7. L. A. Komel'kova, V. P. Kruglenko, O. A. Logunov, M. V. Povstyanoi, A. V. Startsev, Yu. Yu. Stoilov, and A. A. Timoshin, Kvantovaya Élektron., 10, 876 (1983).
8. V. S. Zuev, V. P. Kruglenko, O. A. Logunov, A. V. Startsev, and Yu. Yu. Stoilov, Kvantovaya Élektron., 8, 1567 (1981).
9. A. Streitwieser, Molecular Orbital Theory for Organic Chemists, Wiley, New York (1961).
10. J. Lalezari and Y. Levy, J. Heterocycl. Chem., 11, 327 (1974).

REACTION OF 2-ALKYLAMINOBENZOTHIAZOLES WITH ACRYLIC ACID

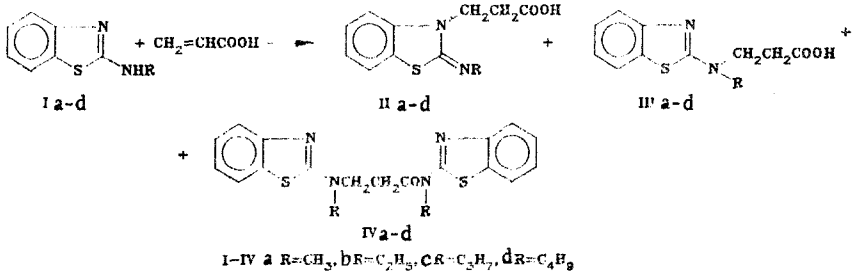
V. A. Saprykina, R. F. Ambartsumova, and N. K. Rozhkova

UDC 547.789.6.07:543.422

The behavior of 2-alkylaminobenzothiazoles in the reaction with acrylic acid was studied and it was shown that under kinetically controlled conditions, the reaction proceeds at the endocyclic nitrogen atom of the ambifunctional system. The formation of amino-isomers is controlled thermodynamically.

The addition of 2-alkylaminobenzothiazoles to reagents containing carbon–carbon multiple bonds has not yet been investigated. There are only a few reports on the reaction of unsubstituted 2-aminobenzothiazole with acetylenecarboxylic acid esters [1-5], leading to the formation of condensed addition products at the endocyclic nitrogen atom of the hetero-system. At the same time, in addition to pyrimidobenzothiazoles, the authors of [3] isolated an adduct with an amino structure, i.e., an addition product at the exocyclic nitrogen atom.

To synthesize potential pesticides, and to examine the paths and conditions of the reaction of 2-aminobenzothiazoles with activated alkenes, we studied the reaction of compounds Ia-d with acrylic acid. The reaction was carried out in aprotic solvents (acetone, toluene) in the temperature range from 30 to 110°C.



I–IV a R=CH3, b R=C2H5, c R=C3H7, d R=C4H9

The ratio of yields of compounds IIa-d–IVa-d depends on the temperature (Table 1). At 30 and 56°C, 2-alkylimino-3-(2-carboxyethyl)benzothiazolines (IIa-d), products of addition of acrylic acid to the endocyclic nitrogen of the heterocycle, become predominant. The isomeric amino analogs IIIa-d are not formed in appreciable amounts. Increase in the temperature to 110°C leads to a sharp increase in the yield of 2-[N-alkyl-N-(2-carboxyethyl) amino]benzothiazoles (IIIa-d). Under the same conditions, benzothiazolylamides of 3-(2-benzothiazolyl)propionic acids (IVa-d) are formed in low yields. The alkyl substituent in compounds Ia-d does not influence the path of the reaction, but the overall yield of the products somewhat decreases with the elongation of the chain. The predominant formation of compounds IIIa-d at 110°C (Table 1) is probably the result of isomerization of the imino analogs IIa-d under the reaction conditions. We shall discuss this fact in a future article.

The structure of the synthesized compunds was established by using IR, UV, and PMR spectroscopy methods (Table 4), and mass spectrometry (Tables 2 and 3), and was also confirmed by elemental analysis data (Table 5) and alternative synthesis.

