CONDENSATION OF ARYLSULFONYL-p-BENZOQUINONES WITH IMINES OF β-DICARBONYL COMPOUNDS

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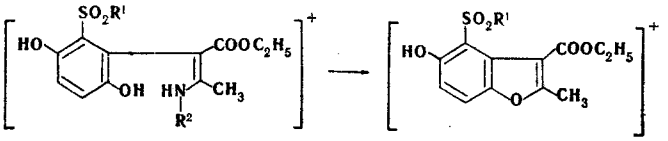
Adducts of 2-arylsulfonyl-p-benzoquinones with imines of β-dicarbonyl compounds were obtained and their conversions to indole and benzofuran derivatives were studied.

Arylsulfonyl-p-benzoquinones, as quinones that contain an electron-acceptor substituent, are of particular interest in connection with the study of orientation during nucleophilic addition reactions. We have found that the arylsulfonyl group orients the entry of substituents into the 3 position, i.e., the ortho position, in the reaction of arylsulfonyl-p-benzoquinones Ia, b with imines of acetoacetic ester, acetylacetone, ethyl benzoylpyruvate, and dimedone.

Adducts IIa-d were obtained under the usual conditions of the Nenitzescu reaction in the condensation of 2-phenylsulfonyl-p-benzoquinone (Ia) with β-alkylaminocrotonate esters. All adducts IIa-d give satisfactorily reproducible mass spectra in which the molecular ion is one of the most intense ions. The absence of $(M - H_2O)^+$, $(M - CH_3)^+$, and $(M - CH_3CHNHR^2)^+$ ions in the spectra reflects the presence of structures of the carbinolamine and 2-alkylaminodihydrobenzofuran type [1]. The presence of $(M - NH_2R^2)^+$ ions (m/e 360) in the spectra of IIa-c does not contradict the IIa-c structure, inasmuch as the driving force of the process may be the formation of a two-ring conjugated system:



m/e 360

The UV spectra of enamines IIa-d contain absorption bands at 280-300 mm, and the IR spectra contain the absorption of a carbonyl group at 1635-1660 cm^{-1}; this constitutes evidence for the presence of the conjugated bonds characteristic for the O=C–C=C–N grouping. Splitting of the signal of the protons of the CH_3–N group (at 2.95 ppm; J = 5 Hz) under the influence of the N–H proton is observed in the PMR spectra of, for example, enamino ketone IIb; there is also a signal of protons of a CH_3 group attached to a double bond (1.34 ppm) and the signal of protons of OH (5, 15, and 10.19 ppm) and NH (9.67 ppm) groups. The PMR spectrum of IId is similar to the spectrum of IIb. However, in contrast to the latter, the signal of the protons of the CH_3 group (2.44 ppm) appear at weaker field, and this, in conformity with the data described for other cases [2], makes it possible to assume a cis-enamine structure for IIb and a trans-enamine structure for IId. When adducts IIa-d are heated briefly in hydrochloric acid they are converted to benzofuran derivatives IIIa, b. We were unable to cyclize IIa-d to indole derivatives by the method in [3]. In addition, indole derivative IV is formed in the condensation of quinone Ia or Ib with β-aminocrotonic ester in acetic acid. These results provide a basis for the assumption that adducts IIa-d

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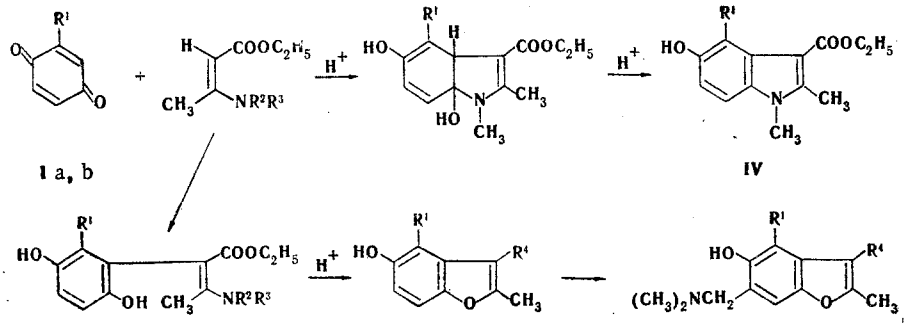
are not intermediates in the synthesis of 5-hydroxyindole derivatives.

