Furan derivatives
202. Nucleophilic substitution reactions of 2-cyano-3-methyl-3-(5-X-2-furyl)acrylonitriles

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Dedicated to Professor Ing. J. Kováč, DrSc., in honour of his 60th birthday

Preparation of 2-cyano-3-methyl-3-(5-X-2-furyl)acrylonitriles by Knoevenagel condensation as well as the study of their substitution nucleophilic reactions with secondary amines is described. The interpretation of UV, IR, ^{1}H NMR spectra of the prepared compounds is given.

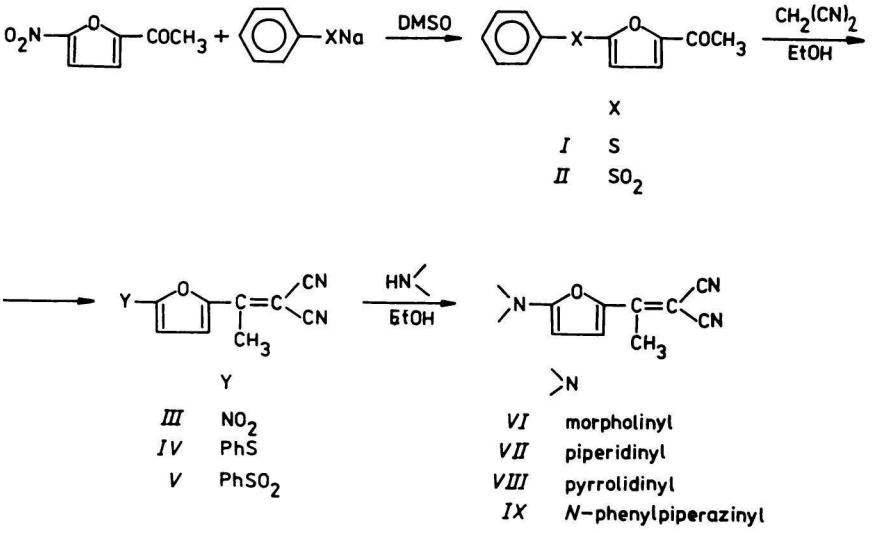
В работе описывается получение 2-циано-3-метил-3-(5-Х-2-фурил)-акрилонитрилов посредством конденсации по Кневенагелю, и обсуждаются их реакции нуклеофильного замещения со вторичными аминами. Интерпретируются УФ-, ИК- и ^{1}Н ЯМР-спектры полученных соединений.

A survey of S_N reactions taking place at the furan ring shows that the most often used leaving groups have been halogen atoms and the nitro group. We have performed nucleophilic substitution reactions of arylthio, heteroarylthio, and arylsulfonyl group at the furan ring.

This report is an extension of our previous papers [1—3] on the preparation and study of nucleophilic reactions of 2-cyano-3-(5-X-2-furyl)acrylonitriles. Special attention was given to the synthesis of acrylonitriles having a methyl group in the β position. Further their nucleophilic displacement reactions with cyclic amines were studied (Scheme 1).

2-Cyano-3-methyl-3-(5-X-2-furyl)acrylonitriles were prepared by Knoevenagel condensation from dinitrile of the malonic acid and the corresponding 5-X-2-acetylfurans (X = nitro [4], phenylthio, phenylsulfonyl) [5, 6]. We have tested the Cope modification of the Knoevenagel method as well, catalyzed by ammonium acetate, but only nitro derivative gave under such conditions yields 10—20-fold higher than the standard procedure.

The reactions of 2-cyano-3-methyl-3-(5-X-2-furyl)acrylonitriles with secondary amines (piperidine, morpholine, *N*-phenylpiperazine, pyrrolidine) were performed in ethanol, dimethylformamide, and dimethyl sulfoxide at various temperatures. The highest yields were achieved in ethanol at laboratory temperature (Table 1).



Scheme 1

Table 1

Physicochemical data of the prepared compounds

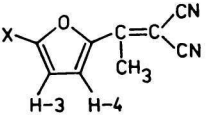
Compound	Formula	M_r	w_i(calc.)/% w_i(found)/%				Yield	M.p.
			C	H	N	S	%	°C
I	$C_{12}H_{10}O_2S$	218.1	66.01	4.62	—	14.70	65.5	56—58
			66.31	4.53	—	14.61		
II	$C_{12}H_{10}O_4S$	250.1	57.57	4.53	—	12.82	35.0	93—94
			57.20	3.82	—	12.58		
III	$C_9H_5N_3O_3$	203.1	53.19	2.48	20.69	—	78.8	144—145
			53.38	2.23	20.40	—		
IV	$C_{15}H_{10}N_2OS$	266.2	67.53	3.79	10.53	12.05	55.6	Oil
			67.51	3.62	10.35	11.89		
V	$C_{15}H_{10}N_2O_3S$	298.2	60.37	3.38	9.40	10.75	38.5	Oil
			60.02	3.20	9.13	10.57		
VI	$C_{13}H_{13}N_3O_2$	243.1	64.17	5.39	17.28	—	64.5	224—225
			63.94	5.21	17.07	—		
VII	$C_{14}H_{15}N_3O$	241.1	69.67	6.27	17.43	—	69.0	154—155
			69.40	6.18	17.20	—		
VIII	$C_{13}H_{13}N_3O$	227.1	68.69	5.77	18.50	—	67.0	190—191
			68.49	5.51	18.23	—		
IX	$C_{19}H_{18}N_4O$	318.2	71.66	5.70	17.61	—	65.0	187—189
			71.38	5.60	17.42	—		

Structure of the synthesized compounds was established by ^{1}H NMR, IR, and UV spectra as well as by elemental analyses.

