lized from petroleum ether. The remaining compounds were obtained as very viscous liquids. The physicochemical constants of the synthesized compounds are presented in Table 3.

LITERATURE CITED

1. M. F. Shostakovskii, F. P. Sidel'kovskaya, and M. G. Zelenskaya, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, 1457 (1957).
2. M. F. Shostakovskii, F. P. Sidel'kovskaya, and A. M. Khomutov, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, 919 (1955).
3. W. Reppe, Polyvinylpyrrolidon, Verlag Chemie, Weinheim (1954).
4. M. F. Shostakovskii and F. P. Sidel'kovskaya, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, 111 (1958).
5. F. P. Sidel'kovskaya, M. G. Zelenskaya, and M. F. Shostakovskii, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, 901 (1959).
6. M. F. Shostakovskii, F. P. Sidel'kovskaya, É. V. Rogova, F. L. Kolodkin, and F. Ibragimov, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, 1111 (1961).
7. É. G. Mesropyan, Yu. A. Bunyatyan, R. K. Aliev, and M. T. Dangyan, Khim. Geterotsikl. Soedin., No. 1, 22 (1974).

RESEARCH IN THE IMIDAZOLE SERIES

LXXXIX.* REACTION OF 1-ALKYL-2-CYANO(ALKOXYCARBONYL)METHYL DERIVATIVES OF IMIDAZOLE AND BENZIMIDAZOLE WITH α-HALO KETONES

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The reaction of 1-alkyl-2-cyano(alkoxycarbonyl)methyl derivatives of imidazole and benzimidazole with α-halo ketones was studied. It was established that the presence of electron-acceptor substituents (CN, $COOC_2H_5$) in the methyl group in the 2 position of the imidazole ring markedly facilitates cyclization of the intermediate imidazolium and benzimidazolium halides to the corresponding cyano (alkoxycarbonyl) derivatives of pyrrolo[1,2-a]imidazoles and pyrrolo[1,2-a]benzimidazoles.

We have established that the reaction of 1-alkyl-2-cyano(alkoxycarbonyl)methyl derivatives of imidazole and benzimidazole with α-halo ketones, which opens up a route to the synthesis of the previously undescribed carboxylic acid derivatives of the pyrrolo[1,2-a]imidazole and pyrrolo[1,2-a]benzimidazole series, does not always proceed unambiguously, in contrast to the analogous reaction in the case of 1,2-dialkyl-substituted imidazoles and benzimidazoles [1]. In some cases quaternary salts, which are readily cyclized to 7-cyano derivatives of pyrrolo[1,2-a]imidazole (IX-XI) without the application of an alkaline agent when they are refluxed in water, are formed when 2-cyanomethyl derivatives of imidazole (I, II) are heated with α-halo ketones in acetone. Treatment with an alcohol solution of sodium ethoxide in the cold was necessary only for the cyclization of bromide VII.

*See [6] for communication LXXXVIII.

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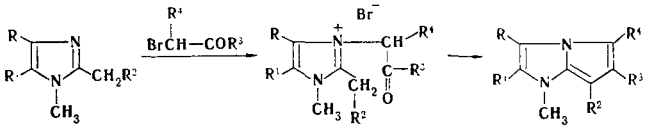

I-IV V-VIII IX-XVI

I $R=R^1=H$, $R^2=CN$; II $R=H$, $R^1=Cl$, $R^2=CN$; III $R+R^1=-CH=CH-CH=CH-$, $R^2=CN$; IV $R-R^1=-CH=CH-CH=CH-$, $R^2=COOC_2H_5$; V $R^2=CN$, $R^3=C_6H_5$, $R=R^1=R^4=H$; VI $R=R^4=H$, $R^1=Cl$, $R^2=CN$, $R^3=CH_3$; VII $R=H$, $R^1=Cl$, $R^2=CN$, $R^3=R^4=CH_3$; VIII $R=R^4=H$, $R^1=Cl$, $R^2=CN$, $R^3=C_6H_5$; IX $R=R^1=R^4=H$, $R^2=CN$, $R^3=C_6H_5$; X $R=R^4=H$, $R^1=Cl$, $R^2=CN$, $R^3=CH_3$; XI $R=R^4=H$, $R^1=Cl$, $R^2=CN$, $R^3=C_6H_5$; XII $R=H$, $R^1=Cl$, $R^2=CN$, $R^3=R^4=CH_3$; XIII $R=R^1=R^4=H$, $R^2=CN$, $R^3=CH_3$; XIV $R=R^1=H$, $R^2=CN$, $R^3=R^4=CH_3$; XV $R+R^1=-CH=CH-CH=CH-$, $R^2=CN$, $R^3=C_6H_5$, $R^4=H$; XVI $R+R^1=-CH=CH-CH=CH-$, $R^2=COOC_2H_5$, $R^3=C_6H_5$, $R^4=H$

