SUBSTITUTION REACTIONS OF 1-(5-NITRO-2-FURYL)-2-BROMOETHYLENE*

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The replacement of halogen by CN in 1-(5-nitro-2-furyl)-2-bromoethylene (*I*) proceeds stereospecifically if 1-methyl-2-pyrrolidone is used as solvent. Both *trans*- and *cis*-stereoisomers of 3-(5-nitro-2-furyl)acrylonitrile were prepared. Reaction of *I* with potassium thiocyanate in aqueous acetone under mild conditions gave a mixture of stereoisomeric 1-(5-nitro-2-furyl)-2-thiocyanatoethylenes, reaction with AgSCN or CuSCN required higher temperature and proceeded predominantly with retention of configuration.

The synthesis of 1-(5-nitro-2-furyl)-2-bromoethylene[1] (*I*) which contains a sufficiently reactive bromine has opened the path for a new synthesis of 5-nitro-2-furylethylene derivatives. In the present paper the replacement of the bromo atom by CN and SCN groups is investigated. The possible use of 3-(5-nitrofuryl)acrylonitrile[2] (*II*) as the starting compound for the synthesis of 3-(5-nitro-2-furyl)vinylene-1,2,4-oxadiazoles and 4-(5-nitro-2-furyl)vinylene-1,2,3-triazoles intensified the investigations of synthesis of this compound. The compound *II* can be prepared by reaction of 3-(5-nitro-2-furyl)acrolein oxime acetate with pyridine[3], by dehydration of 3-(5-nitro-2-furyl)-acrylamide with *p*-toluenesulphonyl chloride[4] or with phosphorus trichloride[2], or by the Wittig reaction of 5-nitro-2-furaldehyde with cyanomethylenetriphenylphosphorane[5]. All authors[2-5] report formation of the *trans*-isomer whereas the *cis*-isomer is mentioned only in the work of Saikachi and Nakamura[5]. Our new preparation of both stereoisomers of 3-(5-nitro-2-furyl)acrylonitrile (*II*) consists of the reaction of the stereoisomeric 1-(5-nitro-2-furyl)-2-bromoethylene with CuCN in 1-methyl-2-pyrrolidone at 100–150°C. We studied also substitution of the bromine atom with the SCN group (Scheme 1).

Replacement of halogen on the double bond of β-bromostyrene by a cyano group was accomplished by Newman and Boden[6] who obtained cinnamonitrile in 92% yield. Lapouyade and coworkers[7] studied the stereochemistry of this reaction and found that in 1-methyl-2-pyrrolidone this reaction is stereospecific. 1-Methyl-2-pyrrolidone is the solvent of choice since it dissolves CuCN already at 90°C and the reaction takes

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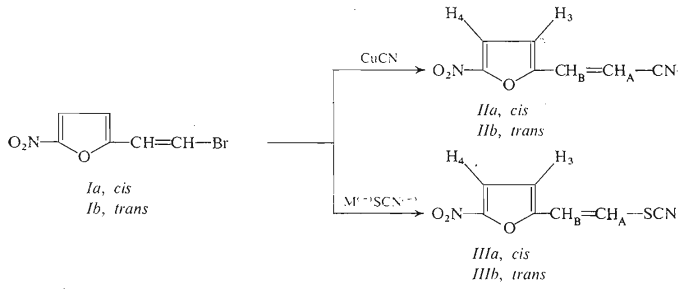
place even with sluggishly reacting halogeno derivatives[7]. We used these results for the study of reactivity of *cis*-1-(5-nitro-2-furyl)-2-bromoethylene[1] (*Ia*) and obtained *cis*-3-(5-nitro-2-furyl)acrylonitrile (*IIa*) in a 55–70% yield by reaction of *Ia* with CuCN in 1-methyl-2-pyrrolidone at 100–150°C in the dark. A mixture of 70% of *Ia* and 30% of *Ib* gave under similar conditions *IIa* and *IIb* in approximately the same ratio as was the ratio of the starting isomers (according to gas–liquid chromatography and ^{1}H-NMR spectroscopy, see Table I). In order to eliminate photoisomerisation, the reactions were carried out under exclusion of light. Gas–liquid chromatography and ^{1}H-NMR spectroscopy did not reveal any thermal isomerisation of *Ia* in 1--methyl-2-pyrrolidone.



