Nitration of methyl 3-(5-nitro-2-furyl)acrylate with fuming nitric acid afforded 5-nitro-2-furancarboxylic acid (II) as a main product (70%) and 5-nitro-2-furaldehyde (III) and methyl ester of 2-nitro-3-(5-nitro-2-furyl)acrylic acid IV as by-products. The nitration of methyl ester of I gave at —10°C the corresponding methyl ester of IV in a 29% yield, whereas the nitration with a solution of N₂O₄ in CCl₄ furnished methyl ester of IV even in a better yield. Both procedures led prevalently to the Z configuration of the ester of IV.

As we have already shown, 3-(5-nitro-2-furyl)acrylic acid (I) undergoes under various reaction conditions of nitration prevalently a decarboxylation nitration [1]. According to preceding findings the reaction of nitrogen oxides with 3-(2-furyl)acrylic acid proceeds in two consecutive steps — nitration and decarboxylation [2], and therefore, we investigated the nitration of methyl ester of I under conditions where the decarboxylation nitration of free acid I takes place aiming to stop the reaction in the first step and isolate the nitration product, since the ester does not undergo a direct decarboxylation, and presuming the obtained products to be of the same structure as compounds prepared by condensation of 5-nitro-2-furaldehyde (III) with methyl nitroacetate [3].
FURAN DERIVATIVES. CIII

Experimental

Melting points were determined on a Kofler micro hot-stage. Infrared spectra were recorded with a UR-20 (Zeiss, Jena) spectrophotometer in KBr discs at a standard concentration 2 mg of substance/1 g of KBr. The instrument was calibrated against a polystyrene foil. 1H-n.m.r. spectra were taken with a Tesla BS 487 C apparatus at an operating frequency 80 MHz in deuterated acetone or chloroform tetramethylsilane being the internal reference substance. Mass spectra were measured with an AEI MS 902 S spectrophotometer. The nitration was carried out with methyl ester of I prepared according to [4].

Nitration of methyl ester of 3-(5-nitro-2-furyl)acrylic acid (I) with nitric acid

Method A

The ester of I (19.7 g; 0.1 mole) was cooled at 0°C, fuming HNO₃ (30 ml) was added and stirring was continued for 1 h. After this time the temperature was allowed to reach 20°C, the mixture was stirred for additional 1 h and then poured into ice containing water (100 ml). The product extracted twice with ether (10 ml each) was washed with 5% aqueous sodium carbonate solution, the dark-red aqueous layer was separated, the ethereal solution dried with MgSO₄ and the solvent distilled off. The product was identified by 1H-n.m.r. spectroscopy and chromatography as consisting of III, methyl nitroacetate (V), and methyl ester of 2-nitro-3-(5-nitro-2-furyl)acrylic acid (IV). This mixture was extracted with boiling heptane (100 ml) from which methyl ester of IV (1.2 g; 4.95%, m.p. 77—79°C) crystallized at room temperature. The ester of IV was identified by spectral means (mass, infrared, and 1H-n.m.r.). The aqueous layer was acidified with HCl and extracted with ether (300 ml) from which II was obtained, in a 70% yield (11 g). This substance was identified also on the basis of spectral evidence (mass, infrared, and 1H-n.m.r.) and mixed melting point with the authentic specimen.

Method B

To the methyl ester of I (19.7 g; 0.1 mole) cooled at −10°C fuming HNO₃ (30 ml) was added under stirring; this being continued for 1 h. After this time the solution was cooled at −20°C, ether (100 ml) was added and stirring was continued for additional 10 min. The ethereal solution was then separated, ether distilled off and the residue extracted with hot heptane, from which methyl ester of IV (7 g; 29%) crystallized at room temperature in long needles; m.p. 77—79°C. Identification as above.

Nitration of methyl ester of I with oxides of nitrogen

Nitrogen(IV) oxide (27.6 g; 0.3 mole) in CCl₄ (250 ml) was dropwise added to a solution of methyl ester of I (19.7 g; 0.1 mole) in CCl₄ (100 ml) placed in a three-necked flask provided with a stirrer, dropping funnel fitted with a CaCl₂ tube under stirring at 0°C. After

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addition of the total amount, stirring was continued for 1 h at 0°C and at room temperature for another 4 h. The mixture was then evaporated under reduced pressure, extracted with heptane (200 ml) and allowed to crystallize. The methyl ester of IV (8.5 g; 35.1%) was obtained within 48 h of standing.

**Action of fuming HNO₃ on 5-nitro-2-furaldehyde (III)**

Fuming HNO₃ (6 ml) was added under efficient cooling and stirring to the solution of III (1 g) in CCl₄ (10 ml) at −10°C. After the intense evolution of nitrous gases discontinued, the reaction mixture was poured onto crushed ice, CCl₄ was separated, washed with 5% sodium carbonate solution and the product was isolated after cooling and acidifying. Yield 0.3 g of II.

**Action of water on methyl ester of IV**

A mixture of Z and E isomers of methyl ester of IV (1 g) was stirred in water (10 ml) at room temperature for 1 h, one part of this solution was separated, extracted with ether and the dried ethereal solution evaporated. The residue dissolved in deuterated chloroform was subjected to ¹H-n.m.r. measurement (O₂NCH₂COOCH₃: δCH₂ = 5.17; δCHO = 3.82; III: δCHO = 9.72). The second part was treated with an excess of standard acid solution of 2,4-dinitrophenylhydrazine, the separated precipitate was filtered off with suction, dissolved in ethyl acetate and identified by t.l.c. on Silufol (developing system CCl₄—ethyl acetate 3:2) as a 2,4-dinitrophenylhydrazone of aldehyde III. The aqueous solution was extracted with ether and identified by t.l.c. as methyl esters of IV and V.

