Synthesis, structure, and properties of β-styryl isothiocyanate

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Synthesis, structure, and reactivity of β-styryl isothiocyanate as a new type of heterodiene were studied. The prepared β-styryl isothiocyanate was a mixture of *cis* and *trans* isomers, the structures of which were proved by spectral methods after their separation by preparative gas chromatography. Kinetics of the nucleophilic addition reaction with glycine as well as the results of spectral measurements pointed to the resemblance of β-styryl isothiocyanate to aromatic isothiocyanates. On the basis of the calculated molecular diagram, the possible courses of cycloaddition reactions of β-styryl isothiocyanate were discussed.

High reactivity of isothiocyanates towards nucleophiles made possible their vast utilization in analytical practice (Edman reaction, gene labelling) as well as in synthesis of organic compounds. Lately, isothiocyanates similarly as other heterocumulenes have been frequently used in cycloaddition reactions with suitable substrates giving 1,2-, 1,3-, and 1,4-cycloaddition compounds [1].

We were interested in the behaviour of a new type of heterodiene having the isothiocyanate group in conjugation with the C=C bond. Till now, there have been only mentions of the synthesis of some isothiocyanates of the vinyl type in the literature [2, 3]. In such heterodiene the C=S, C=N, and C=C bonds could theoretically enable 1,2-, 1,3- or 1,4-cycloaddition reactions. To study this problem we chose β-styryl isothiocyanate which was a suitable model also for following the stereospecificity of the cyclization reactions. This paper deals with the synthesis and reactivity of β-styryl isothiocyanate as well as with isolation and proof of the structure of its *cis* and *trans* isomers.

Experimental

The i.r. spectra of the synthesized compounds were taken on a double-beam UR 20 (Zeiss, Jena) spectrophotometer in the region of 800—3500 cm^{-1} in chloroform. The apparatus was calibrated with a polystyrene foil.

The u.v. spectra were taken on a recording Perkin—Elmer 402 spectrophotometer at 25 ± 0.2°C using 10-mm cells.

The n.m.r. spectra were measured on a Varian 100 apparatus in deuterated acetone and in deuterated chloroform (compound *II*). HMDS was used as the internal standard.

1-Phenyl-1-chloroethyl isothiocyanate (II)

To a mixture of saturated aqueous solution of 1-phenyl-1-chloroethylammonium chloride *I* (12 g; 0.062 mole) [4] and thiophosgene (7.8 g; 0.068 mole) dissolved in chloroform (200 ml), a few drops of phenolphthalein was added and then a 1 M aqueous solution of sodium hydroxide was added dropwise under vigorous stirring till the rose colour of the reaction mixture was durable. The chloroform layer was separated, dried over calcium chloride, evaporated, and the residue was chromatographed on a column of silica gel (300 g; petroleum ether : ether = 8 : 1). Yield 9.8 g (79.5%), b.p. 117—118°C/ /2 torr.

For C_9H_8NSCl (197.71) calculated: 55.51% C, 4.15% H, 7.19% N; found: 55.45% C, 4.19% H, 7.04% N.

The i.r. spectrum ($CHCl_3$) $\nu(NCS) = 2095\ cm^{-1}$; u.v. (cyclohexane) $\lambda_{max} = 245$ ($\log \varepsilon = 3.04$); n.m.r. ($CDCl_3$) $\tau = 2.69$ (aromatic protons), $\tau = 5.04$ triplet (CH), $\tau = 6.12$ doublet (CH_2).

β-*Styryl isothiocyanate (III and IV)*

A solution of *II* (2.4 g; 0.012 mole) in dioxan (12 ml), triethylamine (3 g; 0.029 mole), and a few crystals of hydroquinone were sealed in an ampoule under nitrogen and heated at 100°C for 36 hrs. The precipitated triethylammonium chloride was filtered, washed with ether, and the evaporated filtrate was chromatographed on a column of silica gel (300 g; petroleum ether : ether = 9 : 1). The obtained substance (1.3 g; 67%) had b.p. 83—86°C/0.25 torr.

For C_9H_7NS (161.26) calculated: 67.05% C, 4.38% H, 8.69% N; found: 67.17% C, 4.49% H, 8.56% N.

The obtained β-styryl isothiocyanate was a mixture of *cis* and *trans* isomers in the ratio 1 : 4 (determined by gas chromatography). These isomers were separated by gas chromatography on a Carlo Erba Fractovap 2400 V apparatus. The working conditions used were the same as described in [6].

cis β-*Styryl isothiocyanate (III)*

The i.r. ($CHCl_3$) $\nu(NCS) = 2122\ cm^{-1}$, $\nu(C{=}C) = 1621\ cm^{-1}$; u.v. (cyclohexane) $\lambda_{max} = 301$ nm ($\log \varepsilon = 4.20$); n.m.r. (CD_3COCD_3) $\tau = 3.71$, two doublets $J_{AB} = 8.7$ Hz.

trans β-*Styryl isothiocyanate (IV)*

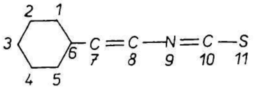
The i.r. ($CHCl_3$) $\nu(NCS) = 2125\ cm^{-1}$, $\nu(C{=}C) = 1628\ cm^{-1}$, $\nu(C{-}H)(trans) = 939\ cm^{-1}$; u.v. (cyclohexane) $\lambda_{max} = 305$ nm ($\log \varepsilon = 4.42$); n.m.r. (CD_3COCD_3) $\tau = 3.22$, two doublets $J_{AB} = 13.9$ Hz.