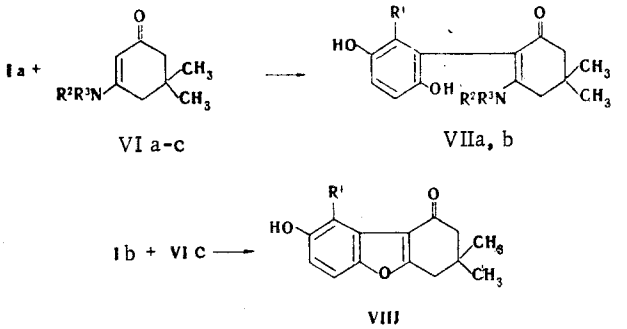


I a, b IV

II a-d III a, b V a, b

I a $R=SO_2C_6H_5$; b $R=SO_2C_6H_4CH_3$; II—V $R^1=SO_2C_6H_5$; II a $R^2=R^3=H$; c $R^2=CH_3$; $R^3=H$; b $R^2=C_6H_5$; $R^3=H$; c $R^2=R^3=C_2H_5$; III, V a $R^4=H$; b $R^4=COOC_2H_5$

The reaction of quinones Ia, b with enamines of dimedone (VIa, b) in acetic acid and dichloroethane gives adducts with a hydroquinone structure (VIIa, b). Enamine VIc reacts with Ib in acetic acid to give benzofuran derivative VIII in low yield. In contrast to similarly constructed compounds [1], adducts VII remain unchanged when they are refluxed in dilute hydrochloric acid.

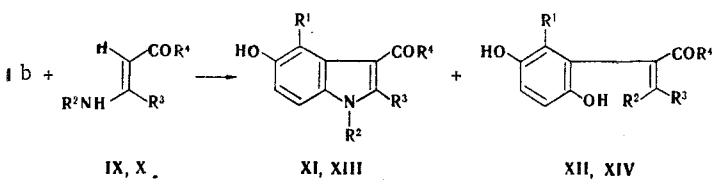


VI a-c VIIa, b

VIII

VI a $R^2=R^3=H$; b $R^2=CH_3$; $R^3=H$; c $R^2=R^3=$ morpholino; VII a $R^2=R^3=H$; b $R^2=CH_3$; $R^3=H$

A mixture of 5-hydroxyindole derivatives (XI, XIII) and an adduct (XII, XIV) is formed in the condensation of quinone Ib with ethyl 2-amino-3-benzoylacrylate (IX) and with 4-methylamino-3-penten-2-one (X).



IX, X XI, XIII XII, XIV

IX—XIV $R^1=SO_2C_6H_4CH_3$-*p*; IX, XI $R^2=H$, $R^3=COOC_2H_5$, $R^4=C_6H_5$; X, XIII $R^2=R^3=R^4=CH_3$; XII $R^2=NH_2$, $R^3=COOC_2H_5$, $R^4=C_6H_5$; XIV $R^2=OH$, $R^3=R^4=CH_3$

Enol XIV is formed as a result of acid hydrolysis of the intermediate.

6-Aminomethyl derivatives Va, b were obtained by the action of bis-(dimethylamino)-methane on benzofurans IIIa, b.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a UR-10 spectrometer. The UV spectra of alcohol solutions of the compounds were obtained with a Hitachi EPS-3 spectrophotometer. The PMR spectra of deuterochloroform solutions were recorded with JNM-4H-100 and C-60-HL spectrometers with tetramethylsilane as the internal standard. The mass spectra were obtained with a Hitachi RMU-6D spectrometer with a system for direct introduction into the ion source at 150-200° and an ionizing-electron energy of 70 eV. Thin-layer

chromatography (TLC) on aluminum oxide in a benzene–ethanol system (10:1) (IV and Va, b) and on Silufol UV-254 plates in chloroform–ethanol (20:3) (VII) and chloroform–methanol (20:4) (XIII and XIV) was used to evaluate the individuality of the substances. We have previously described the synthesis of IIa-d and IIIa, b [8].

