

# Benzothiazole Compounds

## XLVII. Synthesis of 3,4-Substituted 2-Benzothiazolinones as Perspective Plant Growth Stimulators

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The reactions of halogenated alcohols, hydroxy ketones, and unsaturated alcohols with 3-[(chloroformyl)methyl]-2-benzothiazolinone or with 4-chloro-3-[(chloroformyl)methyl]-2-benzothiazolinone gave the corresponding 3-alkoxycarbonylmethyl-2-benzothiazolinones. The structure of the products was confirmed by means of UV, IR, and <sup>1</sup>H NMR spectra. The tests performed on *Triticum aestivum* L. proved the highest stimulating effect for 4-chloro-3-(3-oxa-5-hexyloxycarbonylmethyl)-2-benzothiazolinone ( $\Delta I = 68.08\%$ ).

This work represents a continuation of the study of derivatives of 3- and 4-substituted 2-benzothiazolinones and their biological activity, especially in the area of growth regulation. The knowledge obtained from the previous papers [1—3] was employed in the synthesis of new derivatives that showed the presumed higher stimulation effect. The described compounds were synthesized from 3-[(chloroformyl)methyl]-2-benzothiazolinone or 4-chloro-3-[(chloroformyl)methyl]-2-benzothiazolinone by treatment with appropriate alcohols in the presence of pyridine (Table 1).

The UV, IR, and <sup>1</sup>H NMR spectra of the studied compounds are given in Table 2.

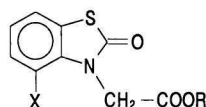
The UV absorption spectra of these compounds, especially the positions of absorption maxima, are very similar to those of the benzothiazolinone compounds described earlier [3]. Like the values of absorption maxima of UV spectra, neither the frequencies of carbonyl absorption in IR nor the chemical shift in <sup>1</sup>H NMR spectra (the values for —CH<sub>2</sub>COOR hydrogens are given) are suitable parameters that would be in any feasible relationship with the change of biological activity of these derivatives.

The synthesized compounds were tested on coleoptile growth of *Triticum aestivum* L. and exhibited stimulating effect which is the highest one observed up to now for the 2-benzothiazolinone derivatives synthesized by us. The chosen concentration was  $1 \times 10^{-5}$  mol dm<sup>-3</sup>. 4-Chloro-3-(3-oxa-5-pentyloxy-carbonylmethyl)-2-benzothiazolinone (XII), with its 68.08 % activity, prevailed over the standard — 2,4-dichlorophenylacetic acid (2,4-D) by  $\Delta I = 16.99\%$ ,

but also the additional five derivatives (II, IV, VIII, XIII, XIV) achieved the activity of the standard. Those compounds are considered to be active in plant growth stimulation that exhibit  $\Delta I > 15\%$ . With the exception of 3-(3-phenyl-2-propenyloxycarbonylmethyl)-2-benzothiazolinone (XVIII), all the compounds have activities of high significance in growth stimulation and they should be subjected to further exacting tests (Table 3).

Upon evaluation of the obtained results, among many active factors, the structure of ester group is of interest as it was being changed whereas the structural base was preserved. In the area of structure—activity relationship, the situation is complicated by the fact that it is usually not known which part of the molecule actually is in an interaction with the receptor. A greater number of atoms or groups can take part in the interaction. In the case of the title compounds, we found that generally the presence of halogen, oxy group or multiple bonds in the ester part of a molecule substantially enhances the stimulation activity. In all these cases, the number of polarized bonds is higher and thus also the extent of possible interaction with the receptor increases. We assume that the carbonyl group represents one of the sites of interaction and, therefore, we study the influence of the alkoxy group structure on the polarization of bonds there. From the obtained results it can be deduced that the lipophilicity of the ester group and the charge density of the carbonyl carbon plays an important role. Growing electron deficit on the carbon of carbonyl increases also the acidity of methylene hydrogens forming thus another

