STUDIES IN THE IMIDAZOLE SERIES

XLIX. SYNTHESIS OF DERIVATIVES OF IMIDAZO[2,1-b]THIAZOLE

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A new synthesis of derivatives of imidazo[2,1-b]thiazole from 2-halogenoimidazoles has been effected. The reaction of 2-bromo-4,5-diphenylimidazoles with phenacyl bromide and its p-substituted derivatives has given the corresponding 2-bromo-1-phenylimidazoles, by the heating of which with thiourea and subsequent cyclization of the resulting 2-mercapto-1-phenacylimidazoles under the action of phosphorus oxychloride a number of 2,5,6-triarylimidazo[2,1-b]thiazoles has been synthesized.

The preparation of derivatives of imidazo[2,1-b]thiazole by the reactions of 2-aminothiazoles with α-bromo ketones [2], of 2-mercaptoimidazoles with α-halogeno ketones [3], and of α-halogeno aldehydes [4, 5], and of α-amino aldehydes with thiocyanates [6] is known. Because of the poor accessibility of α-halogeno aldehydes and α-amino aldehydes and their acetals, these methods for the preparation of 2-substituted imidazo[2,1-b]thiazoles are inconvenient. Consequently, we undertook the synthesis of such compounds from the accessible 2-halogenoimidazoles and α-halogeno ketones, as has been reported in a letter to the editor [7].

The reaction of 2-bromo-4,5-diphenylimidazole with α-bromo ketones (phenylacyl bromide and its p-substituted derivatives) in dimethylformamide gave the 2-bromo-1-phenacyl-4,5-diphenylimidazoles (I-V, Table 1). The structure of these compounds was confirmed by their IR spectra.

When compounds I-V were heated with thiourea, as has been described for the preparation of 2-mercaptobenzimidazole from 2-chlorobenzimidazole [8], we obtained the 2-mercapto-1-phenacyl-4,5-diphenylimidazoles (VI-X, Table 1), which, in the solid state, judging from their IR spectra, have the structures of the corresponding imidazoline-2-thiones. Some compounds of this type have been obtained previously in low yields (8-35%) by the reaction of amino aldehydes with potassium thiocyanate in an acid medium. Heating them in conc. HCl leads to 2,5-dialkylimidazo[2,1-b]thiazoles [6]. The compounds VI-X that we prepared readily split out a molecule of water on being heated with $POCl_3$, being converted into the corresponding 2,5,6-triaryl-substituted imidazo[2,1-b]thiazoles (XI-XV, Table 1).

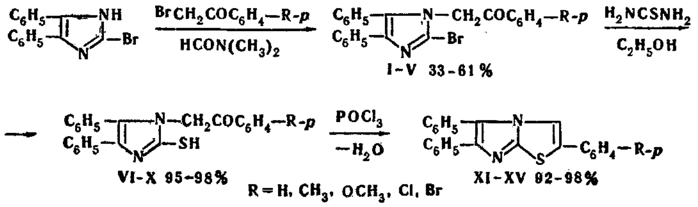

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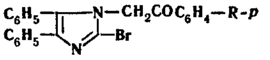
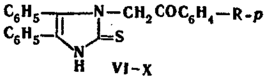
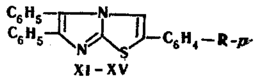
TABLE 1


