after which 400 ml of MC was added and it was washed successively with 0.1 N HCl (4 × 100 ml), and H_2O (4 × 100 ml) and was dried with anhydrous Na_2SO_4. The solution was evaporated in vacuum. The oily residue was dissolved in 100 ml of ethyl acetate, and the solution was kept at 2 ± 2°C for 48 h. The crystalline precipitate was washed with hexane and dried in vacuum at 40°C to constant weight. This gave 28.6 g of a dry white powder (see Table 1).

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SYNTHESIS OF THE C-TERMINAL HEXA- AND HEPTAPEPTIDE SEQUENCES OF OXYTOCIN

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Three schemes for the synthesis of the heptapeptide 3-9 of the oxytocin sequence with different protective groups of the thiol function of the cysteine and the use of two main methods of condensation (the activated-ester method and the mixed-anhydride method) are considered.

Variants of the synthesis of the C-terminal tri- and tetrapeptides of the oxytocin sequence have been considered previously [1, 2]. In order to develop the optimum scheme for the synthesis of oxytocin, we have tried out variants of the synthesis of the heptapeptide starting from the C-terminal tripeptide: a 2 + (2 + 3) and a 2 + (1 + 4) scheme, and stepwise synthesis using the C-terminal tetrapeptide as the starting material.

Table 1 gives the properties of pentapeptides of the 5-9 sequence of oxytocin obtained with the use of activated pentafluorophenyl (PFPE) or paranitrophenyl (PNPE) esters, and also by the mixed-anhydride (MA) method using pivaloyl chloride by a 1 + 4 scheme. As can be seen from Table 1, the highest yield of pentapeptide was observed on the use of a PFPE and the lowest on the use of the MA method. However, if it is borne in mind that to obtain a PFPE or a PMPE a separate stage of synthesis using a strong allergen — DCHC — must be performed, the MA method at this stage has definite advantages.

Table 2 gives the properties of the 4-9 hexapeptides of the oxytocin sequence obtained by a 1 + (1 + 4) scheme. A similar situation with a change in the yield of hexapeptide on the use of the same method of condensation as in the synthesis of the peptapeptide was observed. Furthermore, with the introduction into the peptide molecule of such amino acids as asparagine and glutamine the hydrophilic properties of the compounds rose, which led to a considerable fall in the yield of certain products. Thus, when Pym protection of the thiol function of cysteine was used it was impossible to obtain a hexapeptide in satisfactory yield (∿ 15%). Thanks to its increased solubility in the majority of solvents used for the purification of peptides (water, DMSO, DMFA, THF, acetone, alcohols, ether), it was impossible to isolate this peptide in the pure form.

Attempts to obtain the 3-9 heptapeptide of the oxytocin sequence starting from the hexapeptide by the azide method of condensation and also by the use of MA (pivaloyl chloride)

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TABLE 1. Physicochemical Properties of Pentapeptides of the Type of BOCAsnCys(X)-ProLeuGlyNH$_2$* Obtained by a 1 + 4 Scheme

Compound	Mol. mass	Method of condensation	mp, °C	$[\alpha]_D^{20}$ (c 1:DMFA), deg	Chromatographic mobility, R_f**	Yield, %
I	614.7	PNPE	223-225	− 21.5	0.82	87
I	"	MA	227	− 22.5	0.80	43
II	691.9	PNPE	207-208	− 67.0	0.77	83
II	"	PNPE	207-208	−	0.79	70
II	"	MA	−	− 65.5	0.76	67
III	705.7	PNPE	198-200	− 22.5	0.85	61
III	"	MA	198-200	− 25.0	0.87	50
IV	698.6	MA	144-146	− 61.0	0.40	46
V	844.1	DCHC + HBT***	173	− 21.0	0.60****	63

* X − Pprtective group of the thiol function of cysteine: ME(I), Bzl (II), Bz (III), Pym (IV), Trit (V), Bzm (VI).
** System: ethyl acetate−pyridine−acetic acid−water (30:10:3:5.5).
*** 2 + 3 Scheme of synthesis.
**** The same system at a ratio of the components of (60:10:3:5.5).