Table 1. Characteristics of the Synthesized Compounds



Compound	R	X	Formula	$M_r$	$w_i(\text{calc.})/\%$				Yield %	M.p./°C Solvent ( $\varphi_r$ )
					$w_i(\text{found})/\%$					
					C	H	N	S		
I	CH <sub>2</sub> CH <sub>2</sub> F	H	C <sub>11</sub> H <sub>10</sub> FNO <sub>3</sub> S	255.27	51.81 51.70	3.95 4.06	5.51 5.43	12.57 12.51	63	104—107 Ether—acetone
II	CH <sub>2</sub> CH <sub>2</sub> F	Cl	C <sub>11</sub> H <sub>9</sub> FCINO <sub>3</sub> S	289.71	45.55 45.37	3.12 3.04	4.82 4.96	11.05 11.02	67	87—90 Ether—acetone (3 : 1)
III	CH <sub>2</sub> CH <sub>2</sub> Cl	H	C <sub>11</sub> H <sub>10</sub> ClNO <sub>3</sub> S	271.72	48.57 48.78	3.70 3.52	5.14 5.31	11.78 11.49	64	93—95 Ethanol—water
IV	CH <sub>2</sub> CH <sub>2</sub> Cl	Cl	C <sub>11</sub> H <sub>10</sub> Cl <sub>2</sub> NO <sub>3</sub> S	306.16	43.17 43.26	2.96 3.10	4.57 4.48	10.47 10.53	67	115—118 Ethanol
V	CH <sub>2</sub> CH <sub>2</sub> Br	H	C <sub>11</sub> H <sub>10</sub> BrNO <sub>3</sub> S	316.18	41.81 42.02	3.18 3.22	4.43 4.31	10.14 10.32	58	67—69 Ether
VI	CH <sub>2</sub> CH <sub>2</sub> Br	Cl	C <sub>11</sub> H <sub>9</sub> BrClNO <sub>3</sub> S	350.62	37.75 37.92	2.59 2.41	4.00 4.12	9.16 8.95	62	116—119 Ether—acetone (2 : 1)
VII	CH <sub>2</sub> CCl <sub>3</sub>	H	C <sub>11</sub> H <sub>8</sub> Cl <sub>3</sub> NO <sub>3</sub> S	340.61	38.62 38.80	2.95 2.91	4.10 4.22	9.40 9.24	74	116—119 Ether
VIII	CH <sub>2</sub> CCl <sub>3</sub>	Cl	C <sub>11</sub> H <sub>7</sub> Cl <sub>4</sub> NO <sub>3</sub> S	375.05	35.23 35.08	1.88 1.92	3.73 3.86	8.55 8.79	75	93—96 Ether—petroleum ether (1 : 1)
IX	CH <sub>2</sub> CH <sub>2</sub> OCH <sub>3</sub>	H	C <sub>11</sub> H <sub>13</sub> NO <sub>4</sub> S	267.30	53.98 54.12	4.90 4.77	5.24 5.31	12.00 11.86	53	66—68 Ether—acetone (3 : 1)
X	CH <sub>2</sub> CH <sub>2</sub> OCH <sub>3</sub>	Cl	C <sub>12</sub> H <sub>12</sub> ClNO <sub>4</sub> S	301.75	47.72 47.53	4.00 4.11	4.63 4.48	10.61 10.50	57	60—61 Ether
XI	CH <sub>2</sub> CH <sub>2</sub> OC <sub>3</sub> H <sub>7</sub>	Cl	C <sub>14</sub> H <sub>16</sub> ClNO <sub>4</sub> S	329.80	50.95 51.12	4.88 4.73	4.24 4.37	9.71 9.57	55	Viscous oil
XII	CH <sub>2</sub> CH <sub>2</sub> OCH <sub>2</sub> CH=CH <sub>2</sub>	Cl	C <sub>14</sub> H <sub>14</sub> ClNO <sub>4</sub> S	327.78	51.27 51.08	4.30 4.13	4.27 4.40	9.77 9.91	58	Viscous oil
XIII	CH <sub>2</sub> CH <sub>2</sub> OCH <sub>2</sub> CCH	Cl	C <sub>14</sub> H <sub>14</sub> ClNO <sub>4</sub> S	325.77	51.58 51.34	3.71 3.53	4.29 4.42	9.82 9.76	52	Viscous oil
XIV	CH <sub>2</sub> CH=CHCH <sub>3</sub>	H	C <sub>13</sub> H <sub>13</sub> NO <sub>3</sub> S	263.31	59.36 59.61	4.98 4.69	5.32 5.47	12.19 12.38	62	98—100 Ether—acetone (3 : 1)
XV	CH <sub>2</sub> CH=CHCH <sub>3</sub>	Cl	C <sub>13</sub> H <sub>12</sub> ClNO <sub>3</sub> S	297.76	52.39 52.14	4.05 4.15	4.69 4.57	10.76 10.61	67	61—62 Ether
XVI	CH <sub>2</sub> CH=C(CH <sub>3</sub> )CCH	H	C <sub>15</sub> H <sub>12</sub> NO <sub>3</sub> S	278.33	62.77 62.53	4.56 4.68	4.88 4.71	11.17 11.21	79	80—82 Ethanol
XVII	CH <sub>2</sub> CH=C(CH <sub>3</sub> )CCH	Cl	C <sub>15</sub> H <sub>12</sub> ClNO <sub>3</sub> S	321.78	55.95 55.71	3.75 3.52	4.34 4.46	9.95 9.70	59	78—80 Acetone—ether (2 : 1)
XVIII	CH <sub>2</sub> CH=CHC <sub>6</sub> H <sub>5</sub>	H	C <sub>18</sub> H <sub>15</sub> NO <sub>3</sub> S	325.37	66.52 66.38	4.65 4.75	4.30 4.41	9.86 9.64	68	154—157 Acetone
XIX	CH <sub>2</sub> CH=CHC <sub>6</sub> H <sub>5</sub>	Cl	C <sub>18</sub> H <sub>14</sub> ClNO <sub>3</sub> S	359.83	60.05 60.23	3.92 3.80	3.88 4.02	8.90 9.05	64	77—79 Ether—acetone (1 : 1)

