SYNTHESIS OF SUBSTITUTED γ-PYRONES

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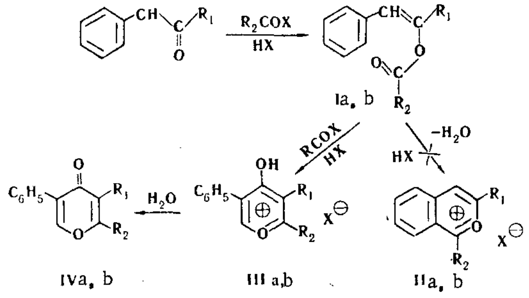
Substituted γ-pyrones were synthesized by the acylation of phenylacetaldehyde and its enol acetate with acetic and propionic anhydrides in the presence of 70% $HClO_4$. The mechanism of the reaction is examined, and the IR and PMR spectra of the synthesized γ-pyrones are presented. Some of their transformations were studied.

In the preparation of 2-benzopyrylium salts by the acylation of benzylacetones and desoxybenzoins [1-3], there is a possibility for initial acylation of the carbonyl oxygen with subsequent cyclization of the resulting enol acetate (I) to the 2-benzopyrylium salt (II).

To verify this assumption, we made attempts to subject the enol acetate of phenylacetaldehyde (I, R_1 = H, $R_2 = CH_3$) to cyclization to the 2-benzopyrylium salt. However, a polymeric product was isolated when the reaction was carried out in polyphosphoric acid (PPA). Similar results were obtained when a mixture of perchloric acid and acetic anhydride (used only to tie up the water present in 70% $HClO_4$ and the water evolved during the cyclization, if the latter occurs) was used.

When excess acetic anhydride is introduced into the reaction, a 52% yield of 2-methyl-4-hydroxy-5-phenylpyrylium perchlorate (IIIa) is obtained. Treatment of IIIa with water gives an almost quantitative yield of 2-methyl-5-phenyl-γ-pyrone (IVa).



I–IV a R_1=H, R_2=CH_3; b R_1=CH_3, R_2=C_2H_5

The optimum conditions for the reaction under consideration proved to be heating a mixture of I (R_1 = H, $R_2 = CH_3$) with a six- to tenfold amount of acetic anhydride in the presence of a small excess of $HClO_4$ at 70°C for 1.5 h.

The direct acetylation of phenylacetaldehyde in the presence of $HClO_4$ also gives the perchlorate (IIIa) but in only 30% yield, which may be evidence for reaction through an intermediate step involving the formation of the enol acetate.

Several cases of the synthesis of γ-pyrones by acylation of the active methyl and methylene groups of ketones with aliphatic acids in PPA or with anhydrides of aliphatic acids in the presence of PF_3 are known

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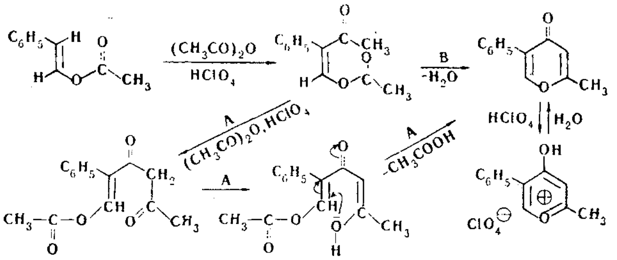
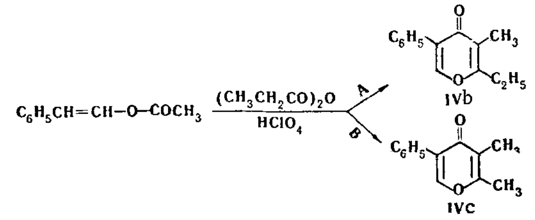
[4, 5]. However, this method was applied only to ketones, and the mechanism of this transformation was not studied in detail.

The reaction under consideration can apparently proceed via one of two mechanisms (A and B):

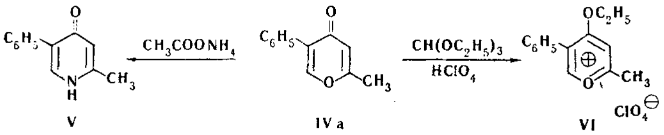


To ascertain the reaction mechanism, we acylated the enol acetate of phenylacetaldehyde with propionic anhydride in the presence of 70% $HClO_4$. In this case, one might expect the formation of two products with different structures (IVb and IVc):



The presence of a quartet centered at 2.55 ppm and a triplet centered at 1.2 ppm, which correspond to the signals of the ethyl group, in the PMR spectrum of the product (54% yield) is irrefutable evidence in favor of structure IVb and thereby in favor of mechanism A.