1,2-Dimethyl-3-carbethoxy-4-phenylsulfonyl-5-hydroxyindole (IV). A solution of 1.24 g (0.005 mole) of 2-phenylsulfonyl-p-benzoquinone (Ia) [4] and 0.79 g (0.005 mole) of ethyl β-methylaminocrotonate in 15 ml of glacial acetic acid was refluxed for 30 min, after which it was cooled, and the precipitated crystals were removed by filtration to give 0.75 g (40%) of IV with mp 205-206° (from glacial acetic acid) and R_f 0.52. IR spectrum, ν_{max}, cm^{-1}: 3230-3270 (OH) and 1660 (CO), UV spectrum, λ_{max}: 222 and 324 nm (log ε 4.48 and 4.17). PMR spectrum, δ: 2.39 (s, 2-CH_3), 3.60 (s, N-CH_3), 9.30 (s, OH), 6.85, and 7.32 ppm (d, 6- and 7-H). Found: C 61.2; H 5.1; N 3.8; S 8.5%. $C_{19}H_{19}NO_5S$. Calculated: C 61.1; H 5.1; N 3.7; S 8.6%.

2-Methyl-4-phenylsulfonyl-5-hydroxy-6-dimethylaminomethylbenzofuran (Va). A 0.45-ml sample of bis(dimethylamino)methane was added to a solution of 0.9 g (0.003 mole) of 2-methyl-4-phenylsulfonyl-5-hydroxybenzofuran (IIIa) in 5 ml of dry dioxane, and the mixture was refluxed for 3 h. It was then cooled and diluted with three to four volumes of water, and the precipitated crystals were separated, washed with water, and dried to give 0.9 g (87%) of Va with mp 186-187° (from alcohol – dioxane) and R_f 0.60. Found: C 62.7; H 5.4; N 4.0; S 9.1%. $C_{18}H_{19}NO_4S$. Calculated: C 62.6; H 5.5; N 4.1; S 9.3%.

2-Methyl-3-carbethoxy-4-phenylsulfonyl-5-hydroxy-6-dimethyl-aminomethylbenzofuran (Vb). This compound, with mp 143-144° (from alcohol) and R_f 0.60, was similarly obtained in 83% yield. PMR spectrum: δ 2.17 [s, $N(CH_3)_2$], 2.54 (s, 2-CH_3), 3.67 (s, CH_2N), 11.2 (s, OH), and 7.54 ppm (s, 7-H). Found: C 60.3; H 5.6; N 3.4; S 7.9%. **$C_{21}H_{23}NO_6S$.** Calculated: C 60.4; H 5.5; N 3.4; S 7.7%.

3-Amino-2-(2-phenylsulfonyl-3,6-dihydroxyphenyl)-5,5-dimethyl-2-cyclohexen-1-one (VIIa). A warm solution of 2.8 g (0.02 mole) of 3-amino-5,5-dimethyl-2-cyclohexen-1-one (VIa) [5] in 40 ml of dichloroethane was added with stirring to a suspension of 4.96 g (0.02 mole) of quinone Ia in 100 ml of dichloroethane, after which the mixture was allowed to stand for 2 days at room temperature. The resulting precipitate was separated and washed with aqueous alcohol to give 3.3 g (43%) of VIIa with mp 211° (dec., from methanol) and R_f 0.62. IR spectrum, ν_{max}, cm^{-1}: 3160-3280, 1680, 1635, and 1540. Found: C 61.9; H 5.4; N 4.2%. $C_{20}H_{21}NO_5S$. Calculated: C 62.0; H 5.5; N 3.6%.

3-Methylamino-2-(2-phenylsulfonyl-3,6-dihydroxyphenyl)-5,5-dimethyl-2-cyclohexen-1-one (VIIb). This compound, with mp 217° (from alcohol–dimethylformamide) and R_f 0.67, was similarly obtained in 31% yield. IR spectrum, ν_{max}, cm^{-1}; 3360 (OH), 3220 (NH), 1670, 1610, and 1540. Found: C 62.7; H 5.6; N 4.0%. $C_{21}H_{23}NO_5S$. Calculated: C 62.8; H 5.8; N 3.5%.

8-Hydroxy-3,3-dimethyl-9-(p-tolylsulfonyl)-1-oxo-1,2,3,4-tetrahydrobenzofuranone (VIII). A solution of 2.1 g (0.01 mole) of 3-morpholino-5,5-dimethyl-2-cyclohexen-1-one (VIc) [5] in 10 ml of acetic acid was added to a suspension of 2.62 g (0.01 mole) of Ib in 40 ml of acetic acid, after which the mixture was allowed to stand at room temperature for 24 h. The solvent was then removed by vacuum distillation, and the resinous residue was triturated with alcohol. The solid was removed by filtration and washed with alcohol to give 0.35 g (9%) of a product with mp 166-168° (from alcohol). IR spectrum, ν_{max}, cm^{-1}: 3100-3200 (OH) and 1705 (CO). Found: C 65.6; H 5.3%. $C_{21}H_{20}O_5S$. Calculated: C 65.6; H 5.3%.

