Isothiocyanates. XXXIII. The synthesis and infrared spectra of benzothiazolyl isothiocyanates

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The synthesis of 2-(X-phenyl)-5-benzothiazolyl isothiocyanates, 4-(2-benzothiazolyl)-, 3-(2-benzothiazolyl)-, and 4-(6-methyl-2-benzothiazolyl)phenyl isothiocyanates is described. The infrared spectra of the synthesized compounds were interpreted in the 1600—1300 and 2200—2000 cm^{-1} range.

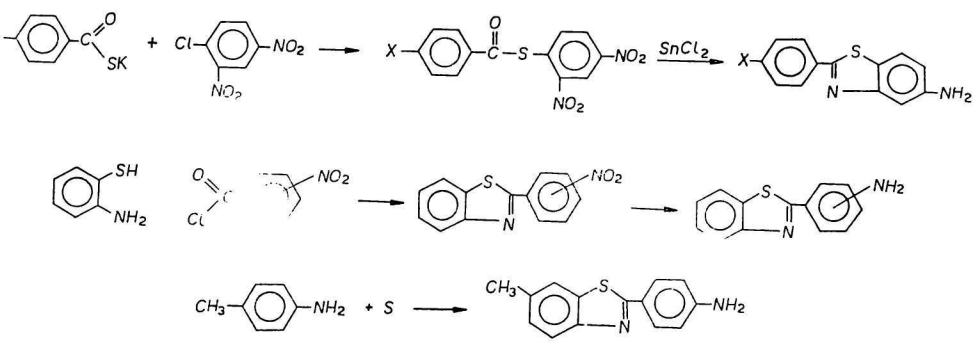
As a part of continuing programme in our research project [1—3] benzothiazolyl isothiocyanates were synthesized in order to examine their biological properties. The goal was to add the —NCS group to a system the derivatives of which exhibit biological activity [4—8]. On the other hand, derivatives of benzothiazole display a strong fluorescence [9, 10], and thereby, also substances with fluorescent properties were obtained.

Experimental

Infrared spectra of chloroform dissolved compounds ($c = 2.5 \times 10^{-2}$ M) were measured with a double-beam UR-20 spectrophotometer in the 3600—800 cm^{-1} range. The apparatus was calibrated against a polystyrene foil.

Amino derivatives of benzothiazole (I—XII)

Intermediates were prepared according to three known methods [11—15] (Scheme 1). According to the first procedure 4-substituted benzoyl chlorides were reacted with



Scheme 1

Table 1

List of the synthesized intermediates

	Compound	Formula	*M*	Calculated/found % N	Calculated/found % S	Yield [%]	M.p. [°C]
I	5-Amino-2-phenylbenzothiazole	$C_{13}H_{10}N_2S$	226.34	—	—	48	202[a]
II	5-Amino-2-(4-methylphenyl)benzothiazole	$C_{14}H_{12}N_2S$	240.36	11.65 11.82	13.56 13.48	42	178 – 180
III	5-Amino-2-(4-methoxyphenyl)benzothiazole	$C_{14}H_{12}N_2OS$	256.36	10.93 10.82	12.73 12.85	56	217 – 219
IV	5-Amino-2-(4-chlorophenyl)benzothiazole	$C_{13}H_9ClN_2S$	260.79	10.74 10.66	12.50 12.35	42	252 – 254
V	5-Amino-2-(4-bromophenyl)benzothiazole	$C_{13}H_9BrN_2S$	305.25	9.35 9.23	10.68 10.91	36	297 – 299
VI	5-Amino-2-(4-iodophenyl)benzothiazole	$C_{13}H_9IN_2S$	352.24	7.98 7.81	9.10 9.38		305 – 310
VII	5-Amino-2-(2-chlorophenyl)benzothiazole	$C_{13}H_9ClN_2S$	260.79	10.78 10.66	12.50 12.31	38	146 – 148
VIII	2-(4-Aminophenyl)benzothiazole	$C_{13}H_{10}N_2S$	226.34	—	—	61	163 – 165[b]
IX	2-(3-Aminophenyl)benzothiazole	$C_{13}H_{10}N_2S$	226.34	—	—	53	140 – 142[b]
X	2-(2-Chloro-4-aminophenyl)benzothiazole	$C_{13}H_9ClN_2S$	260.79	10.78 10.66	12.50 12.62	41	87 – 90
XI	6-Methyl-2-(4-aminophenyl)benzothiazole	$C_{14}H_{12}N_2S$	240.36	—	—	71	190 – 191[c]
XII	6-Amino-2-phenylbenzothiazole	$C_{13}H_{10}N_2S$	226.34	—	—	43	206 – 207[d]

a) Ref. [18] m.p. 202°C; *b*) [21] m.p. 156.2 and 140 – 140.9°C; *c*) [22] m.p. 190 – 191°C; *d*) [21] m.p. 206°C.

