

PREPARATION OF 5-X-2-(2-NITROVINYL)FURANS AND THEIR REACTIONS WITH NUCLEOPHILES*

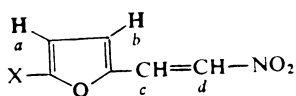
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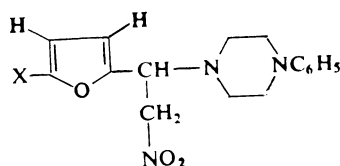
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The title compounds were prepared by condensation of 5-X-2-furaldehydes (X = H, Br, C₆H₅S, C₆H₅SO₂, 4-CH₃-C₆H₄SO₂, 3-O₂N-C₆H₄O) with nitromethane in methanol. 5-Trimethylammonium-2-(2-nitrovinyl)furan bromide (*li*) was obtained from 5-bromo-2-(2-nitrovinyl)furan (*lb*) and trimethylamine in benzene; its thermal decomposition in methanol furnished 5-dimethylamino-2-(2-nitrovinyl)furan (*lh*). Reactions of 5-X-2-(2-nitrovinyl)furans with nitrogen-containing nucleophiles were investigated.

Our preceding papers concerned reaction of furan derivatives with nucleophilic reagents^{1,2}. Nucleophilic substitution of sulfur-functional group in position 5 of the furan ring proceeded quite easily with 5-phenylthio-, 5-heteroarylthio-5-phenylsulfonyl-2-furfurylidene malononitriles¹ and with analogous methyl 2-furfurylidene cyano acetates². These reactions were also kinetically investigated under conditions of pseudomonomolecular reaction at various temperatures, and using various solvents, nucleophilic reagents and substituents in position 5 of the furan ring^{3,4}.



- Ia*, X = H
Ib, X = Br
Ic, X = NO₂
Id, X = C₆H₅S
Ie, X = C₆H₅SO₂
If, X = 4-CH₃-C₆H₄
Ig, X = 3-NO₂-C₆H₄
Ih, X = (CH₃)₂N
Ii, X = (CH₃)₃N⁽⁺⁾-



- IIa*, X = H
IIb, X = C₆H₅S

* Part CLXXXI in the series Furan Derivatives; Part CLXXX: This Journal 49, 2141 (1984).

This paper deals with the preparation of 5-X-2-(2-nitrovinyl)furans *Ia–Ih*, as substrates for reactions with nucleophiles (piperidine, pyrrolidine, morpholine, N-phenylpiperazine). 5-X-2-(2-Nitrovinyl)furans *Ia, Ib, Id–Ig* were prepared by condensation of the corresponding 5-X-2-furaldehydes with nitromethane in methanol under conditions of an aldol condensation. 5-Bromo-2-(2-nitrovinyl)furan *Ib* reacted with trimethylamine in benzene to give 5-nitromethylammonium-2-(2-nitrovinyl)furan bromide (*Ii*), which, when thermally decomposed in methanol afforded 5-dimethylamino-2-(2-nitrovinyl)furan (*Ih*). Experiments to prepare this compound by condensation of 5-dimethylamino-2-furaldehyde with nitromethane failed.

Nucleophiles do not substitute the functional group in position 5 of the furan ring upon reaction with 5-X-2-(2-nitrovinyl)furan, but added to the strongly polarized double bond. As evident, these substrates substantially differ from 5-X-2-furfurylidene malonitriles and methyl 5-X-2-furfurylidene cyanoacetates. Nucleophilic additions with nitrogen-containing nucleophiles well proceeded only with 2-(2-nitrovinyl)furan in ethanol. Structures of the addition products were elucidated with stable N-phenylpiperazine derivatives, since those with piperidine, pyrrolidine and morpholine have a low thermal stability and are, moreover, little soluble. Compounds resulting from reaction of 5-bromo- or 5-nitro-2-(2-nitrovinyl)furans with the above-mentioned nucleophiles in ethanol, acetone, dimethylformamide, or dimethyl sulfoxide were contaminated with tarry products.