^{1}H NMR spectra (Table 2) displayed a singlet of the methyl group of 5-X-2-acetylfurans at $\delta = 2.45$—2.60 ppm, the higher value being that of the nitro derivative, the lower value that of phenylthio and phenylsulfonyl derivatives (2.45 ppm and 2.46 ppm). Doublets of furan ring protons were found at $\delta = 6.63$—7.27 ppm and 7.18—7.38 ppm; again nitro derivative having the most deshielded protons. Coupling constants of the furan protons were found to be 3.5—3.8 Hz. The highest (3.8 Hz) coupling constant was that of the nitro derivative. Benzene ring protons of the phenylthio derivative showed only one multiplet, whereas those of phenylsulfonyl derivative showed two multiplets at $\delta = 7.26$—7.37 ppm and 7.95—8.13 ppm.

Table 2

^{1}H NMR data (δ/ppm)



Compound	CH_3, s	H-3, d	H-4, d	Phenyl, m	H-Het, m	$J_{3,4}$/Hz
I	2.45	6.63	7.18	7.26—7.37	—	3.5
II	2.46	7.15	7.24	7.50—7.71 7.95—8.13	—	3.65
III	2.68	7.45	7.73	—	—	4.0
IV	2.50	6.57	7.47	7.25—7.60	—	3.9
V	2.51	6.59	7.50	7.24—7.55	—	4.0
VI	2.33	5.49	7.24	—	3.45—3.65 3.75—3.90	4.2
VII	2.28	5.47	7.24	—	1.55—1.83 3.40—3.68	4.2
VIII	2.30	5.39	7.25	—	1.95—2.15 3.45—3.71	4.2
IX	2.34	5.55	7.24	6.78—7.05 7.20—7.45	3.24—3.45 3.58—3.84	4.2

Condensation products of 5-X-2-acetylfurans with malonodinitrile displayed their signals in ^{1}H NMR spectra at higher δ values, due to the extended conjugation in their molecules. Signals of methyl groups were found at $\delta = 2.50$—2.68 ppm. H-3 and H-4 protons of the nitro derivative showed their signals at higher δ values, those of the phenylthio and phenylsulfonyl derivatives were

found at both lower (H-3) and higher (H-4) δ values, compared with the starting material. Coupling constants of H-3 and H-4 protons were 3.9—4.0 Hz. Protons of the methyl group of the substitution products *VI—IX* experienced an upfield shift to $\delta = 2.28$—2.34 ppm. Chemical shift of the H-3 proton depends on the character of the substituent ($\delta = 5.39$—5.55 ppm), whereas H-4 proton of the furan ring appeared mostly unaffected by substitution ($\delta = 7.24$—7.25 ppm). Proton of the secondary amines gave two multiplets at $\delta = 3.25$—3.65 ppm and 3.58—3.90 ppm (morpholine, *N*-phenylpiperazine), 1.55—2.15 ppm and 3.40 —3.71 ppm (pyrrolidine, piperidine).

Table 3

Spectral data of the prepared compounds

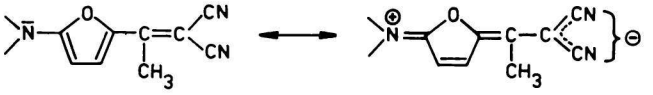
Compound	$\tilde{\nu}$(C=O) / cm^{-1}	$\tilde{\nu}$(C=C) / cm^{-1}	$\tilde{\nu}$(CN) / cm^{-1}	λ_{max}/nm (log {ε})	λ_{max}/nm (log {ε})	λ_{max}/nm (log {ε})
I	1680	—	—	241 (2.82)	270 (2.81)	310 (2.75)
II	1692	—	—	225 (3.04)	272 (3.34)	—
III	—	1591	2217	247 (3.03)	353 (3.39)	—
IV	—	1580	2224	236 (3.02)	382 (3.24)	—
V	—	1589	2216	238 (2.95)	382 (3.07)	—
VI	—	1612	2212	238 (3.22)	285 (2.56)	470 (3.69)
VII	—	1616	2210	238 (3.20)	288 (2.61)	472 (3.74)
VIII	—	1626	2208	237 (3.21)	287 (2.62)	475 (3.81)
IX	—	1598	2216	241 (3.31)	285 (2.71)	472 (3.68)

ε in $dm^3\,mol^{-1}\,cm^{-1}$.

