SYNTHESIS AND PROPERTIES OF ANALOGS OF 5(4)-AMINOIMIDAZOLE-4(5)-CARBOXAMIDE (AICA)

II.* SOME REACTIONS OF 5(4)-HYDRAZINOIMIDAZOLE-4(5)-CARBOXAMIDE

V. I. Nifontov, V. S. Mokrushin,
Z. V. Pushkareva, and A. A. Mukhina

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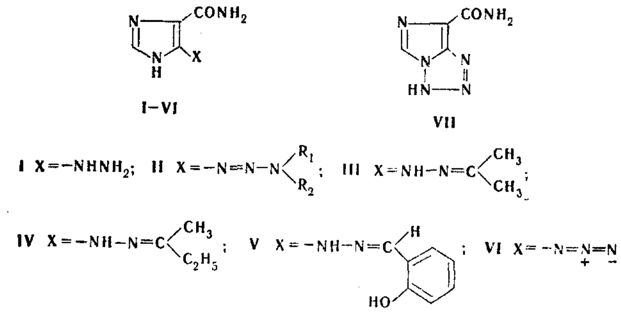
A new analog of AICA – 5(4)-hydrazinoimidazole-4(5)-carboxamide – forms the corresponding hydrazones with carbonyl-containing compounds and reacts with sodium nitrite to give 5(4)-azidoimidazole-4(5)-carboxamide, the structure of which was proved on the basis of IR spectroscopic data.

In addition to the AICA analogs that we previously described [1], we have obtained an analog containing a hydrazino group in the 5(4) position of the imidazole ring – 5(4)-hydrazinoimidazole-4(5)-carboxamide (I).

On the basis of an analysis of the literature data on the proposed mechanism of the antitumorigenic action of 5(4)-(3,3-dialkyl-1-triazeno)imidazole-4(5)-carboxamides (II) [2, 3], the synthesis of hydrazones of 5(4)-hydrazinoimidazole-4(5)carboxamide (III-V), which are structural analogs of biologically active II, seemed of interest for comparative biological tests. Compounds III-V were obtained by the reaction of the hydrochloride of I with the appropriate aldehydes or ketones. The UV spectra (Table 1) of III-V were studied. As one should have expected, the absorption curves of the starting hydrochloride of I and of hydrazones III and IV proved to be similar, except for 5(4)-salicylidenehydrazinoimidazole-4(5)-carboxamide (V), for which the long-wave maximum is shifted to 348 nm.



5(4)-Azidoimidazole-4(5)-carboxamide (VI) was synthesized by the reaction of the hydrochloride of I with $NaNO_2$. To find out which of the two possible structures the synthesized compound has (VI or VII), we studied its IR spectrum in the crystalline state. The presence of a characteristic intense band at 2220 cm^{-1} in the spectrum and the absence of bands at 1060 cm^{-1} make it possible to assume that the investigated compound exists in the azide form (VI) [4, 5]. In all probability, closing of the tetrazole ring is hindered in view of the relatively high electron density on the nitrogen atom of the imidazole ring.

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*See [1] for communication I.

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TABLE 1. Characteristics of the Compounds Obtained

Compound	mp, °C (crystallization solvent)	Empirical formula	Found, %			Calc., %			UV spectra*		Yield, %
			C	H	N	C	H	N	λ_{max}, nm	lg ε	
III	188—190 (chloroform + ether)	$C_7H_{11}N_5O$	46,15	6,16	38,7	46,4	6,08	38,7	4,33; 4,07	204; 286	63,5
IV	156—157 (ethyl acetate)	$C_8H_{13}N_5O$	49,6	7,16	35,3	49,23	6,66	35,89	3,97; 3,78; 4,07	206; 245; 278	25
V	225—226 (water)	$C_{11}H_{12}N_5O$	53,85	4,9	28,74	53,7	4,88	28,5	3,84; 3,23; 3,80	202; 280; 348	70
VI	146	$C_4H_4N_6O$	32,11	2,40	54,15	31,6	2,63	55,26	—	—	50

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*For the hydrochloride of I, λ_{max} (log ε): 198 (4.02), 269 (3.99).

EXPERIMENTAL

5(4)-Isopropylidenehydrazinoimidazole-4(5)-carboxamide (III). A mixture of 1.1 g (6.2 mmole) of the hydrochloride of I in 150 ml of absolute ethanol, 6 ml (81 mmole) of acetone, and 2.5 ml (51.5 mmole) of triethylamine was refluxed for 8 h and evaporated to dryness in vacuo. The residue was treated with chloroform and crystallized. Compounds V and IV were similarly obtained. In the latter case, the residue after evaporation of the reaction mass was dissolved in chloroform and treated with a saturated solution of 5 g of sodium carbonate in water. The layer containing chloroform was separated and vacuum evaporated to dryness. The residue was suspended in a small amount of ether, and the suspension was removed by filtration and crystallized.

5(4)-Azidoimidazole-4(5)-carboxamide (VI). A cooled solution of 1.3 g (18.8 mmole) of $NaNO_2$ in 4 ml of water was added by drops with thorough stirring to 1 g (5.6 mmole) of the hydrochloride of I in 11 ml of water at −5°, and the mixture was held at this temperature for 15 min. The precipitate was removed by filtration and washed with water. IR spectrum: $-N=\underset{+}{\underline{N}}=\underline{N}-$ group at 2210 cm^{-1}. The UV spectra of I and III-V in water were recorded with a Perkin-Elmer spectrophotometer, while the IR spectra of VI were recorded with a UR-20 spectrophotometer at 1900-3600 cm^{-1} as perfluorohydrocarbon pastes and at 700-1700 cm^{-1} as mineral oil suspensions.

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