RESEARCH IN THE IMIDAZOLE SERIES

XC.* MANNICH REACTION IN A SERIES OF PYRROLO[1,2-a]IMIDAZOLE DERIVATIVES

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The Mannich reaction in the 6-aryl-7-cyanopyrrolo[1,2-a]imidazole series was studied, and the corresponding 5-dialkylaminomethyl derivatives of this heterocycle were obtained.

Continuing our study of electrophilic substitution reactions of pyrrolo[1,2-a]imidazole derivatives [2, 3], we have established that 6-phenyl-7-cyanopyrroloimidazoles (I, II) [1] readily react with formaldehyde and secondary amines to give the corresponding 5-dialkyl(cycloalkyl)aminomethyl derivatives III-XI (Table 1) in high yields. Thus the presence of the electron-acceptor CN group in the 7 position of the pyrroloimidazole two-ring system does not lead to substantial redistribution of the electron density in this heterocycle, and electrophilic attack is directed to the α-carbon atom of the pyrrole ring.

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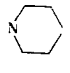
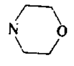
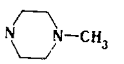
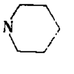
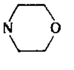
*See [1] for communication LXXXIX.

TABLE 1. 5-Dialkylaminoalkyl Derivatives of Pyrrolo[1,2-a]imidazole (III-XI)

Compound	R	R'	mp, °C*	Empirical formula	Found, %				Calc., %				Yield, %
					C	H	Cl	N	C	H	Cl	N	
III	H	$N(CH_3)_2$	95—97	$C_{17}H_{16}N_4$	73.2	6.7	—	19.9	73,3	6.5	—	20.1	90
IV	H		92—94	$C_{19}H_{20}N_4$	75,2	6,8	—	18,1	75,0	6,6	—	18,4	82
V	H		163—164.5	$C_{20}H_{22}N_4$	75.8	6.9	—	17.5	75,4	7,0	—	17,6	83
VI	H		161—162	$C_{19}H_{20}N_4O$	70,9	6.1	—	17,0	71,2	6.3	—	17,5	47
VII	H		140—141,5	$C_{20}H_{23}N_5$	72,6	7,0	—	21,0	72,0	6,9	—	21,0	91
VIII	Cl	$N(CH_3)_2$	97—99	$C_{17}H_{17}ClN_4$	65.3	5.5	11.1	18.1	65.3	5.5	11,3	17,9	97
IX	Cl	$N(C_2H_5)_2$	88—89	$C_{19}H_{21}ClN_4$	67,3	6.2	10,1	16,2	66,9	6,2	10,4	16,4	83
X	Cl		128—130	$C_{20}H_{21}ClN_4$	68,1	6,1	9.9	15,6	68,1	6,0	10.0	15,9	82
XI	Cl		181—183	$C_{19}H_{19}ClN_4O$	64,4	5.2	9,9	15,5	64,3	5.4	10,0	15,8	85

*The compounds were purified by crystallization: III-V, VII, and VIII-XI from ethanol; VI from acetone.

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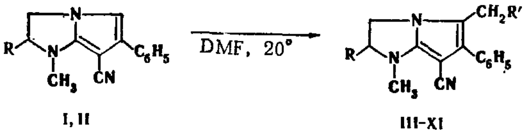

I, II

III-XI

EXPERIMENTAL

1-Methyl-6-phenyl- and 1-methyl-2-chloro-6-phenyl-7-cyanopyrrolo[1,2-a]imidazoles (I, II) were obtained by the method in [1].

5-Dialkylaminomethyl Derivatives of Pyrrolo[1,2-a]imidazole (III-XI, Table 1). A mixture of 0.05 mole of the secondary amine and 0.05 mole of a 37% solution of formaldehyde in 20 ml of dimethylformamide (DMF) was stirred at 20° for 30 min, after which 0.01 mole of the 7-cyano-derivative of pyrroloimidazole (I, II) was added, and the mixture was stirred for another 3 h. The precipitated V, VIII, X, and XI were removed by filtration and washed with aqueous alcohol. In the case of the remaining compounds, no precipitate formed; the reaction mixture was therefore cooled, and crystallization was induced by scratching a glass rod along the wall of the flask or by pouring in a twofold to threefold amount of water; the resulting oil began to crystallize on trituration with petroleum ether.

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RADICAL ADDITION OF THIOLS TO VINYL DERIVATIVES OF 4,5-DIPHENYLIMIDAZOLE-2-THIONE

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It is shown that 2-vinylthio- and 1-vinyl-2-vinylthio-4,5-diphenylimidazoles readily add thiols to the double bond of the vinyl group attached to the sulfur atom. A vinyl group attached to the nitrogen atom undergoes only 7-15% thiylation; this is explained by the electron-acceptor effect of phenyl groups and also by steric factors.

In the present research we investigated the reaction of our previously synthesized [1] 2-vinylthio- (I) and 1-vinyl-2-vinylthio-4,5-diphenylimidazoles (II) with ethane-, butane-, and benzenethiols in order to study the reactivities of the double bonds of vinyl groups attached to different heteroatoms.

In contrast to benzimidazolyl vinyl sulfide, which reacts only with ethanethiol under homolytic conditions [2], imidazolyl vinyl sulfide I readily adds butanethiol and thiophenol, in addition to ethanethiol, to give stable 4,5-diphenyl-2-imidazolyl [β-alkyl(aryl)thioethyl] sulfides (III-V).

The synthesis of thiosulfides III-V in high yields is probably possible becuase of the high stability of the S−C bond due to the effect of two electron-acceptor substituents through the conjugated system of π, p bonds of the heteroring.

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