NEW DERIVATIVES OF IMIDAZO [5, 1-b] BENZOTHIAZOLE

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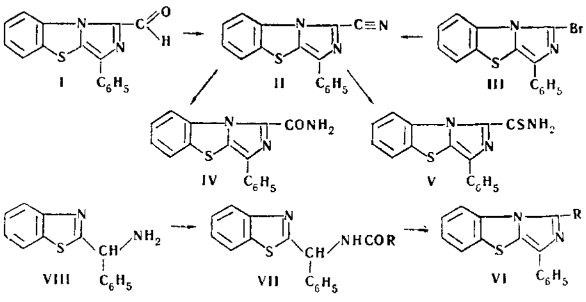
1-Cyano-3-phenylimidazo[5, 1-b]benzothiazole (II) has been obtained from 1-formyl-3-phenylimidazo[5, 1-b]benzothiazole (I) and from 1-brono-3-phenylimidazo[5, 1-b]benzothiazole (III) and has been converted into the corresponding amide (IV) and thioamide (V). New 1-alkyl-3-phenylimidazo[5, 1-b]benzothiazoles (VI) have been synthesized.

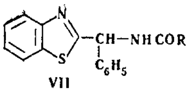
The present work is a continuation of investigations in the field of imidazo[5, 1-b]benzothiazoles [1] and is devoted to the synthesis of new derivatives of this heterocycle in order to study their biological properties. By the reaction of 1-formyl-3-phenylimidazo[5, 1-b[benzothiazole (I) with hydroxylamine and sodium formate [2], we obtained 1-cyano-3-phenylimidazo [5, 1-b] benzothiazole (II). It was also possible to obtain the same substance by the reaction of 1-bromo-3-phenylimidazo[5, 1-b]benzothiazole (III) with potassium cyanide in dimethyl sulfoxide. From the nitrile (II) we then prepared the corresponding amide (IV) and thioamide (V). Some 1-alkyl-3-phenylimidazo[5, 1-b]benzothiazoles (VI) were also synthesized, including 1-trifluoromethyl-3-phenylimidazo [5, 1-b]benzothiazole. The acylamines (VII) required for the synthesis of these compounds were obtained by acylating 2-(α-aminobenzyl)benzothiazole (VIII) with acid chlorides in the presence of pyridine. The cyclization of the acylamines VII to compounds VI was performed by the method described previously [3].



EXPERIMENTAL

1-Cyano-3-phenylimidazobenzothiazole (II). a) A mixture of 1.39 g (0.005 mole) of the aldehyde **I**, 0.4 g (0.0058 mole) of hydroxylamine hydrochloride, 0.63 g (0.0093 mole) of sodium formate, and 10 ml of 99%formic acid was boiled for 1 hr 30 min. The solid matter gradually dissolved and then white crystals separated out. The hot mixture was filtered, and the residue was washed with water and dried in a desiccator. Yield 0.71 g (52%), mp 202.5–203° C (from isobutanol). The filtrate was poured into water to give another 3.2 g of less pure substance. The total yield was 75%. Found, %: C 69.86; H 3.23; N 15.10; S 11.75. Calculated for $C_{16}H_9N_3S$, %: C 69.80 H 3.30; N 15.26; S 11 65. $\nu_{C \equiv N}$ 2230 cm^{-1}, λ_{max} 283, 343 nm; log ε 4.32, 4.0. The IR spectrum was taken on a UR-10 spectrophotometer in paraffin oil. The UV spectrum was taken on an SF-4 instrument in ethanol.

b) A mixture of 0.5 g (0.0018 mole) of the bromide **III**, 0.13 g (0.002 mole) of potassium cyanide, and 5 ml of dimethyl sulfoxide was heated in a sealed tube (under nitrogen) at 160° C (bath temper-


VII

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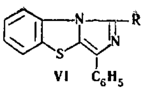
VI

