# BROMINATION OF 2-ACETYLTHIOPHENE AND ITS DERIVATIVES

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A new method has been developed for the bromination of thiophene and its derivatives. The method consists in the action of N-bromosuccinimide in acetic anhydride and glacial acetic acid on the thiophene derivatives. In the bromination of 2-acetylthiophene and its derivatives, the bromine replaces the hydrogen atom in the 5 position of the thiophene ring.

Up to the present time, there have been no indications in the literature of the possibility of replacement of the hydrogen atom in the 5 position of the thiophene ring by bromine by direct bromination of 2-acetylthiophene and its derivatives. The bromination of 2-acylthiophenes in the 4 position of the thiophene ring is known [1, 2]. The bromination of thiophene and its derivatives with N-bromosuccinimide in glacial acetic acid and chloroform was described in 1968 [3]. However, 2- and 3-acetylthiophenes could not be brominated by this method; this was explained by the strong deactivating effect of the acetyl group.

In the present paper we have studied the reaction of 2-acetylthiophene (I); 4-bromo-, 4-nitro-, 5-bromo-, and 5-nitro-2-acetylthiophenes (II-V); 5-acetyl-2,2'-diethienyl (VI); and thiophene (VII) with N-bromosuccinimide in acetic anhydride and in acetic anhydride–glacial acetic acid at 20-130°C.

5-Substituted 2-acetylthiophenes IV and V and 4-nitro-2-acetylthiophene (III) are not brominated under the conditions that we studied. The 5 position of the thiophene ring is brominated by the action of N-bromosuccinimide on I, II, and VI in acetic anhydride–glacial acetic acid. The method that we developed for the bromination was also used to obtain 2-bromothiophenes from thiophene. The yields of 2-bromothiophene were identical (74%) for both bromination in acetic anhydride and in acetic anhydride–glacial acetic acid but were appreciably higher than those given in [3]. A study of the composition of the products obtained in the bromination of I in various media and at different temperatures via the method in [4] demonstrated that II is absent in the mixtures and that the major constituent of the product is IV. We did not detect the corresponding 2-(ω-bromoacetyl) derivative in the products of the bromination of I, II, and VI (negative reaction with an alcohol solution of silver nitrate).

In order to determine the optimum conditions for the bromination of ketones I, II, and VI, we studied the effect of the addition of glacial acetic acid to acetic anhydride and the effect of temperature on the yields of the bromo ketones (see Table 1). The bromination of I in acetic anhydride–glacial acetic acid

TABLE 1. Results of the Bromination of 2-Acetylthiophene and Its Derivatives

| Starting ketone | Ketone:bromosuccinimide:$(CH_3CO)_2O$:$CH_3COOH$ molar ratio | Temp., °C | Time, h | Yield of bromo ketone, % |
|---|---|---|---|---|
| 2-Acetylthiophene | 1 : 1 : 4 : 0 | 40 | 2 | — |
| | 1 : 1 : 4 : 0 | 80 | 2 | 69 |
| | 1 : 1 : 4 : 1 | 20 | 2 | 68 |
| | 1 : 1 : 4 : 1 | 40 | 1 | 72 |
| | 1 : 1 : 4 : 1 | 80 | 1 | 66 |
| 4-Bromo-2-acetylthiophene | 1 : 1 : 4 : 1 | 130 | 1 | — |
| | 1 : 1 : 4 : 1 | 80 | 2 | 33 |
| | 1 : 1,5 : 4 : 1 | 80 | 2 | 42 |
| 5-Acetyl-2,2'-dithienyl | 1 : 2 : 4 : 1 | 80 | 2 | 48 |
| | 1 : 1 : 4 : 84 | 20 | 1 | 91 |
| | 1 : 1 : 0 : 84 | 20 | 1 | 90 |

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proceeds more efficiently than in acetic anhydride. We were able to brominate II only in acetic anhydride–glacial acetic acid at 80°. Dithienyl derivative VI is readily brominated in both acetic anhydride–glacial acetic acid and in acetic acid, and the yields of 5-acetyl-5'-bromo-2,2'-dithienyl in both cases are identical. Thus the catalyzing effect of glacial acetic acid in the bromination of I and II may to a certain extent serve as an indication of the ionic character of the reaction.

