SYNTHESIS OF SEMICARBAZONES AND THIOSEMICARBAZONES OF 1-(2-BENZOTHIAZOLON-3-YL)PROPANONES

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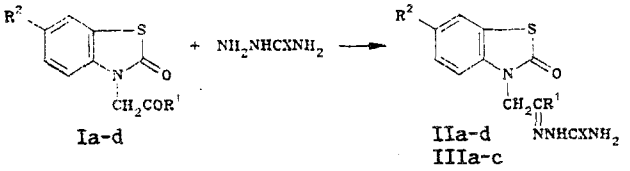
Semi- and thiosemicarbazones were synthesized by the reaction of 1-(2-benzothiazolon-3-yl)propanones with semi- and thiosemicarbazide. These compounds are more active in stimulating plant growth than the starting propanones.

Systems that contain two potentially biologically active segments usually display valuable biological activity. In the present work we discuss the synthesis of such types of compounds, viz., the semicarbazones and the thiosemicarbazones, which usually show pronounced biological properties [1, 2]; they are derived from the benzothiazolonyl ketones, which are known for their physiological activity [3, 4]. Indeed biological tests have shown that activity of these compounds in regulating plant growth is stronger [5] than that of the starting ketones [6].

Compounds (II) and (III) were obtained by the reaction of equimolar amounts of 1-(2-benzothiazolonyl) propanones (I) and semi- or thiosemicarbazide in 68-97% yield (Table 1).



Ia-d

IIa-d
IIIa-c

I—III a—c $R^1=CH_3$, d $R^1=C_6H_5$; a $R^2=H$; b $R^2=Br$; c,d $R^2=NO_2$; II X=O; III X=S

Besides the signals corresponding to segments of the starting propanones [3], the PMR spectra of the synthesized semi- and thiosemicarbazones show the signals of primary amino groups at 6.20-6.35 ppm for (IIa-c), or secondary amino groups at 9.60 ppm for (IIa-c), or 10.12-10.38 ppm for (IIIa-c). The primary amino signals for thiosemicarbazone (III) are overlapped by the multiplet for aromatic protons. The ^{13}C NMR spectra of the semicarbazones and thiosemicarbazones lack the signals of the carbonyl carbon of a ketone (Table 2).

The reaction of ω-(6-nitro-2-benzothiazolon-3-yl)acetophenone (Id) with semicarbazide proceeds with greater difficulty than the reaction with the propanone analog (Ic).

EXPERIMENTAL

IR spectra were obtained with a Specord 71 IR spectrophotometer in mineral oil; PMR spectra, with a Tesla BS 487C unit (80 MHz) in DMSO-D_6 (HMDS external standard (compound (II)) and DMSO-D_6 + $CDCl_3$ (TMS internal standard). ^{13}C NMR spectra were recorded with a Bruker WM-250 unit in DMSO-D_6, with TMS standard. The course of the reaction was monitored by TLC on Kieselgel 60 F_{254} plates (Merck) in 5:1 benzene–ethyl acetate; development was in UV light with iodine vapor. Melting points were determined with a Boetius unit and were not corrected.

The properties of the synthesized compounds are shown in the table. The elemental analyses for C, H, and N agree with the calculated values.

The initial 1-(2-benzothiazolon-3-yl)- (Ia), 1-(6-bromo-2-benzothiazolon-3-yl)- (Ib), and 1-(6-nitro-2-benzothiazolon-3-yl)propanones (Ic) were obtained by the procedure of [3]. 6-Nitro-2(3H)-benzothiazolone was obtained by a direct nitration that differed somewhat from the nitrations described in [7-9].