potential centre for an interaction. These assumptions found the subject of further study aimed at the dependence of stimulation effectivity on structural changes.

## EXPERIMENTAL

The microanalysis of the synthesized compounds is summarized in Table 1. The UV spectra were measured using methanolic solutions ( $c = 1 \times 10^{-4}$  mol dm<sup>-3</sup>) in 1 cm cuvette on HP 8452A spectrophotometer. The position of the absorption maxima

was determined from the fourth derivation of the spectra. The IR spectra in CH<sub>3</sub>Cl were measured on PE 180 apparatus in 0.1 mm NaCl cuvettes. The spectra were corrected for polystyrene absorption (Table 2). The <sup>1</sup>H NMR spectra were obtained (in CDCl<sub>3</sub> solutions) on Tesla BS instrument. The growth regulation tests were performed on the coleoptile growth of wheat (*Triticum aestivum* L.) and the results were compared with those of the standards — 3-indolylacetic acid (IAA) and 2,4-dichlorophenoxyacetic acid (2,4-D) for the concentration of  $1 \times 10^{-5}$  mol dm<sup>-3</sup> according to the used technology [4]. The obtained results are summarized in Table 3.

**Table 2.** UV, IR, and  $^1\text{H}$  NMR Spectral Data of the Synthesized Compounds

Compound	$\tilde{\nu}(\nu(\text{C}=\text{O}))/\text{cm}^{-1}$	$\lambda_{\text{max}}/\text{nm}$ ( $\log(\epsilon/(\text{m}^2 \text{mol}^{-1}))$ )			$\alpha(\text{CH}_2)^*$
I	1679, 1762	220 (3.19)	282 (2.36)	288 (2.35)	4.74
II	1683, 1761	224 (3.36)	286 (2.32)	292 (2.34)	5.21
III	1679, 1762	218 (3.27)	282 (2.48)	288 (2.47)	4.74
IV	1681, 1760	222 (3.36)	284 (2.18)	292 (2.20)	5.20
V	1679, 1761	220 (3.29)	282 (2.48)	288 (2.47)	4.74
VI	1683, 1761	224 (3.42)	284 (2.29)	292 (2.32)	5.20
VII	1680, 1774	218 (3.30)	282 (2.40)	288 (2.40)	4.80
VIII	1681, 1772	220 (3.51)	284 (2.52)	292 (2.29)	5.32
IX	1678, 1757	218 (3.30)	282 (2.42)	288 (2.41)	4.72
X	1683, 1753	224 (3.41)	286 (2.39)	294 (2.41)	5.17
XI	1681, 1754	224 (3.42)	286 (2.33)	294 (2.36)	5.17
XII	1684, 1756	226 (3.32)	286 (2.37)	294 (2.39)	5.17
XIII	1683, 1757	224 (3.29)	286 (2.35)	294 (2.38)	5.18
XIV	1679, 1753	216 (3.43)	282 (2.44)	288 (2.43)	4.67
XV	1682, 1751	224 (3.45)	286 (2.38)	294 (2.40)	4.15
XVI	1680, 1756	222 (3.34)	282 (2.44)	288 (2.43)	4.69
