INVESTIGATIONS IN THE IMIDAZOLE SERIES

LXXIII.* SYNTHESIS OF PYRROLO[1,2-a]BENZIMIDAZOLE DERIVATIVES FROM 2-ALKYL(ARALKYL)BENZIMIDAZOLES

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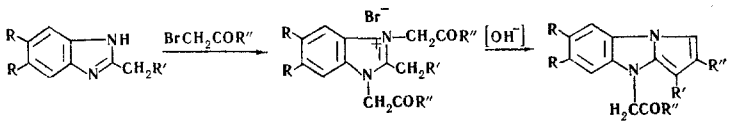
The synthesis of 2-alkyl(aryl)- and 2-aryl-3-alkyl(aryl)-4-acylmethyl-substituted pyrrolo-[1,2-a]benzimidazoles was accomplished by the reaction of 2-alkyl(aralkyl)benzimidazoles with α-haloketones and subsequent cyclization of the resulting 1,3-(diacylmethyl)-2-alkyl-(aralkyl)benzimidazolium halides.

To procure the hard-to-obtain pyrrolo[1,2-a]benzimidazole derivatives [2] with a free 4 position, it seemed of interest to study the quaternization of 1-acyl-2-alkylbenzimidazoles with α-haloketones and, in the case of the formation of 1-acyl-2-alkyl-3-acylalkylbenzimidazolium halides, to subject them to cyclization in anhydrous media and then to saponification of the acyl group. However, we have established that the reaction of equimolecular amounts of 1-acetyl-2-methylbenzimidazole (I) and phenacyl or p-bromophenacyl bromides in anhydrous acetone or benzene, both on heating and in the cold, does not stop at the stage involving formation of the 1-acetyl-2-methyl-3-phenacylbenzimidazolium bromides but proceeds with cleavage of the acetyl group and addition of a second molecule of the bromoketone to give 1,3-(diacylmethyl)-2-methylbenzimidazolium bromides (VII, IX). These same compounds, as well as other quaternary salts of similar structure (VIII-XII, Table 1), are readily formed when 2-alkyl(aralkyl)benzimidazoles (II-VI) are heated with aliphatic and aliphatic-aromatic α-bromoketones in acetone or lower alcohols. The yields of quaternary salts naturally increase when 2-2.5 moles of bromoketone are used per mole of II-VI.

As was reported in [3], when quaternary salts VIII-XII are refluxed in aqueous sodium bicarbonate solution or in lower alcohols in the presence of alkali, they readily cyclize to form the corresponding alkyl-(aryl)-substituted pyrrolobenzimidazoles with ketone residues in the 4 position (XIII-XVII, Table 1). This sort of compound in the condensed pyrrole system with a common nitrogen atom has not been described in the literature.



II-VI VIII-XII XIII-XVII

R=H, Me; R′=H, Me, Ph; R″=Me, Ar

The structures of quaternary salts VIII-XII and pyrrolobenzimidazole derivatives XIII-XVII were confirmed by the IR spectra, in which there are absorption bands of the CO group at 1688-1740 cm^{-1}.

EXPERIMENTAL

2-Benzyl-5,6-dimethylbenzimidazole (VI). This compound was prepared by the method in [4], while the remaining benzimidazole derivatives (I-V) were prepared by well-known methods.

*See [1] for communication LXXII.

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TABLE 1. 1,3-Di(acylmethyl)-2-alkyl(or aralkyl)benzimidazolium Bromides (VIII-XII) and Pyrrolo[1,2-a]benzimidazole Derivatives (XIII-XVII)

Compound	R	R′	R″	Mp, °C (dec.)	ν_{CO}, cm^{-1}	Empirical formula	Found, %				Calc., %				Yield, %
							C	H	Br	N	C	H	Br	N	
VIII	H	H	CH_3	272—274	1730	$C_{14}H_{17}BrN_2O_2$	52.0	5.6	24.4	8.5	51.7	5.3	24.6	8.6	54
IX	H	H	*p*-BrC_6H_4	282—283	1700	$C_{24}H_{19}Br_3N_2O_2$	47.6	3.4	39.2	4.5	47.5	3.1	39.5	4.6	48—66
X	H	H	*p*-$O_2NC_6H_4$	254—256	1708	$C_{24}H_{19}BrN_4O_6$	53.6	3.9	14.5	10.6	53.4	3.5	14.8	10.4	70
XI	CH_3	H	C_6H_5	250—251	1692	$C_{26}H_{25}BrN_2O_2$	—	—	16.8	—	—	—	16.7	—	72
XII	CH_3	C_6H_5	C_6H_5	250—252	1695	$C_{32}H_{29}BrN_2O_2$	69.1	5.4	14.3	5.3	69.4	5.3	14.4	5.1	62
XIII	H	C_6H_5	CH_3	169—171	1740	$C_{14}H_{14}N_2O \cdot C_6H_3N_3O_7$	52.8	3.8	—	15.3	52.7	3.7	—	15.4	74
XIV	H	H	*p*-BrC_6H_4	180—181	1710	$C_{24}H_{16}Br_2N_2O$	56.7	3.3	31.6	5.3	56.7	3.2	31.4	5.5	68
XV	H	H	*p*-$O_2NC_6H_4$	238—240	1692	$C_{24}H_{16}N_4O_5$	65.6	3.7	—	12.5	65.6	3.4	—	12.7	98
XVI	CH_3	H	C_6H_5	164—166	1696	$C_{26}H_{22}N_2O$	82.9	5.8	—	7.7	82.5	6.8	—	7.4	47
XVII	CH_3	C_6H_5	C_6H_5	188—189	1688	$C_{32}H_{26}N_2O$	84.9	5.9	—	6.4	84.5	5.8	—	6.2	67

1,3-Diphenacyl-2-methylbenzimidazolium Bromide (VII). A solution of 4.0 g (0.02 mole) of α-bromoacetophenone in 20-35 ml of acetone was added to a solution of 3.5 g (0.02 mole) of 1-acetyl-2-methylbenzimidazole (I) in 40 ml of anhydrous acetone, and the mixture was refluxed for 23-27 h and cooled. The precipitate was removed by filtration and washed with acetone to give 45% of VII with mp 255-256° [3]. Compound IX was similarly obtained. The yield of VII was 19% when the reaction was carried out in anhydrous benzene at 18-20° for 60 h.

1,3-Di(acylmethyl)-2-alkyl(or aralkyl)benzimidazolium Bromides (VIII-XII, Table 1). A solution of 0.01 mole of II-IV and 0.02 mole of α-haloketone in 50-200 ml of acetone was refluxed for 6-8 h, and the precipitated VIII-X were removed by filtration and washed with acetone. Compounds XI and XII were similarly synthesized, but the reaction was carried out in refluxing methanol (for 8 h for the preparation of XI and for 15 h in the preparation of XII). The compounds were purified for analysis by crystallization from methanol (VIII, IX, XI, XII) or from ethanol–DMF (1:2) (X).

Pyrrolo[1,2-a]benzimidazole Derivatives (XIII-XVII, Table 1). A mixture of 0.01 mole of bromide VIII-X and 0.0105 mole of sodium bicarbonate in 50-350 ml of water was refluxed for 3-8 h and cooled. The precipitate (XIII-XV) was removed by filtration and washed with water. Compounds XVI and XVII were similarly obtained, but the reaction was carried out in methanol with an equimolecular amount of sodium hydroxide. The compounds were purified for analysis by crystallization from ethanol (XIII), ethanol–DMF (2:1) (XIV), DMF (XV), or methanol–DMF (1:1) (XVI, XVII).

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