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TABLE 1. Semicarbazones (II) and Thiosemicarbazones (III)

Compound	Empirical formula	mp, °C	IR spectrum, cm^{-1}	PMR spectrum, δ, ppm	Yield, %
IIa	$C_{11}H_{12}N_4O_2S$	201...203	3470, 3400, 3180 sh, 3270, 1715, 1675, 1590	2,0 (s 3H, CH_3); 4,9 (s 2H, CH_2); 6,35 (2H, NH_2); 7,2...8,0 (m, 4H, arom); 9,62 (1H, NH)	90
IIb	$C_{11}H_{11}BrN_4O_2S$	224...226	3470, 3180 sh, 3280, 1715, 1670, 1590	2,0 (s 3H, CH_3); 4,9 (s 2H, CH_2); 6,25 (2H, NH_2); 7,3...8,3 (m, 3H, arom); 9,6 (1H, NH)	97
IIc	$C_{11}H_{11}N_5O_4S$	223...225,5	3470, 3180 sh, 3280, 3070, 1715, 1670, 1590, 1540, 1520, 1345	2,05 (s 3H, CH_3); 5,0 (s, 2H, CH_2); 6,2 (2H, NH_2); 7,65...9,1 (m, 3H, arom.); 9,6 (1H, NH)	97
IId	$C_{16}H_{13}N_5O_4S$	230...232	3490, 3330, 3220, 1705, 1590, 1510, 1340	5,35 (s 2H, CH_2); 6,48 (2H, NH_2); 7,4...9,05 (9H, Ar)	71
IIIa	$C_{11}H_{12}N_4OS_2$	199...201	3400, 3210, 3130, 1660, 1680, 1600	1,95 (s, 3H, CH_3); 4,7 (s 2H, CH_2); 6,8...7,6 (m, 6H, arom. NH_2); 10,12 (1H, NH)	72
IIIb	$C_{11}H_{11}BrN_4OS_2$	210...212	3420, 3220, 3290, 3160, 1670, 1590	1,95 (s 3H, CH_3); 4,75 (s 2H, CH_2); 6,95...7,95 (m 5H, arom. NH_2); 10,32 (1H, NH)	68
IIIc	$C_{11}H_{11}N_5O_3S_2$	211...213	3480, 3370, 3180, 1690, 1660, 1590, 1570, 1525, 1340	2,0 (s 3H, CH_3), 4,85 (s 2H, CH_2); 6,88...8,5 (m, 5H, arom. NH_2); 10,38 (1H, NH)	92

*Compounds (IIa) and (IIIa, b) were crystallized from ethanol, (IIb) from methanol, (IIc) and (IIIc) from acetonitrile.

TABLE 2. ^{13}C NMR Spectra of Compounds (IIb), (IId), and (IIIb)*

Compound	Chemical shift, ppm†									
	$C_{(2)}$	$C_{(3a)}$	$C_{(5)}$	$C_{(6)}$	$C_{(7)}$	$C_{(7a)}$	CH_2	C=N	C=O(S)	R'
II	167,94	135,58	128,47	113,92	124,29	122,48	46,89	140,83	156,08	12,95
III	167,86	135,56	128,47	113,95	124,26	122,41	46,85	145,09	178,09	13,54
II	168,34	141,13	121,78	141,30	118,28	121,36	46,86	142,01	154,83	

*The authors thank S. D. Simova for obtaining and interpreting the ^{13}C NMR spectra.
†For compound (IId), $C_{(12)}$ 129.80; $C_{(13)}$ 128.25; $C_{(14)}$ 126.44; $C_{(15)}$ 128.83.

1-(2-Benzothiazolon-3-yl)propanone semicarbazone (IIa). To a suspension of 1.03 g (5 mmoles) of propanone (Ia) and 0.56 g (5 mmole) of semicarbazide hydrochloride in 40 ml of ethanol was added 0.4 g (0.4 ml, 5 mmole) of pyridine, and the reaction mixture was stirred with boiling for 30 min. After cooling the precipitate was filtered off and washed with water (5 × 8 ml).

1-(6-Bromo-2-benzothiazolon-3-yl)propanone semicarbazone (IIb) was obtained analogously from (Ib) in 75 ml of ethanol.

1-(6-Nitro-2-benzothiazolon-3-yl)propanone semicarbazone (IIc) was obtained analogously to (IIa) from propanone (Ic) in 60 ml of ethanol.