XVII	1684, 1753	224 (3.48)	284 (2.29)	292 (2.30)	5.15
XVIII	1678, 1754	216 (3.24)	250 (3.10)	282 (2.39)	4.85
XIX	1684, 1753	226 (3.54)	248 (3.52)	284 (2.69)	5.18

\*The methylene of the  $-\text{CH}_2\text{COOR}$  group.

**Table 3.** Growth Regulation Activity of the Synthesized Compounds Tested on *Triticum aestivum* L.

Compound	Stimulation ( $c = 10^{-5} \text{ mol dm}^{-3}$ )		Compound	Stimulation ( $c = 10^{-5} \text{ mol dm}^{-3}$ )	
	$\Delta I/\text{mm}$	$\Delta I/\%$		$\Delta I/\text{mm}$	$\Delta I/\%$
I	2.65	45.61***	XII	3.37	68.08***
II	2.92	62.12***	XIII	2.48	50.10***
III	1.31	27.17***	XIV	2.81	55.53***
IV	2.75	51.40***	XV	1.49	30.10***
V	2.52	43.37***	XVI	2.40	46.24***
VI	2.01	42.76***	XVII	2.65	49.53***
VII	2.79	48.02***	XVIII	0.18	3.46
VIII	2.37	50.42***	XIX	1.89	33.09***
IX	2.09	44.46***	IAA*	5.93	100.33
X	1.93	41.06***	2,4-D**	2.56	51.09
XI	2.27	45.85***			

\*3-Indolylacetic acid. \*\*2,4-Dichlorophenoxyacetic acid. \*\*\*Highly significant activity.

### 3-(R-Oxycarbonylmethyl)-2-benzothiazolinones I—X, XIV—XIX

Into 10  $\text{cm}^3$  of dry acetone, the following materials were added consecutively: 3-[(chloroformyl)methyl]-2-benzothiazolinone (2.27 g; 0.01 mol), pyridine (0.78 g; 0.01 mol), and 2-fluoroethanol (0.015 mol). The reaction mixture was left for 12 h at room temperature followed by 2 h of reflux. After addition of 80—100  $\text{cm}^3$  of water, the crystalline portion was filtered off and after drying crystallized from the mixture of ether and acetone ( $\varphi_r = 2 : 1$ ). Thus 1.7 g (67 %) of the product was obtained (m.p. = 104—107 °C).

### 3-(R-Oxycarbonylmethyl)-2-benzothiazolinones XI—XIII

The mixture of 15  $\text{cm}^3$  of dry acetone (or tetrahydrofuran), 3-[(chloroformyl)methyl]-2-benzothiazolinone (2.27 g; 0.01 mol), pyridine (0.79 g; 0.01 mol), and 2-propoxyethanol (1.56 g; 0.015 mol) was heated under reflux for 5 h. After addition of 50—60  $\text{cm}^3$  of water, the unreacted portion was extracted with ether. The highly viscous liquid, obtained by the usual work-up, was chromatographed on alumina column with benzene—ethanol ( $\varphi_r = 9 : 1$ ) as an eluent affording 1.8 g (55 %) of the product.

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