Institute of Chemistry of Plant Materials. Academy of Sciences of the Uzbek SSR, Tashkent 700170. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 986-991, July, 1986. Original article submitted March 12, 1985.

0009-3122/86/2207 0795$12.50

TABLE 1. Conditions of Preparation and Yields of Products of Alkylation Reaction of Compounds Ia-d

Compound	T_{react}, °C	Time, h	Yield*, %		
			II	III	IV
Ia	30	600	60	24	—
	56	20	62	10	—
	110	5	2	83	6
Ib	30	1600	59	5	—
	56	20	60	8	<1
	110	5	5	71	12
Ic	30	1600	49	8	—
	56	20	60	7	<1
	110	5	6	61	11
Id	30	1600	32	3	—
	56	40	51	8	<1
	110	5	6	53	7

*At a 1:2 ratio between 2-alkylaminobenzothiazole and acrylic acid.

TABLE 2. Mass Numbers (m/z) and Relative Intensities of Fragments (%) in Spectra of Compounds IIa-d and IIIa-d

Compound	M^+	$[M-C_2H_3COOH]^+$	$[M-CH_2COOH]^+$	$I[M-C_2H_3COOH]^+ / I[M-CH_2COOH]^+$	Other fragments
IIa	236 (43)	164 (100)	177 (5)	20	191 (25), 177 (5), 163 (25), 150 (5), 136 (45), 135 (34)
IIb	250 (6)	177 (100)	191 (2)	50	205 (5), 164 (9), 163 (61), 150 (79), 136 (42), 135 (12)
IIc	264 (2)	192 (58)	205 (0,3)	193	177 (14), 164 (17), 163 (100), 150 (60), 136 (21), 135 (7)
IId	278 (23)	206 (73)	219 (0,3)	243	235 (100), 191 (7), 177 (20), 164 (26), 163 (87), 150 (82), 136 (20), 135 (13)
IIIa	236 (100)	164 (63)	177 (53)	1	191 (21), 163 (25), 150 (11), 136 (53), 135 (21)
IIIb	250 (31)	177 (49)	191 (49)	1	205 (15), 177 (49), 163 (100), 164 (7), 150 (14), 136 (30), 135 (19)
IIId	264 (31)	192 (45)	205 (5)	9	177 (20), 164 (16), 163 (100), 150 (60), 136 (22), 135 (11)
IIId	278 (26)	206 (24)	219 (1)	24	177 (21), 164 (18), 163 (100), 150 (40), 136 (27), 135 (12)

It is known that the alkylation of 2-aminobenzothiazoles by alklyl halides, including halocarboxylic acids, in a neutral medium takes place at the endocyclic nitrogen atom [6]. Thus, in the reaction of benzothiazole Ia with β-bromopropionic acid, carboxyethylbenzothiazoline IIa, identical to the above described compound IIa, is formed.

The amino-isomer IIIa was obtained by the saponification of 2-[N-methyl-N-(2-methyoxycarbonylethyl)amino]benzothiazole [7]. It should be noted that an imino structure has been erroneously ascribed previously [8] to compound IIIa.

The alternative synthesis of compounds IVa and IVd has been carried out by acylation of heterocyclic amines Ia and Id by acids IIIa and IIId, respectively.

In the IR spectra of the reaction products, intense stretching vibration bands of carboxylic (1705-1740 cm^{-1}, compounds II, IIIa-d) and amide groups (1660-1680 cm^{-1}, compounds IVa-d) were recorded. Still more intense bands characterize the vibration of the C=N bonds, whereby the absorption of the exocyclic azomethine bond is observed in the higher frequency region (1605-1640 cm^{-1}), than that of the endocyclic azomethine bond (1540-1560 cm^{-1} (Table 4).