TABLE 2. Physicochemical Properties of Hexapeptides of the Type of BOCGlnAsnCys-(X)ProLeuGlyNH$_2$* Obtained by a 1 + 5 Scheme

Compound	Mol. mass	Method of condensation	mp, °C	$[\alpha]_D^{20}$ (c 1: DMFA), deg	Chromatographic mobility, R_f**	Yield, %
VII	744.0	PNPE	179-180	− 47.5	0.29	29
VIII	820.1	PNPE	203-204	− 48.0	0.40	83
VIII	"	PNPE	200-201	− 49.0	0.40	80
VIII	"	MA	199-201	− 50.0	0.40	70
IX	834.0	MA	210	− 38.0	0.26	72
X	826.8	MA	Oil	***	***	15

* X − Protective group of the thiol function of cysteine: Me (VII), Bzl (VIII), Bzm (IX), Pym (X).
** System: ethyl acetate−pyridine−acetic acid−water (30:10:3:5.5).
*** It was impossible to isolate the products in the pure form.

and of 2-ethoxy-N-ethoxycarbonyl: 1,2-dihydroquinoline were unsuccessful. Only the use of a PNPE enabled the product to be obtained, with a yield of about 50%.

In view of the above-mentioned difficulties in the synthesis of the heptapeptide by successive condensation using a 1 + [1 + (1 + 4)] scheme, we performed the synthesis of 3-9 heptapeptides of the oxytocin sequence by a 2 + 5 scheme. Table 3 gives the properties of the compounds obtained by the activated-ester method without their isolation (DCHC + HBT). All the products with the exception of the Bz and Bzm derivatives (yields 50 and 38%, respectively) were obtained in good (more than 60%) yield.

As follows from Tables 1-3 and also from the results of preceding communications [1, 2], the synthesis of the C-terminal hexapeptide of the oxytocin sequence using Bzl as the protective group of the thiol function of cysteine can be achieved with fairly high yield by stepwise synthesis using the C-terminal tetrapeptide. So far as concerns the protective groups, the production of their derivatives by this scheme is unrealistic in view of the low yield and the poor quality of the intermediate compounds so obtained.

On the use of the Trit and, particularly, Pym protective groups for the thiol function of histidine, a preferential variant is the preparation of the C-terminal heptapeptide (2 + 5 scheme) as the starting compound for the synthesis of oxytocin. Since it is impossible to obtain the heptapeptide using benzyl protection of the thiol function of cysteine by the 1 + 6 scheme, the 2 + 5 scheme of synthesis is preferable for protection of this type.

TABLE 3. Physicochemical Properties of Heptapeptides of the Type of BOCIleGlnAsnCys(X)ProLeuGlyNH$_2$* Obtained by a 2 + 5 Scheme Using the Activated-Ester Method (DCHC + HBT) without Isolation

Compound	Mol. mass	mp, °C	$[\alpha]_D^{20}$ (c 1; DMFA), deg	Chromatographic mobility, Rf**	Yield, %
XI	857,2	227	—59,0	0,34	60
XII	934,1	206—207	—50,0	0,50	75
XIII	947,9	207—209	—60,0	0,76	50
XIV	938,9	149—150	—55,5	0,39	82
XV	1085,3	136	—16,0	0,76	88
XVI	948,1	173—174	—51,5	0,47	38

* X – Protective group of the thiol function of cysteine: Me (XI), Bzl (XII), Bz (XIII), Pym (XIV), Trit (XV), Bzm (XVI).
**System: ethyl acetate–pyridine–acetic acid–water (30:10:3:5.5).

To confirm the structure and check the purity of the peptides from the oxytocin sequence and a number of intermediate compounds that we had obtained we used ^{13}C NMR spectroscopy. The chemical shifts found are given in Tables 4-6. The assignment of the resonance signals was based on literature information [3] and a comparison of the shemical shifts in a number of compounds with the inclusion of the results of preceding studies on the N-terminal tripeptide [4, 5] and the C-terminal tetrapeptide [2] of oxytocin. In a number of cases additional information on the nature of the splitting of the signals and the values of the spin-spin coupling constants was used.

