

## SYNTHESES OF 5-NITRO-2-FURYL- AND 5-NITRO-2-THIENYL-ACETONITRILES

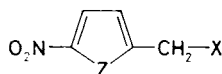
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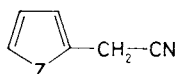
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Syntheses of 5-nitro-2-furyl- and 5-nitro-2-thienylacetonitriles have been accomplished by the reaction of enamines *VIII* with hydroxylamine-O-sulphonic acid and by nitration of furyl- and thienylacetonitriles *V*.

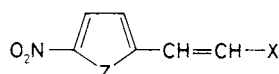
The synthesis of nitrofuryl- and nitrothienylacetic acid derivatives was followed in the context of synthetic problems of antibacterial ethylene derivatives with heterocyclic residues<sup>1</sup>. The acetonitriles substituted with residues of nitro five-membered heterocycles are described only exceptionally<sup>2</sup>. The attempts at syntheses of acetonitriles *I* from easily available furfuryl<sup>3-5</sup> and thenyl<sup>6,7</sup> derivatives *III*, *IV* failed<sup>8-11</sup>.



- I*, X = CN  
*II*, X = H  
*III*, X = Br  
*IV*, X = N(CH<sub>3</sub>)<sub>3</sub> Br<sup>(-)</sup>



*V*

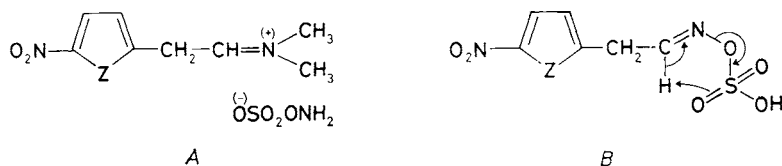


- VI*, X = Br  
*VII*, X = N(CH<sub>3</sub>)<sub>3</sub> Br<sup>(-)</sup>  
*VIII*, X = N(CH<sub>3</sub>)<sub>2</sub>  
*IX*, X = N<sub>3</sub>

In formulae *I-IX*: *a*, Z = O      *b*, Z = S

5-Nitrofuran and 5-nitrothiophene enamines *VIII* react with hydroxylamine-O-sulphonic acid<sup>12,13</sup> at room temperature in water to give the acetonitriles *I* in 22 to 37% yields. Two to three equivalents of hydroxylamine-O-sulphonic acid (which is added gradually, portionwise within several hours) are used for the conversion of enamine *VIII* to acetonitrile *I*. Additions of organic solvents decrease the reaction yields. The corresponding enamines *VIII* were prepared by the reaction of (*Z*)- and (*E*)-isomers, respectively, of the vinyl halides *VI* (refs<sup>14,15</sup>) with dimethylamine<sup>15,16</sup> in 80 to 90% yields or from the methyl derivatives *II* by condensation with dimethylformamide dimethylacetal<sup>17</sup> at 110–120°C in 90 to 95% yields.

The transformation mechanism of enamines and hydroxylamine-O-sulphonic acid into acetonitriles has not been described yet. We presume that an electrophilic attack of hydroxylamine-O-sulphonic acid on the enamine *VIII* produces the salt *A* which condensates with another molecule of hydroxylamine-O-sulphonic acid to give the acetaldehyde oxime-O-sulphonic acid *B*; this compound is thermolabile, giving the acetonitriles *I* already at room temperature (Scheme 1). The relatively low yields of *I* are explained by extensive  $p$ - $\pi$  conjugation in the molecule and lowering of electron density at the  $\beta$  carbon atom with regard to the dimethylamino group, which lowers the reactivity of the enamine *VIII* to electrophilic reagents at this carbon<sup>2</sup>.



SCHEME 1

The attempts at transformations of some other reactive vinyl derivatives, as e.g. vinyl bromides *VI*, vinyltrimethylammonium salts *VII*, and vinyl azides *IX* (refs<sup>15,18</sup>), into the acetonitriles *I* failed. The vinyl azides *IX* are decomposed thermally already at 60–70°C, giving the vinyl nitrene which is stabilized by formation of three-membered 2*H*-azirine cycle<sup>15,18</sup>.

The syntheses of 2-furyl- and 2-thienylacetonitriles were accomplished by reactions of the respective furfuryl and thenyl halides with cyanide in dimethyl sulphoxide according to Satoh<sup>19</sup> and Novitskii<sup>20</sup>. The nitration of *V* in acetanhydride with nitric acid (*d* 1.51) at –10°C produces the nitriles *Ia* and *Ib* in the yields of 7–9% and 11–14%, respectively. The reaction mixture undergoes resinification especially during decomposition of the nitration mixture after the nitration.

Considerable reactivity and acidity of the methylene protons in compounds *I* result in formation of intensely coloured products with basic reagents. The presence of *I* in the reaction mixtures was qualitatively determined by means of TLC (silica gel). The compounds *I* are practically invisible on silica gel (or only slightly yellowish) but turn orange immediately after exposition to ammonia vapours.

