SYNTHESIS AND PROPERTIES OF AZOLES AND THEIR DERIVATIVES

XVIII.* PREPARATION OF 1-SUBSTITUTED 2-(BENZIMIDAZOL-2-YL)IMIDAZOLINES

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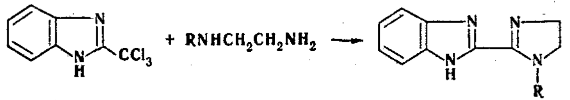
The condensation of 2-trichloromethylbenzimidazole with various N-monosubstituted ethylenediamines has given 1-substitued 2-(benzimidazol-2-yl)imidazolines.

Substituted 2-imidazolines find wide use as biologically active compounds [2, 3]. The present work was devoted to the preparation of N-substituted imidazolines containing a benzimidazole residue in position 2. This type of compound cannot be obtained by the usual methods for the synthesis of 2-imidazolines [4], since the initial benzimidazole-2-carboxylic acid and its derivatives are difficultly accessible compounds or are unreactive (for example, the nitrile). Consequently, for the synthesis of 1-substituted 2-(benzimidazol-2-yl)imidazolines we made use of the capacity of 2-trichloromethylbenzimidazole (I) for taking part in nucleophilic exchange reactions under the influence of amines without undergoing the haloform decomposition [5]. The use in this reaction of N-monosubstituted ethylenediamines (II-VII) enabled the 2-(benzimidazol-2-yl)imidazolines (VIII-XIII) to be obtained.



I II–VII VIII–XIII

II, VIII R=$C_6H_5CH_2$; III, IX R=$HOCH_2CH_2$; IV, X R=$NCCH_2CH_2$; V, XI R= furfuryl
VI, XII R=1-benzotriazolylmethyl VII, XIII R=1α-thienylmethyl

In the IR spectra of compounds (VIII-XIII) there are intense absorption bands in the 1610-1595 cm^{-1} region relating to the vibrations of the C = N bond [6], and there are also bands in the 1430-1420 cm^{-1} region which relate to the deformation vibrations of a C–H bond or to the "scissors" vibrations of the CH_2 groups in an imidazoline ring [7]. In addition, there are absorption bands characteristic for benzimidazoles and for the groupings present in position 1 of the imidazoline ring.

EXPERIMENTAL

Thin-layer chromatography was carried out on Al_2O_3 of activity grade II in the heptane–isopropanol (5 : 1) system.

Compounds (I) [5], (II) [8], (III) [9], (IV) [10], and (V) [11] were prepared by known methods.

N-(α-Thienylmethyl)ethylenediamine (VI). At 15-20°C with stirring, 11.7 g (0.088 mole) of α-chloromethylthiophene was added to 26.5 g (0.44 mole) of 100% ethylenediamine in 30 ml of absolute methanol, the mixture was stirred at 40°C for 4 h and at 60°C for 30 min and was then cooled to 0°C, and a solution of 2.02 g (0.088 mole) of sodium in 15 ml of absolute methanol was added and the resulting mixture was stirred at 0°C for 1 h. The precipitate that deposited was filtered off, the filtrate was evaporated under reduced

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*For Communication XVII, see [1].

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TABLE 1. 1-Substituted 2-(Benzimidazol-2-yl)imidazolines

Compound	Mp, °C*	R_f	Empirical formula	Found, %			Calculated, %			Yield, %
				C	H	N	C	H	N	
VIII	193—194	0,79	$C_{17}H_{16}N_4$	75,1	5,8	20,5	75,0	5,8	20,3	90
IX	183—184†	0,62	—	—	—	—	—	—	—	74
X	170	0,54	$C_{13}H_{13}N_5$	65,0	5,5	29,7	65,2	5,4	29,3	93
XI	209—210	0,72	$C_{15}H_{14}N_4O$	67,5	5,7	21,1	67,3	5,6	20,9	90
XII	188—188,5	0,84	$C_{15}H_{14}N_4S$	63,6	5,1	20,1	63,8	4,9	19,8	88
XIII	205—206	0,75	$C_{17}H_{15}N_7$	63,9	4,6	30,6	64,3	4,7	31,0	75

*Compounds (VIII, X, and XII) were crystallized from acetonitrile, (IX) and (XI) from ethyl acetate, and (XIII) from nitromethane.

†According to the literature [5], mp 180°C.

pressure, and the residual oil was distilled in vacuum giving 10.3 g (75%) of (VI) with bp 115-116°C (7 mm), n_D^{20} 1.5512; d_4^{20} 1.1024. Found: C 53.8; H 7.7; N 18.1%. $C_7H_{12}N_2$. Calculated: C 53.7; H 7.6; N 17.9%. Dipicrate of (VI). Mp, 113-114°C (50% acetone).

N-(Benzotriazol-1-ylmethyl)ethylenediamine (VII). This was obtained in a similar manner to (VI) from 15.0 g (0.25 mole) of 100% ethylenediamine and 8.4 g (0.05 mole) of 1-chloromethylbenzotriazole [12]. Yield of (VII) 7.7 g (81%); viscous undistillable oil. Dipicrate of (VII). Mp, 219-220°C (50% ethanol). Found: C 38.7; H 2.9; N 24.2%. $C_9H_{13}N_5 \cdot 2C_6H_3N_3O_7$. Calculated: C 38.8; H 2.9; N 23.7%.

2-(Benzimidazol-2-yl)-1-benzylimidazoline (VIII). In portions, 1.0 g (0.0042 mole) of (I) was added with stirring at 10°C to 2.5 g (0.017 mole) of (II) in 15 ml of water. The reaction mixture was stirred at 20°C for 1 h and was poured into 30 ml of cold water, and the precipitate was collected, washed with 10% KOH, and dried.

The other 1-substituted 2-(benzimidazol-2-yl)imidazolines (IX-XIII) were obtained similarly (Table 1).

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