In other cases the resulting quaternary imidazolium and benzimidazolium salts proved to be so unstable that they immediately underwent cyclization to pyrrolo[1,2-a]imidazole (VIII, XIV) and pyrrolo[1,2-a]benzimidazole (XV, XVI) derivatives. For preparative purposes, this reaction is more conveniently carried out with 2 moles of starting imidazole per mole of halo ketone, since 1 mole of the starting base, as in the case of 2-cyano(alkoxycarbonyl)methylpyridines [2], is consumed in tying up the hydrogen halide liberated in the reaction.

The ease of cyclization of 1-alkyl-2-cyano(ethoxycarbonyl)methyl-3-acylalkylimidazolium and benzimidazolium bromides to pyrroloimidazole and pyrrolobenzimidazole derivatives is explained by the high reactivity of the methylene group in the 2 position of the imidazole ring activated by strong electron-acceptor substituents (CN and $COOC_2H_5$).

The structures of the synthesized compounds were confirmed by the results of elementary analysis and the IR spectra.

EXPERIMENTAL

The IR spectra of mineral-oil suspensions of the compounds were recorded with a UR-10 spectrometer.

1-Methyl-2-cyanomethylimidazole (I). This compound was obtained by the method in [3].

1-Methyl-2-cyanomethyl-5-chloroimidazole (II). A hot solution of 55 g (0.275 mole) of 1-methyl-2-chloromethyl-5-chloroimidazole hydrochloride [4] in 450 ml of dimethylformamide (DMF) was added with stirring and cooling to a suspension of 27.5 g (0.56 mole) of NaCN in 50 ml of DMF at such a rate that the temperature of the mixture did not exceed 18-20°, after which the mixture was stirred at the same temperature for 5 h. The precipitated NaCl was removed by filtration, the solvent was removed by vacuum distillation, and the residue was washed with water to give 31 g (72%) of a product with mp 142-143° (from benzene) (mp 110-128° [4]). Found: N 23.0%. $C_6H_6ClN_3$. Calculated: N 22.8%.

1-Methyl-2-cyanomethylbenzimidazole (III) and 1-Methyl-2-ethoxycarbonylmethylbenzimidazole (IV). These compounds were obtained by the method in [5].

1-Methyl-2-cyanomethyl-3-acylmethylimidazolium Bromides (V-VIII, Table 1). These compounds were synthesized from I and II and the appropriate α-bromo ketones in acetone by the method in [1].

1-Methyl-6-phenyl-7-cyanopyrrolo[1,2-a]imidazole (IX). A suspension of 1 g of bromide V in 10 ml of water was refluxed for 15 min, after which it was cooled, and the solid material was removed by filtration and washed with water. Compounds X and XI were similarly obtained. Their characteristics are presented in Table 1.

1,5,6-Trimethyl-2-chloro-7-cyanopyrrolo[1,2-a]imidazoles (XII, Table 1). A solution of 0.17 g (2.5 mmole) of sodium ethoxide in 0.5 ml of anhydrous ethanol was added to a solution of 0.6 g (2 mmole) of bromide VII in 2 ml of anhydrous ethanol, and the mixture was allowed to stand at 18-20° for 30 min. The resulting precipitate was removed by filtration and washed with ethanol.

1,6-Dimethyl-7-cyanopyrrolo[1,2-a]imidazole (XIII). A solution of 3.7 g (30 mmole) of I and 1.5 g (15 mmole) of bromoacetone in 20 ml of acetone was refluxed for 2 h, after which it was cooled, and the precipitated hydrobromide of I was removed by filtration. The filtrate was air evaporated to give pyrroloimidazole XIII.

