BECKMANN REARRANGEMENT OF ACETYLTHIOPHENE OXIME BENZENESULFONATES AS A METHOD FOR THE SYNTHESIS OF ACETAMIDOTHIOPHENES

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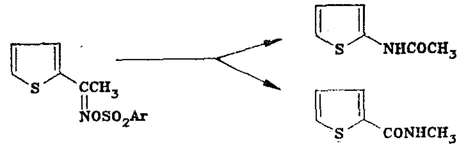
The Beckmann rearrangement of 2-acetylthiophene, 5-methyl-2-acetylthiophene, 5-chloro-2-acetylthiophene, and 2,5-dichloro-3-acetylthiophene oxime benzenesulfonates to the corresponding acetamidothiophenes was carried out by heating with an aqueous methanol solution of sodium acetate. This method can be used for the preparative synthesis of 2-acetamidothiophene and 2,5-dichloro-3-acetamidothiophene.

Acetamidothiophenes are extremely reactive compounds, the acetamido group of which can be thoroughly alkylated, and the thiophene ring of which undergoes electrophilic substitution, particularly Vilsmeier formylation and diazo coupling, as a consequence of which 2- and 3-acetamidothiophenes and their ring-substituted derivatives have often been used for the synthesis of various heterocyclic compounds (for example, see [1]) and azo dyes.

The following methods have been chiefly used for the preparation of acetamidothiophenes, including those that contain substituents in the ring: reductive acetylation of the corresponding nitrothiophenes by various metals [2-4] in acetic anhydride and acetic acid, Hofmann cleavage of thiophenecarboxylic acid amides [5], the Schmidt reaction of acetylthiophenes with hydrazoic acid [5], the action of potassium amide and acetic anhydride on 3-bromothiophene [5], a modified Curtius rearrangement [6],* and, finally, Beckmann rearrangement of acetylthiophene oximes [1].

Phosphorus pentachloride has been most often used as the reagent in the Beckmann rearrangement of ketoximes [7]; however, in the case of the rearrangement of acetylthiophene oximes this reagent has not always given reproducible results, in connection with which modifications of the method have been proposed [8, 9].

Other reagents that have been widely used for the rearrangement of ketoximes are arenesulfonyl chlorides [7]. In particular, the reaction of 2-acetylthiophene oxime with benzene- or p-toluenesulfonyl chloride and rearrangement of the resulting oxime arenesulfonate by passing a solution of it in benzene through activated Al_2O_3 have been proposed for the preparation of 2-acetamidothiophene [10]:



Ar = phenyl or p-tolyl

The direction of the reaction depends on the spatial configuration of the starting oxime.

This method [10] has made it possible to obtain 2-acetamidothiophene in 90% yield, but it is hardly suitable for preparative synthesis because of the low solubility of the 2-acetylthiophene oxime arenesulfonate in benzene and the time required to complete the process.

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*The latter method cannot be regarded as safe, since violent decomposition of the azide occurred when the proposed method was reproduced.

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TABLE 1. Characteristics of the Products of Beckmann Rearrangement

Starting benzenesulfonate	Reaction product	mp, °C	Yield, %
2-Acetylthiophene oxime	2-Acetamidothiophene	156-157*; 160 [10]	80
5-Methyl-2-acetylthiophene oxime†	2-Acetamido-5-methylthiophene	165-167; 166-168 [14]	34
Low-melting 5-chloro-2-acetylthiophene oxime	2-Acetamido-5-chlorothiophene	173-174; 175-176 [12]	40
High-melting 5-chloro-2-acetylthiophene oxime	5-Chloro-2-thiophenecarboxylic acid N-methylamide	165-167; 168 [12]	35
2,5-Dichloro-3-acetylthiophene oxime	3-Acetamido-2,5-dichlorothiophene	107-109; 108‡ [5]	52

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*After sublimation *in vacuo*, this compound had mp 159-160°C.

†The moist oxime benzenesulfonate was used. The yield was based on the oxime.

‡Obtained by the action of hydrazoic acid on 2,5-dichloro-3-acetylthiophene.

Previously, in our laboratory we proposed a method for the synthesis of lactams that contain a thiophene ring by heating the benzenesulfonates of the corresponding ketoximes with an aqueous alcohol solution of sodium or potassium acetate [11]. When we used this method for the preparation of 2-acetamidothiophene from 2-acetylthiophene oxime benzenesulfonate (the oxime had mp 113-114°C), the constant yield of 2-acetamidothiophene was about 80%. This result compelled us to use 5-methyl-, 2-acetyl-, 5-chloro-2-acetyl-, and 2,5-dichloro-3-acetylthiophene oxime benzenesulfonates for the rearrangement.

