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NITRATION OF 2- AND 4-[2-(2-FURYL)VINYL]THIAZOLE DERIVATIVES

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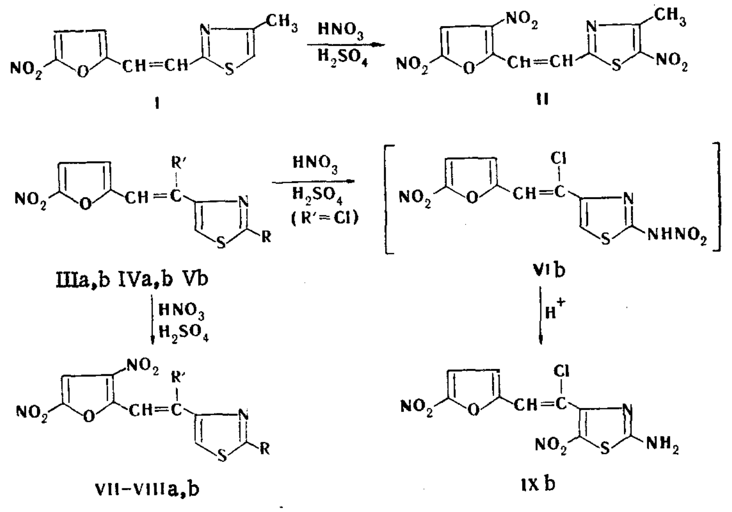
Nitration of 4-methyl-2-[2-(nitro-2-furyl)vinyl]thiazole with a mixture of concentrated nitric and sulfuric acids leads to 4-methyl-5-nitro-2-[2-(3,5-dinitro-2-furyl)vinyl]thiazole. Under the same conditions 2-methyl- and 2-acetamido-4-[1-R-2-(5-nitro-2-furyl)vinyl]thiazoles (R = CH_3, Cl) are nitrated in the 3 position of the furan ring, 2-amino-4-[1-chloro-2-(5-nitro-2-furyl)vinyl]thiazole is nitrated in the 5 position of the thiazole ring and 2-acetamido-5-nitro-4-[2-(2-furyl)vinyl]thiazole undergoes profound changes. Under the influence of a mixture of of nitric acid and acetic anhydride the latter compound is converted quantitatively to the 5-nitro derivative (with respect to the furan ring), whereas 4-[2-(5-nitro-2-furyl)vinyl]thiazole derivatives do not undergo reaction.

It is known that 4-methyl-2-[2-(2-furyl)vinyl]thiazole is converted to 4-methyl-2-[2-(5-nitro-2-furyl)vinyl]thiazole (I) by the action of a mixture of concentrated nitric acid and acetic anhydride [1]; this was proved by alternative synthesis from 5-nitrofurfural and 2,4-dimethylthiazole [2, 3].

We have established that another two nitro groups can be incorporated in I by the further action on I of a mixture of concentrated nitric and sulfuric acids. From a comparison of the PMR spectra of the starting compound and the final product (Table 1) it follows that 4-methyl-5-nitro[2-(3,5-dinitro-2-furyl)vinyl]thiazole (II) was obtained.



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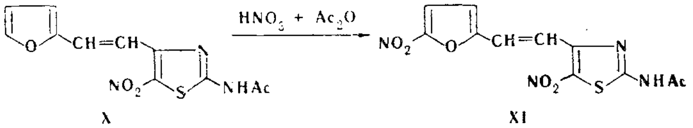


IIIa, VIIa $R=R'=CH_3$; IIIb VIIb $R=CH_3$, $R'=Cl$; IVa, $R=NHAc$, $R'=CH_3$; IVb and VIIIb $R=NHAc$, $R'=Cl$; Vb $R=NH_2$, $R'=Cl$

In contrast to 2-vinylthiazole (I), only one nitro group in the 3 position of the furan ring can be introduced in 2-methyl-4-[1-R-2-(5-nitro-2-furyl)vinyl]thiazoles (IIIa, b) under the same conditions. 2-Acetamido-4-[1-R-2-(5-nitro-2-furyl)vinyl]thiazoles (IVa, b) are nitrated in the same position. This sort of deactivation of the position of the thiazole ring has also been noted in the nitration of 2-alkyl- [4] and 2-acetamido-4-phenylthiazole [5]. As a result of this, nitration is realized only in the phenyl ring. In addition, it has been assumed that 2-acetamido-4-styrylthiazole is nitrated in the thiazole ring [6].