The presence of electron-acceptor groups in the 4 position of the thiophene ring of 2-acetylthiophene (II and III) hinders bromination (III could not be brominated, and about 50% of the starting ketone was isolated in the bromination of II with an equimolecular amount of N-bromosuccinimide). These qualitative data on the effect of substituents in the thiophene ring on the bromination also to a certain degree indicate the ionic character of the reaction.

The fact that ring bromination is not observed in the reaction of N-bromosuccinimide with I as the temperature of the reaction mixture is raised above 90-100° (the starting I is almost completely recovered) while the bromosuccinimide is completely consumed is interesting. It can be assumed that at temperatures above 90-100°, the reaction of N-bromosuccinimide with the reaction mixture components is radical in character, and radical bromination of acetic anhydride is the principal reaction.

The problem of the mechanism of the bromination of 2-acetylthiophene and its derivatives with bromosuccinimide in acetic anhydride–glacial acetic acid at various temperatures requires special study.

## EXPERIMENTAL

The IR spectra of $CCl_4$ solutions of the products of bromination of I were measured with an IKS-14 spectrometer; the spectra of the remaining compounds were obtained from KBr pellets.

5-Bromo-2-acetylthiophene (IV). The component ratios and reaction conditions are indicated in Table 1. At the end of the reaction, the mixture was poured into water. After complete hydrolysis of the acetic anhydride, the reaction product was removed by filtration, washed with water, and steam distilled to give colorless crystals with mp 94-95° (from ethanol) [5]. The IR spectra of the synthesized bromo ketone and the sample obtained by acetylation of 2-bromothiophene were identical.

4,5-Dibromo-2-acetylthiophene. This compound was similarly obtained. After hydrolysis of the acetic anhydride, the reaction product was extracted with ether. The extract was dried, the ether was removed by distillation, and the residue was vacuum distilled to give unchanged II (30-50%), which boiled up to 145° (15 mm), and a bromination product with bp 145-165° (15 mm); the latter was recrystallized from ethanol to give a product with mp 85-86° (mp 84-85° [4]). The IR spectrum of the synthesized compound and that of a sample obtained by the method in [4] were identical.

5-Acetyl-5'-bromo-2,2'-dithienyl. The component ratios and the reaction conditions are indicated in Table 1. At the end of the reaction, the reaction mixture was filtered, and the precipitate was washed successively with a small amount of acetic acid and water. Recrystallization from ethanol gave light-yellow crystals with mp 174-175° (mp 170-172° [6]). The IR spectrum of the synthesized preparation and that of a sample obtained via the method in [6] were identical.

2-Bromothiophene. A 181.6-g (1.02 mole) sample of N-bromosuccinimide was added in the course of 30-40 min to a mixture of 84.1 g (1 mole) of thiophene and 200 ml of acetic anhydride with stirring while maintaining the temperature at 20-30°. After all of the bromosuccinimide had been added, the reaction mixture was allowed to stand at room temperature for 1 h and was then poured into 600 ml of cold water. After hydrolysis of the acetic anhydride, the heavy oil was separated, and the aqueous layer was saturated with salt and extracted with ether. The ether extracts were combined with the bulk of the product, and the mass was washed with water, sodium hydroxide solution, again with water, and dried. The ether was removed by distillation, and the residue was distilled in vacuo or at atmospheric pressure to give 119.2° (74%) of 2-bromothiophene with bp 65-67° (15 mm), 155-156° (760 mm), and $n_D^{20}$ 1.5871, and 10.36 g of 2,5-dibromothiophene with bp 86-87° (1 mm) and $n_D^{20}$ 1.6288.

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