SYNTHESIS OF 6-ARYL-SUBSTITUTED PYRAN-2,4-DIONES

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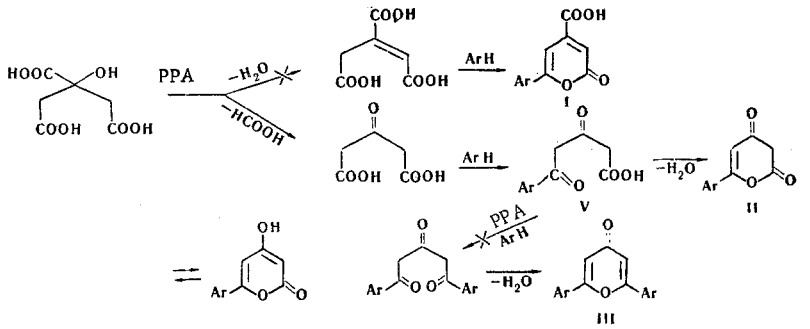
A new method for the synthesis of 6-aryl-substituted pyran-2,4-diones by the acylation of various phenol ethers (anisole, phenol, veratrole) with citric and acetonedicarboxylic acids in the presence of polyphosphoric acid (PPA) has been studied. The mechanism of the reaction and the spectra of the compounds obtained are discussed.

We have previously shown that the catalytic acylation of aromatic compounds (phenol ethers) with dibasic acids (glutaric and homophthalic acids) in the presence of PPA leads to the synthesis of oxygen-containing heterocycles: 2,6-disubstituted pyrylium salts and isocoumarins [1,2].

Continuing these investigations, we have studied the acylation of phenol ethers (anisole, phenol, veratrole) with citric acid. It could be assumed that the direction of this reaction would depend on the nature of the decomposition of the citric acid in PPA (to aconitic acid or to acetonedicarboxylic acid). In the first case, in analogy with the reaction with homophthalic acid [2], the formation of 6-aryl-substituted α-pyrone-4-carboxylic acids (I) and in the second case that of 6-aryl-substituted pyran-2,4-diones (II) might have been expected:



a Ar = p-$CH_3OC_6H_4$; b Ar = p-$C_2H_5OC_6H_4$; c Ar = 3,4-$(CH_3O)_2C_6H_3$

It was found that the end products of this reaction are 6-aryl-substituted pyran-2,4-diones. The known methods of synthesizing the latter consist in the thermal condensation of benzylmalonic esters with enolizing ketones or in the multistage synthesis of β,δ-dioxo acids with their subsequent cyclization: the desired products are obtained in low yields [3-6]. The synthesis of 6-aryl-substituted pyran-2,4-diones was carried out by heating a mixture of a phenol ether with a twofold excess of citric acid in the presence of an 8- to 10-fold (by weight) amount of PPA at 60-70°C for 6 hr. The yields of reaction products do not exceed 20%, since the limiting stage is the formation, difficult to control, of acetonedicarboxylic acid (IV), which decomposes readily under these conditions.

In view of this it appeared of interest to study the acylation of phenol ethers with acetonedicarboxylic acid directly in the presence of PPA. The reaction was carried out by heating equimolecular amounts of acetonedicarboxylic acid and phenol ether in the presence of an 8-10-fold amount of PPA (by weight) at 55-60°C for 4 hr 30 min - 5 hr. After the reaction mixture had been treated with water, the unchanged phenol ether was distilled with steam, and the final product was filtered off. The yields of pyran-2,4-diones under

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these conditions rose to 30-58%. Thus, this method of synthesizing 6-aryl-substituted pyran-2,4-diones is the simplest of those known and can be used to obtain these compounds, which possess physiological activity [7].

Attempts to obtain 2,6-diaryl-substituted γ-pyrones (III) by the diacylation of phenol ethers with acetonedicarboxylic acid proved unsuccessful, since the δ-aryl-β,δ,-dioxovaleric acids (V) formed cyclized immediately under the action of the PPA into 6-aryl-substituted pyran-2,4-diones (II).

The products obtained consist of high-melting compounds sparingly soluble in polar organic solvents. The structure of the compounds obtained was confirmed by IR spectroscopy. The IR spectra of the substances obtained had strong absorption bands in the 1710-1704-cm^{-1} and 1628-1620-cm^{-1} regions which we assigned, respectively, to the characteristic vibrations of the C = O of a lactone grouping and to the characteristic frequencies of an α-pyran ring [8]. The bands of the stretching vibrations of the aromatic substituents at 1600 and 1580 and 1560 cm^{-1} and of the alkoxy groups at 1260-1240 cm^{-1} are also seen.

EXPERIMENTAL

6-(4'-Methoxyphenyl)pyran-2,4-dione (IIa). a. A mixture of 3.84 g (0.02 mole) of citric acid, 1.08 g (0.01 mole, 1.1 ml) of anisole and 40 g of PPA was heated at 65°C with vigorous stirring for 3 hr. The temperature was raised to 70°C and stirring was continued for another 2 hr. The mixture was poured into ice water, and the yellow amorphous product was filtered off, washed with ethanol, and dried. Yield 0.4 g (18%); colorless needles, mp 211-212°C (decomp., from glacial acetic acid [6]). IR spectrum, cm^{-1}; 1704, 1620, 1608, 1560, 1248. Similarly, the acylation with citric acid of phenetole and veratrole gave: 6-(4'-ethoxyphenyl)pyran-2,4-dione (IIb), yellow needles, mp 213-214°C (from acetic acid), yield 20%. Found %: C 67.03: H 5.20. Calculated for $C_{13}H_{12}O_4$, %: C 67.24: H 5.17. IR spectrum, cm^{-1}: 1704, 1612, 1600, 1558, 1248; and 6-(3',4'-dimethoxyphenyl)pyran-2,4-dione (IIc) colorless plates mp 220-221°C (from acetic acid), yield 9%; C 62.86; H 4.94. Calculated for $C_{13}H_{12}O_5$, %; C 62.90; H 4.84. IR spectrum, cm^{-1}: 1710, 1628, 1614, 1560, 1260.

b. A mixture of 15 g (0.011 mole) of acetonedicarboxylic acid, 1.08 g (1.1 ml, 0.01 mole) of anisole, and 20 g of PPA was heated at 60-62°C with vigorous stirring for 4 hr 30 min. After the treatment of the reaction mixture with water, the unchanged anisole was distilled off with steam. Yield of IIa 1.2 g (58%). Compound IIb was obtained similarly with a yield of 55% (time of heating 4 hr 30 min) and IIc with a yield of 30% (time of heating 3 hr). Mixtures of the compounds obtained (IIa-c) with samples obtained in experiment (a) gave no depression of the melting point.

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