**Discussion**

Nitration of methyl ester of I with fuming HNO₃ at 0—20°C was accompanied with an intense evolution of nitrous gases. A considerable amount of acid products was extracted with ether after decomposition of the nitration mixture with water. This procedure was utilized for separation of the mixture, since acid components can be extracted from the ethereal layer into water with sodium carbonate solution.

In addition to the methyl ester of IV, substances III and V were found in the neutral ethereal solution, whereas acid II was obtained in a 70% yield from the aqueous layer after extraction of the ethereal extract with sodium carbonate solution.

According to experience [1], the C=C bond in 3-(5-nitro-2-furyl)acrylic acid derivatives is stable towards oxidation reagents and therefore, the formation of II as a main reaction product has to proceed otherwise than by oxidation of the side-chain double bond. The most probable route for formation of II under the
given conditions is considered the oxidation of III which has to originate, if decomposition of the primary addition product in the reaction mixture resulting from methyl ester of I and nitric acid or alternatively from methyl ester of IV and water, takes place.

This reaction course is supported by the appearance of aldehyde III in products of decomposition of the reaction mixture by water determined both by 1H-n.m.r. spectrum and t.l.c.

The small amount of methyl ester of IV obtained in addition to the main product of reaction II indicates that two concurrent reactions of different rate took place under the given conditions, addition is the main, substitution the side reaction.

To evidence the suggested mechanism of the main reaction the individual steps presumed were analyzed. Addition of water to methyl ester of IV (Scheme 1)

afforded a compound identical with that formed by addition of HNO₃ to methyl ester of I. Decomposition of the product in water to give V and III (which has been experimentally proved) confirms the second step of the scheme. Oxidation of III with HNO₃ to yield II proceeded vigorously, although it was performed under mild conditions; it can be brought under control only in solution and at temperatures not exceeding —20°C. This argument confirms the suggested mechanism of the main reaction.

This conclusion is in accordance with the hydration rate constant of water to the double bond of 2-nitrocrotonate [5], the order of magnitude of which was found to be 10⁻² s⁻¹.

Aiming to enhance the yield of the substitution by-product, methyl ester of I was nitrated at —10°C; to avoid addition of water to the originating methyl ester of IV, the nitration mixture was deeply cooled and extracted with ether. This procedure

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led to a 29% yield of methyl ester of IV. To prevent proceeding of further reactions after addition of HNO₃ to the double bond, the reaction was carried out with nitrogen oxides in CCl₄; yield of the nitration product was thus raised to 35%.

Methyl ester of IV exists in Z and E configurations according to the preparation mode. During the decarboxylation nitration of 3-(5-nitro-2-furyl)acrylic acid the leaving and the approaching nitro groups are on the same side of the double bond, and consequently, the E isomer was formed [1]. This process is possible only under a presumption that the decarboxylation nitration proceeds by an addition-elimination mechanism and after addition of HNO₃ to the C = C double bond of the acrylic acid the molecule occupies a more favourable spatial arrangement during the elimination, enabling the generation of the E isomer.

A characteristic differentiation feature in the ¹H-n.m.r. spectra of esters of IV are differences in chemical shifts of protons associated with position 3 of acrylic acid: protons of E isomers resonate in a lower field than those of Z isomers. This chemical shift of ethylene protons is due to a greater magnetic anisotropy of the nitro group when compared with the carboxyl group. Chemical shifts of olefinic protons in E and Z isomers were calculated on the basis of additive increments for substituents in cis and trans positions towards the proton according to [6]:

$$\delta_{CH=C} = 5.25 + Z_{gem} + Z_{cis} + Z_{trans}$$

The obtained values differ by 1 p.p.m. evidencing thus the nonplanarity of the molecule.

Both isomers could be distinguished also by stretching vibrations $\nu_s(NO_2)$ and $\nu_{as}(NO_2)$ of the methyl ester of IV (Table 1). Stretching vibrations of the nitro group of the E isomer, having the nitro group in a trans arrangement towards furan ring, appear at lower wavelength than in the Z isomer.

Condensation of III with V [3], where the latter compound could be oriented toward the aldehyde in both directions, furnished methyl ester of IV as a mixture of Z and E isomers in a 1:8 ratio.

The ¹H-n.m.r. spectrum of methyl ester of IV, obtained by nitration of methyl ester of I with HNO₃, proved the existence of Z and E isomers in a 9.2:1 ratio. It means that the nitration led to a substance of less favourable configuration, which

### Table 1

<table>
<thead>
<tr>
<th>Isomer</th>
<th>$\delta_{CH=C}$ (p.p.m.)</th>
<th>OCH₃ (p.p.m.)</th>
<th>$\nu_s(NO_2)$ cm⁻¹</th>
<th>$\nu_{as}(NO_2)$ cm⁻¹</th>
<th>M.p. °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>E</td>
<td>8.75</td>
<td>7.77</td>
<td>4.01</td>
<td>1330</td>
<td>102—103</td>
</tr>
<tr>
<td>Z</td>
<td>8.10</td>
<td>7.28</td>
<td>3.86</td>
<td>1375</td>
<td>77—79</td>
</tr>
</tbody>
</table>

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could exist in a nonplanar form only under a presumption that the furan ring and nitro group are located above each other [7]. Formation of the Z isomer as a prevailing form is of importance for determination of the reaction mechanism, since this isomer can be exclusively generated in a case, when hydrogen in position 2 of acrylic group undergoes displacement under maintaining the original molecular geometry; nevertheless, this was not observed during nitration of free I.

Similarly as in the former case, nitration of methyl ester of I with N₂O₄ leads to formation of Z and E isomers of methyl ester of IV in a 4:1 ratio indicating thus that also radical substitution favourizes maintaining the same molecular geometry.

References


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