2-(4-X-2-Nitrophenylhydrazino)benzothiazoles

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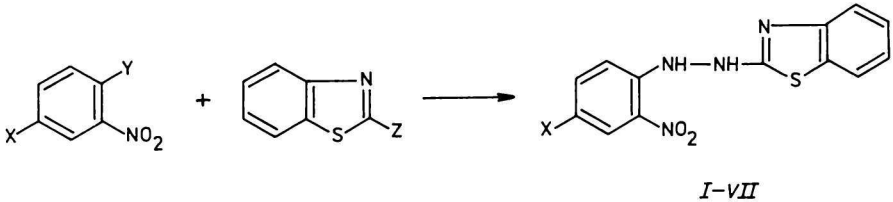
2-(4-X-2-Nitrophenylhydrazino)benzothiazoles were prepared by the nucleophilic substitution of either fluorine atom in 2-fluorobenzothiazole with 4-substituted 2-nitrophenylhydrazine or a halogen atom in the molecule of 4-substituted 2-nitro-1-halobenzene with 2-hydrazinobenzothiazole.

Compounds which contain the benzothiazole skeleton are known as physiologically active compounds with an influence on plant growth [1]. Our aim was to prepare compounds with such a complex substituent being on the mentioned structure as would enable us to build a heterocyclic skeleton as a substituent. Compounds here described are namely precursors of compounds with benzotriazole 1-oxide system in connection with the mentioned skeleton of benzothiazole.

2-(4-X-2-Nitrophenylhydrazino)benzothiazoles *I*—*VII* were prepared by the nucleophilic substitution. In case the substituent in position 4 was CH_3O, CH_3, Cl, Br, or it was unsubstituted derivative (compounds *I*—*V*) as the substrate 2-fluorobenzothiazole [2] was used. 4-Substituted 2-nitrophenylhydrazines served as nucleophiles. In case of strongly electronwithdrawing substituents in position 4 (compounds *VI* and *VII*) 2-hydrazinobenzothiazole was used as reagent and 2,4-dinitro-1-fluorobenzene and 4-cyano-2-nitro-1-chlorobenzene were used as substrates. Compound *V* was prepared *via* both ways, *i.e.* from 4-bromo-2-nitrophenylhydrazine and 2-nitro-1,4-dibromobenzene (Scheme 1).

4-Substituted 2-nitrophenylhydrazines were prepared from the appropriate anilines by diazotation and following reduction with stannous chloride. The diazonium salt was dropwise added into solution of stannous chloride in hydrochloric acid. In this way we prevented side reactions. After the reaction complex salts of these hydrazino derivatives with stannous chloride were formed. An exception was 4-methoxy-2-nitrophenylhydrazine that formed corresponding hydrazinium chloride. Substituted hydrazines were isolated from these complexes through hydrazones prepared by the reactions with acetone. In this way the organic part was quite easily separated from the inorganic one. The formed acetone hydrazones then were hydrolyzed by a short boiling in hydro-

chloric acid (36 %). After cooling down the crystalline hydrazinium chlorides were separated. But these are rather well soluble in concentrated hydrochloric acid. The only small change in pH, for instance by the dilution of the reaction mixture was accompanied by the reverse reaction with present acetone in the reaction mixture to hydrazone. In order to increase the yield of the reaction we found the removal of all the solvent from mother liquor inclusive acetone on a vacuum evaporator to be very effective. The corresponding substituted hydrazine was then precipitated from the aqueous solution of hydrazinium chloride in the crystalline form.



I–VII

	X	Y	Z
I	CH_3O	NH_2NH	F
II	CH_3	NH_2NH	F
III	H	NH_2NH	F
IV	Cl	NH_2NH	F
V	Br	NH_2NH resp. Br	F resp. NH_2NH
VI	CN	Cl	NH_2NH
VII	NO_2	F	NH_2NH

Scheme 1

The nucleophilic substitution was carried out in ethanol. The method using in the reaction mixture 2-fluorobenzothiazole (1 mol) with substituted phenylhydrazine (2 mol; 1 mol was used to bind released hydrogen fluoride) was shown to be the best method of preparation. An application of another base than the corresponding phenylhydrazine (for example pyridine or sodium hydrogen carbonate) led to the catalysis of the consequent reaction, *i.e.* the cyclization to 6-substituted 2-(2-benzothiazolyl)benzotriazole 1-oxide. The preparation of 2-(4-methoxy-2-nitrophenylhydrazino)benzothiazole (*I*) needed changed amount of substance ratio of components to 1 1 because a higher amount of 4-methoxy-2-nitrophenylhydrazine caused the consequent cyclization due to its fairly high basicity.