In our previous investigations[8–11] we have found that the presence of a thiocyanato group in a side chain of a nitrofurane derivative affects significantly its biological properties. Also 1-(5-thiocyanato-2-furyl)-2-nitroethylene[12], in which the

TABLE I

^{1}H-NMR Data for the Stereoisomeric 3-(5-Nitro-2-furyl)acrylonitriles

Parameter	*IIa*				*IIb*			
	H_A	H_B	H_3	H_4	H_A	H_B	H_3	H_4
δ, ppm[a]	5·59	7·01	6·73	7·27	6·06	7·08	6·68	7·27
J, Hz	12·5		4·0		16·3		4·0	
δ, ppm[b]	6·02	7·33	7·23	7·67	6·41[c]	7·57[c]	7·18[c]	7·67[c]
J, Hz	12·5		4·0		16·3		4·0	

[a] Measured in $CDCl_3$; [b] measured in hexadeuteriodimethyl sulphoxide; [c] the chemical shifts agree with those given in ref.[2].

SCN group is bonded to the furan ring, was found to exhibit bacteriostatic properties. We tried to prepare 1-(5-nitro-2-furyl)-2-thiocyanatoethylene with the aim to study biological properties of mutually conjugated nitro and thiocyanato groups. Saikachi and Takai[13] prepared the analogous 1-(5-nitro-2-furyl)-2-isocyanatoethylene. For the preparation of 1-(5-nitro-2-furyl)-2-thiocyanatoethylene the possibility appeared to replace the bromine in *I* by an SCN group. The replacement of a vinylic halogen by SCN group is described only for activated vinylene halides which in addition to the halogen contain strongly electron-withdrawing groups attached to the double bond. This reaction was found for 2-halogenovinylene ketones[14,15], 1-arylsulphonyl-2-halogenoethylenes[16] and 1-nitro-2-halogenoethylenes[17]. In some cases the halogen attached to a non-activated double bond was replaced by SCN using Cu as catalyst[18]. Reaction of compounds *I* with alkali metal thiocyanates at room temperature is not stereospecific. Treatment of *Ia* with KSCN in aqueous acetone afforded *IIIa* and *IIIb* in the ratio 65 : 35. The compound *Ia* reacted with silver or cuprous thiocyanate only under substantially more vigorous conditions. The reaction with AgSCN was carried out in acetonitrile in sealed ampoules at 130–140°C and its course was followed by visual observation of the formation of the insoluble silver bromide. Optimum yields of the thiocyanates were about 50% and were achieved after 18 hours. Also in this case a mixture of *IIIa* and *IIIb* was formed, in which the isomer of the same configuration as had the starting compound *I* predominated. A mixture of *Ia* and *Ib* afforded a mixture of *IIIa* and *IIIb* with approximately the same ratio as the ratio *Ia* : *Ib*. The isomer ratio in the reaction mixtures was determined by ^{1}H-NMR spectroscopy (Table II).

TABLE II

^{1}H-NMR Data for the Stereoisomeric 1-(5-Nitro-2-furyl)-2-thiocyanatoethylenes

Parameter	*IIIa*				*IIIb*			
	H_A	H_B	H_3	H_4	H_A	H_B	H_3	H_4
δ, ppm[a]	6·58[c]		6·56	7·29	6·46[c]		6·50	7·26
J, Hz	—		4 0		—		4·0	
δ, ppm[b]	6 96	7·00	6·93	7·68	6·98[d]	7·77[d]	7·10[d]	7·70[d]
J, Hz	10·7		4·0		15·3		4·0	

[a] Measured in $CDCl_3$; [b] measured in hexadeuteriodimethyl sulphoxide; [c] singlet (2 H); [d] measured in 1-methyl-2-pyrrolidone.

EXPERIMENTAL

The melting points were determined on a Kofler block and are uncorrected. ^{1}H-NMR spectra were taken in deuteriochloroform or hexadeuteriodimethyl sulphoxide at 25°C on a Tesla BS 487C 80 MHz spectrometer, using tetramethylsilane as internal standard. The IR spectra were measured in $CHCl_3$ on a UR-20 (Zeiss, Jena) spectrophotometer. Gas–liquid chromatographic analyses were performed on a Hewlett-Packard 7620A GC chromatograph and the mass spectra were obtained on an MS 902S AEI instrument.

