

Benzothiazole compounds

XXXVII. Synthesis and spectral characteristics of 3,3'-disubstituted 2,2'-polymethylenedibenzothiazolium salts

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Received 3 October 1988

It was ascertained that 2,2'-methylenedibenzothiazole reacts in the first step with CH_3I or $(\text{CH}_3)_2\text{SO}_4$ in enamine form, *i.e.* 2-(2-benzothiazolinylidenemethyl)benzothiazole gives 2-(2-benzothiazolinylidenemethyl)-3-methylbenzothiazolium iodide, resp. methylsulfate. 2,2'-Ethylene-, 2,2'-trimethylene-, and 2,2'-tetramethylenedibenzothiazole react with CH_3I and $(\text{CH}_3)_2\text{SO}_4$ under formation of appropriate dibenzothiazolium salts. The structure of reaction products was proved by UV, ^1H NMR, and ^{13}C NMR spectroscopy. The compounds were tested on *Triticum aestivum* L. as growth-regulators. 2-(2-Benzothiazolinylidenemethyl)-3-methylbenzothiazolium methylsulfate exhibits a high-noticeable activity, while the activity of 2,2'-ethylene-dibenzothiazolium di(methylsulfate) is noticeable.

Показано, что 2,2'-метилендибензотиазол реагирует на первой стадии с CH_3I или $(\text{CH}_3)_2\text{SO}_4$ в енаминовой форме, т.е. в виде 2-(2-бензотиазолинилиденметил)бензотиазола с образованием 2-(2-бензотиазолинилиденметил)-3-метилбензотиазолий иодида или метилсульфата. 2,2'-Этилен-, 2,2'-триметилен- и 2,2'-тетраметилендибензотиазол взаимодействуют с CH_3I и $(\text{CH}_3)_2\text{SO}_4$ с образованием соответствующих солей дибензотиазолия. Строение продуктов реакции было подтверждено с помощью УФ, ^1H ЯМР и ^{13}C ЯМР спектроскопии. Полученные соединения испытывались в качестве регуляторов роста *Triticum aestivum* L. 2-(2-Бензотиазолинилиденметил)-3-метилбензотиазолий метилсульфат проявляет высокую активность, а ди(метилсульфат) 2,2'-этилендибензотиазолия проявляет заметную активность.

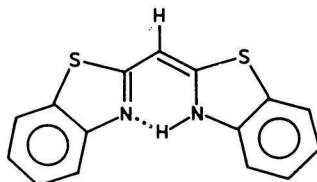
The synthesis of 3,3'-disubstituted 2,2'-polymethylenedibenzothiazolium salts is a continuation of investigations in the area of structure and growth-regulating activity of benzothiazolium salts [1—3]. The starting 2,2'-polymethylenedibenzothiazoles were prepared from 2-aminothiophenol and polyphosphoric acid

(PPA) [4], or by application of the method used by synthesis of 2-methylbenzothiazole, 2-methylbenzimidazole, 2-methylbenzoxazole, and others using trimethylsilyl ester of polyphosphoric acid (PPSE) [5]. PPSE is a very effective cyclocondensation agent, which enables to work at moderate conditions (85 °C against more than 130 °C in the case of PPA). This method was employed by preparation of 2,2'-ethylenedibenzothiazole. The quaternization was carried out in the medium of DMF at 60–70 °C.

The alkylation of 2-(2-benzothiazolinyldenemethyl)benzothiazole with CH_3I or $(\text{CH}_3)_2\text{SO}_4$ takes place only in the first step under formation of 2-(2-benzothiazolinyldenemethyl)-3-methylbenzothiazolium iodide, resp. methylsulfate (*I*, *II*; Table 1), which was confirmed by composition and ^1H NMR spectra (Table 2). In the spectra of *I* a singlet of three protons of CH_3 group on the quaternary nitrogen at $\delta = 4.12$ ppm and a multiplet corresponding to nine protons in the region of $\delta = 7.5\text{--}8.1$ ppm was observed, which indicates that these compounds (*I*, *II*) exist in an enamine form. This is in agreement with Ref. [6], which gives an evidence on the existence of 2,2'-methylene-dibenzothiazole in enamine form.

