

**XXXVIII. Synthesis and spectral characteristics
of 3,3'-dimethyl-2,2'-(polymethylenedithio)dibenzothiazolium salts**

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2,2'-(Methylenedithio)dibenzothiazole reacts with CH_3I or $(\text{CH}_3)_2\text{SO}_4$ to afford 3,3'-dimethyl-2,2'-(methylenedithio)dibenzothiazolium diiodide resp. di(methylsulfate). From 2,2'-(ethylenedithio)dibenzothiazole 2,3-dihydrothiazolo[2,3-*b*]benzothiazolium iodide is obtained and 2,2'-(trimethylenedithio)dibenzothiazole gives 3,4-dihydro-2*H*-1,3-thiazino[2,3-*b*]benzothiazolium iodide. The mechanism of the formation of these tricyclic compounds is reported. The structure of the compounds was confirmed using ^1H NMR, ^{13}C NMR, and UV spectroscopy.

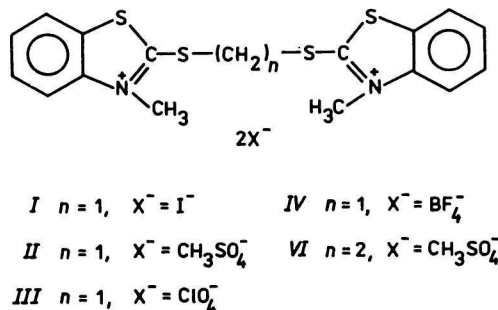
2,2'-(Метилендитио)дибензотиазол взаимодействует с CH_3I или $(\text{CH}_3)_2\text{SO}_4$ с образованием диодида и диметилсульфата 3,3'-диметил-2,2'-(метилендитио)дибензотиазолия, соответственно. Из 2,2'-(этилендитио)дибензотиазола образуется иодид 2,3-дигидротиазоло[2,3-*b*]бензотиазолия, а из 2,2'-(триметилендитио)дибензотиазола образуется 3,4-дигидро-2*H*-1,3-тиазино[2,3-*b*]бензотиазолий иодид. Описывается механизм образования этих трициклических соединений. Строение полученных соединений было подтверждено с помощью ^1H и ^{13}C ЯМР, а также УФ-спектроскопии.

It follows from the existing knowledge that benzothiazole belongs to the weakest bases and nucleophiles in the series of pyridine type compounds [1]. A difficult course of the quaternization reactions indicates a low reactivity of benzothiazole derivatives having in the position 2 an alkyl chain attached through a sulfur atom. By alkylation of these compounds usually a mixture of products is generated [2, 3]. The above facts were significantly manifested upon the quaternization of 2,2'-(polymethylenedithio)dibenzothiazoles synthesized in the framework of study of relation between the structure and growth-regulating activity of these compounds.

The starting 2,2'-(methylenedithio)dibenzothiazole was prepared by treating potassium salt of 2-mercaptobenzothiazole with diiodomethane in ethanol. 2,2'-(Polymethylenedithio)dibenzothiazoles were prepared by the reaction with

1,2-dichloroethane, 1,3-dibromopropane, and 1,4-dibromobutane. The quaternary salts were synthesized with CH_3I and $(\text{CH}_3)_2\text{SO}_4$ in anhydrous dimethylformamide. The preparation of quaternary salts with other alkylating agents like ethyl iodide, allyl iodide, and benzyl bromide was unsuccessful. The reaction rate depends on the length of polymethylene chain.

2,2'-(Methylenedithio)dibenzothiazole gave with CH_3I 3,3'-dimethyl-2,2'-(methylenedithio)dibenzothiazolium diiodide (*I*) and with $(\text{CH}_3)_2\text{SO}_4$ the appropriate di(methylsulfate) (*II*) (Formula 1, Table 1). In the ^1H NMR spectra



Formula 1

of these compounds the singlets of methylene group hydrogens at $\delta = 3.3$ ppm and CH_3 group hydrogens on the quaternary nitrogen at $\delta = 4.1$ ppm were observed. The multiplets of aromatic protons are in the region of $\delta = 7.5\text{--}8.2$ ppm and the singlet of six hydrogens of methylsulfate anions at $\delta = 3.4$ ppm is observed. The above values unambiguously confirm the assumed structure (Formula 1). To investigate the influence of anion on the biological activity, the salts *III* and *IV* were prepared from compound *I* by exchange of I^- for ClO_4^- and BF_4^- , respectively.

