FUNCTIONAL DERIVATIVES OF THIOPHENE

V.* SYNTHESIS OF NITRO DERIVATIVES OF 3-ETHOXYCARBONYL-4-HYDROXY-2-METHYL- AND 4-CHLORO-3-ETHOXYCARBONYL-2-METHYLTHIOPHENES

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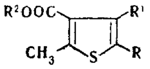
The nitration of 3-ethoxycarbonyl-4-hydroxy-2-methyl- and 4-chloro-3-ethoxycarbonyl-2-methylthiophenes has given the corresponding 5-nitro derivatives of thiophene. The 4-chloro-3-ethoxycarbonyl-2-methylthiophene was synthesized by the decarboxylation of 3-chloro-4-ethoxycarbonyl-5-methylthiophene-2-carboxylic acid, which is formed by the oxidation of 3-chloro-4-ethoxycarbonyl-5-methylthiophene-2-carbaldehyde.

The action on 3-ethoxycarbonyl-4-hydroxy-2-methylthiophene (I) of concentrated nitric acid in concentrated sulfuric acid under the conditions for the nitration of 2-ethoxycarbonyl-3-hydroxythiophene leads to the formation of resins. We have obtained 3-ethoxycarbonyl-4-hydroxy-2-methyl-5-nitrothiophene (II) by the nitration of (I) with acetyl nitrate in acetic anhydride at a temperature of –30 to –40°C.

4-Chloro-3-ethoxycarbonyl-2-methylthiophene (III) and its 5-nitro derivative (IV) are of definite interest, being key compounds in the synthesis of various thiophene derivatives.

The treatment of (I) with the Vilsmeier reagent leads not only to the introduction of an aldehyde group into the molecule of (I) but also to the replacement of the hydroxy group by chlorine [3]. The 3-chloro-4-ethoxycarbonyl-5-methylthiophene-2-carbaldehyde (V) obtained in this way was oxidized with sodium hypobromite to 3-chloro-4-ethoxycarbonyl-5-methylthiophene-2-carboxylic acid (VI). The action of mercuric acetate on (VI) formed an acetoxymercury derivative which was converted by boiling with dilute hydrochloric acid into (III). The nitration of (III) with fuming nitric acid (d 1.5) in acetic anhydride at –5°C gave the chloronitrothiophene (IV). We found no replacement of the formyl and carboxy groups by a nitro group in the action of nitric acid on (V) and (VI). Attempts to synthesize the chloro derivatives (II) and (IV) by boiling the hydroxythiophenes (I) and (II) with phosphorus oxychloride, phosphorus pentachloride, a mixture of them, or thionyl chloride were also unsuccessful.



I $R=H$, $R^1=OH$, $R^2=C_2H_5$, II $R=NO_2$, $R^1=OH$, $R^2=C_2H_5$, III $R=H$, $R^1=Cl$, $R^2=C_2H_5$ IV $R=NO_2$, $R^1=Cl$, $R^2=C_2H_5$, V $R=CHO$, $R^1=Cl$, $R^2=C_2H_5$, VI $R=COOH$, $R^1=Cl$, $R^2=C_2H_5$, VII $R, R^2=H$, $R^1=Cl$

The action of ethanolic caustic soda on (III) led to 4-chloro-2-methylthiophene-3-carboxylic acid (VII).

The introduction of the nitro group into the substituent-free α position of the thiophenes (I) and (III) is confirmed by the disappearance from the IR spectra of the absorption band at 3120 cm^{-1} that is characteristic of the vibrations of the α-CH group and the appearance of two absorption bands in the 1320- and 1550-cm^{-1} regions (ν_{NO_2}).

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*For Communication IV, see [1].

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EXPERIMENTAL

The IR spectra of the substances obtained were taken in paraffin oil on a UR-10 spectrometer.

3-Ethoxycarbonyl-4-hydroxy-2-methyl-5-nitrothiophene (II). At a temperature of −30 to −40°C with stirring, 11 ml (0.26 mole) of nitric acid (d 1.5) in 30 ml of acetic anhydride was added to 10 g (0.053 mole) of (I) in 100 ml of acetic anhydride. The reaction mixture was stirred at the same temperature for 30 min and was then poured onto ice. The precipitate was separated off, washed on the filter with water, and recrystallized. The yield of (II) was 7.4 g (59%), mp 102-103°C (from methanol). Found, %: C 41.5; H 4.2; N 6.0; S 14.0. $C_8H_9NO_5S$. Calculated,%: C 41.5; H 3.9; N 6.1; S 13.9.