This structure was also confirmed by UV spectra of compounds *I* and *II* (Table 2), in which a bathochromic shift of CT bands was observed in the region of $\lambda = 380\text{--}400$ nm as compared with 3,3'-disubstituted 2,2'-polymethylene-dibenzothiazolium salts (*III*–*VIII*). In the IR spectra relatively intensive bands were observed at $\tilde{\nu} = 1527$ and 1545 cm^{-1} . These bands, which can be assigned to the formed conjugated system, were not observed in the case of other compounds.

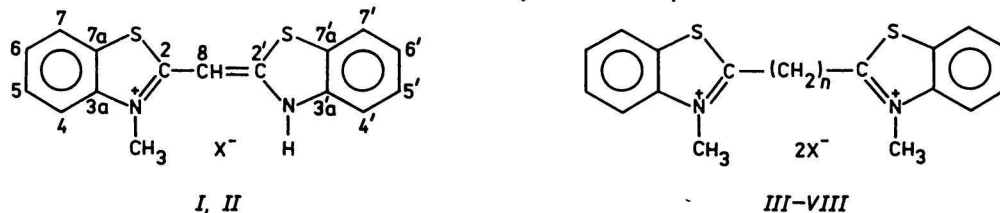
An unambiguous evidence of enamine grouping in compound *I* was obtained by analysis of ^{13}C NMR spectrum: δ/ppm : 170.5 (C-2), 168.0 (C-2'), 142.7 (C-3a), 140.8 (C-3'a), 132.2 (C-5), 132.1 (C-5'), 131.2 (C-6), 132.0 (C-6'), 130.0 (C-7a), 130.0 (C-7'a), 124.6 (C-7), 124.2 (C-7'), 119.1 (C-8), 117.4 (C-4), 117.1 (C-4'), 38.2 (CH_3). In the aliphatic region only one signal corresponding to CH_3 group on the quaternary nitrogen was observed, while the signal of $\text{>CH}_2\text{<}$ carbon was absent. At $\delta = 119.07$ ppm a signal corresponding to the carbon with sp^2 hybridization was observed and assigned to the —CH= group in enamine form. For the remaining carbons of both benzothiazole skeletons individual signals with very similar values of chemical shifts were observed.



Formula 1

Table 1

Characterization of the synthesized compounds



Compound	X	n	Formula	M_r	w_i (calc.)/% w_i (found)/%					Yield %	M.p. °C
					C	H	N	S	I		
I ^a	I	1	C ₁₆ H ₁₃ IN ₂ S ₂	424.39	45.28	3.09	5.10	16.60	29.90	79	219–221
					44.98	3.09	5.05	16.45	30.04		
II ^a	CH ₃ SO ₄	1	C ₁₇ H ₁₆ N ₂ O ₄ S ₃	408.59	49.98	3.95	6.86	23.54	—	63	270–275
					49.71	3.90	6.73	23.38	—		
III	I	2	C ₁₈ H ₁₅ I ₂ N ₂ S ₂	580.28	37.26	3.12	4.83	11.05	43.74	61	268–272
					37.48	3.11	4.98	11.02	43.70		
IV	CH ₃ SO ₄	2	C ₂₀ H ₂₄ N ₂ O ₈ S ₄	548.66	43.78	4.41	5.10	23.37	—	56	225–227
					43.71	4.38	5.17	23.17	—		
V	I	3	C ₁₉ H ₂₀ I ₂ N ₂ S ₂	594.30	38.37	3.40	4.71	10.79	42.59	81	224–228
					38.40	3.34	4.55	10.43	42.81		
VI	CH ₃ SO ₄	3	C ₂₁ H ₂₆ N ₂ O ₈ S ₄	562.69	44.88	4.66	4.98	22.81	—	60	228–231
					44.91	4.76	4.81	22.69	—		
VII	I	4	C ₂₀ H ₂₂ I ₂ N ₂ S ₂	608.30	39.49	3.65	4.60	10.54	41.72	67	300–303
					39.70	3.64	4.69	10.53	41.40		
VIII	CH ₃ SO ₄	4	C ₂₂ H ₂₈ N ₂ O ₈ S ₄	576.38	45.89	4.89	4.86	22.23	—	62	254–258
					46.16	4.81	4.86	22.04	—		

a) A monosalt is generated upon the reaction.

