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REACTION OF ETHYL ESTER AND NITRILE OF 5-METHYL-2-FURANCARBOXYLIC ACID WITH MIXTURE OF NITRIC AND SULFURIC ACIDS

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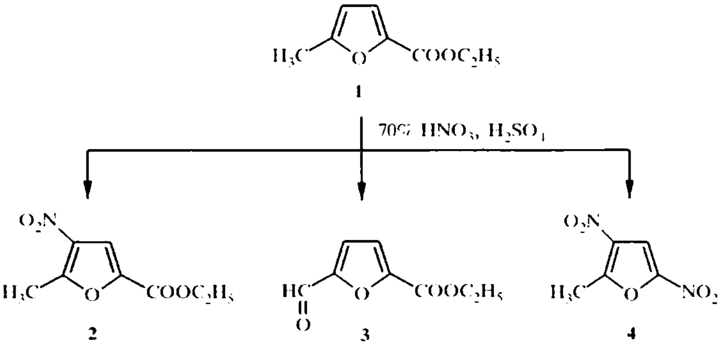
The reaction of 70% HNO_3 with ethyl 5-methyl-2-furancarboxylate in concentrated H_2SO_4 gave the corresponding 4-nitro derivative and ethyl 5-formyl-2-furancarboxylate. Only 4-nitro derivative, which was converted into amidoxime, was obtained from 5-methyl-2-furonitrile.

Keywords: 4-nitrofurans, furan compounds, nitration.

A mixture of 4-nitro derivatives (yield up to 4%), the products of nitrodecarboxylation, namely 2-methyl-5-nitrofuran (30%), and the products of the oxidation of the 5-methyl group to formyl group (yields up to 39%) [1, 2] were obtained from the reaction of nitric acid and acetic anhydride with 5-methyl-2-furancarboxylic acid [3-5] and its methyl ester [1,2,6].



In this report the results of nitration of ethyl 5-methyl-2-furancarboxylate (**1**) and 5-methyl-2-furonitrile (**5**) with a mixture of nitric and sulfuric acids are presented.

Reaction of ester **1** in concentrated sulfuric acid with 1.5 mol of 70% nitric acid at -10 to -5°C gave a mixture of ethyl 5-methyl-4-nitro-2-furancarboxylate (**2**) and ethyl 5-formyl-2-furancarboxylate (**3**) in yields of 12 and 18% respectively, calculated from the ^1H NMR spectrum of the mixture, i.e., an analogy was observed with the reaction of ester **1** with a mixture of nitric acid and acetic anhydride [1,2]. The formyl ester **3** had been obtained earlier by Sommelet's method [7] and by a multistage synthesis from furfural diethyl acetal [8].

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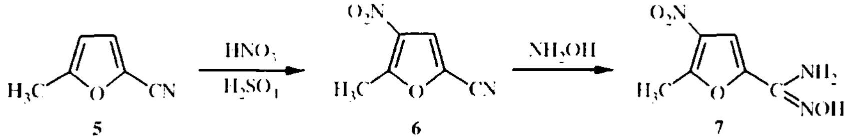
The predominant product of the reaction is a polymeric substance containing some quantities of compounds **2-4**. The ether extract of the residue after separation of the polymers contained a mixture of esters **2** and **3** which, after treatment with thiosemicarbazide, gave a 5:3 mixture of the *E*- and *Z*-isomers of semicarbazone of ester **3** and nitro ester **2**. The configurations were assigned based on their ^{1}H NMR spectra: the isomer with the chemical shift of the CH=N proton at 8.01 ppm has the *E*-configuration, while that with the shift at 7.35 ppm has the *Z*- configuration as a result of the deshielding effect of the C=N group. For the same reason the furan ring proton signals are deshielded in the *Z*-isomer.

According to the ^{1}H NMR spectrum, the reaction mixture contains a small amount of 3,5-dinitro-2-methylfuran **4**, the product of *ipso* nitration of nitro ester, but 2-methyl-5-nitrofuran was not observed, although it was obtained from the nitration of 5-methyl-2-furancarboxylic acid [3] and 2-furanaldehyde [9] in acetic anhydride. Nitration of 2-cyano-5-methylfuran (**5**) proceeded somewhat more easily under the same conditions to give 26-30% of 4-nitro derivative along with polymeric products*



The reaction of nitronitrile **6** with hydroxylamine gave 4-nitro-5-methyl-2-furancarboxamidoxime **7** as a 2:5 mixture of *E*- and *Z*-isomers. The assignment of the isomers was based on the chemical shifts of the 3-H protons [11]. Screening of the signals of the NH_2 protons is not a strict criterion for determination of the isomers because the chemical shift is largely determined by the concentration of the solution.