TABLE 3. Mass Spectra of Compounds IVa-d

Compound	Values of m/z (relative intensity, %)					
	M^+	Type of rupture				Other fragments
		A_1	A_2	B	C_1	
IV	382 (27)	163 (27)	219 (100)	177 (91)	191 (36)	189 (30), 164 (64), 150 (9), 136 (45), 135 (27)
IV	410 (41)	177 (35)	233 (58)	191 (65)	205 (41)	203 (35), 178 (76), 164 (18), 163 (100), 150 (65), 136 (70), 135 (24)
IV	438 (11)	191 (46)	247 (100)	205 (11)	219 (8)	217 (23), 164 (19), 163 (57), 150 (68), 136 (32), 135 (2)
IV	466 (22)	205 (66)	261 (100)	219 (51)	233 (68)	231 (78), 206 (66), 192 (32), 178 (17), 163 (86), 150 (68), 136 (29), 135 (92)

TABLE 4. Spectra Characteristics of Compounds II-IVa-d

Compound	UV spectrum, λ_{max}, nm (log ε)		IR spectrum, ν, cm^{-1}		PMR spectrum, δ, ppm (CF_3COOH)				
	Ethanol	0.1N. HCl	C=O	C=N	$N-CH_2$	CH_2CO	CH_2 (others)	CH_3	Aromatic protons
II a	223 (4,44) 264 (3,97) 281 (3,70) 306 (3,59)	223 (4,33) 256 (4,04) 281 (3,98) 290 (4,02)	1720	1620	4,20 (T, 2H)	2,79 (T, 2H)	—	2,88 (d, 3H)	6,95—7,55 (M, 4H)
II b	223 (4,26) 264 (3,80) 281 (3,57) 290 (3,52) 306 (3,39)	223 (4,19) 256 (3,82) 280 (3,74) 289 (3,78)	1720	1630	4,15 (T, 2H) 3,0—3,4 (M, 2H)	2,71 (T, 2H)	—	1,05 (T, 3H)	6,95—7,50 (M, 4H)
II c	222 (4,39) 263 (3,94) 281 (3,79) 290 (3,81) 306 (3,37)	219 (4,34) 258 (3,91) 281 (3,89) 290 (3,91)	1710	1640	4,20 (T, 2H) 2,90—3,35 (M, 2H)	2,80 (T, 2H)	1,25—1,75 (M, 2H)	0,65 (T, 3H)	6,95—7,60 (M, 4H)
II d	222 (4,47) 265 (4,01) 283 (3,84) 290 (3,82) 305 (3,65)	215 (4,30) 258 (3,89) 280 (3,86) 290 (3,89)	1705	1605	4,18 (T, 2H) 2,95—3,35 (M, 2H)	2,76 (T, 2H)	0,85—1,60 (M, 4H)	0,56 (T, 3H)	7,00—7,50 (M, 4H)
III a	227 (4,50) 274 (4,23) 305 (3,65)	215 (4,47) 262 (4,10) 280 (4,04) 290 (4,08)	1710	1560	3,62 (T, 2H)	2,62 (T, 2H)	—	3,05 (s, 3H)	6,85—7,30 (M, 4H)
III b	226 (4,59) 275 (4,31) 302 (4,01)	220 (4,43) 265 (4,12) 282 (4,08) 291 (4,10)	1725	1550	3,72 (T, 2H) 3,30—3,67 (M, 2H)	2,69 (T, 2H)	—	1,08 (T, 3H)	7,00—7,50 (M, 4H)
III c	227 (4,39) 275 (4,13) 302 (3,83)	220 (4,30) 265 (4,00) 282 (3,98) 291 (4,00)	1725	1548	3,72 (T, 2H) 3,05—3,50 (M, 2H)	2,67 (T, 2H)	1,15—1,82 (M, 2H)	0,65 (T, 3H)	6,95—7,50 (M, 4H)
III d	227 (4,27) 275 (4,00) 302 (3,52)	220 (4,14) 265 (3,84) 283 (3,81) 290 (3,85)	1707	1555	3,70 (T, 2H) 3,15—3,45 (M, 2H)	2,68 (T, 2H)	1,15—1,65 (M, 4H)	0,70 (T, 3H)	6,90—7,40 (M, 4H)
IV a	223 273 300	210 (4,55) 259 (4,18) 281 (4,12) 289 (4,13)	1680	1550	3,75 (T, 2H)	3,08 (T 2H)	—	3,10 (s, 3H) 3,52 (s, 3H)	6,70—7,35 (M, 8H)
IV b	224 (4,56) 278 (4,36) 301 (4,12)	210 (4,53) 259 (4,27) 281 (4,10) 289 (4,10)	1660	1540	3,80—4,15 (T, 4H) 3,05—3,65 (M, 2H)	3,05—3,65 (M 2H)	—	1,17 (T, 3H)	7,00—7,80 (M, 8H)
IV c	227 (4,53) 279 (4,29) 302 (4,11)	212 (4,54) 260 (4,22) 282 (4,14) 290 (4,12)	1670	1550	3,70—4,10 (M 4H) 3,10—3,50 (M 2H)	3,10—3,50 (M, 2H)	1,42—1,70 (M, 4H)	0,68 (T, 6H)	7,05—7,65 (M, 8H)
IV d	224 (4,54) 278 (4,37) 301 (4,18)	210 (4,57) 260 (4,32) 281 (4,13) 289 (4,13)	1670	1550	3,65 (T 2H) 2,90—3,50 (M, 2H)	2,90—3,50 (M 2H)	1,00—1,25 (M, 8H)	0,52 (T, 3H) 0,65 (T, 3H)	6,90—7,40 (M, 8H)

