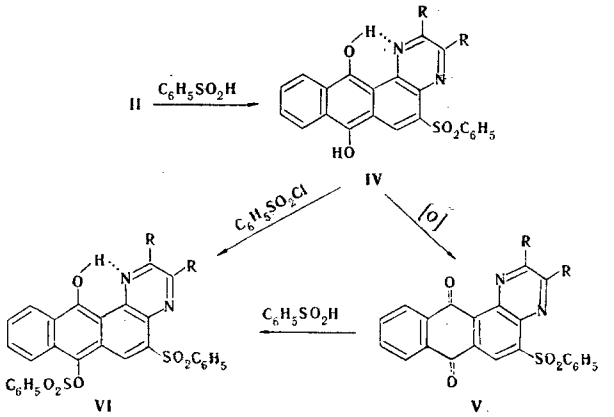
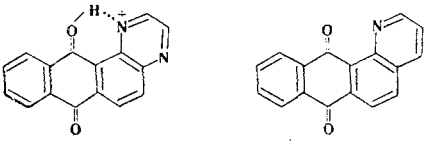


a R=H; b R=COOC$_2$H$_5$; c R=C$_6$H$_5$

Quinones Va,b add another molecule of benzenesulfinic acid to give benzenesulfonate esters VI. Identical substances were obtained by acylation of hydroquinones IV with benzenesulfonyl chloride. In addition to bands of vibrations of the S=O bond of the sulfone group at 1160 cm^{-1}, the IR spectra of these compounds contain the band at 1195 cm^{-1} that is characteristic for the ν_{SO} vibrations in sulfonate [6]. At the same time, the spectra do not contain absorption bands of the carbonyl groups of anthraquinone and OH group absorption at 3100-3600 cm^{-1}. The latter circumstance is explained by tying up of the OH group in a strong intramolecular hydrogen bond and indicates that the ester grouping is attached to the oxygen atom farther away from the heteroring.

Thus, compounds II behave like quinonazines I in reactions with benzenesulfinic acid. The difference consists in the fact that C-addition in the case of quinonazines II is accompanied by reduction of the quinone grouping, as compared with reduction of the azine grouping in the case of quinonazines I. This is explained by the greater energetic stability of the N,N'-dihydrophenazine structure as compared with the N,N'-dihydroquinoxaline structure.

Neither quinoxalinediones nor linear naphthoquinoxalinediones III react under these conditions with benzenesulfinic acid. The reaction of quinones II and V with sodium benzenesulfinate does not proceed in the absence of protic acids. Consequently, the protonated form of naphtho[2,3-f]quinoxaline-7,12-dione, in which the formation of an intramolecular hydrogen bond (VII) is possible, undergoes nucleophilic attack. A comparison of the ionization constants of isomeric quinones IIa and IIIa confirm the existence of VII. Angular pyrazinoanthraquinone IIa (pK_a 8.0) is at least three orders of magnitude more basic than linear isomer IIIa (pK_a < 5.0). The increase in the basicity of quinone IIIa is due to stabilization of cation VII due to a gain in energy on closing of the chelate ring.



VII VIII

Protonation with closing of an intramolecular hydrogen bond activates the molecule, intensifying the coordinated electron-acceptor effect of the peri-oriented nitrogen atoms of the heteroring and the oxygen atom of the carbonyl group, an effect which is transmitted along the conjugation chain to the positions that undergo nucleophilic attack. In this respect, anthraquinonepyrazines II are similar to anthraquinonepyridine VIII [7, 8]. One should expect a similar mechanism of activation in nucleophilic addition reactions in all cases in which the nitrogen atom of a condensed six-membered aromatic heteroring is in the peri position relative to the carbonyl group of the anthraquinone.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were measured with a UR-20 spectrometer. The ionization constants were determined by potentiometry by the method described in [9]. The authors thank B. A. Korolev for measuring the pK_a values.

Naphtho[2,3-f]quinoxaline-7,12-diones (II and V) (Table 1). A 0.015-mole sample of the appropriate α-dicarbonyl compound was added to a suspension of 0.01 mole of 1,2-diaminoanthraquinone or 3-phenyl-

