2-HYDROXYBENZINDOLEQUINONE

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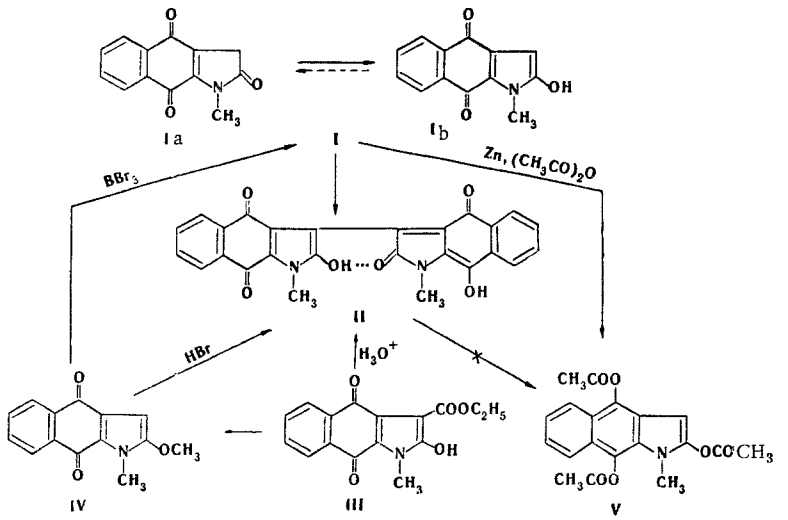
UDC 547.756.757'759.3.07

The demethylation of 2-methoxy-1-methylbenz[f]indolo-4,9-quinone with boron tribromide at −80°C gave 2-hydroxy-1-methylbenz[f]indole-4,9-quinone, which is converted quantitatively to the 3,4' dimer by the action of acids and bases and by heating. The state of the tautomeric equilibrium of the 2-hydroxybenzindolequinone in the crystalline state and in solutions was investigated by IR, PMR, and electronic spectroscopy.

We have previously shown [1, 2] that the compound to which the 2-hydroxybenzindolequinone structure I was assigned [3] is actually its 3,3' dimer (II). It seemed of interest to synthesize the heretofore unknown monomeric I and study its properties.

As we have already noted [2], the hydrolysis and decarboxylation of ethyl 2-hydroxybenzindolequinone-3-carboxylate (III), like the demethylation of 2-methoxybenzindolequinone IV by heating with hydrobromic acid, lead to dimer II even when air oxygen is absent. We were able to obtain monomeric 2-hydroxybenzindolequinone I by treatment of methoxy derivative IV with boron tribromide [4] at −80°C. The monomeric structure of quinone I is confirmed by its conversion by reductive acetylation to triacetoxybenzindole V, the molecular mass of which was determined by mass spectrometry. Under the same conditions dimer II gives only the corresponding hexaacetyl derivative [2].

2-Hydroxybenzindolequinone I is labile and readily undergoes dimerization when it is heated and under the influence of acids or bases; this explains the earlier failures in attempts to isolate it [3, 5]. This reaction is evidently analogous to the oxidative dimerization of oxindoles under the influence of potassium ferricyanide [6] or air oxygen in the presence of a base [7], in which 3,3'-bis(oxindolyls) are formed. The quinone grouping of one molecule of I, which accepts an electron from the pyrrole ring of another molecule to give a semiquinone which subsequently undergoes disproportionation to the quinone and hydroquinone [2], acts as the oxidizing agent in this case.



Like oxindole [8], oxindolequinone I exists entirely in keto form Ia in an aprotic solvent with low polarity, viz., chloroform: Its IR spectrum contains a band of a lactam CO group at 1730 cm^{-1} but does not contain the band of an OH group at 3000-3600 cm^{-1}, and its PMR spectrum contains two signals at 3.52 and 3.58 ppm with

Scientific-Research Institute of Organic Intermediates and Dyes, Moscow 103787. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 927-929, July, 1979. Original article submitted October 2, 1978.