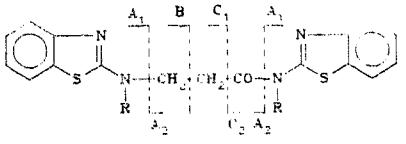
In the UV spectra in ethanol, the imino isomers IIa-d display a finer structure than the amino compounds IIIa-d and IVa-d. On transition from alcoholic solutions to 0.1 N hydrochloric acid, the spectra of the two types of isomers average out (Table 4).

In the PMR spectra, the CS values of the CH_2 group protons at the endocyclic nitrogen atom are shifted to the weaker field (4.15-4.20 ppm, compounds IIa-d), compared with CS of the same protons at the exocyclic nitrogen atom (3.05-3.72 ppm, compounds IIIa-d; see Table 4).

We have previously developed in association with Ya. V. Rashkes [7, 9, 10] a method for the identification of amino- and imino-isomers in the series of 2-aminobenzothiazoles, using mass spectrometery. The most important indication distinguishing these groups of compounds is the distribution of intensities of ions formed as a result of α and β-ruptures (with respect to the heterocycle) of the alkyl chain. The above characteristics were applied in the present work to confirm the structure of compounds IIa-d-IVa-d (Tables 2, 3).

The great prevalence of the $[M-C_2H_3COOH]^+$ ions and the low (or completely absent) peaks of the characteristic $[M-CH_2COOH]^+$ ions indicate the presence of imino compounds IIa-d. Sharp decrease in ratio $I[M-C_2H_3COOH]^+/I[M-CH_2COOH]^+$ (Table 2) is characteristic for amino-benzothiazoles IIIa-d. The peaks of the molecular ions in the mass spectra of IIa-d are less intense than the corresponding peaks in the spectra of the amino isomers IIIa-d, since a decrease in the degree of aromatization destabilizes the molecular ion. The difficulties in the interpretation of the spectra of compounds IId and IIId due to the elongation of the readily decomposing alkyl substituent should be noted.

Compounds IVa-d decompose similarly to the fragmentation of both 2-alkylaminobenzothiazoles [7] and 2-acylaminobenzothiazoles [9] (Table 3). The conversion of the carboxylic group in compounds IIIa-d into an amide group (compounds IVa-d), in general, decreases the stability of the molecule to electron impact. In the mass spectra of amides IVa-d, a successive splitting of the molecular ion according to type A, B, C is observed, the dominating fragmentation process being the α-rupture (type A).



