

Furan derivatives. CXXXV.

Anhydrides of 3-(5-nitro-2-furyl)acrylic acid as starting materials for the synthesis of 1-(5-nitro-2-furyl)-2-(1,3,4-oxadiazol-2-yl)ethenes

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A new method for preparation of substituted 1-(5-nitro-2-furyl)-2-(5-X-1,3,4-oxadiazol-2-yl)ethenes from 5-substituted tetrazoles and mixed anhydrides of 3-(5-nitro-2-furyl)acrylic acid was worked out.

В работе описывается новый способ приготовления замещенных 1-(5-нитро-2-фурил)-2-(5-X-1,3,4-оксадиазол-2-ил)этиленов по реакции 5-замещенных тетразолов и ангидридов 3-(5-нитро-2-фурил)акриловой кислоты.

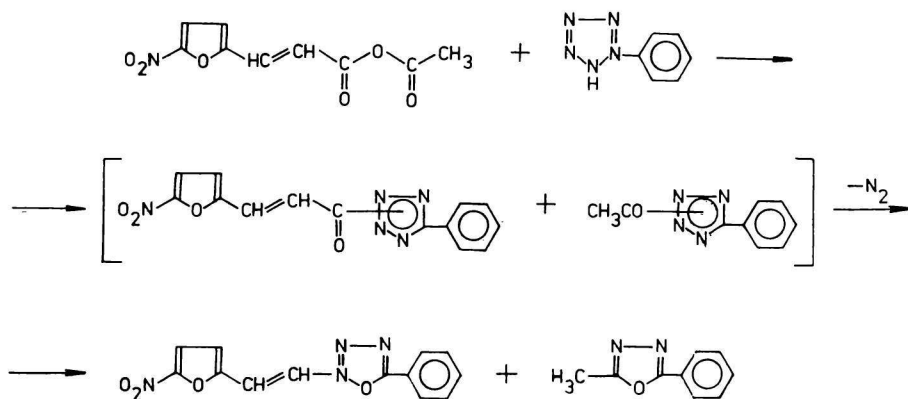
The appearance of Panfuran (1-(5-nitro-2-furyl)-2-(3-amino-1,2,4-triazin-6-yl)ethene) and Furamizol (1-(2-furyl)-2-(5-nitro-2-furyl)-1-(5-amino-1,3,4-oxadiazol-2-yl)ethene) [1], two preparations of a high antimicrobial activity, stimulated the search for further (5-nitro-2-furyl)vinyl substituted derivatives of nitrogen-containing heterocycles. Consequently, new approaches to those derivatives in high yields were investigated. Substituted 1-(5-nitro-2-furyl)-2-(5-X-1,3,4-oxadiazol-2-yl)ethenes, where X = aryl or heteroaryl, were so far prepared by cyclization of *N,N'*-disubstituted hydrazides of acids [2], or by oxidation of arylidenehydrazides of 3-(5-nitro-2-furyl)acrylic acid [3]. A general method for preparation of 1,3,4-oxadiazoles from tetrazoles [4] was tried to be applied for the synthesis of 2-[(5-nitro-2-furyl)vinylidene]-1,3,4-oxadiazoles [5], nevertheless 5-substituted tetrazoles gave with 3-(5-nitro-2-furyl)acryloyl chloride in boiling xylene the corresponding oxadiazoles in low yield only.

The goal of this paper was to examine the convenience of 3-(5-nitro-2-furyl)acrylic acid derivatives for preparation of 1,3,4-oxadiazoles of 2-(5-nitro-2-furyl)vinylene series. The experiment to increase the yield by modification of the above-mentioned reaction failed. Reaction of 2-furyltetrazole with the complex of 3-(5-nitro-2-furyl)acryloyl chloride with pyridine at a low temperature did not take

place, the increase of temperature to 50°C had an exothermic course and furnished tarry products. Successful were found reactions with 3-(5-nitro-2-furyl)acrylic anhydride (*I*) and 3-(5-nitro-2-furyl)acrylic anhydride (*II*).

The reaction of 5-phenyltetrazole with *I* without a solvent at 120°C was quite vigorous, got out of control and afforded 1-(5-nitro-2-furyl)-2-(5-phenyl-1,3,4-oxadiazol-2-yl)ethene (*III*) in a 12% yield. The reaction could be controlled by using xylene as a solvent; also the yield was fairly improved. This way prepared 1-(5-nitro-2-furyl)-2-[5-(5-X-2-furyl)-1,3,4-oxadiazol-2-yl]ethenes are listed in Table 2.