Infrared spectra (Table 3) of 5-X-2-acetylfurans showed the peaks of carbonyl groups at $\tilde{\nu} = 1680$—1693 cm^{-1}, nitro group of the nitro derivative appeared at $\tilde{\nu}_{as} \approx 1530\ cm^{-1}$, $\tilde{\nu}_s \approx 1350\ cm^{-1}$, phenylsulfonyl derivative displayed the SO_2 bands at $\tilde{\nu}_{as}(SO_2) \approx 1345\ cm^{-1}$ and $\tilde{\nu}_s(SO_2) \approx 1150\ cm^{-1}$. Infrared spectra of condensation products lacked C=O group bands and contained characteristic bands of nitrile group. Ultraviolet spectra of 5-phenylsulfonyl-2- -acetylfuran showed two absorption maxima at 225 nm and 272 nm. The longwave maximum of 5-nitro-2-acetylfuran was bathochromically shifted to 305 nm. 5-Phenylthio-2-acetylfuran displayed three absorption maxima at 241 nm, 270 nm, and 310 nm due to the presence of the lone electron pairs at the sulfur atom. UV absorption maxima of 5-X-2-acetylfurans correspond to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ electronic transitions localized in the furan, benzene, 5-nitro, 5-phenylsulfonyl, 5-phenylthiofuran moiety, respectively. 2-Cyano-3-methyl-3- -(5-X-2-furyl)acrylonitrile showed in its electronic spectra two absorption maxima at $\lambda = 236$—247 nm and $\lambda = 353$—382 nm, the first one corresponding to

$\pi \rightarrow \pi^*$ or $n \rightarrow \pi^*$ electronic transitions localized in the 5-phenylthio, 5-phenylsulfonyl, and 5-nitrofuran moiety, the second one being the result of electronic oscillations over the entire conjugated system of the molecule (*K*-band).

Substitution products of the condensation derivatives displayed three maxima in their UV spectra. The bands at $\lambda = 238$—241 nm and $\lambda = 285$—288 nm correspond to the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions of the furan or benzene. The third maximum was strongly shifted toward the visible part of the spectrum, testifying to the presence of polar quinonoid structures, which account for the intensive colour as well (Scheme 2).



Scheme 2

Experimental

5-Phenylsulfonyl-2-acetylfuran (II)

To 5-nitro-2-acetylfuran (1.55 g; 0.01 mol) and urea (1.2 g; 0.02 mol) in 40 cm^3 of dimethyl sulfoxide was during 1 h added sodium benzenesulfinane (1.64 g; 0.01 mol) dissolved in 10 cm^3 of dimethyl sulfoxide at laboratory temperature. The mixture was kept stirred at 100 °C for 48 h, then poured into 40 cm^3 of water—ice mixture and extracted with ether. The ethereal extract was dried by sodium sulfate and concentrated. The crude residue was crystallized from ethanol.

5-Phenylthio-2-acetylfuran (I)

To the stirred solution of 5-nitro-2-acetylfuran (1.55 g; 0.01 mol) in 30 cm^3 of dimethyl sulfoxide was added at laboratory temperature sodium thiophenolate (2 g; 0.015 mol) in 10 cm^3 of dimethyl sulfoxide. The mixture was then stirred for 48 h at 70 °C, then poured on 50 g of broken ice. The crude product was sucked off and crystallized from ethanol.

2-Cyano-3-methyl-3-(5-X-2-furyl)acrylonitriles (III—V)

To the solution of 5-X-2-acetylfuran (0.02 mol) in 40 cm^3 of ethanol was added malonodinitrile (0.02 mol) in 10 cm^3 of ethanol and the mixture kept stirred at laboratory temperature for further 48 h. The product was isolated by column chromatography on silica gel, eluted by chloroform. Nitro derivative *III* was crystallized from chloroform.

2-Cyano-3-methyl-3-(5-X-2-furyl)acrylonitriles (VI—IX)

To the solution of *III—V* (0.0025 mol) in 25 cm^3 of ethanol was added secondary amine (0.0075 mol) in 5 cm^3 of ethanol. The mixture was stirred and kept for 4—6 h at laboratory temperature. The solvent was then evaporated and the residue separated on a silica gel column eluted by chloroform—ethyl acetate mixture (volume ratio = 5 : 1). Products were crystallized from ethanol.

Spectral measurements

Infrared spectra were measured with a double-beam spectrometer PYE UNICAM SP-100 in a NaCl cuvette 0.1 mm thick. The spectrometer was calibrated using a polystyrene film with 25 μm thickness. Electronic spectra were taken with a Specord UV VIS apparatus (Zeiss, Jena) from $2—5 \times 10^{-5}$ M methanolic solutions. The cuvette was 9.99 mm thick. ^{1}H NMR spectra were measured on the Tesla BS 487 C, 80 MHz spectrometer in C^2HCl_3, using tetramethylsilane as internal standard.

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