

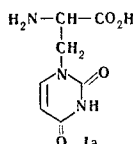
PEPTIDES OF DL-WILLARDIINE. HOMO- AND  
HETERODIPEPTIDES FROM WILLARDIINE

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One of the types of pyrimidinylpeptides (i.e., peptides constructed of pyrimidinyl- and purinyl- $\alpha$ -amino acids) consists of peptides including residues of only those  $\alpha$ -amino acids the lateral radicals of which contain nucleic bases. Below, such amino acids will be called nucleoamino acids and the peptides derived from them nucleopeptides. The latter are hybrid analogs of nucleic acids and proteins. Their study may lead to important theoretical and practical results.

In order to develop methods for the controlled synthesis of nucleopeptides including residues of the natural nucleoamino acid  $\beta$ -(uracil-N<sub>1</sub>-yl)- $\alpha$ -alanine (willardiine) [1-9], we have obtained a series of the simplest homo- and heteropeptides of DL-willardiine (Ia). To create the peptide bond, we used the mixed anhydride method, the activated ester method, and the carbodiimide method, and for masking the  $\alpha$ -amino group we used benzyloxycarbonylation.



The following previously unknown compounds were synthesized:  $\alpha$ -N-cbo-DL-willardiine (I),\* the p-nitrophenyl ester of  $\alpha$ -N-cbo-DL-willardiine (II), the methyl ester of DL-willardiine (III), the methyl ester

\*Here and below, the abbreviation "cbo" denotes the benzyloxycarbonyl group.

TABLE 1. Dipeptides Based on Willardiine

Com- pound	mp, °C	R <sub>f</sub> in system		Yield, %	Com- pound	mp, °C	R <sub>f</sub> in system		Yield, %
		<i>n</i> -C <sub>6</sub> H <sub>5</sub> OH- -CH <sub>3</sub> CO <sub>2</sub> H- -H <sub>2</sub> O (9 : 1 : 2)	<i>i</i> -C <sub>6</sub> H <sub>5</sub> OH- -NH <sub>4</sub> OH- -H <sub>2</sub> O (7 : 1 : 2)				<i>n</i> -C <sub>6</sub> H <sub>5</sub> OH- -CH <sub>3</sub> CO <sub>2</sub> H- -H <sub>2</sub> O (9 : 1 : 2)	<i>i</i> -C <sub>6</sub> H <sub>5</sub> OH- -NH <sub>4</sub> OH- -H <sub>2</sub> O (7 : 1 : 2)	
I	143	0,87	0,71	52	VIII <sup>b</sup>	133	0,11	0,32	72
II	200	0,09	0,19	59	IX <sup>c</sup>	—	0,96	0,72	59
III	216	0,24 <sup>a</sup>	0,38	78	X <sup>c</sup>	260	0,99	0,69	59
IV	101	0,48	0,33	58	(decomp)				
V	131	0,17	0,11	66	XI <sup>d</sup>	—	0,89	0,73	61
VI	193	0,55	0,30	71	XII	211	0,69	0,48	69
VII	136	0,31	0,35	74	XIII	330	—	0,10	58
					(decomp)				
					XIV <sup>b</sup>	—	0,94	0,76	88

- a. Hydrochloride.
- b. Hydrobromide.
- c. Monohydrate.
- d. Monohydrate-hydrobromide.

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of N-cbo-glycyl-DL-willardiine (IV), the methyl ester of  $\alpha$ -N-cbo-DL-willardiyl-L-tyrosine (V), N-cbo-glycyl-DL-willardiine (VI),  $\alpha$ -N-cbo-DL-willardiylglycine (VII),  $\alpha$ -n-cbo-DL-willardiyl-L-tyrosine (VIII), DL-willardiylglycine (IX), glycyl-DL-willardiine (X), DL-willardiyl-L-tyrosine (XI), the methyl ester of  $\alpha$ -N-cbo-DL-willardiyl-DL-willardiine (XII),  $\alpha$ -N-cbo-DL-willardiyl-DL-willardiine (XIII), and DL-willardiyl-GL-willardiine (XIV). The last-mentioned compound is the simplest representative of the family of poly(pyrimidin-N-yl)- $\alpha$ -amino acids and the first member of the series of monotonic nucleopeptides containing a uracil nucleus as the repeating side chain.

The constants and yields of compounds I-XIV are given in Table 1.

We are continuing the synthesis and study of the properties of the pyuranylpeptides and nucleopeptides.

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