5-Methyl-2-acetylthiophene oxime benzenesulfonate proved to be an unstable compound and decomposed violently as it was being dried; it was therefore not analyzed and was used in moist form for the rearrangement. The yield of 5-methyl-2-acetamidothiophene was 33% based on the starting oxime.

5-Chloro-2-acetylthiophene exists in the form of two difficult-to-separate isomers [12]. 2-Acetamido-5-chlorothiophene was obtained in 40% yield by rearrangement of the benzenesulfonate synthesized from the oxime with mp 137-139°C; 5-chloro-2-thiophenecarboxylic acid N-methylamide was formed in 34% yield from the oxime benzenesulfonate (the oxime had mp 175°C). 3-Acetamido-2,5-dichlorothiophene was obtained in 50% yield from 2,5-dichloro-3-acetylthiophene oxime benzenesulfonate. When the acetamidothiophenes obtained were heated with hydrochloric acid, they decomposed with H_2S evolution; 5-chloro-2-thiophenecarboxylic acid was formed in the hydrolysis of 5-chloro-2-thiophenecarboxylic acid N-methylamide.

EXPERIMENTAL

2-Acetyl-, 5-methyl-2-acetyl-, 5-chloro-2-acetyl-, and 2,5-dichloro-3-acetylthiophene oximes were obtained by the action of hydroxylamine by the methods in [12-15], and their melting points were close to those presented in the literature; 2,5-dichloro-3-acetylthiophene oxime had mp 112-113°C (mp 102°C [15]).

The benzenesulfonates of all of the oximes were synthesized by the action of a solution of benzenesulfonyl chloride in acetone on an acetone solution of the oxime at reduced temperatures in the presence of an aqueous solution of sodium hydroxide. 2-Acetylthiophene oxime benzenesulfonate was obtained in 94% yield and had mp 85°C (dec.) (mp 85-86°C [10]). The characteristics of the newly obtained benzenesulfonates are presented below. 5-Chloro-2-acetylthiophene oxime benzenesulfonate, with mp 75-77°C, was obtained in 92% yield. Found, %: N 4.2. $C_{12}H_{10}ClNO_3S_2$. Calculated, %: N 4.4. 5-Chloro-2-acetylthiophene oxime benzenesulfonate, with mp 118-119°C, was obtained in 95% yield. Found, %: C 45.4, H 3.3, Cl 11.1, S 19.9. $C_{12}H_{10}ClNO_3S_2$. Calculated, %: C 45.6, H 3.2, Cl 11.2, S 20.3. 2,5-Dichloro-3-acetylthiophene oxime benzenesulfonate, with mp 83-85°C, was obtained in 87% yield. Found, %: N 4.0. $C_{12}H_9Cl_2NO_3S_2$. Calculated, %: N 4.0.

Beckmann Rearrangement of Acetylthiophene Oxime Benzenesulfonates (General Method). A 0.05-mole sample of the oxime benzenesulfonate was added to a solution of 0.25 mole of anhydrous sodium acetate in a mixture of 100 ml of water and 40 ml of methanol, and the mixture was stirred at 60-70°C until a red solution had formed. The latter was treated with activated charcoal and filtered, and the methanol was removed from the yellow filtrate by distillation up to a vapor temperature of 80°C. The residue was allowed to stand in a refrigerator, and the precipitate was removed by filtration, washed with cold water, and, where necessary, was recrystallized from a suitable solvent as, for example, from alcohol or acetic acid diluted with water (in both cases).

The characteristics of the rearrangement products are presented in Table 1.

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ELECTRONIC STRUCTURES AND SPECTRAL AND ACID–BASE PROPERTIES OF PYRROL-, THIOPHEN-, AND FURANANTHRONES

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The IR spectra, electronic absorption and luminescence spectra, solvatochromism, and basicities of compounds of the 6H-dibenz[cd,g]indol-6-one, 6H-anthra[9,1-bc]thiophen-6-one, and 6H-anthra[9,1-bc]furan-6-one groups were studied. The interrelationship between the indicated properties and such structural factors as the 1,10-anthraquinoid structure, the presence of a π-surplus heteroring, and the presence of substituents was examined.

Compounds with compositions that include an anthrone ring annelated with a heteroring in the peri positions and are arbitrarily called heterocyclic derivatives of anthrone occupy a prominent position in the chemistry of intermediates and dyes [1]. We have previously used spectral methods to study the electronic structures of anthrone derivatives with a six-membered heteroring in the case of their most important representatives, viz., pyridonanthrones (2-hydroxyazabenzanthrones) [2, 3]. The recently accomplished [4, 5] synthesis of the uninvestigated group of anthrone derivatives of the I type with five-membered pyrrole, thiophene, and furan rings, which have a formally 1,10-anthraquinoid distribution of bonds, makes it possible to examine their spectral properties as compared with the previously known 9,10-anthraquinoid isomers, viz., pyrrol- and thiophenanthrones of the II type.

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