## EXPERIMENTAL

The melting points were determined with a Kofler apparatus and are not corrected. The infrared spectra were measured in chloroform with a UR-20 spectrophotometer (Zeiss, Jena). The

$^1\text{H}$  NMR spectra were measured in deuteriochloroform with a Tesla NMR BS 487 C (80 MHz) apparatus using tetramethylsilane as the internal standard. The mass spectra were measured with an AEI MS 902 S spectrometer.

1-(5-Nitro-2-furyl)-2-(N,N-dimethylamino)ethene (*VIIIa*)

A solution of 25.5 g (0.25 mol) 5-nitro-2-methylfuran<sup>3</sup> (*IIa*) in 75 ml dimethylformamide dimethylacetal<sup>17</sup> was heated under argon at 110–120°C 7 h. The solvent was distilled off under reduced pressure, and the residue was purified by column chromatography (silica gel 200  $\mu\text{m}$ ; benzene for *IIa*, benzene-ethyl acetate for *VIIIa*). Yield 41 g (90%) enamine *VIIIa*, m.p. 65–67°C (ref.<sup>16</sup> gives m.p. 65–67°C).

1-(5-Nitro-2-thienyl)-2-(N,N-dimethylamino)ethene (*VIIIb*)

The same procedure as for *VIIIa* was applied to 5-nitro-2-methylthiophene (*IIB*); yield 92%, m.p. 125–127°C (ref.<sup>15</sup> gives m.p. 124–127°C).

5-Nitro-2-furylacetonitrile (*Ia*)

*a*) From the enamine *VIIIa*: A suspension of 18.2 g (0.1 mol) *VIIIa* in 500 ml distilled water was intensively stirred at room temperature, and 35 g hydroxylamine-O-sulphonic acid was added thereto within two hours<sup>12</sup>. After 24 h standing at room temperature, the reaction mixture was heated at 70°C for a short time, cooled, and extracted with dichloromethane. Dichloromethane was distilled off under reduced pressure, and the residue was purified by column chromatography (silica gel 200  $\mu\text{m}$ ; benzene-ethyl acetate 1 : 1). Yield 4.8 g (32%), m.p. 38–39°C. For  $\text{C}_6\text{H}_4\text{N}_2\text{O}_3$  (152.1) calculated: 47.38% C, 2.65% H, 18.42% N; found: 47.33% C, 2.70% H, 18.47% N. Mass spectrum ( $m/z$ ): 152 ( $\text{M}^+$ ).  $^1\text{H}$  NMR spectrum: 6.95 dt, 1 H (H-3); 7.34 d, 1 H (H-4); 3.97 d, 2 H ( $\text{CH}_2$ ),  $J(3, 4) = 4.0$ ;  $J(\text{H-3}, \text{CH}_2) = 0.7$ . IR spectrum: 2 257  $\text{cm}^{-1}$  ( $\text{C}\equiv\text{N}$ ).

*b*) By nitration of *Va*: 9.45 g (0.15 mol) nitric acid ( $d$  1.51) was added dropwise to 42.5 g (0.42 mol) acetic anhydride at 0°C. After 15 min stirring, the nitration mixture was cooled to  $-10^\circ\text{C}$ , and 10.7 g (0.1 mol) 2-furylacetonitrile (*Va*) in 14 g acetic anhydride was added thereto during 1 h. Then intensive stirring was continued at  $-10^\circ\text{C}$  1 h and at 0°C 1 h. The mixture was poured onto 600 g ice and treated with a solution of 40 g NaOH in 120 ml water added dropwise with intensive stirring (pH 6.0–6.6). The product was extracted with ether ( $5 \times 100$  ml). The extract was mixed with 20 ml pyridine and dried with  $\text{MgSO}_4$  24 h. The solid was removed by filtration, the ether was distilled off, and the residue was purified by column chromatography (silica gel as sub *a*). Yield 1.1 g (7%) 5-nitro-2-furylacetonitrile (*Ia*), m.p. 38–39°C.

5-Nitro-2-thienylacetonitrile (*Ib*)

*a*) From enamine *VIIIb*: The procedure was analogous to that starting from *VIIIa*. Yield 6.2 g (37%) *Ib*, orange-yellow oil. For  $\text{C}_6\text{H}_4\text{N}_2\text{O}_2\text{S}$  (168.2) calculated: 42.85% C, 2.39% H, 16.66% N; found: 42.80% C, 2.35% H, 16.60% N. Mass spectrum ( $m/z$ ): 168 ( $\text{M}^+$ ).  $^1\text{H}$  NMR spectrum: 7.10 dt, 1 H (H-3); 7.84 d, 1 H (H-4); 4.02 d, 2 H ( $\text{CH}_2$ ,  $J(3, 4) = 4.15$ ;  $J(\text{CH}_2, \text{H-3}) = 0.7$ ). IR spectrum: 2 253  $\text{cm}^{-1}$  ( $\text{C}\equiv\text{N}$ ).

*b*) By nitration of *Vb*: The procedure was analogous to that starting from *Va* and gave 14% yield of orange-yellow oily 5-nitro-2-thienylacetonitrile ( $R_F = 0.15$ ; benzene as the eluent).

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