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3-Substituted 6-Bromo-2-benzothiazolinones and Their Antialgal and Plant Growth Regulating Activity

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6-Bromo-2-benzothiazolinone and its 3-substituted derivatives were synthesized. The compounds were tested for plant growth regulating and antialgal activity.

6-Acetamido-3-alkyl-2-benzothiazolinones and especially 3-alkyl-6-nitro-2-benzothiazolinones [1] were found to be active as stimulators of fresh green mass and chlorophyll production in *Zea mays* L. Stimulation of green algae *Chlorella vulgaris* by the above-mentioned compounds was not significant. 3-(2-Alkylthio-6-benzothiazolylaminomethyl)-6-bromo-2-benzothiazolinones with alkyls C_3 to C_6 proved good antialgal activity [2]. These facts pointed to the necessity of testing the related 6-bromo-2-benzothiazolinones with different substituents at position 3. Of the synthesized group of compounds, *III*—*V*, *VIII* and *IX* (Table 1) are new.

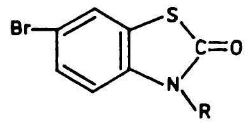
The starting compound, 6-bromo-2-benzothiazolinone (*I*) was synthesized using a convenient newly developed method. According to it, 2-benzothiazolinone was brominated with *N*-bromosuccinimide in chloroform [2, 3].

Alkylation of 6-bromo-2-benzothiazolinone with alkyl halides was carried out in aqueous ethanol in the presence of equivalent amount of potassium hydroxide at reflux temperature.

Compound *VIII* (Table 1) is the product of amidomethylation of 6-bromo-2-benzothiazolinone with two equivalents of *N*-hydroxymethylbenzamide in 85 % formic acid at reflux temperature. Originally the compound was gained by chance in the course of a reaction using 1 : 1 mole ratio. Later on in order to get a better yield the reaction was repeated using the due mole ratio according to the structure verified by IR spectra. The benzoyl derivative *IX* was prepared by benzoylation of 6-bromo-2-benzothiazolinone with benzoyl chloride in pyridine at reflux temperature. IR spectra are in accordance with the expected structures (Table 1).

The synthesized compounds were tested for growth-regulating activity and for synthesized chlorophyll content of green algae *Chlorella vulgaris* and of wheat plants. Further their influence on the prolongation of roots and stems of maize germinating in dark was investigated.

Table 1. Characterization of 6-Bromo-3-R-2-benzothiazolinones



Compound	R	Formula M_r	w_i(calc.)/% w_i(found)/% C	H	Br	N	S	Yield/%	M.p./°C	$\tilde{\nu}$/cm^{-1} ν(CO)	Others
III	$(CH_2)_2CH_3$	$C_{10}H_{10}BrNOS$	44.13	3.70	29.35	5.15	11.78	80.90	116.5—118.5	1670 s	
		272.17	44.09	3.51	29.60	5.00	11.84				
IV	CH_2—CH=CH_2	$C_{10}H_8BrNOS$	44.46	2.98	29.58	5.18	11.87	95.0	108.5—111.5	1650 s	1635 sh ν(C=C)
		270.15	44.23	2.86	29.46	5.20	11.94				
V	CH_2—C≡CH	$C_{10}H_6BrNOS$	44.79	2.26	29.80	5.22	11.96	84.6	158—159	1672 s	3296 m ν(≡C—H)
		268.14	44.49	2.15	30.09	5.14	12.04				
VIII	CH_2—N—CO—C_6H_5	$C_{23}H_{18}BrN_3O_3S$	55.65	3.66	16.10	8.47	6.46	72.0	186.5—187.5	1665 s, 1696 s,	3320 w ν(NH)
	| CH_2—NH—CO—C_6H_5	496.39	55.33	3.64	16.40	8.31	6.58			1702 sh	
IX	CO—C_6H_5	$C_{14}H_8BrNO_2S$	50.31	2.41	23.91	4.19	9.59	68.3	152.5—155	1668 s, 1727 sh	
		334.20	50.59	2.36	24.24	4.24	9.64				

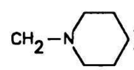
Compound *I* (R = H), $\tilde{\nu}$/cm^{-1}: 1670 s (ν(CO)), 3125 w (ν(NH)). Compound *II* (R = C_2H_5), yield 72.7 %, $\tilde{\nu}$/cm^{-1}: 1662 s (ν(CO)). Compound *VI* (R = CH_2—CH_2—OH), yield 62.0 %, $\tilde{\nu}$/cm^{-1}: 1652 s (ν(CO)), 3445 m (ν(OH)). Compound *VII* (R = ), yield 61.2 %, 1648 s (ν(CO)).