By the reaction of 2,2'-(ethylenedithio)dibenzothiazole with dimethyl sulfate 3,3'-dimethyl-2,2'-(ethylenedithio)dibenzothiazolium di(methylsulfate) (*V*) was prepared. Upon the reaction with CH_3I a derivative was formed, which in the ^1H NMR spectra reveals a triplet at $\delta = 4.55$ ppm ($J = 8$ Hz) and 5.1 ppm ($J = 8$ Hz) and a multiplet of aromatic protons in the region of $\delta = 7.6\text{--}8.1$ ppm (Table 2). The intensity ratio of these signals (1 : 1 : 2) as well as the results of elemental analysis confirm that upon the reaction 2,3-dihydrothiazolo[2,3-*b*]benzothiazolium iodide (*V*) (Scheme 1) is formed. The structure of compound was confirmed by ^{13}C NMR spectrum, in which the signals of two CH_2 groups were found and proved by DEPT and APT methods: δ/ppm : 181.61 (C-2), 137.29 (C-3a), 115.50 (C-4), 128.59 (C-5), 126.61 (C-6), 124.71 (C-7), 133.75 (C-7a). The above values of chemical shifts are in a good agreement with the data cal-

Table 1
Characterization of the synthesized benzothiazolium salts

Compound	Formula	M_r	w_i (calc.)/% w_i (found)/%					Yield %	M.p. °C
			C	H	N	S	I (Cl)		
<i>I</i>	$C_{17}H_{16}I_2N_2S_4$	630.38	32.39 32.14	2.56 2.87	4.44 4.12	20.34 20.18	40.26 40.11	60	143—146
<i>II</i>	$C_{19}H_{22}N_2O_8S_6$	598.81	38.39 38.09	3.89 3.98	2.62 2.83	32.28 31.97	— —	50	138—142
<i>III</i>	$C_{17}H_{16}Cl_2N_2O_8S_4$	575.48				22.28 21.97	12.32 12.06	75	181—183
<i>IV</i>	$C_{17}H_{16}B_2F_8N_2S_2$	474.18				23.38 23.27	— —	60	169—172
<i>V</i>	$C_9H_8INS_2$	321.19	33.36 33.62	2.51 2.38	4.36 4.12	19.99 20.08	39.51 39.22	80	242—245
<i>VI</i>	$C_{20}H_{24}N_2O_8S_6$	612.78	39.18 39.41	3.94 3.79	4.57 4.44	31.38 31.53	— —	45	224—228
<i>VII</i>	$C_{10}H_{10}INS_2$	335.22	35.83 36.07	3.01 2.93	4.18 3.98	19.13 19.22	37.86 37.53	80	278—282