3-Chloro-4-ethoxycarbonyl-5-methylthiophene-2-carbaldehyde (V). At 5-10°C with stirring, 137 g (81 ml; 0.9 mole) of phosphorus oxychloride was added to a solution of 56 g (0.3 mole) of (I) in 150 ml of dimethylformamide. The reaction mixture was heated at 80°C for 1 h and was then poured onto ice, and the resulting solution was neutralized with sodium acetate. The precipitate that formed was separated off, washed with water, and dried, and it was then dissolved in petroleum ether (bp 70-100°C). The solution was filtered and the solvent was distilled off from the filtrate. The yield of (V) was 46 g (65.9%), mp 62-63°C (from methanol). Found, %: C 46.6; H 3.9; Cl 15.3; S 14.0. $C_9H_9ClO_3S$. Calculated, %: C 46.5; H 3.9; Cl 15.2; S 13.8.

3-Chloro-4-ethoxycarbonyl-5-methylthiophene-2-carboxylic Acid (VI). At 0-5°C with stirring, 1.1 ml (0.068 mole) of bromine was added to a solution of 2.7 g (0.068 mole) of caustic soda in 13 ml of water, and this was followed by a solution of 4.6 g (0.02 mole) of (V) in 20 ml of dioxane at a temperature not exceeding 10°C. The reaction mixture was kept at 0-5°C for 40 min and was then poured onto ice and filtered. The filtrate was acidified with dilute hydrochloric acid (1:1). The precipitate was filtered off, washed with water to neutrality, and dried. Yield of (VI) 4 g (81%), mp 159-160°C (from aqueous acetone). Found,%: C 43.4; H 3.9; Cl 14.2; S 12.9. $C_9H_9ClO_4S$. Calculated, %: C 43.5; H 3.7; Cl 14.3; S 12.9.

4-Chloro-3-ethoxycarbonyl-2-methylthiophene (III). A mixture of 7.7 g (0.03 mole) of (VI) and 9.6 g (0.03 mole) of mercuric acetate in 150 ml of acetic acid was boiled for 15 min. The resulting solution was cooled to 50°C, 150 ml of concentrated hydrochloric acid and 600 ml of water were added to it, and this mixture was boiled for 15 min. Then it was cooled to room temperature and the oil that separated out was extracted with ether. The ethereal extract was washed with water to neutrality and dried with magnesium sulfate, the solvent was evaporated off, and the residue was distilled in vacuum. Yield of (III) 4.3 g (68%), bp 93-94°C (1 mm), n_D^{20} 1.5348. Found, %: C 47.0; H 4.5; Cl 17.6; S 15.3. $C_8H_9ClO_2S$. Calculated, %: C 46.9; H 4.4; Cl 17.3; S 15.7.

4-Chloro-3-ethoxycarbonyl-2-methyl-5-nitrothiophene (IV). At a temperature not exceeding −2°C, with stirring, 2.6 ml (0.06 mole) of nitric acid (d 1.5) in 7.5 ml of acetic anhydride was added to 2.6 g (0.012 mole) of (III) in 8 ml of acetic anhydride. The reaction mixture was stirred at −5°C for 15 min and was then poured onto ice. The precipitate that deposited was separated off, washed on the filter with water to neutrality, and dried. The yield of (IV) was 2.6 g (87%), mp 81-82°C (from methanol). Found, %: C 38.7; H 3.2; Cl 14.1; N 5.7; S 12.8. $C_8H_8ClNO_4S$. Calculated, %: C 38.5; H 3.2; Cl 14.2; N 5.6; S 12.8.

4-Chloro-2-methylthiophene-3-carboxylic Acid (VII). A mixture of 2 g (0.01 mole) of (III) and a solution of 1.2 g (0.03 mole) of caustic soda in 20 ml of ethanol was boiled for 30 min. The solution obtained was diluted with three volumes of water and the ethanol was distilled off. The solution of the salt was acidified with dilute hydrochloric acid (1:1) to an acid reaction to Congo Red. The precipitate of the acid was separated off, washed with water, and dried. Yield of (VII) 1.1 g (65%), mp 204-205°C (from acetone). Found, %: C 40.6; H 2.9; Cl 20.0; S 18.2. $C_6H_5ClO_2S$. Calculated, %: C 40.8; H 2.9; Cl 20.1; S 18.2.

LITERATURE CITED

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