Table 2. Influence of 3-Substituted 6-Bromo-2-benzothiazolinones on *Chlorella vulgaris* Algae

Compound	c/(mol dm^{-3})	Relative chlorophyll production/%[a]	Absorbance/%[a]
I	10^{-4}	26.1 ± 4.2	31.1 ± 7.6
	10^{-5}	84.6 ± 1.9	79.6 ± 1.8
	10^{-9}	98.4 ± 0.4	100.4 ± 1.6
II	10^{-4}	23.4 ± 4.0	47.0 ± 4.9
	10^{-5}	70.8 ± 5.2	75.8 ± 5.8
	10^{-9}	101.1 ± 14.3	97.5 ± 5.3
III	10^{-4}	74.7 ± 15.7	73.6 ± 7.5
	10^{-5}	85.0 ± 3.6	84.9 ± 3.3
	10^{-9}	91.4 ± 11.5	93.1 ± 4.1
IV	10^{-4}	43.2 ± 10.0	48.1 ± 7.3
	10^{-5}	87.5 ± 14.3	83.8 ± 8.6
	10^{-9}	99.8 ± 4.1	91.4 ± 0.9
V	10^{-4}	69.8 ± 10.3	74.2 ± 8.0
	10^{-5}	83.4 ± 8.6	83.6 ± 6.7
	10^{-9}	93.8 ± 3.0	89.3 ± 8.8
VI	10^{-4}	66.9 ± 1.7	74.7 ± 1.3
	10^{-5}	88.9 ± 15.0	93.3 ± 2.5
	10^{-9}	99.3 ± 2.1	92.0 ± 5.4
VII	10^{-4}	39.3 ± 2.1	51.6 ± 2.8
	10^{-5}	71.4 ± 26.0	80.1 ± 15.9
	10^{-9}	91.8 ± 21.0	92.2 ± 7.9
VIII	10^{-4}	57.0 ± 4.2	32.7 ± 3.8
	10^{-5}	89.6 ± 12.0	87.1 ± 12.3
	10^{-9}	96.5 ± 2.5	97.9 ± 4.4
IX	10^{-4}	0	29.9 ± 4.3
	10^{-5}	75.0 ± 16.0	95.8 ± 0.8
	10^{-9}	108.8 ± 11.9	96.0 ± 6.1

a) Related to the control ± standard deviation.

All the investigated compounds showed antialgal efficiency at higher concentrations (Table 2), whereby the inhibitory effect on the synthesized chlorophyll content was in general more pronounced than the inhibition of the *Chlorella vulgaris* growth (with the exception of compound *VIII*). Using the expression of inhibitory concentration IC_{50}/(mol dm^{-3}) (corresponding to 50 % inhibition) for the chlorophyll synthesis in algae, the inhibitory efficiency of the tested 3-substituted derivatives decreased in the following order: *IX* (2.2 x 10^{-5}), *II* (2.8 x 10^{-5}), *I* (3.9 x 10^{-5}), *VII* (4.4 x 10^{-5}), *IV* (6.9 x 10^{-5}), *VIII* (1.6 x 10^{-4}), *VI* (4.1 x 10^{-4}). The lowest activity was obtained with derivatives *III* and *V*. In the whole concentration range investigated no stimulation effect on the growth and on synthesized chlorophyll content of green algae was found.

In contradistinction to the results obtained with algae, a partial stimulation of the synthesized chlorophyll content caused by 6-bromo-2-benzothiazolinones in wheat plants was found at c = 1 x 10^{-5} mol dm^{-3} (Table 3); at a lower concentration (1 x 10^{-9} mol dm^{-3}) the corresponding values were similar to the control values. The stimulation effect on the fresh green mass production in wheat plants was shown only by three derivatives, namely the compound *II* (at c = 1 x 10^{-5} mol dm^{-3}) and the compounds *VII* and *IX* (at c = 1 x 10^{-9} mol dm^{-3}). Neither stimulation at low concentrations was manifested by prolongation of the roots and stems of maize germinating in dark (Table 4). Also the corresponding inhibitory effect at c = 1 x 10^{-4} mol dm^{-3} was small (smaller than the algicidal effect of the studied compounds). By comparing the growth-regulating activity of 6-acetamido- and 6-nitro-2-benzothiazolinones [1] with that of 6-bromo derivatives it is evident that the introducing of Br-substituent to the position 6 leads in general to the decrease of the stimulation activity at low concentrations, especially with plants. It is also obvious that the substituent in the position 3 of

Table 3. The Effect of 3-Substituted 6-Bromo-2-benzothiazolinones on the Wheat Growth and the Synthesized Chlorophyll

Compound	c/(mol dm^{-3})	Relative chlorophyll production/%[a]	Relative seedlings mass/%[a]
I	10^{-5}	111.7 ± 2.0	102.8 ± 3.3
	10^{-9}	99.1 ± 4.3	91.3 ± 2.9
II	10^{-5}	102.2 ± 7.9	117.2 ± 3.8
	10^{-9}	101.7 ± 3.7	103.0 ± 1.3
III	10^{-5}	110.6 ± 3.4	97.7 ± 1.8
	10^{-9}	93.7 ± 5.5	104.3 ± 1.9
VI	10^{-5}	107.0 ± 3.4	107.2 ± 4.8
	10^{-9}	104.8 ± 7.9	91.2 ± 1.2
VII	10^{-5}	111.1 ± 7.1	85.6 ± 1.4
	10^{-9}	105.6 ± 6.0	112.9 ± 6.8
VIII	10^{-5}	106.9 ± 2.2	105.1 ± 2.6
	10^{-9}	102.1 ± 2.7	100.6 ± 1.5
IX	10^{-5}	119.7 ± 3.6	–
	10^{-9}	102.3 ± 7.4	120.2 ± 1.2

a) Related to the control ± standard deviation. – not tested.