Anhydride *II* was found to afford *III* in better yields than *I*, nonetheless the laborious separation of 3-(5-nitro-2-furyl)acrylic acid from *III* considerably deteriorates the use of *II*. The xylene solution after reaction of 5-phenyltetrazole with *I* contained, in addition to acetic acid and *III*, 5-methyl-2-phenyl-1,3,4-oxadiazole. This fact evidences that the mixed anhydride *I* reacts with 5-phenyltetrazole under formation of both possible acylated tetrazoles, which undergo decomposition to the corresponding 1,3-oxadiazoles. The result of this side reaction is seen in a lowered yield of *III* upon reaction of phenyltetrazole with *I* (Scheme 1)



Scheme 1

Experimental

Infrared and ultraviolet spectra were recorded with UR-20 (Zeiss, Jena) and UV VIS Specord spectrophotometers, respectively. Melting points were measured on a Kofler block. The starting substances, synthesized according to [6] are listed in Table 1.

Table 1

Characteristic data of 5-X-2-furonitriles (A) and 5-X-2-furyltetrazoles (B)

Type	X	Formula	M	Calculated/found				Yield %	M.p. °C	C=N cm ⁻¹	λ_{\max} nm	log ϵ
				% C	% H	% N	% Cl					
A	3-Cl-C ₆ H ₄	C ₁₁ H ₆ ClNO	203	65.10	2.95	6.91	17.43	52.4	104—105	2229	215	4.22
				65.09	2.84	7.04	17.10				298	4.53
A	2-Cl-C ₆ H ₄	C ₁₁ H ₆ ClNO	203	65.10	2.95	6.91	17.43	62	74—75	2230	214	4.27
				65.18	2.89	7.05	17.15				235	4.01
B	3-Cl-C ₆ H ₄	C ₁₁ H ₇ ClN ₄ O	246	53.57	2.86	22.71	14.37	65	241—242	—	291	4.57
				53.71	2.85	22.81	14.20				203	4.11
B	2-Cl-C ₆ H ₄	C ₁₁ H ₇ ClN ₄ O	246	53.57	2.86	22.71	14.37	63	211—212		313	4.40
				53.60	2.90	22.89	14.45				203	4.07
											238	4.09
											301	4.25

Table 2

Characteristic data of 1-(5-nitro-2-furyl)-2-[5-(5-X-2-furyl)-1,3,4-oxadiazol-2-yl]ethenes

X	Formula	M	Calculated/found			Yield %	M.p. °C	$\nu(\text{C}=\text{C})_{\text{arom}}^e$ cm^{-1}	$\nu(\text{C}=\text{N})$ cm^{-1}	λ_{max} nm	log ϵ
			% C	% H	% N						
2-NO ₂ C ₆ H ₄	C ₁₈ H ₁₀ N ₄ O ₇	394.30	55.05 54.93	2.55 2.54	14.21 14.11	75	230—231	1585	1630	390	4.54
4-BrC ₆ H ₄ ^a	C ₁₈ H ₁₀ BrN ₃ O ₅	428.21	50.60 50.38	2.36 2.44	9.83 9.71	72	225—226	1580	1635	395	4.53
3-ClC ₆ H ₄ ^b	C ₁₈ H ₁₀ ClN ₃ O ₅	383.75	56.55 56.68	2.63 2.71	10.95 10.68	68	234—235	1580	1640	390	4.43
4-CH ₃ OC ₆ H ₄	C ₁₉ H ₁₃ N ₃ O ₆	379.33	60.20 60.29	3.46 3.50	11.09 10.88	65	234—235	1585	1640	410	4.54
III ^d	C ₁₄ H ₉ N ₃ O ₄	283.23				64 ^c	215—217 ^f	1590	1640	370	4.16

a) % Br calculated/found: 18.67/18.75; b) % Cl: 9.26/9.23; c) crystallized from ethanol, all remaining compounds were crystallized from ethylene glycol monomethyl ether; d) III is 1-(5-nitro-2-furyl)-2-(5-phenyl-1,3,4-oxadiazol-2-yl)ethene; e) $\nu_s(\text{NO}_2) = 1360 \text{ cm}^{-1}$, $\nu_{\text{as}} = 1520 \text{ cm}^{-1}$ of all derivatives; f) melting point reported in [3].

Reaction of 5-X-tetrazoles with 3-(5-nitro-2-furyl)acrylic acetic anhydride

The mixture of 5-X-tetrazole (5 mmol) and 3-(5-nitro-2-furyl)acrylic acetic anhydride (1.35 g; 6 mmol) was heated in xylene (30 ml) at 130—140°C for 30 min. The crude oxadiazole was after cooling filtered off, washed with ethanol and crystallized from ethylene glycol monomethyl ether. Characteristic data of this series of compounds are given in Table 2.

The xylene filtrate after removal of *IIId*, which was left from the reaction of *I* with 5-phenyltetrazole, was divided in two equal portions. Titration with 0.1 N-NaOH revealed the content of acetic acid in the first portion to be 66—71%, the second portion gave, after concentration under diminished pressure, 5-methyl-2-phenyl-1,3,4-oxadiazole in 20—25% yield; its melting point 65—66°C is in accordance with that reported in [4].

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