The electron absorption spectra of 5-X-2-(2-nitrovinyl)furans reveal three absorption bands at 207–210, 234–255 and 322–428 nm. The first two can be ascribed to $\pi-\pi^*$ and $n\rightarrow\pi^*$ electronic transitions in the furan, benzene, or furylvinyl grouping. The effect of substituent X upon the shift of the last absorption (K-band) is evident from Table I. Electron-donating substituents cause its bathochromic shift, whilst the electron-accepting ones a hypsochromic shift. The values of coupling constants of protons in positions 3 and 4 of the furan ring vary within 3.47 to 4.03 Hz. The coupling constant values for protons of 2-nitrovinyl grouping evidence all the compounds under investigation to have *E*-configuration.

The nucleophilic addition of 5-X-2-(2-nitrovinyl)furans with saturated secondary amines was also kinetically studied under conditions of a pseudomonomolecular reaction in an excess of the nucleophile. The reaction is of second order; in relation to the substrate and nucleophile, it is of first order. The velocity constant values obtained at three various temperatures, as well as thermodynamic parameters of the reaction are listed in Tables II, III and IV. The velocity Ad_N of reaction of 2-(2-nitrovinyl)furan (*Ia*) with nucleophiles at 25–45°C raises with the increasing nucleophilicity (in parentheses) of the reagent: morpholine (5.29) < piperidine (5.59) < pyrrolidine (5.67). Reaction of *Ia* with pyrrolidine served for examination of the solvent effect upon the reaction course. The highest velocity constant was found for non-polar solvents; it decreases with an increasing polarity of the solvent (Table III).

The effect of group X in position 5 of the furan ring upon velocity of the Ad_N reac-

TABLE I
Characteristic data of 5-X-2-(2-nitrovinyl)furans I

Com- pound	Formula (M_f)	M.p., °C yield, %	Calculated/Found				λ_{\max} , nm log ϵ	$^1\text{H NMR}$ (δ , ppm, J, Hz)						
			% C	% H	% N	% S		H _b	H _a	H _c	H _d	J	J	
<i>Ia</i>	C ₆ H ₅ NO ₃ (139.1)	74—75 61	51.80 51.68	3.62 3.54	10.06 9.88	— —	207 3.58	238 3.60	346 4.23	6.56 d 3.53	6.89 d	7.53 m 13.1	7.70 d 13.1	
<i>Ib</i>	C ₆ H ₄ BrNO ₃ (218.0)	112—113 55	33.05 32.92	1.84 1.80	12.84 12.75	— —	208 3.78	234 3.80	355 4.29	6.83 d 3.51	6.51 d	7.50 d 13.1	7.66 d 13.1	
<i>Ic</i>	C ₆ H ₄ N ₂ O ₅ (184.1)	137—138 29	39.14 39.05	2.21 2.17	15.21 15.08	— —	208 3.49	246 3.91	350 4.28	6.21 d 4.03	5.33 d	6.72 d 13.1	6.78 d 13.1	
<i>Id</i>	C ₁₂ H ₉ NO ₃ S (247.2)	59—61 53	58.30 58.21	3.66 3.60	5.66 5.58	12.97 12.81	207 4.19	242 4.02	370 4.14	6.74 d 3.50	6.50 d	7.29 d 13.0	7.51 d 13.0	
<i>Ie</i>	C ₁₂ H ₉ NO ₅ S (279.2)	118—120 36	51.62 51.49	3.24 3.15	5.01 4.97	11.48 11.4	208 3.13	241 3.12	335 3.33	7.24 d 3.47	6.89 d	7.55 d 13.8	7.66 d 13.8	
<i>If</i>	C ₁₃ H ₁₁ NO ₅ S (293.2)	92—94 53	53.25 53.08	3.78 3.72	4.79 4.71	10.93 10.88	210 3.18	255 3.20	335 2.93	7.22 d 3.59	8.87 d	7.54 d 13.3	7.66 d 13.3	
<i>Ig</i>	C ₁₂ H ₈ N ₂ O ₆ (276.2)	131—133 58	36.20 36.08	2.91 2.88	10.14 9.98	— —	207 4.26	248 4.17	370 4.35	7.53 d 3.80	6.25 d	7.80 d 13.4	7.95 d 13.4	
<i>Ih</i>	C ₈ H ₁₀ N ₂ O ₃ (182.1)	130—132 51	52.76 52.63	5.53 5.44	15.38 15.22	— —	208 3.67	262 4.18	428 4.42	7.38 d 3.79	7.16 d	8.07 d 13.5	8.15 d 13.5	