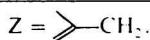
Compounds having a structure like salts *I* and *II* are known in the chemistry of cyanin dyes [7]. The intramolecular hydrogen bond raises the thermodynamic stability in comparison with 2,2'-methylenedibenzothiazole and lowers the basicity of the more basic nitrogen (Formula 1), which causes a decrease of the reaction rate of alkylation. The alkylation of 2-(2-benzothiazolynilidene-methyl)benzothiazole in the first step causes a decrease of activation energy of the process connected with the rotation of molecular fragment around the C-2—C-8 bond and leads to a conformation of compound *I*, in which the sterical hindrance of alkylation in the second step is rather unprobable (Scheme 1).

This fact can be explained first of all by the weak basicity of nitrogen. From this point of view the exocyclic C=C bond is less advantageous than the C=N bond. In the case of derivatives with $n > 1$, from the viewpoint of thermodynamics the existence of enamine form is practically impossible. On that account these compounds undergo alkylation to the second step. In this case the

Table 2

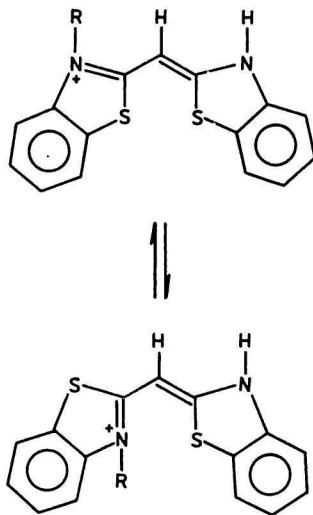
UV and ¹H NMR data of the synthesized compounds

Compound	λ nm			δ /ppm
	$\log(\epsilon (\text{m}^2 \text{mol}^{-1}))$			
<i>I</i>	240	385	400	4.12 (s, 3H, N ⁺ CH ₃), 7.5–8.1
	3.43	3.64	3.71	(m, 9H, H _{arom=C(H)})
<i>II</i>	225	380	400	4.29 (s, 3H, N ⁺ CH ₃), 3.5 (s, 3H,
	3.40	3.70	3.71	CH ₂ SO ₄), 7.6–8.0 (m, 9H, H _{arom=C(H)})
<i>III</i>	240	290	370	4.01 (s, 6H, N ⁺ CH ₃), 3.97 (s, 4H,
	3.56	3.11	3.05	CH ₂ —CH ₂), 7.43–7.74 (m, 8H, H _{arom})
<i>II'</i>	235	290	490	4.25 (s, 6H, N ⁺ CH ₃), 3.46 (s, 6H,
	3.39	3.22	2.92	CH ₂ SO ₄), 4.25 (s, 4H, CH ₂ —CH ₂),
<i>I'</i>	240	290		7.7–8.6 (m, 8H, H _{arom})
	3.62	3.14		3.97 (s, 6H, N ⁺ CH ₃), 3.6 (t, 4H, Z, $J = 8$ Hz), 2.4 (q, 2H, CH ₂ —CH ₂ —CH ₂ , $J = 7$ Hz)
<i>II'</i>	240	280		3.99 (s, 6H, N ⁺ CH ₃), 3.53 (t, 4H, Z, $J = 7$ Hz), 2.4 (q, 2H, CH ₂ —CH ₂ —CH ₂ , $J = 7$ Hz), 3.41 (s, 6H, CH ₂ SO ₄),
	3.35	3.13		7.4–7.8 (m, 8H, H _{arom})
<i>I''</i>	240	275	320	4.2 (s, 6H, N ⁺ CH ₃), 3.6 (t, 4H, Z, $J = 8$ Hz), 2.3 (m, 4H, Z—CH ₂),
	3.51	2.99	2.61	7.7–8.0 (m, 8H, H _{arom})
<i>I'''</i>	235	280	590	3.95 (s, 6H, N ⁺ CH ₃), 2.0 (m, 4H,
	3.39	3.08	3.29	Z—CH ₂), 3.3 (t, 4H, Z, $J = 8$ Hz), 3.44 (s, 6H, CH ₂ SO ₄), 7.4–7.8 (m, 8H, H _{arom})



rate of alkylation is determined by the nature and the access of alkylation agent to the reaction centre.

