$$[C_6H_5CH_2C(CH_3)_2OCO]_2O+H_2NCHRCO_2^- \rightarrow C_6H_5CH_2C(CH_3)_2OCONHCHRCO_2^- + C_6H_5CH_2C(CH_3)_2OH+CO_2$$

The pyrocarbonate (I) was taken 20% excess and was added to the reaction mixture in the form of a 1 M solution in acetone. The time and temperature of the reaction was varied according to the reactivity of the amino acid. The Pboc derivatives of the amino acids were isolated by the method generally used in similar cases [5, 6] and were crystallized from the solvent mixtures shown in Table 1 or were converted into the dicyclohexylammonium salts.

Table I gives the reaction conditions and the characteristics of the compounds obtained. The melting points were determined in capillaries and are not corrected. The angles of optical rotation were determined on a Perkin–Elmer 141 polarimeter. The results of elementary analysis for C, H, and N corresponded to the calculated figures.

LITERATURE CITED

1. R. Hirschmann and D. Veber, in: The Chemistry of the Polypeptides [in Russian], Moscow (1977), pp. 143-165.
2. V. F. Pozdnev, Khim. Prirodn. Soedin., 384 (1971).
3. V. F. Pozdnev, Khim. Prirodn. Soedin., 402 (1972).
4. V. F. Pozdnev, Zh. Organ. Khim., 7, 1078 (1971).
5. V. F. Pozdnev, Khim. Prirodn. Soedin., 764 (1974).
6. V. F. Pozdnev, Bioorg. Khim., 3, 1605 (1977); V. F. Pozdnev, Zh. Org. Khim., 13, 2531 (1977).

SYNTHESIS OF ANALOGS OF THE C-TERMINAL PART OF FIBRINOPEPTIDE A

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The role of the configuration of the amino-acid residues of substrates (inhibitors) in the manifestation of the catalytic properties of thrombin have been studied little [1]. To investigate the stereospecificity of thrombin and to analyze the influence of the configurations of the amino acids of the immediate surroundings of the bond sensitive to hydrolysis by thrombin we have performed the synthesis of all the possible steroisomers of esters of tosylvalyl- (or tosylphenylalanyl)arginine of the L-L, D-D, L-D, and D-L types.

The hydrochlorides of Tos-X-Arg-OCH_3 (where X = Val, Phe, Z-Pro-Ala) were synthesized by condensing free arginine with the N-hydroxysuccinimide esters of the corresponding tosylamino acids obtained similarly to the N-hydroxysuccinimide esters of benzyloxycarbonylamino acids [2]. The condensation products were converted into the corresponding esters by treatment by thionyl chloride in absolute ethanol. The method of synthesizing peptides with unsubstituted C-terminal arginine, which possesses a number of advantages, has been widely used to obtain bradykinin analogs [3, 4]. It also proved convenient for the compounds Tos-X-Arg-OH and we used it in the present work. On the following page, we give the characteristics of the compounds synthesized (their individuality was shown by TLC on silica gel, paper electrophoresis at pH 6.5, and the results of elementary analysis).

Tosylphenylalanyl- (or Tosylvalyl)arginine (I, II). A mixture of 5.7 mmole of the N-hydroxysuccinimide ester of the appropriate tosylamino acid in 7.5 ml of dioxane and 6 mmole of arginine in 4.5 ml of water was stirred at room temperature for 12-16 h. The precipitate that deposited was filtered off, washed with water, ethyl acetate, and dioxane, and recrystallized from n-butanol or isopropanol.

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	Yield, %	mp, °C	Optical activity $[\alpha]_D^{25}$, c=1		$R_f^{\ddagger}$	E_{Arg} pH 6,5
I. Tos-*L*-Phe-*D*-Arg-OH	99	253—254	−35,0	CH_3OCH	0,37	0,11
II. Tos-*D*-Val-*D*-Arg-OH	96	137—139†	+33,1*	"	0,42	0,18
III. Z-Pro-Ala-Arg-OH	90	139—140†	−40,5	"	0,39	0,15
IV. Tos-*L*-Phe-*D*-Arg-OCH_3	97	92—93	−28,5	"	0,51	0,67
V. Tos-*D*-Val-*D*-Arg-OCH_3	95	107—108	+36,7	"	0,52	0,60
VI. Z-Pro-Ala-Arg-OCH_3	86	74—75	−58,0	"	0,51	0,60
VII. Tos-*L*-Val-*L*-Arg-OCH_3	51	100†	−45,0	"	0,49	0,66
VIII. Tos-*D*-Val-*D*-Arg-OC_3H_7	72	102—103†	+41,5	"	0,58	0,57

*c = 0.2.

†The decomposition temperatures are given.

‡Butanol—pyridine—acetic acid—water (30:20:6:10).

Benzyloxycarbonylprolylalanylarginine (III). A solution of 3.1 mmole of Z-Pro-Ala-OH and 3.1 mmole of N-hydroxysuccinimide in 15-20 ml of absolute tetrahydrofuran was stirred with 3.1 mmole of dicyclohexylcarbodiimide at 0°C for 2 h and at room temperature for another 4 h. The dicyclohexylurea was filtered off, the solvent was evaporated off, and the residue in 5 ml of dioxane was treated with 3.1 mmole of arginine in 3 ml of water. The subsequent working up was the same as described for compounds (I) and (II).

The tosylpeptides (I-III) were converted into the esters (IV-VIII) by the following method. At −25°C, 5 mmole of thionyl chloride was added to a suspension of 4.8 mmole of compound (I-III), the temperature of the reaction mixture was slowly raised to room temperature, and it was kept there for 6-8 h. The ethanol was driven off in vacuum at 40°C, the residue was kept over caustic soda in a vacuum desiccator, and then solutions of the esters (IV-VIII) in methanol were purified by passage through a small column of alumina.

LITERATURE CITED

1. D. M. Fedoryak, V. K. Kibirev, A. A. Sereiskaya, and S. V. Serebryanyi, in: Molecular Biology [in Russian], No. 17, Kiev (1977), pp. 64-75.
2. G. W. Anderson, J. E. Zimmerman, and Z. M. Callahan, J. Am. Chem. Soc., 86, 1839 (1964).
3. M. P. Filatova, N. A. Krit, G. S. Suchkova, G. A. Ravdel', and V. T. Ivanov, Bioorg. Khim., 1, 437 (1975).
4. N. A. Krit, G. A. Ravdel', and V. T. Ivanov, Bioorg. Khim., 2, 1455 (1976).