I-V


VI-X


XI-XV

Compound	R	mp (decomp.), °C	Empirical formula	Found, %[a]					Calculated, %					Yield, %
				C	H	Hal	N	S	C	H	Hal	N	S	
I	H	180—181	$C_{23}H_{17}BrN_2O$[b]	—	—	—	—	—	—	—	—	—	—	46
II	CH_3	205—206	$C_{24}H_{19}BrN_2O$	66,42	4,54	18,79	6,44	—	66,83	4,44	18,53	6,49	—	40
III	OCH_3	187—188	$C_{24}H_{19}BrN_2O_2$	64,18	4,42	17,58	6,25	—	64,44	4,28	17,86	6,26	—	41
IV	Cl	219—220	$C_{23}H_{16}ClBrN_2O$	60,84	3,37	25,60	6,67	—	61,15	3,57	25,72	6,20	—	33
V	Br	227—228	$C_{23}H_{16}Br_2N_2O$	55,78	2,94	32,37	5,51	—	55,67	3,25	32,21	5,65	—	61
VI	H	[illegible]-266	$C_{23}H_{18}N_2OS$	74,28	4,87	—	7,74	8,64	74,56	4,90	—	7,56	8,65	96
VII	CH_3	269—271	$C_{24}H_{20}N_2OS$	74,15	5,27	—	7,19	8,08	74,97	5,24	—	7,29	8,34	98
VIII	OCH_3	222—223	$C_{24}H_{20}N_2O_2S$	72,75	4,89	—	7,10	—	71,96	5,03	—	6,99	—	97
IX	Cl	226—228	$C_{23}H_{17}ClN_2OS$	68,02	4,19	—	6,61	7,51	68,22	4,23	—	6,92	7,92	98
X	Br	238—239	$C_{23}H_{17}Br_2N_2OS \cdot H_2O$	59,32	4,44	17,25	5,32	6,16	59,10	4,10	17,10	5,99	6,86	95
XI	H	175—177	$C_{23}H_{16}N_2S$[c]	—	—	—	8,05	—	—	—	—	7,95	—	92
XII	CH_3	181—182	$C_{24}H_{18}N_2S$	77,80	4,95	—	7,59	8,56	78,66	4,95	—	7,64	8,75	98
XIII	OCH_3	177—178	$C_{24}H_{18}N_2OS$	74,70	4,50	—	7,26	8,19	75,36	4,74	—	7,32	8,38	98
XIV	Cl	214—216	$C_{23}H_{15}ClN_2S$	71,79	3,94	—	6,90	8,08	71,40	3,91	—	7,24	8,29	97
XV	Br	236—238	$C_{23}H_{15}BrN_2S$	—	—	—	6,57	7,19	—	—	—	6,49	7,43	97

[a] For analysis the compounds were purified by crystallization: I and III from methanol; II, V, VI, and IX from ethanol; XI from dioxane; XII from dioxane–water (2:1); XV from dioxane–water (5:1); IV, VII, and XIV from ethanol–dioxane (1:1); VIII and XIII from ethanol–dioxane (3:1); and X from ethanol–dioxane–water (2:4:1). IR spectra (UR-10 instrument, in paraffin oil): I, 1700 (CO); II, 1696 (CO); III, 1696 (CO); IV, 1702 (CO); V, 1700 (CO); VI, 1710 (CO) and 3100 NH; VII, 1700 (CO) and 3100 (NH); IX, 1705 (CO) and 3100 (NH); X, 1700 (CO) and 3110 (NH). We express our thanks to V. V. Kolpakova, Yu. N. Sheinker and their colleagues for performing the microanalysis and recording the IR spectra. [b] According to [7], mp 180-181°C. [c] According to [7], mp 175-177°C.

EXPERIMENTAL

2-Bromo-1-phenacyl-4,5-diphenylimidazoles (I-V, Table 1).* a) A solution of 0.015 mole of 2-bromo-4,5-diphenylimidazole [9] in 15 ml of dimethylformamide was treated with 0.02 mole of NaOH and 5 ml of water, and then with 0.015 mole of an α-bromo ketone. The mixture was heated in the boiling water bath for 10 min and cooled, and the precipitate of I, II, IV, or V was filtered off and washed with water and then with a small amount of methanol.

b) A solution of 0.02 mole of 2-bromo-4,5-diphenylimidazole and 0.02 mole of a bromo ketone in 20 ml of dimethylformamide was heated in the boiling water bath for 5-6 h, cooled and poured into water, and the precipitate of I, III, or V was filtered off and washed with water and methanol. Colorless crystalline substances soluble in organic solvents, insoluble in water, not forming picrates, hydrobromides, and hydrochlorides.

1-Phenacyl-4,5-diphenylimidazoline-2-thiones (VI-X, Table 1). A mixture of 0.01 mole of a compound I-V and 0.05 mole of thiourea in 75 ml of ethanol was boiled for 6 h (in the preparation of VII), 11 h (IX), or 17 h (VI, VIII, X), cooled, poured into water, and neutralized with $NaHCO_3$, and the precipitate was filtered off and washed with water. Colorless crystalline substances soluble in organic solvents and insoluble in water.

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* Compounds I, III, and V were obtained with the participation of B. A. Priimenko.

2,5,6-Triarylimidazo[2,1-b]thiazoles (XI-XV, Table 1). A mixture of 1.5 g of a compound VI-X in 15 ml of $POCl_3$ was boiled for 1 h, the excess of $POCl_3$ was distilled off in vacuum, the residue was treated with water and neutralized with aqueous ammonia, and the precipitate was filtered off and washed with water. Colorless crystalline substances soluble in organic solvents and mineral acids, insoluble in water.

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