Table 2

UV and ^1H NMR spectra of the synthesized benzothiazolium salts

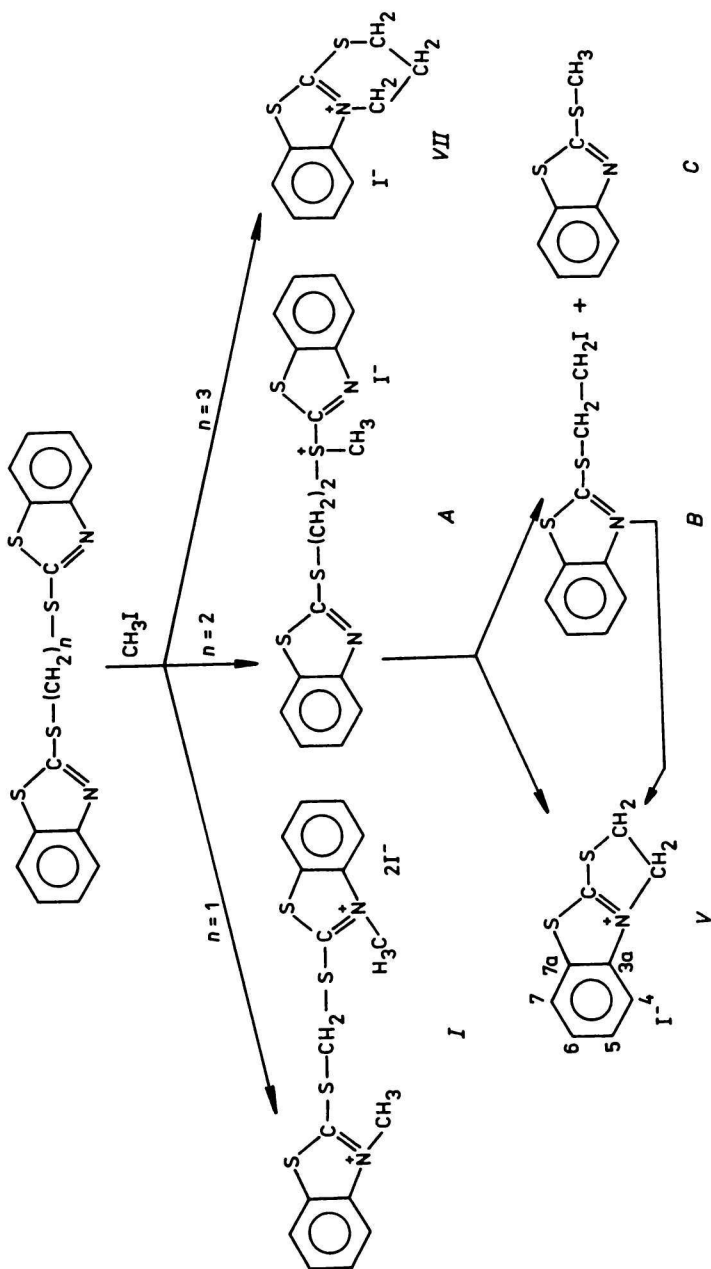
Compound	λ/nm $\log(\epsilon/(\text{m}^2 \text{mol}^{-1}))$		δ/ppm
<i>I</i>	248	307	"3.3 (s, 2H, S—CH ₂), 4.1 (s, 6H, N ⁺ —CH ₃), 7.5—8.2 (m, 8H, H _{arom})
<i>II</i>	225	365	"3.3 (s, 2H, S—CH ₂), 3.4 (s, 6H, CH ₃ SO ₄ ⁻), 3.38 3.37 4.1 (s, 6H, N ⁺ —CH ₃), 7.5—8.1 (m, 8H, H _{arom})
<i>V</i>	225	280	"4.55 (t, 2H, S—CH ₂ , $J = 8$ Hz), 5.1 (t, 2H, 3.53 3.32 N ⁺ —CH ₂ , $J = 8$ Hz), 7.6—8.1 (m, 4H, H _{arom})
<i>VI</i>	225	300	"3.6 (s, 4H, S—CH ₂), 3.45 (s, 6H, CH ₃ SO ₄ ⁻), 3.56 3.29 4.05 (s, 6H, N ⁺ —CH ₃), 7.6—8.0 (m, 8H, H _{arom})
<i>VII</i>	248	309	"3.52 (t, 2H, S—CH ₂ , $J = 7$ Hz), 2.65 (m, 2H, CH ₂ —CH ₂ —CH ₂), 4.59 (t, 2H, N ⁺ —CH ₂ , $J = 7$ Hz), 7.58—7.9 (m, 4H, H _{arom})

a) Measured in DMSO; *b*) measured in CF₃COOH.

culated using additive increments for a chosen model system: SCN—CH₂—CH₂—N[±] [4]. For SCN—CH₂— a value of $\delta = 35.2$ ppm and for —CH₂—N[±] a value of $\delta = 47.2$ ppm was calculated. On the basis of these data the carbon in —CH₂—S— was assigned the value of $\delta = 37.34$ ppm and the carbon in >N⁺—CH₂— the value $\delta = 51.34$ ppm. It follows from the comparison of ^{13}C NMR spectra of pyridine, thiazole and benzothiazole derivatives measured in DMSO and CF₃COOH that the redistribution of charge density due to the protonization causes a change in the values of chemical shifts of all carbons of the above heterocycles [5].

2,2'-(Trimethylenedithio)dibenzothiazole reacts only with CH₃I to give 3,4-dihydro-2*H*-1,3-thiazino[2,3-*b*]benzothiazolium iodide (*VII*). The alkylation with (CH₃)₂SO₄ does not take place even after prolongation of the reaction time for 4 d and the increase of reaction temperature to 100 °C. In the ^1H NMR spectra of *VII* two triplets at $\delta = 3.52$ ppm and 4.59 ppm, $J = 7$ Hz, a multiplet with a centre at $\delta = 2.65$ ppm and signals of the multiplet of aromatic protons in the region of $\delta = 7.58$ —7.90 ppm were observed. The ratio of signals intensities was 1 : 1 : 1 : 2, which indicates that a tricyclic compound is formed.