EXPERIMENTAL

The purity of individual products was determined by TLC on Silufol UV-254 strips with the eluent systems (1) 3:1 benzene–ethyl acetate, and (2) 48:6:1 benzene–tetrahydrofuran–acetic acid, and also by ^{1}H NMR spectra in DMSO-d_6 (TMS as internal standard) obtained with Bruker WH-90/DS instrument. IR spectra of Nujol mulls were recorded with a Perkin Elmer 580B spectrometer. Melting points were determined with a Boetius apparatus and were not corrected.

Ethyl 5-Methyl-4-nitro-2-furancarboxylate (3) and Ethyl 5-Formyl-2-furancarboxylate (3). Ethyl 5-methyl-2-furancarboxylate (**1**) (7.70 g, 50 mmol) was added with vigorous stirring to concentrated H_2SO_4 (50 ml) at -10 to -5°C, followed by mixture of 70% HNO_3 (4.73 ml, 75 mmol) in concentrated H_2SO_4 (10 ml). Stirring and cooling were maintained for 2 h, after which the reaction mixture was poured onto ice (300 g) with water. The precipitate was filtered off, washed many times with water, and dried in air to give a yellow amorphous precipitate (5 g); mp 120-160°C, which dissolved well in organic solvents but did not crystallize from them. According to the ^{1}H NMR spectrum, this polymer contained a small amount of esters **2** and **3** and also 2-methyl-3,5-dinitrofuran **4**. 1:1 mixture of esters **2** and **3** (80 mg) was obtained by vacuum sublimation from the precipitate (1 g). The filtrate was extracted with ether, the extract (300 ml) was washed with $NaHCO_3$ solution, then water, and dried over $MgSO_4$. After removal of the solvent a reddish oil was obtained (2.68 g) which consisted of 2:3 molar ratio mixture of esters **2** and **3** and traces of 2-methyl-3,5-dinitrofuran **4**. The yields calculated from the ^{1}H NMR spectrum were **2** ~ 12%, **3** ~ 18%. 1 g of the evaporated ether extract was extracted with boiling hexane (50 ml) and then kept in the refrigerator. Ethyl 5-formyl-2-furancarboxylate (3) (0.2 g) was obtained; mp 29-36°C, R_f^1 0.57, R_f^2 0.66. After second recrystallization from hexane plus activated charcoal, mp 37-39°C. ^{1}H NMR spectrum: 1.33 (3H, t, J = 7 Hz, CH_3); 4.36 (2H, q, J = 7 Hz, CH_2); 7.48 (1H, d, J = 3.5 Hz, 3-H); 7.62 (1H, d, J = 3.7 Hz, 4-H); 9.77 ppm (1H, s, CHO). Found, %: C 57.30; H 4.83. $C_8H_8O_4$. Calculated, %: C 57.14; H 7.49.

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* Syntheses of this 4-nitro derivative from 2-methylthio-2-alkyl/aryl-1-nitroethene, and also by other methods, are characterized by small yields [10].

2,4-Dinitrophenylhydrazone of Formyl Ester; mp 190-191°C (washed with hot ethanol). ^{1}H NMR spectrum: 7.15 (1H, d, *J* = 3.7 Hz, 4-H); 7.41 (1H, d, *J* = 3.7 Hz, 3-H); 8.65 (1H, s, CH=N); 10.80 (1H, s NH); protons of the benzene ring: 8.00 (1H, d, *J* = 9.7 Hz, 6-H); 8.42 (1H, dd, *J* = 9.7 Hz, *J* = 2.6 Hz, 5-H); 8.86 ppm (1H, d, *J* = 2.6 Hz, 3-H). Found, %: C 48.48; H 3.51; N 16.00. $C_{14}H_{12}N_4O_7$. Calculated, %: C 48.28; H 3.47; N 16.09.