Table 2

List of the synthesized benzthiazolyl isothiocyanates

	Compound	Formula	*M*	Calculated/found % N	Calculated/found % S	Yield [%]	M.p. [°C]
XIII	2-Phenyl-5-benzothiazolyl isothiocyanate	$C_{14}H_8N_2S_2$	268.34	10.43 10.34	23.89 23.85	47	147—149
XIV	2-(4-Methylphenyl)-5-benzothiazolyl isothiocyanate	$C_{15}H_{10}N_2S_2$	282.37	9.92 10.18	22.71 22.70	38	132—134
XV	2-(4-Methoxyphenyl)-5-benzothiazolyl isothiocyanate	$C_{15}H_{10}H_2OS_2$	298.38	9.38 9.48	21.49 21.66	49	140—141
XVI	2-(4-Chlorophenyl)-5-benzothiazolyl isothiocyanate	$C_{14}H_7ClN_2S_2$	302.80	9.25 9.34	21.22 21.20	32	173—175
XVII	2-(4-Bromophenyl)-5-benzothiazolyl isothiocyanate	$C_{14}H_7BrN_2S_2$	347.26	8.06 8.09	18.46 18.28	31	175—176
XVIII	2-(4-Iodophenyl)-5-benzothiazolyl isothiocyanate	$C_{14}H_7IN_2S_2$	394.26	7.10 7.20	16.26 16.37	30	177—178
XIX	2-(2-Chlorophenyl)-5-benzothiazolyl isothiocyanate	$C_{14}H_7ClN_2S_2$	302.80	9.25 9.34	21.51 21.20	42	150—152
XX	4-(2-Benzothiazolyl)phenyl isothiocyanate	$C_{14}H_8N_2S_2$	268.34	10.43 10.52	23.89 23.90	57	153—155
XXI	3-(2-Benzothiazolyl)phenyl isothiocyanate	$C_{14}H_8N_2S_2$	268.34	10.43 10.60	23.89 23.70	51	120—123
XXII	2-Chloro-4-(2-benzothiazolyl)phenyl isothiocyanate	$C_{14}H_7ClN_2S_2$	302.80	9.25 9.33	21.51 21.62	41	143—145
XXIII	4-(6-Methyl-2-benzothiazolyl)phenyl isothiocyanate	$C_{15}H_{10}N_2S_2$	282.37	9.92 9.87	22.71 22.69	61	182—183
XXIV	2-Phenyl-6-benzothiazolyl isothiocyanate	$C_{14}H_8N_2S_2$	268.34	10.43 10.52	23.89 23.72		110—112

Table 3

Characteristic infrared data of benzothiazolyl isothiocyanates [cm^{-1}]

Compound	δ(CH)	$\tilde{\nu}_s$(NCS)	$\tilde{\nu}$(skelet.)	$\tilde{\nu}$(arom.)	$\tilde{\nu}_{as}$(NCS)	Other absorption bands
XIII	820, 850, 877	970	1310, 1448 1540, 1595	1605 1470	2028, 2090 2115, 2170	1060, 1080 1150, 1260
XIV	820, 855, 875	967	1310, 1450 1540, 1595	1605 1482	2030, 2090 2120, 2170	1060, 1080 1150, 1260
XV	820, 855, 875	967	1305, 1450 1540, 1600	1600 1482	2040, 2090 2120, 2170	1060, 1080 1175, 1250
XVI	840, 855, 875	963	1310, 1447 1540, 1585	1585 1472	2030, 2090 2115, 2170	1015, 1095, 1080 1250
XVII	830, 855, 875	970	1310, 1450 1540, 1580	1600 1473	2030, 2090 2115, 2170	1015, 1075 1180, 1260
XVIII	840, 860, 885	970	1310, 1465 1540, 1595	1615 1485	2050, 2090 2120, 2170	1020, 1070 1060, 1260
XIX	845, 860, 882	965	1320, 1440 1528, 1590	1490 1610	2070, 2110 2190, 2190	1065, 1260
XX	820, 860, 882	950	1320, 1445 1520, 1590	1478 1610	2080, 2115 2190	1130, 1180 1260
XXI	830, 860, 870	970	1310, 1450 1520, 1600	1470 1600	2030, 2080 2110, 2170	1130, 1070 1260
XXII	830, 855, 880	970	1320, 1430 1520, 1605	1480 1610	2030, 2080 2110, 2170	1050, 1070 1085, 1160
XXIII	858, 930	980	1320, 1450 1500, 1590	1470 1610	2070, 2110 2190	1050, 1070
XXIV	830, 870, 940	980	1310, 1450 1520, 1580	1480 1600	2080, 2110 2180	1100, 1140