1-(2-Benzothiazolon-3-yl)propanone thiosemicarbazone (IIIa). A suspension of 1.03 g (5 mmole) of propanone (Ia) and 0.46 g of thiosemicarbazide in 25 ml of methanol was stirred with boiling for 2 h. The thiosemicarbazone precipitate was filtered off, washed with ethanol (2 × 2 ml), and crystallized from ethanol.

1-(6-Bromo-2-benzothiazolon-3-yl)propanone thiosemicarbazone (IIIb) was obtained analogously from (Ib) in 40 ml of ethanol.

1-(6-Nitro-2-benzothiazolon-3-yl)propanone thiosemicarbazone (IIIc) was obtained analogously to (IIIa) from propanone (Ia) in 40 ml of n-propanol.

6-Nitro-2(3H)-benzothiazolone ($C_7H_4N_2O_3$). To 15 ml of nitric acid (d 1.4) was added 3.02 g (20 mmoles) of 2(3H)-benzothiazolone portionwise with stirring [10]. The reaction mixture was gradually heated to 50-60° and stirred at that temperature for 2.5 h. Then it was cooled and treated with ice. The precipitate was filtered off and washed with cold water until the washings were neutral. Recrystallization from ethanol gave 3 g (77%) of 6-nitro-2(3H)-benzothiazolone, mp 246-248°C (according to [7-9], mp 248-252°C). IR spectrum: 3220, 1715, 1515, 1345 cm^{-1}.

ω-(6-Nitro-2-benzothiazolon-2-yl)acetophenone (Id, $C_{15}H_{10}N_2O_4S$). To a solution of 1.15 g (50 mmoles) of sodium in 110 ml of ethanol was added 9.81 g (50 mmoles) of 6-nitro-2(3H)-benzothazolone, and the mixture was heated to complete solution. Gradually over 1 h 9.96 g (50 mmoles) of phenacyl bromide was added. The mixture was stirred with boiling for 4 h, cooled and filtered, and the solid was washed with ethanol (4 × 10 ml). Yield 12.1 g (77%), mp 198-199.5°C (from ethanol). IR spectrum: 1670, 1695, 1650, 1580, 1330 cm^{-1}. PMR spectrum (DMSO-D_6): 5.95 (s, 2H, CH_2); 7.55-9.02 ppm (m, 8H, arom.).

ω-6-Nitro-2-benzothiazolon-3-yl)acetophenone semicarbazone (IId, $C_{16}H_{13}N_5O_4S$). A suspension of 1.57 g (5 mmoles) of acetophenone (Id) and 0.56 g (5 mmoles) of semicarbazide hydrochloride in 20 ml of propanol containing 0.4 ml (5 mmoles) of pyridine was stirred with boiling for 4 h. The precipitate of semicarbazone (IId) was filtered off, washed with water (5 × 10 ml), and recrystallized from butanol.

LITERATURE CITED

1. G. A. Melent'eva, Pharmaceutical Chemistry [in Russian], Vol. 1, Meditsina, Moscow (1976), p. 405.
2. N. N. Mel'nikov, Chemistry and Technology of Pesticides [in Russian], Khimiya, Moscow (1974), p. 442.
3. V. B. Kalcheva, A. Ts. Antonova, D. Simov, and N. H. Mincheva, Compt. Acad. Bulg. Sci., 39, No. 12, 59 (1986).
4. V. B. Kalcheva, A. Ts. Antonova, D. Simov, and N. H. Mincheva, Compt. Acad. Bulg. Sci., 40, No. 1, 71 (1987).
5. A. Ts. Antonova, D. S. Antonov, V. B. Kalcheva, G. N. Vasilev, and Z. P. Dimcheva, Bulgarian Auth. Cert. 83,682.
6. D. S. Antonov, A. Ts. Antonova, N. Kh. Mincheva, V. B. Kalcheva, and G. N. Vasilev, Bulgarian Auth. Cert. 72,099.
7. P. Jacobson and A. Kwaysser, Annalen, 277, 237 (1893).
8. R. Hunter and E. Parken, J. Chem. Soc., 1755 (1935).
9. S. G. Fridman, Zh. Obshch. Khim., 24, 642 (1954).
10. L. S. Efros and L. P. Davidenkov, ibid., 21, 2046 (1951).