The complete assignment of the resonance signals of the C=O group for peptides containing five and more amino acid residues is difficult, as a rule, because the positions of the signals are determined not only by the structure of the particular peptide but also by the amount of water in the sample. In the spectra of all the peptides considered in the present work, the signals of the C_δ nuclei of Gln, C_α of Leu and Cys^6 and of the C=O protective groups of the thiol function of cysteine were identified in the 160-201 ppm region; in some cases a fairly reliable assignment of other resonance signals was possible. At the same time, in the majority of the spectra it was possible to single out in this region one or two groups out of the three or more signals within which the identification of the signals was impossible. In Tables 4 and 5, parentheses are used to denote such groups; brackets of different types for different groups correspond to two groups in one spectrum. In the case of peptides with benzoyl protection of the thiol function of the Cys^6 residue, not only the assignment of the signals but also their combination into groups (this is discussed in more detail below) was difficult, since the majority of the signals of this frequency region were enclosed in parentheses. It must be mentioned that it would be undesirable to omit this part of the spectral range from consideration, since the total positioning, number, and relative intensities of the signals give information on the purity and, to some extent, on the structure of a peptide even if no complete assignment is made.

Analysis of the resonance signals in the 10-160 ppm range was substantially facilitated by available information on the terminal peptides of oxytocin with different protective groups for the thiol function of cysteine [2, 4, 5].

Table 6 gives the chemical shifts for the carbon nuclei present in the protective groups. In the main, these figures are in good agreement with the results of preceding studies. An exception is the Bz group in the Cys^6 residue. Beginning from the pentapeptide (when a Asn residue appears before Cys^6), there is a change in the chemical shifts of all the carbon nuclei of the Bz group, the most substantial shift (10 ppm downfield) being observed for the C=O nucleus. The spectrum of the Asn residue undergoes equally considerable changes (Tables 4 and 5). Thus, the signal of the C_α nucleus shifts downfield by 4 ppm, and one of the signals of the C=O (C_α or C_γ) upfield by 4 ppm. Apparently, we are observing the result of an interaction of the Bz group with the Asn residue through their spatial propinguity. However, a more detailed consideration of this effect requires a number of model compounds with other amino acid residues preceding Cys. It must be mentioned that the above-mentioned feature of the spectra of peptides with protective Bz groups introduces additional difficulties

TABLE 4. Chemical Shifts in the ^{13}C NMR Spectra of the C-Terminal Penta- and Hexapeptides of the Oxytocin Sequence*

Residue	Nucleus	Compound I	II	III	IV	V	VII	VIII	IX
Gln	C_0						(171,8)	(171,5)	(171,5)
	C_α						54,3	54,3	54,1
	C_β						27,9	27,8	27,8
	C_γ						31,6	31,6	31,6
	C_δ						174,1	174,1	174,1
Asn	C_0	(171,5)	(171,4)	166,5[a]	(171,6)	171,4	170,9[b]	170,8[c]	171,0
	C_α	51,5	51,5	57,7	51,5	51,5	49,7	49,7	49,6
	C_β	37,4	37,5	36,9	37,5	37,2	37,1	37,1	37,2
	C_γ	171,5)	(171,4)	170,9[a]	(171,7)	171,4	(171,6)	(171,6)	(171,8)
Cys	C_0	169,2	169,0	169,0	169,2	168,1	169,2	169,0	169,2
	C_α	50,2	50,5	51,3	50,5	50,4	50,5	50,8	51,3
	C_β	35,2	32,7	29,6	32,6	32,9	35,0	32,4	32,1
Pro	C_0	(171,6)	(171,6)	171,7	(171,7)	171,4	(171,8)	(171,7)	(171,8)
	C_α	60,0	60,0	59,9	60,0	59,6	60,2	60,0	60,0
	C_β	28,9	29,0	28,9	29,0	23,5	28,9	28,9	29,0
	C_γ	24,4	24,5	24,5	24,4	24,4	24,5	24,4	24,4
	C_δ	46,9	47,0	46,9	47,0	46,6	47,0	46,9	46,7
Leu	C_0	172,1	172,1	172,2	172,2	172,2	172,2	172,2	172,2
	C_α	51,5	51,5	51,5	51,5	51,5	51,6	51,5	51,5
	C_β	40,2	40,2	40,1	40,2	40,3	40,1	40,2	40,2
	C_γ	24,2	24,3	24,3	24,3	24,2	24,3	24,2	24,3
	C_{δ_1}	23,0	23,0	23,0	23,1	22,9	23,1	23,0	23,0
	C_{δ_2}	21,5	21,6	21,6	21,5	21,7	21,6	21,5	21,5
Gly	C_0	170,9	170,9	170,9	171,0	171,0	171,0[b]	171,0[c]	171,0
	C_α	42,0	42,1	42,1	42,1	42,0	42,1	42,1	42,0
BOC	C=O	155,1	155,1	155,0	155,2	155,1	155,4	155,4	155,4
	—C	78,5	78,5	78,9	78,5	78,4	78,4	78,4	78,4
	CH_3	28,2	28,2	28,1	28,2	28,2	28,3	28,2	28,3