IV a-d

Taking compound IVd as an example and using high resolution mass spectrometry, it was shown that in the compounds studied the rupture of the CH_2—CO bond leads to the appearance of two types of fragmentary ions in the spectrum. The determination of the elemental composition of the ion with m/z 233 made it possible to establish the empirical formula $C_{13}H_{17}N_2S$ (type C_1). However, only 60% of the ions with mass number 231 ($C_{13}H_{15}N_2S$ composition) have been formed by this path. The remaining 40% of the ions were formed as the result of type C_2 fragmentation ($C_{12}H_{11}N_2OS$ composition).

EXPERIMENTAL

The IR spectra were recorded in KBr tablets on a UR-20 spectrophotometer; the UV spectra, on a Hitachi EPS-3T spectrometer; and the PMR spectra, on a Jeol C-60 HL spectrometer, using TMS as internal standard. The mass spectra of compounds IIa-d-IVa-d were run on an MX-1303 mass spectrometer (direct introduction of the sample), at the temperature of the input tube of 100-120°C and ionizing voltage of 40 eV. The summary spectra of compounds IVc-d and the elemental compositions of the ions were determined on a MX-1310 apparatus, at the temperature of the direct introduction system of the sample of 100-130°C, ionizing voltage of 50 eV, using perfluorokerosene as a reference substance.

The compounds obtained were separated by preparative column chromatography, using silica gel L 100/160 as sorbent, and eluting the products successively with benzene and ethanol. The purity of the compounds obtained was controlled on Silufol UV-254 plates.

Reaction of 2-alkylaminobenzothiazoles with Acrylic Acid. A mixture of 10 mmoles of acrylic acid and 5 mmoles of the corresponding heterocyclic amine is held in 10 ml of a solvent (acetone or toluene) at the corresponding temperature (Table 1). After evaporation

TABLE 5. Characteristics of Synthesized Compounds

Compound	mp, °C	R^*_f	Found, %				Empirical formula	Calculated, %			
			C	H	N	S		C	H	N	S
IIa	147—148	0,41	55,7	5,1	11,8	13,4	$C_{11}H_{12}N_2O_2S$	55,9	5,1	11,9	13,6
IIb	110—111	0,46	57,8	5,8	11,1	12,6	$C_{12}H_{14}N_2O_2S$	57,6	5,6	11,2	12,8
IIc	122—123	0,50	59,1	6,2	10,5	12,0	$C_{13}H_{16}N_2O_2S$	59,0	6,1	10,6	12,1
IId	110—111	0,61	60,2	6,3	10,0	11,2	$C_{14}H_{18}N_2O_2S$	60,4	6,5	10,1	11,5
IIIa	167—168	0,20	55,6	5,0	11,8	13,4	$C_{11}H_{12}N_2O_2S$	55,9	5,1	11,9	13,6
IIIb	129—130	0,31	57,4	5,6	11,2	13,5	$C_{12}H_{14}N_2O_2S$	57,6	5,6	11,2	13,6
IIIc	89—90	0,45	59,3	6,0	10,6	12,2	$C_{13}H_{16}N_2O_2S$	59,0	6,1	10,6	12,1
IIId	96—97	0,39	60,0	6,4	10,0	11,1	$C_{14}H_{18}N_2O_2S$	60,4	6,5	10,1	11,5
IVa	209—210	0,52	59,6	4,7	14,8	16,8	$C_{19}H_{18}N_4OS_2$	59,7	4,7	14,6	16,8
IVb	107—108	0,64	61,3	5,2	13,6	15,5	$C_{21}H_{22}N_4OS_2$	61,4	5,4	13,7	15,6
IVc	91—92	0,83	63,2	6,0	12,7	14,3	$C_{23}H_{26}N_4OS_2$	63,0	6,0	12,8	14,6
IVd	105—107	0,89	64,0	6,3	11,9	13,6	$C_{25}H_{30}N_4OS_2$	64,3	6,5	12,0	13,7

*For compounds Ia-d in a 2:1 ethanol—water mixture; for IIIa-d and IVa-d in a 4:1 benzene—acetone mixture.

of the solvent, the residue is chromatographed on a column with silica gel. Compounds IIa-d and IIIa-d are recrystallized from ethanol and compounds IVa-d, from benzene. The characteristics of the synthesized compounds are listed in Table 5.