The results of our studies show that the thiazolylvinyl grouping, like the vinyl group [7], has pronounced electron-donor character, which ensures the ready introduction of a second nitro group in the furan ring, as occurs in the nitration of 2-methyl-5-nitrofuran [8]. Our observed incorporation of a second nitro group in the furan ring is the first time this has been noted in the furylvinylheterocycle series.

However, nitration of 2-amino-4-1-chloro-2-(nitro-2-furyl)vinyl]thiazole (Vb) with 1 mole of nitric acid leads to a nitro derivative involving the 5 position of the thiazole ring. The reaction in this case evidently proceeds through intermediate nitro amine VIb, which undergoes rearrangement to IXb, in a manner similar to that established for 2-aminothiazole [9] and its 4-methyl-substituted derivative [10].

The direction of nitration of 4-vinylthiazoles (III-V) as a function of the character of the substitutent in the 2 position was proved by means of PMR spectroscopy (Table 1).

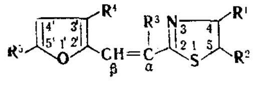
The PMR spectra confirm the correctness of the previously expressed assumption that the product of nitration of 2-acetamido-5-nitro-4-[2-(2-furyl)vinyl]thiazole (X) with a mixture of concentrated nitric acid and acetic anhydride is the 5-nitro-substituted derivative with respect to the furan ring (XI) [11] and has a trans structure ($J_{\alpha,\beta}$ 15.2 Hz). We established by thin-layer chromatography (TLC) that nitro-substituted derivative XI rather than the product of the addition of acetyl nitrate is formed directly during nitration under these conditions, and the nitro product can therefore also be isolated in quantitative yield without treatment of the reaction mixture with potassium acetate or pyridine. 2-Acetamido-5-nitro-4-[2-(5-methyl-2-furyl)vinyl]thiazole (XII) and substituted 4-[2-(5-nitro-2-furyl)vinyl]-thiazoles (IIIa, b-Va, b) were found to be inert to acetyl nitrate. Compound X underwent profound changes under the influence of a mixture of sulfuric and nitric acids.

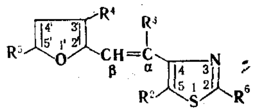
The 4-[2-(2-furyl)vinyl]thiazole derivatives synthesized for the first time in this research are presented in Table 2.

According to the data in Table 3, each type of nitro-substituted derivative in the series of 4-[2-(2-furyl)vinyl]thiazole derivatives has a UV spectrum peculiar to its character. Whereas there are two absorption maxima at 275-285 and 380-395 nm in each of the spectra of 2-methyl- (IIIa, b) and 2-acetamido-4-[2-(5-nitro-2-furyl)-1-R'-vinyl]thiazoles (IVa, b), a shift of the shortwave band to the UV region (< 250 nm) is observed in the spectra of their 3-nitro-substituted derivatives (with respect to the furan ring) (VIIa, b and VIIIa, b) with retention of the long-wave band. Instead of the two bands of strong absorption at 300 and 400 nm in the spectrum of 2-acetamido-5-nitro-4-[2-(2-furyl)vinyl]thiazole (X), not only a hyposchromic shift on the shortwave maximum (from 300 to 280 nm) but also intense absorption at 345 nm is observed in the product of its nitration in the 5 position of the furan ring, and the long-wave maximum is retained.

Moreover, instead of the expected (in analogy with XI) three absorption maxima, the spectrum of the product of nitration of aminothiazole Vb, which, according to the PMR spectrum, has structure IXb, contains only two maxima; this may be due to the noncoplanarity of the molecule. It was established by means of Stuart–Briegleb models that in the case of the bulkier (as compared with the hydrogen atom) chlorine atom in the vinylene group, the nitro group in the 5 position of the thiazole ring cannot be situated in the plane of the molecule.