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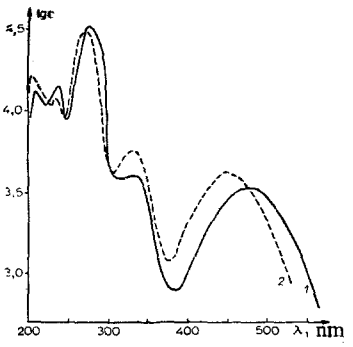

Fig. 1. Electronic spectra in ethanol: 1) 2-hydroxy-1-methylbenz[f]indole-4,9-quinone (I); 2) 2-methoxy-1-methylbenz[f]indole-4,9-quinone (IV).

an intensity ratio of 3:2 that corresponds to methyl and methylene groups. However, in contrast to oxindole, hydroxybenzindolequinone I exists in hydroxy form Ib in ethanol and in the crystalline state, since in ethanol its electronic spectrum is similar to the spectrum of methoxy derivative IV (Fig. 1), whereas the band of a lactam carbonyl group is not observed in the IR spectrum of a KBr pellet, and there is a broad band of an associated hydroxy group at 3400 cm^{-1}.

According to the data from the electronic and IR spectra, oxindole exists exclusively in the keto form in ethanol solution [9] and in the crystalline state [10]. Hydroxybenzindolequinone I exists in dimethyl sulfoxide (DMSO) in the form of a mixture of tautomers Ia and Ib in a ratio of 1:3 with predominance of the hydroxy form. Evidence for this is provided by the presence of the signal of the β-H proton of the pyrrole ring at 5.80 ppm with an intensity of ~0.75 of a proton unit and a broad singlet of methyl and methylene groups at 3.75 ppm with an intensity of 3.3 protons. The signal of an enol hydroxy proton is not observed, evidently because of exchange with traces of water or association. The shift of the tautomeric equilibrium to favor the hydroxy form in the case of hydroxybenzindolequinone I as compared with oxindole is probably due to the effect of conjugation of the hydroxy group with the quinone carbonyl group, which stabilizes form Ib.

EXPERIMENTAL

The IR spectra of the compounds were recorded with a UR-20 spectrometer. The electronic spectra were recorded with a Specord UV-vis spectrophotometer. The PMR spectra were obtained with a Jeol C-60 HL spectrometer with tetramethylsilane as the internal standard.

2-Hydroxy-1-methylbenz[f]indole-4,9-quinone (I). A solution of 1 g (4.15 mole) of methoxy derivative IV in 150 ml of absolute methylene chloride was cooled to −80°C, 3.6 g (14.4 mmole) of BBr_3 was added dropwise, and the mixture was stirred at −80°C for 1 h and at 20°C for 8 h. It was then poured into 0.5 liter of ice water, and the organic layer was dried with sodium sulfate and filtered. The filtrate was evaporated in vacuo, and the residue was recrystallized from methylene chloride at −80°C to give 0.37 g (39%) of orange crystals of oxindolequinone I. The latter was converted completely to dimer II when it was heated to 70-90°C; dimer II was readily soluble in aqueous alkali and gave a bright-blue solution, upon acidification of which dimer II was isolated. Found: C 68.4; H 4.0; N 6.0%. $C_{13}H_9NO_3$. Calculated: C 68.7; H 4.0; N 6.2%.

2,4,9-Triacetoxy-1-methylbenz[f]indole (V). A 0.23-g (1 mmole) sample of oxindole I was suspended in 5 ml of acetic anhydride, 0.3 g of zinc dust was added, and the mixture was shaken until it became colorless. Pyridine (3 ml) was added, and the mixture was refluxed for 1 h, after which it was cooled and poured into ice water. The precipitated triacetoxy derivative V was removed by filtration, dried, and recrystallized from chloroform to give 0.32 g (90%) of a product with mp 220-222°C. The product was identical to the compound described in [2] with respect to its melting point and IR spectrum.