The remaining 2,2'-polymethylenedibenzothiazoles afford with CH_3I and $(\text{CH}_3)_2\text{SO}_4$ disalts (compounds *III--VIII*). In the ^1H NMR spectra of these salts the singlets of hydrogens of CH_3 groups on the quaternary nitrogen in the region of $\delta = 3.95\text{--}4.35$ ppm and the signals of hydrogens of polymethylene chains in the region of $\delta = 2.00\text{--}4.25$ ppm were observed (Table 2). In the ^{13}C NMR spectrum of compound *VIII* the signals of seven sp^2 hybridized carbons corresponding to the chemical shifts of a benzothiazolium cation and signals of four aliphatic carbons were observed: δ/ppm : 180.11 (C-2), 142.82 (C-3a), 116.67 (C-4), 131.47 (C-5), 130.30 (C-6), 124.35 (C-7), 129.29 (C-7a), 36.36 ($\text{N}^+\text{--CH}_3$), 27.48, 30.94 ($\text{CH}_2\text{--CH}_2$), 56.91 (CH_3SO_4^-).



Scheme 1

The fact that the molecule consists of 22 carbon atoms and that the ^{13}C NMR spectrum exhibits only eleven signals testifies a high degree of the molecular symmetry. In the UV spectra of *III--VIII*, besides bands corresponding to $\pi \rightarrow \pi^*$ transitions in conjugated system of multiple bonds ($\lambda = 235\text{--}240$ nm) and bands belonging to CT transitions in anion--benzothiazolium cation system ($\lambda = 275\text{--}290$ nm), intense bands in the long-wave region are observed (Table 2). The molar absorption coefficient but not the wavelength of this maximum does change with the polarity of solvent. For example, the band at $\lambda_{\text{max}} = 590$ nm (compound *VIII*) has in CH_3CN a value of $\log \varepsilon 3.29 \text{ m}^2 \text{ mol}^{-1}$, in

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>	0.29	5.99	10^{-5}	1.65	34.10	10^{-3}
<i>II</i>	0.68 ^c	14.04	10^{-5}	1.75	36.16	10^{-3}
	0.45 ^d	9.29	10^{-7}			
	0.43 ^d	8.88	10^{-9}			
<i>III</i>	0.26	5.31	10^{-5}	1.41	28.84	10^{-3}
<i>IV</i>	0.44 ^d	8.99	10^{-7}	1.59	32.51	10^{-3}
<i>V</i>	0.23	4.70	10^{-5}	1.29	26.39	10^{-3}
<i>VI</i>	0.31	6.40	10^{-4}	1.72	35.54	10^{-3}
<i>VII</i>	0.13	2.46	10^{-7}	1.76	33.91	10^{-3}
<i>VIII</i>	0.14	2.65	10^{-9}	2.01	38.07	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. *d)* Noticeable activity; *e)* high-noticeable activity.

CH₃OH 3.61 and in H₂O 3.47 m² mol⁻¹. Similarly the intensity of the long-wave band of compound *IV* ($\lambda_{max} = 490$ nm) does change with the polarity of solvent.

It is evident from the above facts that these salts, mainly in polar solution form intramolecular CT complexes. It follows from the roentgenographic investigation of 3-benzylbenzothiazolium bromide (unpublished results) that relatively strong nonbonding interactions exist between the bromide anion and the CH₂ group of benzyl moiety. It is probable that these interactions, also in the case of compounds *III*–*VIII*, have a significant influence upon the resultant geometry of the molecules and consequently on the electronic transitions connected with the long-wave absorption band. The absorption bands of disalts *IV* and *VIII* with methylsulfate anions are observed at longer wavelengths in comparison with the bands of analogous disalts bearing iodide anions (λ_{max}/nm : 490 for *IV*, 590 for *VIII*, 370 for *III*, 320 for *VII*). Besides the character of anion also the length of the polymethylene chain does influence the wavelength and the intensity of these bands. The highest intensity and the largest bathochromic shift was observed with the salt *VIII* having a methylsulfate anions and a tetramethylene chain. We suppose that this is caused by the flexibility of such a chain, as well as by a different strength of the afore-mentioned nonbonding interactions of methylsulfate anions with respect to shorter chains and iodide anions.