2,2'-(Tetramethylenedithio)dibenzothiazole does not react with CH₃I and neither with (CH₃)₂SO₄. At the formation of tricyclic salts (*V* and *VII*), a significant role is played by a different character of the reaction centres, *i.e.* of the nitrogen of heterocycle and the exocyclically bonded sulfur in the molecule of starting benzothiazole compound, on the one hand and the character of carbons in CH₃I and (CH₃)₂SO₄ on the other hand [6]. Dimethyl sulfate is a harder acid



Scheme I

with respect to CH_3I and therefore preferentially reacts with the benzothiazole ring nitrogen representing a harder centre compared to the exocyclically bonded sulfur. In the reaction with CH_3I the softer centre, *i.e.* the exocyclically bonded sulfur is activated (Scheme 1). By interaction of CH_3I with sulfur an intermediate *A* is formed, which can undergo immediately an S_N reaction to give a cyclic product *V* or *VII*. It is reasonable to assume that a nucleophilic attack of the iodide anion takes place to afford 2-(2-iodoethylthio)benzothiazole (*B*), which renders by cyclization compound *V*. We regard as more probable a direct attack of heterocycle nitrogen, without formation of *B*. 2-Methylthiobenzothiazole (*C*) was proved in the reaction mixture by gas chromatography. The low solubility in dimethylformamide has a favourable influence on the yields of tricyclic products. Stanovnik and Tišler [7] reported on the preparation of analogues *V* with bromide anion by the reaction of 2-mercaptobenzothiazole with 1,2-dibromoethane and the structure of compound proved by IR spectra. The compound can be prepared also by the reaction of 2-(2- or 3-(2-hydroxyethylthio)benzothiazole or 3-(2-hydroxyethyl)-2-benzothiazolinethione with PBr_3 or SOCl_2 [8]. The intermediate bromo and chloro derivatives were identified by the authors only with difficulties as these immediately undergo cyclization to 2,3-dihydrothiazolo[2,3-*b*]benzothiazolium salts. The reported ^1H NMR spectrum is in a good agreement with that measured by us. In the UV spectra of salts *I*, *II* and *V*—*VII* a band in the region of $\lambda = 225$ — 248 nm with $\log \epsilon = 3.25$ — 3.56 $\text{m}^2 \text{mol}^{-1}$ and a less intense band in the region of $\lambda = 300$ — 309 nm was observed. The shorter-wave band was assigned to the $\pi \rightarrow \pi^*$ transition in the system of conjugated multiple bonds. In the case of salts with methylsulfate anion the maximum of this band is observed at shorter wavelength like in the case of compounds with an iodide anion (Table 2). A similar difference was found with 3-methyl-2-styrylbenzothiazolium iodide and methylsulfate [9]. The observed differences occur as the consequence of a different interaction of benzothiazolium cation with appertaining anions. The anomaly observed in the case of tricyclic compound *V*, which has an iodide anion, but the position of its short-wave band corresponds to those of salts *II* and *VI* with methylsulfate anions, indicates that the exocyclic sulfur atom is turned aside of the plane of thiazole ring. The band in the region of $\lambda = 300$ — 309 nm was assigned according to [10] to the charge transfer in the anion—cation system. The compound *V* exhibits in this region a broad band with a maximum at $\lambda = 280$ nm and a shoulder at 300 nm. In the IR spectra of the afore-mentioned compounds the bands corresponding to stretching vibrations of $\text{C}=\text{C}$ and $\text{C}=\text{N}$ bonds at $\tilde{\nu} \approx 1505$ cm^{-1} and 1600 cm^{-1} and the bands of bending vibrations of CH_3 and CH_2 groups at $\tilde{\nu} \approx 1320$, 1390 , and 1470 cm^{-1} were observed. The bands are relatively of a low intensity and their wavenumbers are only

a little affected by the change of substituents in position 2 and 3, which makes the study of structure by means of IR spectroscopy difficult.

The activity of prepared compounds when tested as growth-regulators of wheat (*Triticum aestivum* L.) was found to be low. Not even one derivative exhibited a noticeable activity in the stimulating region. The tricyclic derivatives *V*, *VII* were found to be active in the inhibitory region (Table 3).

Table 3

Growth-regulating activity of the synthesized compounds tested on *Triticum aestivum* L.

Compound	Stimulation			Inhibition		
	+ $\Delta l/mm$	+ $\Delta l/\%$	$c/(mol\ dm^{-3})$	- $\Delta l/mm$	- $\Delta l/\%$	$c/(mol\ dm^{-3})$
<i>I</i>	0.24	4.55	10^{-5}	1.93	36.62	10^{-3}
<i>II</i>	0.25	4.74	10^{-7}	2.16	40.99	10^{-3}
<i>III</i>	0.33	6.08	10^{-11}	2.37	43.73	10^{-3}
<i>IV</i>	0.27	5.52	10^{-5}	1.54	31.50	10^{-3}
<i>V</i>				2.21	41.94	10^{-3}
<i>VI</i>	0.16	3.27	10^{-7}	1.62	33.12	10^{-3}
<i>VII</i>				2.08	39.47	10^{-3}
IAA ^a	5.93	100.33	10^{-5}	2.77	46.72	10^{-3}
2,4-D ^b	2.56	51.09	10^{-5}	2.01	40.12	10^{-3}
CCC ^c				1.75	32.35	10^{-3}

a) 2-Indolylacetic acid; *b*) 2,4-dichlorophenoxyacetic acid; *c*) (2-chloroethyl)trimethylammonium chloride.