hydrogen sulfide in alkaline medium to yield potassium thiobenzoates, which, when condensed with 2,4-dinitrochlorobenzene afforded 2,4-dinitrophenyl thiobenzoates. The latter furnished, upon mild reduction and simultaneous cyclization, the desired amino derivatives.

Further method starts from zinc *o*-aminothiophenolate, which was condensed with the proper nitrobenzoyl chloride. In the third procedure 4-(6-methyl-2-benzothiazolyl)-phenylamine was prepared by direct reaction of toluidine with elemental sulfur. Characteristic data of synthesized derivatives are listed in Table 1.

Isothiocyanates (XIII—XXIV)

Chloroform (80 ml) and dichloroethane (60 ml) were placed into a three-necked flask. To this mixture water (150 ml) and thiophosgene (6 g; 0.052 mole) were added. The content of the flask on intensive stirring and cooling (up to 10°C) afforded an emulsion to which a solution of the amine (*I—XII*) (0.05 mole) in chloroform was gradually added. During reaction the pH of the mixture was kept at about 7; after addition of the amine stirring was continued for 3 hours. The organic layer was then separated, dried with $CaCl_2$ and distilled off. The dry reaction residue was dissolved in the necessary amount of benzene, heated with charcoal, filtered, and evaporated. To this hot solution light petroleum was added to a turbulence and the product was allowed to crystallize.

Spectral and other characteristic data of isothiocyanates prepared are listed in Tables 2 and 3.

Results and discussion

This paper deals with the synthesis of twelve intermediates for the synthesis of isothiocyanates of which compounds *II—VII*, *X*, and twelve final products are hitherto not reported. Low yields in the last step of the preparation of intermediates are largely due to the complex isolation of the amines after reduction followed by cyclization. Similarly, lower yields were encountered also in the synthesis of isothiocyanates due to a diminished solubility of intermediates and final products what has been observed namely with derivatives *XVI—XVIII*. The highest yields were noticed with compounds *XX*, *XXI*, *XXIII*, *XXIV*, the common feature of which is that all originated from derivatives having an amino group attached to a phenyl group.

There are relatively few papers dealing with the infrared spectra of benzothiazoles. As reported [16, 17], benzothiazole and its derivatives display four absorption bands in the 1600—1300 cm^{-1} region.

Derivatives prepared by us also reveal strong and medium absorption bands in the above-mentioned range. The spectra of our derivatives showed, however, more than four absorption bands in the 1600—1300 cm^{-1} region. Studying the 1610—1590 cm^{-1} absorption band in more detail we ascertained that there are involved two bands which are quite distinct in the case of the iodo derivative, whereas in some other derivatives they are manifested as an inflex on the absorption band of great intensity with maximum at 1590 cm^{-1}.

As seen in Table 3, there are three absorption bands corresponding to deformation C—H vibrations in the 900—800 cm^{-1} region. These absorption bands lie constantly at 820, 850, and 875 cm^{-1}.

In our previous papers [18—20] we reported that the isothiocyanato group attached to the aromatic ring exhibits a great absorption band in the 2200—2000 cm^{-1} region,

this being split into three maxima at about 2060, 2100, and 2180 cm^{-1}. The position of the first absorption band, due to the substituent effect, undergoes changes, so that the correlation with σ_p constants was possible. Derivatives *XIII*—*XIX* of 2-(X-phenyl)--5-benzothiazolyl isothiocyanates display a new maximum on the absorption band at 2030 cm^{-1}. There has not been observed the substituent effect on the absorption band position of derivatives under study.

Both the shape and the position of the above-mentioned maximum in the spectra of derivatives (*XX*—*XXIII*) having the —NCS group attached directly to the benzene ring resemble those of other aromatic isothiocyanates.

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