TABLE 1. Naphtho[2,3-f]quinoxaline Derivatives

Compound	mp, °C (crystallization solvent)	Empirical formula	Found, %				Calc., %				Yield, %
			C	H	N	S	C	H	N	S	
IIa	277—278 (chlorobenzene)	$C_{16}H_8N_2O_2$	73,8	3,1	10,8	—	73,8	3,1	10,8	—	32
IIc	245—246 (dioxane)	$C_{28}H_{16}N_2O_2$	81,6	3,9	6,7	—	81,5	3,9	6,8	—	72
IVa	215—216,5 (acetic acid)	$C_{22}H_{14}N_2O_4S$	—	—	6,8	8,0	—	—	7,0	8,0	71
IVb	185—186 (acetic acid)	$C_{28}H_{22}N_2O_8S$	61,3	4,1	5,0	5,7	61,5	4,0	5,1	5,9	87
IVc	281—282 (isobutanol)	$C_{34}H_{22}N_2O_4S$	73,5	3,8	5,2	5,6	73,6	4,0	5,0	5,8	75
Va	294—295 (chloroform)	$C_{22}H_{12}N_2O_4S$	—	—	6,9	7,9	—	—	7,0	8,0	20*
Vb	235—236 (alcohol)	$C_{28}H_{20}N_2O_8S$	61,9	3,6	5,1	5,7	61,8	3,7	5,1	5,9	77*
Vc	300—302 (dioxane)	$C_{36}H_{20}N_2O_4S$	73,8	3,5	4,9	5,6	73,9	3,6	5,1	5,8	70*
VIa	270—271.5 (acetic acid)	$C_{28}H_{18}N_2O_6S_2$	—	—	5,3	11,6	—	—	5,2	11,8	82†
VIb	199,5—200,5 (alcohol)	$C_{34}H_{26}N_2O_{10}S_2$	59,7	3,7	3,9	9,5	59,5	3,8	4,7	9,2	88†

* From 3-phenylsulfonyl-1,2-diaminoanthraquinone.
† By reaction of quinone V with benzenesulfinic acid.

sulfonyl-1,2-diaminoanthraquinone in 30 ml of alcohol, and the mixture was refluxed for 5 h. It was then cooled, and the precipitated II or V was removed by filtration and purified by column chromatography on Al_2O_3 with elution by chloroform and subsequent crystallization. Quinones IIc and Vc were obtained similarly in 15 ml of acetic acid.

Naphtho[2,3-g]quinoxaline-7,12-diones (III). Quinones IIIa,b were synthesized like quinones II by heating 2,3-diaminoanthraquinone with glyoxal or diacetyl in alcohol, respectively. Quinone IIIa, with mp 299-300° (from chlorobenzene), was obtained in 80% yield. Found, %: C 73.7; H 3.1; N 11.0. $C_{16}H_8N_2O_2$. Calculated, %: C 73.8; H 3.1; N 10.8. Quinone IIIb, with mp 279-280° (from alcohol), was obtained in 73% yield. Found, %: C 74.8; H 4.2; N 9.9. $C_{18}H_{12}N_2O_2$. Calculated, %: C 75.0; H 4.2; N 9.7.

5-Phenylsulfonyl-7,12-dihydroxynaphtho[2,3-f]quinoxalines (IV). A solution of 3 mmole of sodium benzenesulfinate in 5 ml of acetic acid was added to a solution of 2 mmole of quinone II in 30-40 ml of boiling acetic acid in a nitrogen atmosphere, and the mixture was refluxed for 2 min. It was then cooled, and the dark-red crystals of hydroquinone IV were separated (Table 1). Hydroquinone IVa (70%) was similarly obtained from quinone IIa but in dioxane with the use of benzenesulfinic acid. Quinone IIa remains unchanged when the reaction is carried out in dioxane with sodium benzenesulfinate.

The unchanged quinone (96%) was isolated after refluxing naptho[2,3-g]quinoxaline-8,13-dione (IIIa) with benzenesulfinic acid in acetic acid. A mixture of 0.52 g (4 mmole) of quinoxaline and 0.71 g (5 mmole) of benzenesulfinic acid was heated for 5 min in 6 ml of refluxing acetic acid, after which the mixture was poured into 25 ml of water, and 5 ml of saturated oxalic acid solution was added. Long colorless needles of the quinoxaline oxalate (90%) with mp 170° (decomp.,) (mp 169° [10]), the IR spectrum of which was identical to that of a genuine sample, were isolated.

5-Phenylsulfonylnaphtho[2,3-f]quinoxaline-7,12-diones (V). A solution of 2 mmole of hydroquinone IVc in acetic acid was mixed with 5 ml of 40% ferric chloride, and the mixture was refluxed for 2-3 min. Heating was continued while water was added until crystallization began. The mixture was then cooled, and yellow crystals of quinone V (82-87%) were removed by filtration; according to a mixed-melting-point determination and the IR spectra, this product was identical to the product obtained by condensation of 3-phenylsulfonyl-1,2-diaminoanthraquinone with glyoxal (Va), diethyl diketosuccinate (Vb), or benzil (Vc), respectively (Table 1).

O^7-Benzenesulfonate Esters of 5-Phenylsulfonyl-7,12-dihydroxynaphtho[2,3-f]quinoxalines (VIa,b). A) A mixture of 1 mmole of quinone Va or Vb, 2 mmole of sodium benzenesulfinate, and 15 ml of acetic acid was refluxed for 2 min, after which it was diluted with water, and the resulting precipitate of monoester VIa or VIb, respectively, was separated; the products were crystallized from alcohol or acetic acid were obtained as orange needles (Table 1).

B) Benzenesulfonyl chloride (2 mmole) was added to a solution of 1 mmole of hydroquinone IVa or IVb in 4 ml of pyridine, and the mixture was heated up to the boiling point, cooled, and diluted with water. The resulting precipitate was removed by filtration and recrystallized. Substances that were identical to the compounds obtained by method A with respect to mixed melting point determinations and IR spectra were isolated in yields of 78-81%.

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