TABLE II

Rate constants k_2 ($l \text{ mol}^{-1} \text{ s}^{-1}$) and thermodynamic parameters of nucleophilic addition to 2-(2-nitrovinyl)furan (*Ia*) in methanol at 25–45°C

Reagent	$T, ^\circ\text{C}$	k_2	E_A^a	ΔH^a	$-\Delta S^b$	ΔG^a
Pyrrolidine	25.2	1.13	16.13	13.65	236.9	84.33
	36.3	1.30				
	45.0	1.67				
Piperidine	25.2	0.47	25.33	22.85	213.4	86.52
	36.3	0.59				
	45.0	0.87				
Morpholine	25.2	0.10	27.36	24.88	219.2	90.28
	36.3	0.14				
	45.0	0.20				

^a in KJ mol^{-1} ; ^b in $\text{J mol}^{-1} \text{ K}^{-1}$.

TABLE III

Rate constants k_2 ($l \text{ mol}^{-1} \text{ s}^{-1}$) of reaction of 2-(2-nitrovinyl)furan (*Ia*) with pyrrolidine in various solvents at $25.2 \pm 0.2^\circ\text{C}$

Solvent	k_2	Solvent	k_2
n-Heptane	7.86	Dimethyl sulfoxide	2.23
Toluene	6.59	Methanol	1.13
Diethyl ether	5.12		

TABLE IV

Rate constants k_2 ($l \text{ mol}^{-1} \text{ s}^{-1}$) of reaction of 5-X-2-(2-nitrovinyl)furan with pyrrolidine and piperidine at $25.2 \pm 0.2^\circ\text{C}$

X	Pyrrolidine	Piperidine
H	1.13	0.47
Br	2.35	1.44
$\text{C}_6\text{H}_5\text{S}$	2.23	1.48
$4\text{-CH}_3\text{-C}_6\text{H}_4\text{SO}_2$	3.42	2.58
$\text{C}_6\text{H}_5\text{SO}_2$	4.60	4.09

tion was investigated in the reaction with pyrrolidine and piperidine at 25·2°C (Table II). The strong electron-accepting group (phenylsulfonyl) bound in position 5 of the furan ring causes an increase of velocity of the Ad_N reaction with both nucleophilic reagents. The Ad_N reaction velocity could not be measured when X = NO₂, since at these conditions a concurrent displacement S_N reaction of the nitro group could take place. As it follows from thermodynamic parameters, the Ad_N reaction proceeds at high negative values of activation entropy (Table II).

EXPERIMENTAL

5-Nitro-2-(2-nitrovinyl)furan (*Ic*) was synthesized by nitration of 2-(2-nitrovinyl)furan⁵.

5-X-2-(2-Nitrovinyl)furans *I*

Aqueous solution of KOH (0·2 mol) was added to a stirred mixture of 5-X-2-furaldehyde (0·1 mol) and nitromethane (0·1 mol) in methanol (300 ml) at 0 ± 2°C. The mixture was stirred for additional 2 h, diluted with ice-cold water (20 ml) and poured into 0·1M-HCl. The separated precipitate was filtered off, dried and crystallized from ethanol. Physicochemical properties of compounds prepared are listed in Table I.