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OXIDATION OF THE 2-HYDROXYBENZINDOLEQUINONE DIMER

EXPANSION OF THE QUINONE RING TO AN OXEPINE RING*

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UDC 547.756'759.3:542.943

One of the quinone rings of the 3,3' dimer of 2-hydroxybenzindolequinone undergoes expansion to an oxepine ring during oxidation with nitric acid. A benzisatinquinone structure was previously erroneously assigned to this compound. The structure was proved by spectral methods and stepwise degradation to be the monomeric 2-hydroxybenzindolequinone derivative. The possible oxidation pathways are discussed.

We have shown [2] that the 3,3' dimer (III) rather than 2-hydroxybenzindolequinone (II), as assumed in [3], is formed in the decarboxylation of 2-hydroxybenzindolequinone-3-carboxylic acid (I). A benzisatinquinone structure (IV) was assigned in [3] and later in [4] to the product of decarboxylation of I and subsequent oxidation with nitric acid in sulfuric acid. We have established that this substance is actually a dimeric quinonelactone (V).

The mass spectrum of lactone V and of the corresponding nitrogen-unsubstituted compound and the results of elementary analysis show that the oxidation proceeds with retention of the dimeric structure as a result of splitting out of two hydrogen atoms from the III molecule and the addition of one oxygen atom.

Under the influence of an aqueous solution of potassium hydroxide lactone V is hydrolyzed to an acid (VI), treatment of which with dehydrating agents (sulfuric acid, acetic anhydride) does not result in the reversible formation of lactone V. Potentiometric titration of acid VI with a solution of tetramethylammonium hydroxide in dimethyl sulfoxide (DMSO) reveals the presence of two acidic groups (pK_a 3.5 and 12.9). When the first acidic group is neutralized, the color of the solution changes from red to blue, and this indicates the presence of an enol grouping conjugated with the quinone carbonyl groups. The formation of blue anions is also observed for other 2-hydroxybenzindolequinone derivatives [4]. The second acidic group is a carboxy group and is eliminated by heating to 200-220°C to give an enol (VII). Its structure is confirmed by its PMR spectrum, which contains signals of two N-methyl groups, and nine aromatic protons and the signal of an enol proton at 8.48 ppm. Methylation of enol VII with dimethyl sulfate gives a methoxy derivative (VIII), the PMR spectrum of which does not contain a signal at 8.48 ppm but does contain a signal of a methoxy group.

Both lactone V and its hydrolysis product (VI) are cleaved to give phthalic acid and an enol (IX) when they are refluxed in a mixture of hydrobromic and acetic acids. The PMR spectra of the methoxy and benzoxy derivatives of the latter (Xa,b) contain signals of four aromatic protons, two N-methyl groups, and a vinyl proton; in addition, the spectrum of Xa contains the signal of the protons of a methoxy group, while the spectrum of Xb contains the signal of the protons of another phenyl ring.

When methoxy derivative Xa is heated with a solution of potassium hydroxide, the N-methylmaleinimide ring is hydrolytically cleaved to give a dicarboxylic acid (XIa), the carboxy groups in which are evidently cis-oriented, since it is converted to an anhydride (XIb) during crystallization. The structure of acid XIa is confirmed by its mass spectrum, the PMR spectrum of its dimethyl ester (XIc) (signals of a vinyl proton, four methyl groups, and four aromatic protons), and its IR spectrum (ν_{CO} bands of quinone and ester groupings at 1667 and 1733 cm^{-1}). As expected, the electronic spectrum of diester XIc is similar to the spectrum of 2-methoxy-3-carbethoxybenzindolequinone [2] (see Fig. 1).

*See [1] for our preliminary communication.

Scientific-Research Institute of Organic Intermediates and Dyes, Moscow 103787. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 930-936, July, 1979. Original article submitted June 7, 1978.

0009-3122/79/1507-0759$07.50