Pyrroloimidazole XIV was similarly obtained from I and α-bromoethyl methyl ketone. The characteristics of XIII and XIV are presented in Table 1.

TABLE 1. Characteristics of the Compounds Obtained

Compound	mp, °C*	Empirical formula	Found, %				Calc., %				Yield, %
			C	H	N	Hal	C	H	N	Hal	
V	216—218†	$C_{14}H_{14}BrN_3O$	—	—	—	25,1	—	—	—	25,0	80
VI	201—203†	$C_9H_{11}BrClN_3O$	—	—	—	39,0	—	—	—	39,4	48
VII	205—207†	$C_{10}H_{13}BrClN_3O$	—	—	—	37,9	—	—	—	37,6	30
VIII	270—272†	$C_{14}H_{13}BrClN_3O$	—	—	—	32,5	—	—	—	32,5	75
IX	135—137	$C_{14}H_{11}N_3$	75,9	5,0	19,1	—	76,0	5,0	19,0	—	79
X	127—128	$C_9H_8ClN_3$	55,8	3,8	21,9	17,8	55,8	4,2	21,7	18,3	38
XI	130—131	$C_{14}H_{10}ClN_3$	66,0	3,9	16,4	13,8	65,8	3,9	16,4	13,9	95
XII	138—140	$C_{10}H_{10}ClN_3$	57,4	5,1	—	16,7	57,8	4,9	—	17,0	74
XIII	114—116	$C_9H_9N_3$	67,5	5,7	26,6	—	67,9	5,7	26,4	—	20
XIV	111—113	$C_{10}H_{11}N_3$	69,3	6,5	24,4	—	69,3	6,4	24,3	—	45
XV	160—161	$C_{18}H_{13}N_3$	79,7	5,0	15,5	—	79,7	4,8	15,5	—	45
XVI	94—95	$C_{20}H_{18}N_2O_2$	75,6	5,5	8,7	—	75,4	5,7	8,8	—	41

* The compounds were purified for analysis by crystallization: V, VI, and XVI from anhydrous ethanol, VII-XIV from ethanol, and XV from methanol–DMF (4 : 1). IR spectra, cm^{-1}: V 1705 (CO), 2250 (CN); VI 1728 (CO), 2250 (CN); VII 1730 (CO), 2190 (CN); VIII 1705 (CO), 2260 (CN); IX 2210 (CN); XI 2200 (CN).
† With decomposition.

2-Phenyl-3-cyano-4-methylpyrrolo[1,2-a]benzimidazole (XV, Table 1). A solution of 5.1 g (30 mmole) of III and 2.98 g (15 mmole) of phenacyl bromide in 30 ml of acetone was refluxed for 4 h, and the precipitated hydrobromide of III was removed by filtration. The filtrate was vacuum evaporated, and the residue was extracted with chloroform. The chloroform solution was washed with water, the solvent was removed by distillation, and the residue was washed with water and methanol.

2-Phenyl-3-ethoxycarbonyl-4-methylpyrrolo[1,2-a]benzimidazole (XVI, Table 1). A solution of 13.08 g (60 mmole) of IV and 5.97 g (30 mmole) of phenacyl bromide in 60 ml of acetone was allowed to stand at 18-20° for 96 h, after which the resulting precipitate was removed by filtration, washed with 10% sodium bicarbonate solution and water, and crystallized from anhydrous ethanol.

LITERATURE CITED

1. P. M. Kochergin, A. A. Druzhinina, and R. M. Palei, Khim. Geterotsikl. Soedin., 148 (1966).
2. D. R. Bragg and D. G. Wibberley, J. Chem. Soc., 3277 (1963).
3. P. C. Jocelyn, J. Chem. Soc., No. 7, 3305 (1957).
4. A. Sonn, E. Hotes, and H. Sieg, Chem. Ber., 57, 953, 2134 (1924).
5. W. Ozegowski and D. Krebs, J. Prakt. Chem., 29, 18 (1965).
6. P. M. Kochergin, M. D. Mashkovskii, A. A. Druzhinina, and M. É. Kaminka, Khim.-farm. Zh., 59 (1976).