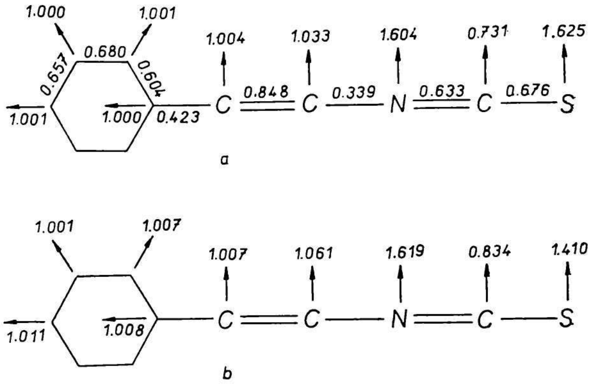
Kinetic measurements

Kinetic measurements of the reaction of isothiocyanates with glycine were accomplished spectrophotometrically in 0.1 M borate buffer by the described method [7] at 325 nm in the case of β-styryl isothiocyanate and at 275 nm in the case of phenyl isothiocyanate. The initial concentrations of the isothiocyanates were $4 \times 10^{-5}\ mol\ l^{-1}$ and the concentration of glycine was $4 \times 10^{-3}\ mol\ l^{-1}$. For the reaction of β-styryl isothiocyanate with glycine, the found value of k was $42.7\ l\ mol^{-1}\ min^{-1}$ and for that of phenyl isothiocyanate with glycine $k = 23.5\ l\ mol^{-1}\ min^{-1}$ under the same conditions.

Calculation of molecular diagram

The molecular diagram of β-styryl isothiocyanate was calculated by a simple HMO method using the same parameters as in the case of aryl isothiocyanates [8].





Scheme 1

Molecular diagram of the ground and excited states of β-styryl isothiocyanate.
a) ground state; *b*) excited state.

Scheme 1 shows the calculated total π-electron densities of both the ground and the excited states of β-styryl isothiocyanate as well as the orders of bonds of the ground state. The calculated superdelocalizabilities of the individual positions of β-styryl isothiocyanate with the same numbering as in Scheme 1 are given in Table 1.

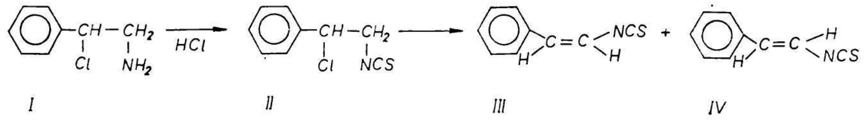
Table 1

The calculated superdelocalizabilities of the individual positions
of β-styryl isothiocyanate

Position	$S_{\mathrm{N,r}}$	$S_{\mathrm{E,r}}$
1	−0.958	0.968
2	−0.829	0.829
3	−0.934	0.945
6	−0.752	0.752
7	−1.045	1.088
8	−1.177	1.177
9	−0.379	0.822
10	−1.630	0.494
11	−0.517	2.324

Results and discussion

The starting compound for the synthesis of β-styryl isothiocyanate was the known 1-phenyl-1-chloroethylammonium chloride (*I*) [4] from which 1-phenyl-1-chloroethyl isothiocyanate (*II*) was obtained by thiophosgene method [5]. Dehydrohalogenation of this compound by triethylamine gave β-styryl isothiocyanate (see Scheme 2).



Scheme 2

The obtained product was a mixture of *cis* and *trans* isomers (*III* and *IV*) in the ratio 1 : 4. This mixture was separated by preparative gas chromatography and the structures of the individual isomers were unambiguously proved by spectral methods.

While the n.m.r. spectrum of 1-phenyl-1-chloroethyl isothiocyanate (*II*) showed the appropriate doublet and triplet of the vicinal protons of CH and CH_2 groups in the region of 5—6.2 τ, in the spectrum of the β-styryl isothiocyanate isomers two doublets of olefinic protons characteristic of *trans* (Fig. 1*a*) and *cis* (Fig. 1*b*) derivatives appeared.