2-Carbethoxy-3-benzoyl-4-(p-tolylsulfonyl)-5-hydroxyindole (XI) and Ethyl 2-Amino-3-benzoyl-3-[2-(p-tolylsulfonyl)-3,6-dihydroxyphenyl]acrylate (XII). A solution of 2.75 g (0.0125 mole) of ethyl 2-amino-3-benzoylacrylate (IX) [6] in 10 ml of glacial acetic acid was added with stirring to a suspension of 3 g (0.012 mole) of Ib in 30 ml of glacial acetic acid, after which the resulting solution was filtered, and allowed to stand at room temperature for 24 h. Half of the solvent was removed by vacuum evaporation, and the residue was removed by filtration and washed with acetic acid. The yield of the mixture of XI and XII was 2.5 g. It was separated with a column filled with LS 5/40 nm silical gel with elution by chloroform to give hydroxyindole XI with mp 210-212° (from aqueous alcohol) and R_f 0.47 [chloroform–ethanol (20:1)]. IR spectrum, ν_{max}, cm^{-1}: 3245 and 3270-3290 (OH and NH); 1680-1710 (CO). Found: C 64.6; H 4.4; N 3.0%. $C_{25}H_{21}NO_6S$. Calculated: C 64.8; H. 4.6; N 3.2%. Adduct XII had mp 190° (dec., from aqueous alcohol) and R_f 0.38. IR spectrum, ν_{max}, cm^{-1}:

3250 (broad, NH and OH), 1655, 1725 (CO). Found: C 62.2; H 4.8; N 3.1%. $C_{25}H_{23}NO_7S$. Calculated: C 62.4; H 4.8; N 2.9%.

1,2-Dimethyl-3-acetyl-4-(p-tolylsulfonyl)-5-hydroxyindole (XIII) and 3-[2-p-Tolylsulfonyl)-3,6-dihydroxyphenyl]acetyl acetone (XIV). A solution of 2.26 g (0.02 mole) of 4-methylamino-3-penten-2-one (X) [7] was added with stirring to a suspension of 5.25 g (0.02 mole) of Ib in 80 ml of glacial acetic acid, and the mixture was allowed to stand at room temperature for 2 days. The solvent was then vacuum evaporated to a residual volume of 10 ml, and the precipitate was separated and washed with methanol to give 2.65 g (37%) of XIII with mp 209-210° (from methanol) and R_f 0.84. IR spectrum, ν_{max}, cm^{-1}(3190-3340 (OH, NH) and 1625 (CO). Found: C 63.9; H 5.4; N 4.3%. $C_{19}H_{19}NO_4S$. Calculated: C 63.8; H 5.4; N 3.9%. The mother liquor remaining after separation of hydroxyindole XIII was diluted with water, and the resulting precipitate was removed by filtration to give 1.55 g (21%) of XIV with mp 146-148° (from methanol) and R_f 0.70. IR spectrum, ν_{max}, cm^{-1}: 3250 (OH) and 1725 and 1755 (CO). Found: 59.6; H 4.9%. $C_{18}H_{18}O_6S$. Calculated: C 59.7; H 5.0%.

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2-BENZOPYRLIUM SALTS.

XVIII.* SYNTHESIS OF 2-BENZOPYRYLIUM SALTS BASED ON SOME ENOL ACYLATES

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The fundamental possibility of the synthesis of 2-benzopyrylium salts by intramolecular cyclization of enol acylates of suitable structure is shown. An assumption is made regarding the mechanism of the formation of pyrylium salts from enol acetates in the presence of acylating agents.

The possibility of primary acylation of the carbonyl oxygen atom and, in analogy with the Pictet–Gams reaction [2], subsequent cyclization of the resulting enol acylate to a 2-benzopyrylium salt exists in the preparation of 2-benzopyrylium salts by acylation with various benzyl ketones.

*See [1] for communication XVII.

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