TABLE 1. PMR Spectra of 2- and 4-[2-(2-Furyl)vinyl]thiazoles


I, II


IIIb, Vb, VII-IXb, XI, XII

Compound	R^1	R^2	R^3	R^4	R^5	R^6	Chemical shifts, δ, ppm						$J_{3',4'}$, Hz
							3'-H	4'-H	α-H	β-H	5-H	protons of groups	
I	CH_3	H	H	H	NO_2	—	7,10	7,71	7,40	7,40	7,35	2,38 (4-CH_3)	3,9
II	CH_3	NO_2	H	NO_2	NO_2	—	—	8,43	8,05	8,05	—	2,77 (4-CH_3)	
IIIb	—	H	Cl	H	NO_2	CH_3	7,33	7,76	—	7,69	7,94	2,71 (2-CH_3)	4,0
Vb	—	H	Cl	H	NO_2	NH_2	7,26	7,76	—	7,10	7,42	7,20 (2-NH_2)	4,1
VIIb	—	H	Cl	NO_2	NO_2	CH_3	—	8,46	—	8,20	8,41	2,74 (2-CH_3)	
VIIIb	—	H	Cl	NO_2	NO_2	NHAc	—	8,04	—	7,63	8,04	2,16 (2-$NHCOCH_3$)	
IXb	—	NO_2	Cl	H	NO_2	NH_2	7,37	7,74	—	7,48	—	7,78 (2-NH_2)	4,0
XI	—	NO_2	H	H	NO_2	NHAc	7,37	7,74	8,06	7,55	—	2,33 (2-$NHCOCH_3$)	3,5 15,2[a]
XII	—	NO_2	H	H	CH_3	NHAc	6,27	6,77	7,55	7,41	—	2,87 (5-CH_3) 2,19 (2-$NHCOCH_3$)	2,7 18,3[a]

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[a] The $J_{\alpha,\beta}$ data are presented.

TABLE 2. Products of the Nitration of 4-[2-(2-Fyryl)vinyl]-thiazole Derivatives

Compound	mp, °C[a]	Found, %			Empirical formula	Calc., %			Yield, %
		C	H	N		C	H	N	
VIIa	180—182	44,9	3,7	14,0	$C_{11}H_9N_3O_5S$	44,7	3,7	14,2	60
VIIb	180—183	38,4	2,0	13,3	$C_{10}H_6ClN_3O_5S$	38,1	1,9	13,3	55
VIIIa	225[b]	42,4	3,0	16,2	$C_{12}H_{10}N_4O_6S$	42,6	3,0	16,5	52
VIIIb	280—283[b]	36,6	1,7	15,3	$C_{11}H_7ClN_4O_6S$	36,7	1,9	15,6	59
IXb	274—275	34,4	1,5	17,4	$C_9H_5ClN_4O_5S$	34,1	1,6	17,7	49
XI	274—275	40,5	2,6	17,7	$C_{11}H_8N_4O_6S$	40,7	2,8	17,3	99

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[a] Crystallization from glacial acetic acid; VIIIa was crystallized from dioxane, and XI was crystallized from dimethylformamide.
[b] With decomposition.

TABLE 3. Chromatographic Characteristics and UV Spectra of 4-[2-(2-Furyl)vinyl]thiazole Derivatives

Compound	$R_f^1 \times 100$	$R_f^2 \times 100$	UV spectrum, λ_{max}, nm (log ε)			
IIIa	70	68	—	275 (4,22)	—	397 (4,35)[a]
IIIb	73	76	—	289 (4,02)	—	383 (4,26)
IVa	47	43	245 (4,10)	280 (4,16)	—	395 (4,28)[a]
IVb	52	71	246 (4,03)	280 (4,04)	—	381 (4,20)[a]
Vb	52	70	249 (4,04)	302 (3,97)	—	390 (4,27)
VIIa	78	70	250 (4,15)	—	—	383 (4,43)
VIIb	83	83	250 (4,0)	—	—	374 (3,94)
VIIIa	61	57	240 (4,10)	—	—	387 (4,07)
VIIIb	62	91	242 (4,33)	—	—	400 (4,14)
IXb	39	43	238 (4,09)	—	362 (4,25)	—
X	45	41	—	300 (4,37)	340 (3,95)	400 (4,25)[a]
XI	39	18	—	280 (4,13)	345 (4,20)	407 (4,32)
				278 (4,15)	339 (4,32)	401 (4,37)[a]

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[a] In alcohol [11].