Experimental

The melting points determined on a Kofler block and elemental analyses of the synthesized compounds are listed in Table 1.

The UV spectra of compounds were taken on a Specord M 40 UV/VIS instrument (Zeiss, Jena) in acetonitrile solutions ($c = 5 \times 10^{-5}$ mol dm⁻³). The ¹H NMR spectra were measured with a Tesla BS 587 (80 MHz) and a Jeol FX-100 (100 MHz) spectrometer. For measurement of ¹³C NMR spectra a Varian VXR (75 MHz) instrument was used. The compounds were measured in hexadeuterodimethyl sulfoxide and trifluoro-deuteroacetic acid using hexamethyldisiloxane as an internal standard.

The growth-regulating tests were aimed at the prolongative growth of primary roots of wheat (*Triticum aestivum* L.) according to a common method [11].

2,2'-(Methylenedithio)dibenzothiazole

In a solution of KOH (5.6 g; 0.1 mol) in ethanol (150 cm³) 2-mercaptobenzothiazole (16.7 g; 0.1 mol) was dissolved. After the solution was clarified diiodomethane (13.4 g;

0.05 mol) was added during 30 min. The reaction mixture was heated for 6 h at the boiling temperature. After cooling the precipitate was filtered off and the ethanolic solution was concentrated to 1/3 of volume and poured into water (150 cm³). The formed precipitate was filtered off, joined with the first portion and crystallized from ethyl acetate. Yield = 31.2 g (90 %), m.p. = 94—95.5°C. For C₁₅H₁₀N₂S₄ (*M_r* = 346.51) *w_i*(calc.): 51.99 % C, 2.91 % H, 8.08 % N, 37.01 % S; *w_i*(found): 52.12 % C, 2.82 % H, 7.87 % N, 37.20 % S.

Using an analogous procedure 2,2'-(*ethylenedithio*)dibenzothiazole was prepared from 1,2-dichloroethane. Yield = 75 %, m.p. = 137—140°C. For C₁₆H₁₂N₂S₄ (*M_r* = 360.54) *w_i*(calc.): 35.62 % S; *w_i*(found): 35.38 % S.

2,2'-(*Trimethylenedithio*)dibenzothiazole was obtained from 1,3-dibromopropane. After pouring into water the mixture was extracted with ether. Yield = 65 %, high-viscous liquid. For C₁₇H₁₄N₂S₄ (*M_r* = 374.53) *w_i*(calc.): 34.28 % S; *w_i*(found): 34.36 % S.

2,2'-(*Tetramethylenedithio*)dibenzothiazole was prepared from 1,4-dibromobutane. Yield = 73 %, m.p. = 130—132°C. For C₁₈H₁₆N₂S₄ (*M_r* = 388.59) *w_i*(calc.): 32.96 % S; *w_i*(found): 32.78 % S.

3,3'-Dimethyl-2,2'-(*methylenedithio*)dibenzothiazolium diiodide (*I*)

2,2'-(*Methylenedithio*)dibenzothiazole (3.5 g; 0.01 mol) and CH₃I (7 g; 0.05 mol) in anhydrous DMF (15 cm³) were heated for 24 h at 60°C. If after cooling a crystalline compound did not originate, anhydrous acetone (10 cm³) was added to decrease the solubility of the synthesized compound and the mixture was heated for 1 h. After isolation the compound was recrystallized from methanol.

By a similar procedure 2,3-dihydrothiazolo[2,3-*b*]benzothiazolium iodide (*V*) was prepared from 2,2'-(*ethylenedithio*)dibenzothiazole, and 3,4-dihydro-2*H*-1,3-thiazino[2,3-*b*]benzothiazolium iodide (*VII*) was synthesized from 2,2'-(*trimethylenedithio*)dibenzothiazole.

Using (CH₃)₂SO₄ as an alkylating agent compounds *II* and *VI* were isolated.

3,3'-Dimethyl-2,2'-(*methylenedithio*)dibenzothiazolium diperchlorate (*III*) and di(*tetrafluoroborate*) (*IV*)

Compound *I* (0.002 mol) was dissolved in warm water (10 cm³) and NaClO₄ or NaBF₄ (0.01 mol) was added. The reaction mixture was heated for 30 min to boil. After cooling the precipitate was crystallized from methanol.

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