The preparation of quaternary salts with another alkylation agents (ethyl iodide, alkyl iodide, esters of bromoacetic acid) was unsuccessful. 2-(2-Benzothiazolinylidenemethyl)benzothiazole does not react at all. In the remaining cases after heating for 24 h with ethyl iodide in DMF a mixture of mono- and disalts was isolated in the yield of 3—5 % (verified by ^1H NMR spectroscopy), the separation of which was unsuccessful.

The prepared compounds were tested for growth-regulating activity on the prolongative growth of primary roots of wheat (*Triticum aestivum* L.) in concentrations from 10^{-13} to 10^{-3} mol dm $^{-3}$ (Table 3). Compound *II* exhibits a high activity in a wide range from 10^{-9} to 10^{-5} mol dm $^{-3}$, which seems to be convenient for a practical use. A good stimulating activity was shown also by 2,2'-ethylenedibenzothiazolium di(methylsulfate) (*IV*). The activity of the remaining derivatives was negligible. The inhibitory activity at the concentration of 10^{-3} mol dm $^{-3}$ was found to be on a level with CCC. It is interesting to compare compounds *IV*, *VI*, and *VIII* bearing methylsulfate anions and a prolongating polymethylene bridging at which the stimulating activity decreases and the inhibitory one increases. The analogical compounds with iodide anions exhibit also a decreasing stimulating activity.

Experimental

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

The IR spectra were measured with a Specord 75 IR instrument (Zeiss, Jena) in paraffin oil and corrected according to the standard spectra of polystyrene. The UV spectra of compounds were taken on a Specord M 40 spectrometer (Zeiss, Jena) in acetonitrile ($c = 5 \times 10^{-5}$ mol dm $^{-3}$). The ^1H NMR spectra were measured on a Tesla BS 587 instrument (80 MHz) and a Jeol FX-100 spectrometer (100 MHz). For measurement of ^{13}C NMR spectra a Varian VXR spectrometer (75 MHz) was used. The compounds were measured in hexadeuterodimethyl sulfoxide and trifluorodeuteroacetic 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 [8].

2,2'-Ethylenedibenzothiazole

A mixture of P_2O_5 (28.4 g; 0.2 mol) and hexamethyldisiloxane (48.7 g; 0.3 mol) in anhydrous 1,2-dichloroethane (150 cm 3) was heated for 30 min at the boiling temperature. At this temperature a mixture of 2-aminothiophenol (12.5 g; 0.1 mol) and malonic acid (11.8 g; 0.1 mol) was added dropwise. The reaction mixture was heated for

3 h and after cooling poured into a cool solution of KOH (28 g; 0.5 mol) in water (1000 cm³) under stirring. After 30 min stirring the aqueous layer was separated and extracted with CH₂Cl₂. After drying with Na₂SO₄ the solvent was distilled off and 2,2'-ethylenedibenzothiazole crystallized from ethanol. M.p. = 136—138 °C, yield = 84 %.

2-(2-Benzothiazolinyliidenemethyl)-3-methylbenzothiazolium and 3,3'-dimethyl-2,2'-polymethylenedibenzothiazolium salts I, II, resp. III—VIII

2-(2-Benzothiazolinyliidenemethyl)benzothiazole or appropriate 2,2'-polymethylenedibenzothiazoles (0.01 mol) and methyl iodide or dimethyl sulfate (0.015 mol) were heated in anhydrous DMF (15 cm³) at 60—70 °C for 5 h. If a solid compound did not originate, anhydrous acetone (10 cm³) was added, the mixture was heated for an additional hour and crystallized under cooling. The crystalline portion was washed with acetone.

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Translated by A. Perjéssy