EXPERIMENTAL

The melting points of the compounds were determined with a Boetius microheating apparatus and were not corrected. The individuality of the compounds was established by TLC on Silufol UV-254 in benzene–dioxane–glacial acetic acid (20:4:1) (R_f^1) and benzene–ethyl acetate (1:1) (R_f^2) system. The PMR spectra of 5% solutions of the compounds in hexadeuterodimethyl sulfoxide were obtained with a Perkin–Elmer R-12A spectrometer (60 MHz) with tetramethylsilane as the internal standard. The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer. The UV spectra of $5 \cdot 10^{-5}$ M solutions of the compounds in dioxane were recorded with a Specord UV-vis spectrophotometer.

4-Methyl-2-[2-(5-nitro-2-furyl)vinyl]thiazole (I). This compound, with mp 175-176° (from glacial acetic acid, R_f^1 0.73, and R_f^2 0.60, was obtained by the method in [2]. UV spectrum, λ_{max} (log ε): 256 (3.85), 303 (3.99), 400 (5.15) 520 nm (3.33); IR spectrum: 970 cm^{-1} (trans-substituted ethylenes).

4-Methyl-5-nitro-2-[2-(3,5-dinitro-2-furyl)vinyl]thiazole (II). A 2.36-g (0.01 mole) sample of I was added in portions with stirring at room temperature to a nitrating mixture consisting of 50 ml of 93% sulfuric acid and 3 ml (0.05 mole) of 70% nitric acid, after which stirring was continued for 1 h. The mixture was poured over a mixture of ice and water, and the resulting precipitate was removed by filtration was washed with water to give 1.8 g (64%) of yellow prisms with mp 195-197° (from glacial acetic acid), R_f^1 0.77, and R_f^2 0.87. UV spectrum, λ_{max} (log ε): 252 (4.01), 325 (3.94), 390 nm (4.00); IR spectrum: 970 cm^{-1} (trans-substituted ethylenes). Found: C 36.9; H 2.2; N 17.2%. $C_{10}H_6N_4O_7S$. Calculated C 36.8; H 1.9; N 17.2%.

Synthesis of VIIa, b and VIIIa, b. (Table 2). A solution of 0.9 ml (15 mmole) of 70% nitric acid in 50 ml of 95% sulfuric acid was added gradually to a solution or suspension of 10 mmole of thiazole (IIIa, b or IVa, b) in 50 ml of 95% sulfuric acid, after which the mixture was stirred for 1 h. It was then poured over ice, and VIIIa, b were separated by filtration; VIIa, b were precipitated by neutralization to pH 6 with sodium hydroxide solution.

2-Amino-5-nitro-4-[2-(5-nitro-2-furyl)-1-chlorovinyl]thiazole (IXb). A 5.42-g (20 mmole) sample of Vb was dissolved with cooling (ice water) and stirring in 60 ml of 95% sulfuric acid, after which a mixture of 1.26 ml (20 mmole) of 70% nitric acid and 5 ml of 95% sulfuric acid was added dropwise, and the mixture was stirred at room temperature for 1 h and at 60-80° for 2 h. It was then poured over a mixture of ice and water, and the dark-cherry-red precipitate was removed by filtration to give 3.04 g (49%) of IXb.

2-Acetamido-5-nitro-4-[2-(5-nitro-2-furyl)vinyl]thiazole (XI). A 1-ml (15 mmole) sample of 70% nitric acid and two drops of 95% sulfuric acid were added at 15-20° to 12 ml of acetic anhydride, after which a suspension of 2.79 g (10 mmole) of thiazole X in a mixture of 13 ml of acetic anhydride and 10 ml of acetic acid was added at 10-15° in the course of 15 min to the resulting nitrating mixture. The mixture was stirred for another 30 min, after which it was poured over a mixture of ice and water. The product was removed by filtration after 3 h.

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