The i.r. spectra of the synthesized compounds revealed a broad absorption band in the region of 2100 cm^{-1} characteristic of the —NCS group. With 1-phenyl-1-chloroethyl isothiocyanate the absorption band was split; besides a significant absorption at

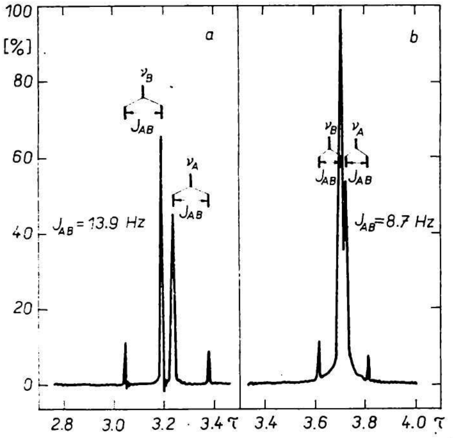


Fig. 1. The n.m.r. spectrum of *cis* and *trans* β-styryl isothiocyanates in the region of olefinic protons.
a) *trans* β-styryl isothiocyanate; *b*) *cis* β-styryl isothiocyanate.
J_{AB} = 13.9 Hz (*a*); J_{AB} = 8.7 Hz (*b*).

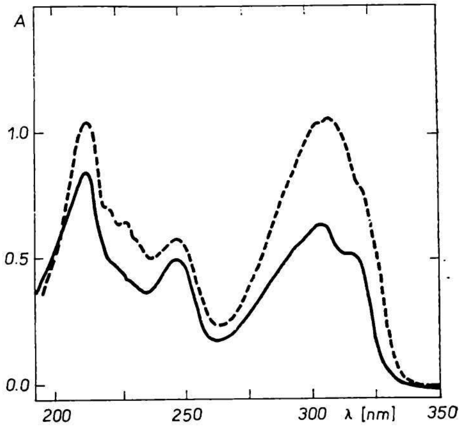


Fig. 2. The u.v. spectra of *cis* and *trans* β-styryl isothiocyanates.
——— *cis* β-styryl isothiocyanate;
- - - - - - *trans* β-styryl isothiocyanate.

2095 cm^{-1} a further maximum appeared at 2235 cm^{-1}. The shape of this absorption band is characteristic of the —NCS group that is not in conjugation with the aromatic ring. The i.r. spectra of the β-styryl isothiocyanate isomers showed a broad absorption band characteristic of aromatic isothiocyanates with the maximum at 2122 cm^{-1} (*cis* isomer) and 2125 cm^{-1} (*trans* isomer). Moreover, they revealed a significant absorption band belonging to the stretching vibration of the C=C bond at 1621 cm^{-1} (*cis* isomer) and 1628 cm^{-1} (*trans* isomer). The *trans* isomer showed a further significant band at 939 cm^{-1} belonging to the deformation vibrations of the C—H bond in *trans* derivatives.

The u.v. spectrum of 1-phenyl-1-chloroethyl isothiocyanate showed only absorption at 246 nm ($\log \varepsilon = 3.04$). β-Styryl isothiocyanate isomers (Fig. 2), in which the —NCS group was in conjugation with the double bond and the aromatic ring showed a pronounced maximum at 301 nm ($\log \varepsilon = 4.20$; *cis* isomer) and 305 nm ($\log \varepsilon = 4.42$; *trans* isomer).

The results of spectral methods unambiguously proved not only the structures of the β-styryl isothiocyanate isomers but also their resemblance to aromatic isothiocyanates. The kinetics of nucleophilic addition reaction of the obtained mixture of the β-styryl isothiocyanate isomers and for comparison also that of phenyl isothiocyanate with glycine at pH 9.8 under the conditions of pseudomonomolecular reaction were also followed. For β-styryl isothiocyanate the reaction rate constant k was found to be 42.7 l mol^{-1} min^{-1} and for phenyl isothiocyanate 23.5 l mol^{-1} min^{-1} under the same conditions. The rate constants of the substituted benzyl isothiocyanates varied in the range of 3—7 l mol^{-1} min^{-1} [5]. Comparison of the rate constants showed that β-styryl isothiocyanate was approximately twice more reactive than phenyl isothiocyanate and its reactivity differed orderly from that of benzyl isothiocyanate. These results similarly as those obtained by spectral methods proved the resemblance of β-styryl isothiocyanate to aromatic isothiocyanates.

To study the reactivity of the synthesized β-styryl isothiocyanate in cycloaddition reactions, its molecular diagrams in the ground and excited states were calculated by a simple Hückel method (Scheme 1).

The values of the molecular diagram did not point to a significant mesomeric interaction of the —NCS group with the conjugated system. However, the obtained values need not be determining for the orientation of cycloaddition reactions considering the high polarizability of the mentioned conjugation system and the possible electromeric effects.

On the basis of the obtained quantum-chemical calculations it can be assumed that 1,2-cycloadditions will predominantly proceed on the C=S bond (higher π-electron density on the sulfur atom) while 1,4-cycloadditions will require dienophiles with significant nucleophilic character because the terminal carbon of the heterodiene shows only negligible effective charge.

If the studied compound is considered as a styrene derivative there appears a further possibility of using it as 1,3-dipolarophile for 1,3-cycloadditions on the C=C bond.

The mentioned assumptions will be discussed later.

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