Thiosemicarbazone of Formyl Ester; mp 300°C (aqueous DMF). ^{1}H NMR spectrum: *E*-isomer: 1.31 (3H, t, *J* = 7 Hz, CH_3); 4.31 (2H, q, *J* = 7 Hz, CH_2); 7.18 (1H, d, *J* = 3.7 Hz, 4-H); 7.36 (1H, d, *J* = 3.7 Hz, 3-H); 7.40 (1H, br. s, NH_2); 8.01 (1H, s, CH=N); 8.36 (1H, br. s, NH_2); 11.65 ppm (1H, s, NH). *Z*-isomer: 1.32 (3H, t, *J* = 7 Hz, CH_3); 4.32 (2H, q, *J* = 7 Hz, CH_2); 7.31 (1H, d, *J* = 3.7 Hz, 4-H); 7.36 (1H, d, *J* = 3.7 Hz, 3-H); 7.20 (1H, br. s, NH_2); 7.35 (1H, s, CH=N); 7.80 (1H, br. s, NH_2); 9.75 ppm (1H, s, NH). Ratio of *E*:*Z* = 5:3. Found, %: C 45.01; H 4.72; N 17.27. $C_9H_{11}N_3O_3S$. Calculated, %: C 44.78; H 4.60; N 17.42.

Ethyl 5-Methyl-4-nitro-2-furancarboxylate (2). Volatile liquid, R_f^1 0.74, R_f^2 0.78. ^{1}H NMR spectrum: 1.31 (3H, t, *J* = 7 Hz, CH_3); 4.33 (2H, q, *J* = 7 Hz, CH_2); 2.76 (1H, d, *J* = 0.4 Hz, 5-CH_3); 7.76 ppm (1H, q, *J* = 0.4 Hz, 3-H).

5-Methyl-4-nitro-2-furancarbonitrile (6) was obtained by the preceding method by the nitration of 5-methyl-2-furancarbonitrile (10.7 g, 0.1 mol), prepared by a known method [12] with 70% HNO_3 (9.4 ml, 0.15 mol) at -10 to -5°C. The reaction mixture was poured onto ice, the floating precipitate was filtered off, washed with water, and dried in the air to give 0.35 g of a yellow amorphous powder; mp 168-173°C; the polymer-containing starting material and the nitronitrile **6**. The filtrate was extracted with ether (4 × 150 ml), the extract was washed with aqueous $NaHCO_3$ solution, then water, and was dried over $MgSO_4$. Removal of the solvent left an oil (4.3 g) which crystallized on standing; mp of the crude product 30-32°C. Yellow crystals; mp 37-39°C (ethanol), R_f^2 0.78. ^{1}H NMR spectrum: 2.76 (3H, d, *J* = 0.4 Hz, 5-CH_3); 8.28 ppm (1H, q, 0.4 Hz, 3-H). IR spectrum, cm^{-1}: 2240 (C=N), 1540 and 1320 (NO_2). Mass spectrum, *m/z* (I_{rel}, %): 152 (68, M$^+$), 136 (5), 135 (6), 122 (21), 107 (26), 105 (15), 78 (26), 77 (44), 54 (35), 52 (47), 51 (100), 28 (29), 27 (26), 18 (38). Found, %: C 47.22; H 2.47; N 18.28. $C_6H_4N_2O_3$. Calculated, %: C 47.37; H 2.65; N 18.42.

5-Methyl-4-nitro-2-furancarboxamide Oxime (7). Mixture of nitronitrile **6** (0.76 g, 5 mmol) and hydroxylamine hydrochloride (0.35 g, 5 mmol), and KOH (0.28 g, 5 mmol) in absolute ethanol (25 ml) was boiled for 10 min, KCl precipitate was filtered off, and the filtrate was evaporated to one third of its original volume. The product was filtered off. Yield 0.47 g (51%); mp 187-192°C (ethanol). ^{1}H NMR spectrum: *E*-isomer: 2.69 (3H, d, *J* = 0.4 Hz, 5-CH_3); 5.9 (2H, br. s, NH_2); 7.36 (1H, q, *J* = 0.4 Hz, 3-H); 9.94 ppm (1H, s, OH). *Z*-isomer: 2.71 (3H, d, *J* = 0.4 Hz, 5-CH_3); 7.6 (2H, br. s, NH_2); 7.39 (1H, q, *J* = 0.4 Hz, 3-H); 10.90 ppm (1H, s, OH). *E* : *Z* ratio = 2:5. Found, %: C 39.14; H 3.63; N 22.46. $C_6H_7N_3O_4$. Calculated, %: C 38.92; H 3.81; N 22.70.

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