The course of the nucleophilic substitution was followed by TLC. It was shown that the rate of the reaction depends on the substituent in position 4. The reactions of 4-substituted 2-nitrophenylhydrazines with electrondonating sub-

stituents were always quicker than those with electronwithdrawing groups as it might be expected. The reaction time was in the range of 6—25 h.

2-Hydrazinobenzothiazole was prepared from potassium 2-benzothiazolesulfonate [3] by the substitution with hydrazine hydrate. Potassium 2-benzothiazolesulfonate was prepared from 2-mercaptobenzothiazole by the oxidation of its corresponding salt with hydrogen peroxide [4]. The nucleophilic substitution also here was carried out in ethanolic solution in amount of substance ratio of components 1 1. The substitution of the fluorine atom in 2,4-dinitro-1-fluorobenzene was finished within 7 h but the substitution of the chlorine atom in 4-cyano-2-nitro-1-chlorobenzene lasted longer (45 h).

2-(4-Bromo-2-nitrophenylhydrazino)benzothiazole (*V*) was prepared *via* both ways.

The structure of the synthesized compounds was proved by the elemental analysis (Table 1), IR and ^{1}H NMR spectra. In the IR spectrum of compounds *I*—*VII* one can find two significant bands at $\tilde{\nu} \approx 3220\ \mathrm{cm}^{-1}$ and $3320\ \mathrm{cm}^{-1}$ corresponding to the stretching vibration of N—H. The band of the NO_2 group appeared in the region of $\tilde{\nu} = 1320$—$1345\ \mathrm{cm}^{-1}$ (symmetrical stretching vibration) and 1525—$1580\ \mathrm{cm}^{-1}$ (asymmetrical vibration). Stretching vibration of C=N was observed at $\tilde{\nu} = 1610\ \mathrm{cm}^{-1}$

Also ^{1}H NMR spectra (Table 3) support the structure. Two singlet signals of hydrogen atoms bound at nitrogen atoms disappeared after addition of D_2O due to fast exchange against deuterium. One of those singlets the chemical shift of which changes with the changed substituent in position 4 is the signal of that hydrogen bound at nitrogen atom connected with benzene ring bearing the nitro group.

In all the spectra of compounds with substituents in position 4 with a significant influence, the signal of hydrogen atom in position 3 (next to nitro group) of the aromatic ring is always situated down-field of the other aromatic hydrogen atoms and split into doublet by the interaction with the hydrogen atom in position 5. The integral intensity corresponds to the whole amount of hydrogen atoms.

Experimental

Melting points were measured on a Kofler hot-stage 79-2106 (Wägetechnik Rapido). Elemental analysis (Table 1) was performed with an elemental analyzer CHN 1102 (Erba). TLC was carried out on silufol UV 254 (Kavalier, Votice), eluent chloroform, detection with Fluotest Universal (Quarzlampen, Hanau). Infrared spectra were taken on a spectrometer SP 1000 (Unicam) in $CHBr_3$, electronic spectra (Table 2) on an SP 1800 (Unicam) in ethanol and ^{1}H NMR spectra (Table 3) on a BS 567 (Tesla) (100 MHz) in DMSO-d_6, internal standard TMS.

Table 1

Characterization of the synthesized compounds

Compound	Formula	M_r	w_i(calc.)/% w_i(found)/%			Yield	M. p./°C
			C	H	N	%	Solvent
I	$C_{14}H_{12}N_4O_3S$	316.32	53.16	3.82	17.71	29	134—136
			53.32	3.68	17.12		50 % ethanol
II	$C_{14}H_9N_4O_2S$	300.33	55.99	4.02	18.65	45	164—166
			55.93	4.13	18.22		50 % ethanol
III	$C_{13}H_{10}N_4O_2S$	286.31	54.54	3.52	19.57	59	183—185
			54.22	3.24	19.29		Ethanol
IV	$C_{13}H_9ClN_4O_2S$	320.75	48.68	2.83	17.47	37	183
			48.35	2.74	16.99		50 % ethanol
V	$C_{13}H_9BrN_4O_2S$	365.20	42.75	2.48	15.34	87	190—191
			42.43	2.31	15.20		50 % ethanol
VI	$C_{14}H_9N_5O_2S$	311.30	54.01	2.91	22.40	24	228—229
			53.98	2.76	22.18		Ethanol
VII	$C_{13}H_9N_5O_4S$	331.29	47.13	2.73	21.13	71	222—223
			46.87	2.59	20.89		Ethanol