As should have been expected, the γ-pyrones obtained have high reactivities. For example, the corresponding γ-pyridine (V) is formed when IVa is fused with ammonium acetate, and the 4-alkoxy-substituted pyrylium salt (VII) was obtained in almost quantitative yield when IVa was allowed to react with ethyl orthoformate in the presence of $HClO_4$:



EXPERIMENTAL

2-Methyl-4-hydroxy-5-phenylpyrylium Perchlorate (IIIa). A) A total of 5 ml of 70% $HClO_4$ was added gradually to an ice-cooled mixture of 8 g (0.05 mole) of the enol acetate of phenylacetaldehyde [7] and 60 ml (0.6 mole) of acetic anhydride. The resulting dark solution was heated for 1.5 h at 70°C and allowed to stand overnight. The precipitated crystals were removed by filtration and washed with ether to give 7.3 g (52%) of colorless crystals with mp 218° (from acetic acid). Found: C 50.3; H 3.7; Cl 12.7%. $C_{12}H_{11}ClO_6$. Calculated: C 50.3; H 3.9; Cl 12.4%. IR spectrum, cm^{-1}: 1636, 1578, 1520, and 1090.

B) A total of 10 ml of 70% $HClO_4$ was added with cooling to a mixture of 12 g (0.1 mole) of phenylacetaldehyde and 80 ml (0.8 mole) of acetic anhydride. The reaction mixture was heated at 80-90° for 2 h and allowed to stand overnight to give 8 g (28%) of product. This product did not depress the melting point of the sample obtained from experiment A.

2-Ethyl-3-methyl-4-hydroxy-5-phenylpyrylium Perchlorate (IIIb). A total of 5 ml of 70% $HClO_4$ was added carefully to a mixture of 8 g (0.05 mole) of the enol acetate of phenylacetaldehyde and 60 ml (0.45 mole) of propionic anhydride. The mixture was heated at 70° for 1 h and cooled, and ether was added to it without stirring. After 24 h, the precipitated crystals were removed by filtration and washed with ether to give 8.5 g (54%) of colorless crystals with mp 173° (from acetic acid). Found: C 53.6; H 4.8; Cl 11.2%. $C_{14}H_{15}ClO_6$. Calculated: C 53.5; H 4.8; Cl 11.4%. IR spectrum, cm^{-1}: 1620, 1570, 1490, and 1100.

2-Methyl-5-phenyl-γ-pyrone (IVa). A suspension of 5.9 g (0.02 mole) of perchlorate IIIa in 50 ml of water was refluxed until the solid material dissolved. The hot solution was filtered and allowed to stand for 24 h. The resulting colorless needles were separated and dried to give 3.28 g (88%) of a product with mp 118°. Found: C 77.4; H 5.4%. $C_{12}H_{10}O_2$. Calculated: C 77.4; H 5.4%. IR spectrum, cm^{-1}: 1650, 1618, and 1591.

2-Ethyl-3-methyl-5-phenyl-γ-pyrone (IVb). This compound was similarly obtained from IIIb in 92% yield as colorless needles with mp 62° (from water). Found: C 78.3; H 6.5%. $C_{14}H_{14}O_2$. Calculated: C 78.8; H 6.6%.

2-Methyl-5-phenyl-γ-pyridone (V). A 0.37 g (0.002 mole) sample of 2-methyl-5-phenyl-γ-pyrone was introduced with stirring into a melt of 10 g of ammonium acetate. The mixture was heated until most of the CH_3COONH_4 had decomposed and was then cooled. The mixture was treated with the minimum amount of water, and the product was removed by filtration and dried to give 0.31 g (77%) of colorless needles with mp 263° (from 2-propanol). Found: C 78.0; H 6.0%. $C_{12}H_{11}NO$. Calculated: C 77.8; H 5.9%. IR spectrum, cm^{-1}: 3180, 3090, 1624, and 1600.

2-Methyl-4-ethoxy-5-phenylpyrylium Perchlorate (VI). A mixture of 3.72 g (0.02 mole) of γ-pyrone IVa, 30 ml of ethyl orthoformate, and 1.6 ml of 70% $HClO_4$ was heated on a water bath (90-100°) for 3-5 min. The mixture was then cooled and diluted with ether. The precipitated product was removed by filtration and dried to give 5.35 g (85%) of colorless crystals with mp 140° (after reprecipitation from glacial acetic acid solution by the addition of ether). Found: C 53.6; H 5.0; Cl 11.2%. $C_{14}H_{15}ClO_6$. Calculated: C 53.3; H 4.8; Cl 11.3%.

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