

NITRO DERIVATIVES OF THE THIOPHENE SERIES.

4.* NITRATION OF THIOPHENE DERIVATIVES
WITH METAL NITRATES IN ACETIC ANHYDRIDE

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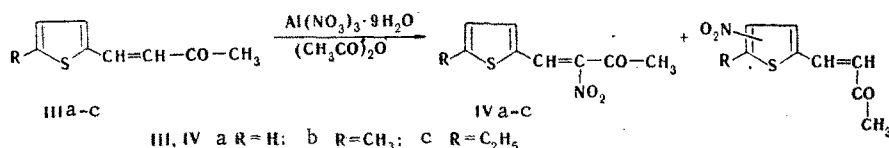
The nitration of 2-formylthiophene, 2-acetothienone, and unsaturated ketones of the thiophene series with copper and aluminum nitrates in acetic anhydride at various temperatures was studied. At low temperatures 2-acetothienone gives a mixture of 4- and 5-nitro isomers, while 2-formylthiophene gives only a 5-nitro-substituted compound in the diacetate form; α,β -unsaturated ketones are not nitrated under these conditions. When the reaction is carried out at 70-90°C, one can obtain mixtures of nitro ketones in the case of unsaturated ketones; 2-formylthiophene is oxidized to thiophene-2-carboxylic acid, while 2-acetothienone gives a substance, the structure of which could not be established. The reaction of copper and aluminum nitrates with acetic anhydride was investigated by means of thermal and x-ray diffraction analysis. It is shown that the reaction is accompanied by the formation of free nitric acid, and the nitrating agent in these mixtures is consequently the nitronium cation.

It is known that carbonyl derivatives of thiophene can be protonated by nitric acid and copper nitrates in acetic anhydride [2-4]. The nitration of 2-acetothienone (I) with nitric acid in acetic anhydride is accompanied by the formation of a mixture of 4- and 5-nitro-substituted ketones [2], while the nitration of 2-formylthiophene (II) leads either to a mixture of 4- and 5-nitro derivatives [3] or to only 5-nitro-2-formylthiophene [4].

Continuing our study of the nitration of carbonyl derivatives of thiophene, we investigated the possibility of the nitration of I and II and α,β -unsaturated methyl ketones (IIIa-c) with copper and aluminum nitrates at various temperatures. To ascertain the specificity of the process and to determine the isomer ratio we investigated the unpurified reaction mixtures by PMR spectroscopy.

The nitration of aldehyde II with cupric nitrate by the method in [4] actually gives only 5-nitro-2-formylthiophene in the diacetate form. The nitration of ketone I with cupric nitrate in acetic anhydride (mixture 1) at 0-5°C leads to the formation of the 4- and 5-nitro isomers in approximately equal amounts. The nitration of ketones IIIa-c under the same conditions was accompanied by pronounced resinification, and this made it impossible to isolate the individual substances. However, at 50-60°C we obtained a mixture of nitro isomers in low yield (18%), in which we were able to identify only α -nitro ketones IVa-c by PMR spectroscopy.

Aluminum nitrate proved to be a less active nitrating agent than cupric nitrate. Thus at low (0-5°C) and room (20°C) temperatures nitration of I, II, and IIIa-c with a mixture of aluminum nitrate and acetic anhydride (mixture 2) does not occur, and the starting substances are isolated. We were able to nitrate α,β -unsaturated ketones with mixture 2 only at 70-90°C.



*See [1] for communication 3.

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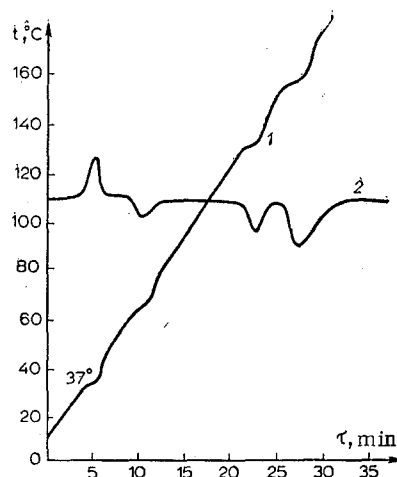
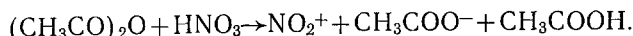
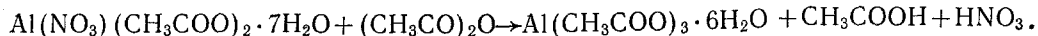
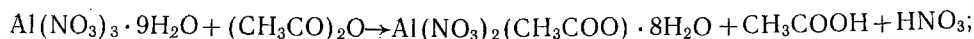


Fig. 1. Thermal curves of the aluminum nitrate-acetic anhydride mixture (2:3): 1) temperature curve; 2) differential curve.