Table 2

Electronic spectra of the synthesized compounds *I*—*VII*

Compound	λ_{max}/nm (ε/(m^2 mol^{-1}))		
I	230 (2766)	262 (1230)	400 (1120)
II	226 (3445)	269 (1520)	386 (460)
III	241 (3810)	274 (1880)	386 (539)
IV	230 (3576)	266 (1890)	389 (620)
V	228 (1938)	266 (1150)	388 (340)
VI	216 (3130)	254 (2013)	350 (1040)
VII	213 (4269)	262 (1660)	370 (1240)

2-Mercaptobenzothiazole was a commercial product (Research Institute of Chemical Technology, Bratislava) as well as 2,4-dinitrophenylhydrazine (Fluka). 2-Nitrophenylhydrazine was prepared according to [5, 6], 4-methyl-2-nitrophenylhydrazine to [7], 4-methoxy-2-nitrophenylhydrazine to [8], 4-chloro-2-nitrophenylhydrazine to [6], 4-bromo-2-nitrophenylhydrazine according to [9] and 4-cyano-2-nitro-1-chlorobenzene according to [10].

4-X-2-Nitrophenylhydrazines

Suspension of 4-substituted 2-nitroaniline (0.07 mol) in concentrated hydrochloric acid (90 cm^3) was heated up to 60 °C and then after cooling down at the temperature of

Table 3

^{1}H NMR spectral characteristics of the synthesized compounds *I*—*VII*

Compound	δ				
	(s, s, 1H, NH)		(m, H_{arom})		(H_{arom} and others)
I	10.27	9.61	6.99—7.76	(7H)	8.03 (d, 1H, J = 6.4 Hz) 3.78 (s, 3H, CH_3O)
II	10.37	9.71	7.08—8.08	(7H)	2.29 (s, 3H, CH_3)
III	9.86	9.24	6.93—8.28	(8H)	
IV	10.41	9.96	7.01—7.84	(7H)	8.13 (d, 1H, J = 2.3 Hz)
V	10.41	9.97	7.08—7.88	(7H)	8.24 (d, 1H, J = 2.3 Hz)
VI	10.76	10.40	7.10—8.04	(7H)	8.59 (d, 1H, J = 1.8 Hz)
VII	10.64	3.32	7.10—8.41	(7H)	8.89 (d, 1H, J = 2.64 Hz)

3 °C the solution of sodium nitrite (5 g; 0.07 mol) in water (15 cm^3) was dropwise added. The formed solution was filtered and dropwise added under agitation into solution of stannous chloride (32 g; 0.14 mol) in concentrated hydrochloric acid (32 cm^3) not to exceed the temperature of 8 °C. Then the stirring continued for another 30 min. The formed precipitate of stannous complex salt was filtered off, washed with cold water and finally dissolved in hot water. The hot solution was filtered and mixed with acetone (about 10 cm^3). A formation of crystalline acetone hydrazone was immediately observed. After cooling down the precipitate was filtered off and washed with water. Hydrolysis was carried out boiling in concentrated hydrochloric acid (25 cm^3) under condenser. The end of the reaction was manifested by the change of the reaction mixture colour. After crystallization hydrazinium chloride from the reaction mixture was collected, washed with concentrated hydrochloric acid and dissolved in water. Setting pH of the solution with sodium acetate caused formation of hydrazine free base crystals. Those were filtered off, washed properly with water and dried. Another portion of hydrazine was obtained from mother liquor after hydrolysis of hydrazone evaporating on a vacuum evaporator to dryness. The dry rest was dissolved in water and pH set up again with sodium acetate.

2-(4-X-2-Nitrophenylhydrazino)benzothiazoles I—VII

Method A (for preparation of compounds *I*—*V*). 4-Substituted 2-nitrophenylhydrazine (0.02 mol) is combined with 2-fluorobenzothiazole (1.54 g; 0.01 mol) in ethanol (50 cm^3) and refluxed. The course of the reaction is followed by TLC. The reaction is stopped after 2-fluorobenzothiazole disappeared. Then the reaction mixture is cooled down, crystals are separated and recrystallized.

Method B (for preparation of compounds *V*—*VII*). 2-Hydrazinobenzothiazole (2 g; 0.01 mol) was dissolved in ethanol (30 cm^3) and 4-substituted 2-nitro-1-halobenzene (0.01 mol) was added. The mixture was refluxed till 2-hydrazinobenzothiazole disappeared (followed by TLC). Then the reaction mixture was cooled down, crystals were separated and recrystallized.

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