2-Methylimino-3-(2-carboxyethyl)benzothiazoline (IIa). A 1.52 g portion (10 mmoles) of 3-bromopropionic acid is added to a solution of 0.82 g (5 mmoles) of compound Ia in 15 ml of acetone, and the mixture is boiled for 10 h. The solvent is evaporated, and the residue is treated by water, with heating, then cooled, and triethylamine is added to pH 6. Unreacted initial amine is extracted by benzene. The aqueous solution is evaporated to dryness, and residue is crystallized from absolute ethanol to yield 0.34 g (41%) of compound Ia. The compound does not depress the melting point in a mixture with compound IIa, obtained by reacting amine Ia with acrylic acid.

2-[N-(2-Carboxyethyl)-N-methylamino]benzothiazole (IIIa). A 0.1 g portion (0.4 mmole) of 2-[N-methyl-N-(2-methoxycarbonylethyl)amino]benzothiazole [7] is dissolved in 1.5 ml of ethanol, 1 ml of concentrated hydrochloric acid is added, and the solution is boiled for 3 h. The reaction mixture is evaporated to dryness, the residue is treated with 5 ml of a saturated solution of sodium carbonate, the mixture is filtered, and the product is isolated by neutralization of the filtrate with 10% hydrochloric acid. Yield, 0.04 g (43%). The reaction product does not depress the melting point in a mixture with compound IIIa, obtained from amine Ia and acrylic acid.

N-Alkyl-N-(2-benzothiazolyl)amides of 3-[N-alkyl-N-(2-benzothiazolyl)-amino]propionic acids (IVa, d). An equimolar mixture of aminobenzene Ia or Id and amino acid IIIa or IIId is boiled in toluene for 20 h. The solvent is removed, and the residue is extracted by hot hexane. Hexane is evaporated, and the dry residue is washed with dilute hydrochloric acid and recrystallized from benzene. Yields, 21 (IVa) and 15% (IVd). The compounds do not depress melting points in a mixtures with samples of IVa and IVd obtained in a reaction of amines Ia and Id with acrylic acid.

LITERATURE CITED

1. D. W. Dunwell and D. Evans, J. Chem. Soc., No. 11, 2094 (1971).
2. H. Ogura, M. Kowano, and T. Itch, Chem. Pharm. Bull., 21, 2019 (1973).
3. H. Reimlinger, M. A. Peiren, and R. Merenyi, Chem. Ber., 108, 3894 (1975).
4. H. N. Al-Yallo and M. A. Muniem, J. Heterocycl. Chem., 15, 849 (1978).
5. J. J. Wade, R. F. Hegel, and C. B. Toso, J. Org. Chem., 44, 1811 (1979).
6. Y. Matsunaga and S. Takagi, Yakugaku Zasshi, 88, 1003 (1968); Chem. Abstr., 70, 19971 (1969).
7. Ya. V. Rashkes, R. F. Ambartsumova, V. A. Saprykina, and N. K. Rozhkova, Zh. Org. Khim., 14, 1981 (1978).
8. N. K. Rozhkova and V. A. Saprykina, Uzb. Khim. Zh., No. 3, 60 (1974).
9. Ya. V. Rashkes, R. F. Ambartsumova, V. A. Saprykina, and N. K. Rozhkova, Zh. Org. Khim., 16, 1744 (1980).
10. Ya. V. Rashkes, R. F. Ambartsumova, V. A. Saprykina, and N. K. Rozhkova, Zh. Org. Khim., 17, 614 (1981).