Table 4. The Effect of 3-Substituted 6-Bromo-2-benzothiazolinones on the Prolongation of Roots and Stems of Maize

Compound	c/(mol dm^{-3})	Relative root length/%[a]	Relative stem length/%[a]
III	10^{-4}	76.0 ± 1.7	90.9 ± 3.2
	10^{-6}—10^{-10}	85.8 ± 4.3	95.9 ± 6.0
VI	10^{-4}	91.3 ± 1.6	87.9 ± 4.1
	10^{-6}—10^{-10}	105.0 ± 5.0	101.4 ± 4.4
VII	10^{-4}	87.7 ± 6.2	81.4 ± 5.5
	10^{-6}—10^{-10}	104.9 ± 3.9	102.4 ± 4.1
VIII	10^{-4}	83.9 ± 2.3	98.9 ± 5.2
	10^{-6}—10^{-10}	86.0 ± 3.3	104.4 ± 6.5
IX	10^{-4}	85.5 ± 5.7	80.7 ± 4.8
	10^{-6}—10^{-10}	100.1 ± 5.0	109.2 ± 10.6

a) Related to the control ± standard deviation.

6-bromo-2-benzothiazolinones significantly influences the algicidal efficiency of the compounds at higher concentrations.

EXPERIMENTAL

Analytical data, melting points determined on a Kofler block, and the yields of new synthesized 6-bromo-2-benzothiazolinones are given in Table 1. Compound *VII* was prepared according to [4]. The infrared spectra of compounds *I*—*IX* were measured on a spectrophotometer IR 75 (Zeiss, Jena) in nujol suspension (Table 1).

The effect of 6-bromo-2-benzothiazolinones on the growth and the synthesized chlorophyll content in green algae *Chlorella vulgaris* was investigated according to [1, 5]. The investigation of the prolongation of the roots and stems in the presence of these compounds was carried out as described in [6].

For the investigation of the growth-regulating activity of studied compounds and the synthesized chlorophyll content in wheat plants, wheat grains were soaked in aqueous solutions of the compounds with 1×10^{-5} and 1×10^{-9} mol dm^{-3} concentrations. Next, the grains were placed on cotton-wool pads moistened with the same solutions and left to germinate for 72 h in the dark. The germinating seeds were subsequently grown in a cultivation box, with the illumination regime 14 h of light, 10 h of dark. After 3 d of cultivation the green portion of the seedlings was weighed (10 sets, each of them containing 10 seedlings) and the synthesized chlorophyll contents were determined after extraction with *N*,*N*-dimethylformamide [7].

3-Alkyl-6-bromo-2-benzothiazolinones *II*—*VI*

6-Bromo-2-benzothiazolinone (*I*) (6.9 g; 0.03 mol) was dissolved in the solution of potassium hydroxide (2.0 g; 0.03 mol) in the mixture of water (10 cm^3) and ethanol (20 cm^3). Alkyl halide (0.03 mol) was added to the reaction mixture which was refluxed for 2 h and afterwards kept overnight at 5 °C.

The precipitated solid products were recrystallized using charcoal from ethanol (*II*, *III*, *VI*), ethanol—water (*V*) or benzene—cyclohexane (*IV*).

3-[*N*-Benzoyl-*N*-(benzoylaminomethyl)aminomethyl]-6-bromo-2-benzothiazolinone (*VIII*)

Compound *I* (4.6 g; 0.02 mol) and *N*-hydroxymethylbenzamide (6.0 g; 0.04 mol) in 85 % formic acid (20 cm^3) were kept under reflux for 30 min and afterwards at 5 °C overnight. White crystals precipitated from the mixture. The raw product was recrystallized from ethanol using charcoal.

3-Benzoyl-6-bromo-2-benzothiazolinone (*IX*)

To the mixture of 6-bromo-2-benzothiazolinone (11.5 g; 0.05 mol) and benzoyl chloride (7.05 g; 0.05 mol) anhydrous pyridine (25 cm^3) was added. The reaction mixture was heated to reflux and after dissolution of the solid the mixture was poured onto crushed ice (600 g). Cold water was added (800 cm^3) and after sucking out the precipitated solid was thoroughly washed with cold water.

The raw product was boiled with ethanol (150 cm^3) for 10 min, then the solid was sucked out and washed with cold ethanol (150 cm^3). Finally the product was recrystallized from ethanol—water mixture using charcoal.

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