R	VII		VI										
	Mp, ° C	Yield, %	Mp, ° C (solvent (for crystallization)	Empirical formula	Found, %				Calculated, %				Yield, %
					C	H	N	S	C	H	N	S	
C_2H_5	154—157	60.0	104—105 (Methanol)	$C_{17}H_{14}N_2S$	73.33	5.16	9.90	11.25	73.35	5.07	10.06	11.52	68.0
C_3H_7	139—141	70.5	152.5—153.5 (Ethanol)	$C_{18}H_{16}N_2S$	73.87	5.30	9.28	11.04	73.93	5.52	9.58	10.97	98.5
i-C_4H_9	145—147	65.6	117—118 (60% Ethanol)	$C_{19}H_{18}N_2S$	74.21	5.88	9.08	10.47	74.47	5.92	9.14	10.47	86.1
C_5H_{11}	121—122	74.5	101.5—102.0 (Hexane)	$C_{20}H_{20}N_2S$	74.80	6.11	9.02	9.89	74.96	6.29	8.74	10.01	100.0
C_6H_{13}	108—109	86.3	85.0—90.0 (Acetonitrile)	$C_{21}H_{22}N_2S$	74.87	6.68	8.46	9.54	75.41	6.63	8.38	9.59	93.2
$C_6H_5CH_2$	166—168	79.5	141.5—142.5 (Methanol)	$C_{22}H_{16}N_2S$	77.52	4.80	8.26	9.57	77.61	4.74	8.23	9.42	100.0
CF_3	170—170,5	67.4	169—169.5 (80% Ethanol)	$C_{16}H_9F_3N_2S$	—	—	8.44	10.08	—	—	8.80	10.07	99.5

ature) for 3 hr. The clear brownish mass was cooled, and the crystals were filtered off, washed with water, and dried. Yield 0.34 g (69%), mp 201–202° C (from formic acid). There was no depression of the melting point in admixture with the analyzed sample. The IR spectra of the substances obtained by methods (a) and (b) were identical.

3-Phenylimidazo[5, 1-b]benzothiazole-1-carboxylic acid amide (IV). A solution of 0.65 g (0.0024 mole) of the nitrile **II** in 10 ml of concentrated sulfuric acid was left at room temperature for 98 hr. The mixture was poured onto ice, and the precipitate was separated off, washed with water, and dried. Yield 0.68 g (98%), mp 266–267° C (decomp., from isobutanol). Found, %: C 65.38; H 3.66; N 13.79; S 11.03. Calculated for $C_{16}H_{11}N_3OS$. %: C 65.51; H 3.78; N 14.33; S 10.93.

3-Phenylimidazo[5, 1-b]benzothiazole-1-carboxylic acid thioamide (V). Dry hydrogen sulfide was passed for 3 hr through a suspension of 0.67 g (0.0024 mole) of the nitrile **II** in 10 ml of dry pyridine containing 0.3 g (0.003 mole) of triethylamine. The solution was poured into 100 ml of water, and the yellow precipitate was separated off, washed with water, and dried. Yield 0.73 g (99.5%), mp 199.5–200.5° C (from isobutanol). Found, %: C 62.04; H 3.30; N 13.92; S 20.77. Calculated for $C_{16}H_{11}N_3S_2$, %: C 62.11; H 3.58; N 13.58; S 20.73.

2-(α-Propionylaminobenzyl)benzothiazole (VII, R = C_2H_5). A solution of 2 g (0.0083 mole) of the amine **VIII** in 20 ml of absolute ether was treated with 1 ml of dry pyridine, and then 1 ml (0.0115 mole) of propionyl chloride in 4 ml of ether was added rapidly with shaking. After 1 hr 30 min, 20 ml of water was added to the mass and it was triturated and the solid matter was filtered off, washed, and dried. Yield, 1.48 g (60%). The substance was used for the cyclization reaction without purification. The other acyl derivatives (VII) were obtained similarly, their constants being given in the table.

2-(α-Trifluoroacetamidobenzyl)benzothiazole (VII, R = CF_3). A solution of 1.8 ml of trifluoroacetic anhydride in 10 ml of ether was added dropwise with vigorous cooling to a solution of 1.91 g (0.00792 mole) of the amine **VIII** in 20 ml of absolute ether. The precipitate was filtered off and washed with ether. Yield 1.80 g (67.4%), mp 170–170.5° C.

The 1-alkyl-3-phenylimidazo[5,1-b]benzothiazoles (VI) were obtained by a published method [2]. Their constants and analytical results are given in the table.

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