FORMATION OF 2-PHENYL-γ-BENZPYRONE (FLAVONE) IN NUCLEOPHILIC THIYLATION OF 1-(2'-HYDROXYPHENYL)-3-PHENYLPROP-1-YN-1-ONE BY POTASSIUM p-THIOCRESOLATE

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The mechanism of formation of 2-phenyl-γ-benzpyrone (flavone) in nucleophilic thiylation of 1-(2'hydroxyphenyl)-3-phenylprop-2-yn-1-one by potassium p-thiocresolate has been established by IR and PMR spectroscopy.

It has already been shown [1] that in the absence of catalysts, 1-(2'hydroxyphenyl)-3-phenylprop-2-yn-1-one I adds thiophenols to form the corresponding β-arylthiovinyl ketones II. However, when a similar reaction is carried out with the participation of potassium thiocresolate, besides the normal adduct II, a noticeable amount of flavone III is obtained. The formation of this heterocyclic compound may proceed by one of the two most probable mechanisms. The first includes splitting of a proton from the hydroxyl group of the acetylenic ketone I by external nucleophile (the thiolate anion), followed by attack of an internal nucleophile (the phenolate anion) on the β-acetylenic carbon atom. The second path comprises the addition of the thiolate anion to the triple bond, followed by proton transfer from the hydroxylic group of the intermediate to the carbanion center (formation of adduct II). The subsequent intramolecular substitution of the thioaryl fragment added by a phenoxyl group leads to the formation of flavone III.

To determine the role of one or other product in the formation of flavone, we used IR and PMR spectroscopy to study the transformation of the reaction products in the thiylation of compound I by potassium thiocresolate in a CCl_4 medium with an equimolar addition of 18-crown-6-polyether at room temperature.

In the PMR spectrum of the acetylenic ketone I, the signal of the hydroxyl group proton appears at 11.62 ppm, and the signals of the aromatic ring protons in the 6.9-7.7 ppm region. In the PMR spectrum, as in [2], stretching vibrations of the triple bond appear in the 2220 cm^{-1} region and those of the carbonyl group at 1630 cm^{-1}.

Immediately after the addition of an equimolar amount of $4\text{-}CH_3PhSK$ to the solution of compound I, proton signals appear in the PMR spectrum that are characteristic of the E- and Z-isomers IIa and IIb of arylthiovinyl ketone II [3]. In the spectrum there are singlets belonging to the protons of the methyl group of the CH_3PhS fragment and the double bond of the E-isomer at 2.38 and 6.6 ppm, respectively, and of the methyl group of the CH_3PhS fragment of the Z-isomer at 2.25 ppm. The signal of the vinyl proton of this isomer, as in all other similar adducts with a Z-configuration [3], is superimposed on the signals of the aromatic rings. The ratio of the integral intensities of the signals of the CH_3 group protons of the adducts with the two configurations IIa and IIb is close to 1:1. In the PMR spectrum of the reaction mixture, the signal of the hydroxyl group proton simultaneously disappears. The IR spectrum of the reaction mixture corresponds well to the data of the PMR spectra. In the IR spectrum, two stretching vibration bands of the carbonyl group of the isomers of the adduct appear at 1668 and 1643 cm^{-1}, and the absorption band corresponding to the stretching vibrations of the $C\equiv C$ bond at 2220 cm^{-1} disappears. After the reaction mixture has been held for 24 h, the proton signals of the CH_3 and $-CH{=}C<$ fragments of the E-adduct (2.38 and 6.6 ppm) completely disappear, the band at 1668 cm^{-1} in the IR spectrum also disappears, and an intense band in the 1680 cm^{-1} region appears that is characteristic of the stretching vibrations of the flavone $C{=}O$ group [3]. After the reaction mixture has been treated with hydrochloric acid, almost equimolar amounts of Z-thiovinyl ketone IIb, flavone III and thiocresol could be isolated.

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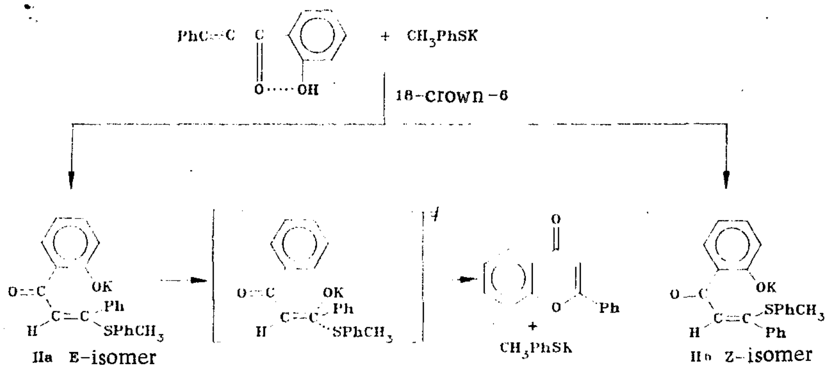
The above data thus show that the formation of flavone in the reaction of 1-(2'-hydroxyphenyl)-3-phenylprop-2-yn-1-one with potassium p-thiocresolate proceeds according to the addition–substitution scheme:



The process includes conjugated addition of a thiolate anion and hydroxyl group proton to form β-arylthiovinyl ketones IIa, IIb, followed by intramolecular substitution of the thioaryl group by a phenoxyl anion present in the trans-position with respect to the leaving group of the adduct with the E-configuration. For the β-adducts IIb, in which the intramolecular attack on the β-carbon atom by the phenoxyl anion is hindered, cyclization under these conditions practically does not occur. A similar transformation of the E-isomer IIa into flavone is also observed when adduct IIa is boiled with metallic potassium in toluene.

EXPERIMENTAL

The IR spectra were recorded on a UR-20 spectrophotometer and PMR spectra on a Tesla BS-4870 spectrometer (80 MHz), using HMDS as an internal standard.

1-(2'-Hydroxyphenyl)-3-phenylprop-2-yn-1-one was prepared by organomagnesium synthesis from phenylacetylene and salicylaldehyde, following by the oxidation of the acetylenic carbinol obtained by active manganese dioxide in acetone [2]. p-Thiocresol was obtained by reduction of p-toluenesulfonyl chloride [4]. Immediately before the experiments, p-thiocresol was distilled in a nitrogen atmosphere.

Reaction of 1-(2'-Hydroxyphenyl)-3-phenylprop-2-yn-1-one with Potassium Thiocresolate. A suspension of 1.5 mmoles of potassium cresolate and 15 mmoles of 18-crown-6 ether in 5 ml of CH_2Cl_2 was added dropwise at 0°C to a solution of 1.5 mmoles of compound I in 20 ml of methylene chloride. After 24 h, the solvent was evaporated, the mixture was treated with 20 ml of methanol with addition of a small amount of HCl, and the crystals of the Z-isomer of IIb were separated. Freezing of the mother liquor gave an additional amount of IIb, and precipitation with water gave flavone III and thiocresol. The molar ratio of compounds IIb–III–CH_3PhSH was 1:0.9:0.85.

A similar result was obtained in the reaction of compound I with potassium thiocresolate in absolute methanol.

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