Cuprous cyanide was freshly prepared and dried at 150°C for 24 h, 1-methyl-2-pyrrolidone was twice distilled. *cis*-1-(5-Nitro-2-furyl)-2-bromoethylene[1] (m.p. 38—39·5°C) was synthesised by 6 hours' refluxing a mixture of *erythro*-2,3-dibromo-3-(5-nitro-2-furyl)propionic acid[19] and sodium carbonate in acetone. The mixture of *cis* and *trans*-1-(5-nitro-2-furyl)-2-bromoethylene was prepared by an analogous reaction in water. *trans*-1-(5-Nitro-2-furyl)-2-bromoethylene (*Ib*) was obtained by photoisomerisation of *Ia* (UV lamp). The purity of *Ib* was checked by gas–liquid chromatography and ^{1}H-NMR spectra.

cis-3-(5-Nitro-2-furyl)acrylonitrile (*IIa*)

A mixture of 2·18 g (0·01 mol) of *cis*-1-(5-nitro-2-furyl)-2-bromoethylene (*Ia*) and CuCN (1·8 g) in 1-methyl-2-pyrrolidone (20 ml) was heated to 130°C for 2 h under exclusion of light. The mixture was poured into water and worked up as described in ref.[20]. Extraction with toluene afforded 1·05 g (65%) of the pure *IIa*, m.p. 73—74·5°C (ethanol). Ref.[5] reports m.p. 71—79°C. For $C_7H_4N_2O_3$ (164·2) calculated: 51·22% C, 2·44% H, 17·07% N; found: 51·39% C, 2·11% H, 17·10% N. IR spectrum ($CHCl_3$): 2221 cm^{-1} (C≡N); for the ^{1}H-NMR data see Table I.

Mixture of IIa *and* IIb: A 70 : 30 mixture (2·18 g; 0·01 mol) of *Ia* and *Ib* and CuCN (1·8 g) in 1-methyl-2-pyrrolidone (20 ml) was heated to 150°C for 5 h, poured into water and worked up according to ref.[20]. Extraction with toluene afforded 1·2 g (75%) of 3-(5-nitro-2-furyl)acrylonitrile, m.p. 98°C (68% *IIa* and 32% *IIb*, according to gas–liquid chromatography and ^{1}H-NMR spectra).

1-(5-Nitro-2-furyl)-2-thiocyanatoethylene (*III*)

a) A solution of *cis*-1-(5-nitro-2-furyl)-2-bromoethylene (*Ia*) (2·18 g; 0·01 mol) in acetone (40 ml) was mixed with KSCN (2 g) in water (10 ml). The mixture was stirred at room temperature for 5 h and at 50°C for 1 h and poured into cold water (50 ml). The separated oil slowly crystallised and was filtered. It was purified by chromatography on a silica gel column (150—250 μm) with benzene as eluant, affording successively: *I* (0·43 g; 20%), m.p. 37—39°C, R_F 0·87; *IIIb* (0·4 g; 20%), m.p. 103—104·5°C, R_F 0·45; *IIIa* (0·9 g; 55%), m.p. 86—89°C, R_F 0·42. For $C_7H_4N_2O_3S$ (196·2) calculated: 42·84% C, 2·05% H, 14·27% N, 16·34% S; found: 42·60% C, 1·94% H, 14·04% N, 16·10% S. IR spectra ($CHCl_3$): ν(SCN) 2175 cm^{-1}, $\nu_{as}(NO_2)$ 1540 cm^{-1}, $\nu_s(NO_2)$ 1360 cm^{-1}. For the ^{1}H-NMR data see Table II.

b) A mixture of *Ia* (1·09 g; 0·005 mol), AgSCN (1·65 g) and acetonitrile (18 ml) was heated to 130°C for 18 h in a sealed ampoule. The precipitate was filtered off and the acetonitrile was evaporated on a rotary evaporator. The residue was dissolved in benzene and purified by column chromatography, yield 55% (82% *IIIa*, 18% *IIIb*).

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