Mixture 2 oxidizes 2-formylthiophene to thiophene-2-carboxylic acid at 70-90°C. The nitration of ketone I under these conditions proceeds in an unusual manner and leads to the formation of a compound, the structure of which we were unable to establish by PMR and mass spectroscopy. The nitration of 2-acetothienone with free nitric acid in 1,2-dichloroethane at 83°C leads to the same compound. This compelled us to make an assumption regarding the presence of free nitric acid in the metal nitrate-acetic anhydride system. We feel that under the conditions of this reaction the nitrating agent is the nitronium cation, which is formed either as a result of autoprotolysis of nitric acid molecules (since acetic acid, which is also liberated in the hydrolysis of copper and aluminum nitrates, is too weak to protonate nitric acid [5]) or by the reaction of nitric acid and acetic anhydride [6, 7]:



Since acetyl nitrate has been previously regarded [8, 9] as the nitrating agent in such mixtures, it seemed of interest to make a more detailed study of the reaction of copper and aluminum nitrates with acetic anhydride; for this study we selected the less active mixture 2. We found that the reaction of aluminum nitrate with acetic anhydride is a slow spontaneous process that takes place without external initiation in 1.5-2 h. An increase in the amount of acetic anhydride as compared with the metal nitrate by a factor of five to 10 makes it possible to carry out this reaction without an appreciable increase in the temperature even in the case of prior heating of the mixture to 30-35°C. A study of mixture 2 by means of thermal analysis showed that several phase transformations commencing at 37, 63, 134, and 160°C occur in the system (Fig. 1). The following transformations of aluminum nitrate, which are accompanied by the liberation of free nitric acid, evidently correspond to the first phase transformation:



X-ray diffraction analysis of the compound isolated from the mixture after this step of the reaction showed that aluminum nitrate is converted completely to the acetate derivative. An additional study by means of IR spectroscopy confirmed the absence in this substance of a NO_3 group and the presence of acetate and hydroxy groups. Further phase transformations (hydrolysis of aluminum acetate and splitting out of crystallization water) occur at 63 and 134°C and terminate at 160°C with the formation of an x-ray-amorphous aluminum oxide phase.

The reaction of cupric nitrate with acetic anhydride also proceeds similarly:



The formation in this case of cupric acetate monohydrate was confirmed by its IR spectrum and the results of x-ray diffraction analysis, which were identical to the data from the x-ray diffraction pattern in [10].

The formation in the aluminum nitrate-acetic anhydride system of free nitric acid and the nitronium cation is also confirmed by the results in [9]. Thus, in particular, the distinct phase transformation on the melting and crystallization diagram of mixture 2 at -42°C demonstrates the presence of free nitric acid in the system [11]. It is known that the intense absorption bands in the cited Raman spectra at 1400 and 1050 cm^{-1} are characteristic for the nitronium cation and are used for its identification [12] but by no means can be ascribed to acetyl nitrate, as asserted by Zimichev and Lipkin [9]. Thus the reaction of cupric and aluminum nitrates with acetic anhydride leads to the formation of free nitric acid and, as a consequence of this, to the development of the nitronium cation, which is also the direct nitrating agent in mixtures 1 and 2.

EXPERIMENTAL

2-Formylthiophene was obtained by the method in [13], 2-acetothienone was obtained as in [14], and α,β -unsaturated ketones IIIa-c were synthesized by crotonic condensation of acetone with the corresponding formylthiophenes by the method in [15]. The thermal studies were carried out by differential thermal analysis (DTA). Platinum crucibles, platinum stirrers, and a platinum-platinorhodium thermocouple were used in the study. The heating curves were recorded with a DTA apparatus constructed on the basis of a KSP-4 automatic electronic potentiometer and an F 116/1 photoamplifier. X-ray diffraction analysis was carried out with a Dron-2 diffractometer by means of $\text{CuK}\alpha$ emission with a nickel β filter. The recording rate was 4 deg/min.

Nitration with Cupric and Aluminum Nitrates in Acetic Anhydride. A 0.01-mole sample of IIIa-c was dissolved in 30 ml of acetic anhydride at the temperature at which the reaction was carried out ($0-5$ or $70-90^{\circ}\text{C}$), after which a previously prepared (at $0-5^{\circ}\text{C}$) mixture of 0.01 mole of the metal nitrate in 30 ml of acetic anhydride was added slowly dropwise. The reaction mixture was maintained at the reaction temperature for another 1.5 h, after which it was poured over ice. The precipitate was removed by filtration, washed with water to remove traces of acid, and dried. The yields ranged from 34 to 50%.

The physicochemical characteristics of nitro ketones IVa-c are presented in [7].

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