5-Dimethylamino-2-(2-nitrovinyl)furan (*Ih*)

Gaseous trimethylamine (2 g, 33 mmol) was introduced in a solution of 5-bromo-2-(2-nitrovinyl)furan (*Ib*) (5·7 g, 26 mmol) in benzene (100 ml). The red ammonium salt which separated after several hours was filtered off and well washed with ether. The salt (0·9 g, 3·2 mmol) was dissolved in methanol and the solution was heated on a steam bath for 2 h, during which gaseous methyl bromide was freed. The mixture was concentrated to 5 ml, the separated red compound was filtered off, dried and crystallized from ethanol.

Reaction of *Ia* or *Id* with nucleophiles

To the respective furan derivative (10 mmol) dissolved in ethanol (20–30 ml) a slight excess of nucleophile in methanol was added with stirring. A precipitate, which successively separated, was filtered off and dried. The products of addition are yellow crystalline compounds undergoing decomposition at temperatures close to melting points; the N-phenylpiperazine derivatives, which could be crystallized from chloroform, are an exception. Yields of this reaction varied within 80–90%.

1-(Phenylpiperazino)-1-(2-furyl)-2-nitroethane (IIa): m.p. 115–116°C (CHCl₃). For C₁₆H₁₉·N₃O₃ (301·3) calculated: 63·77% C, 6·35% H, 13·95% N; found: 63·58% C, 6·21% H, 13·85% N. UV spectrum, nm (log ε): 209 (4·38), 250 (4·12). ¹H NMR spectrum (δ, ppm): 7·38 (d, 1 H, H_c), 7·00–7·25 (m, 5 H, C₆H₅), 6·35 (dd, 1 H, H_b), 6·23 (d, 1 H, H_a), 4·50–5·12 (m, 3 H, CH₂—CH), 3·15 (t, 4 H, CH_{2c}), 2·44–3·00 (m, 4 H, CH_{2d}), J_{AB} = 3·3 Hz, J_{BC} = 1·7 Hz.

1-(4-Phenylpiperazino)-1-(5-phenylthio-2-furyl)-2-nitroethane (IIb): m.p. 135·5°C (CHCl₃). For C₂₂H₂₃N₃O₃S (409·5) calculated: 64·52% C, 5·66% H, 10·26% N, 7·83% S; found: 64·31% C, 5·48% H, 10·07% N, 7·75% S. UV spectrum, nm (log ε): 207 (4·25), 244 (4·11). ¹H NMR spectrum (δ, ppm): 6·75–7·37 (m, 10 H, C₆H₅), 6·69 (d, 1 H, H_a), 6·33 (d, 1 H, H_b), 4·50–5·12 (m, 3 H, CH₂—CH), 3·15 (t, 4 H, CH_{2c}), 2·44–3·00 (m, 4 H, CH_{2d}), J_{AB} = 3·2 Hz.

Measurement

The reaction kinetics was measured with a Specord UV-VIS spectrophotometer (Zeiss, Jena) in 1 cm tempered cells within 25–45°C in various solvents. Investigated was the maximum drop of the absorption band of the starting *Ia* or *Ib*. The mixture consisted of 0.04–0.1 ml of the respective 2-(2-nitrovinyl)furan (final concentration in the mixture was $4 \cdot 10^{-5}$ – $1 \cdot 10^{-4}$ mol \cdot l $^{-1}$), the stock solution of the nucleophile (2 ml, pyrrolidine, piperidine, morpholine — the final concentration in the mixture was $1 \cdot 10$ mol l $^{-1}$) and that of the solvent (7.90–7.95 ml).

The electron absorption spectra were recorded with the same apparatus in the 200–600 nm range in 1 cm-cells at $5 \cdot 10^{-4}$ – $5 \cdot 10^{-5}$ mol l $^{-1}$ concentration in methanol; the reading accuracy was ± 1 nm. The ^1H NMR spectra of CDCl_3 solutions were taken with a Tesla BS 487 spectrometer operating at 80 MHz; internal reference was tetramethylsilane.

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