*For each pair of signals marked by the letters a, b, and c the opposite assignment is possible. For the groups of signals in parentheses, see the explanation in the text.

into the identification of the signals in the 160-201 ppm region, since it is impossible on the basis of available materials to determine which of the signals of the Asn residue (C_0 or C_γ) undergoes the upfield shift by 4 ppm and what takes place with the second signal.

EXPERIMENTAL

Melting points, chromatographic mobilities, and purities, and also angles of optical rotation of the peptides, were determined as in [5]. ^{13}C NMR spectra of solutions of the peptides in deuterated dimethyl sulfoxide (DMSO-d_6, c = 50-100 mg/ml) were recorded on a Bruker WP-80 DS spectrometer (FRG) with a frequency of 20.115 MHz for ^{13}C nuclei. The recording conditions have been described previously [4]; the time of recording one spectrum ranged from 5 to 20 h.

For synthesis we used PNPEs of BOC derivatives of amino acids produced by Reanal (Hungary), while the PSPEs of BOC derivatives of amino acids were obtained by the procedure described in [6]. The peptides were obtained by a unified procedure. The isolation of the products from the reaction mixtures was carried out individually in view of their different solubilities.

1. Synthesis of Peptides by the Mixed-Anhydride Method. With vigorous stirring, 16 mmole of pivaloyl chloride was added to a solution of 15 mmole of BOCAsnOH or BOCGlnOH in 50 ml of a mixture dimethylformamide (DMFA) and CH_2Cl_2 (1:1 and 2:1, respectively) and 15.5

TABLE 5. Chemical Shifts in the ^{13}C NMR Spectra of C-Terminal Heptapeptides of the Oxytocin Sequence*

Residue	Nucleus	Compound					
		XI	XII	XIII	XIV	XV	XVI
Ile	C_o	(171.6)	(171,3)	(171,5)	(171,1)	(171,2)	(171,1)
	C_α	59,1	58,9	59,0	59,0	59,0	59,0
	C_β	36,6	36,5	36,6	***	36,5	36,6
	C_{γ_1}	24,5	24,5	24,5	24,5	24,4	24,5
	C_{γ_2}	15,5	15,5	15,5	15,5	15,5	15,5
	C_δ	11,1	11,0	11,0	11,0	11,0	11,0
Gln	C_o	[171,1]	[170,7]	(170,7)	[170,8]	(171,0)	[170,9]
	C_α	52,2	52,1	52,0	52,1	52,1	52,1
	C_β	**	**	**	**	**	**
	C_γ	31,4	31,4	31,4	31,4	31,4	31,4
	C_δ	174,2	173,8	174,0	173,9	174,1	174,0
Asn	C_o	[171,1]	[170,6]	166,7[a]	[170,7]	(170,7)	[170,7]
	C_α	49,8	49,7	56,0	49,7	49,6	49,7
	C_β	37,1	37,0	***	***	37,3	***
	C_γ	(171,5)	(171,1)	(171,5)[a]	(171,3)	171,4	(171,3)
Cys	C_o	169,3	168,9	169,1	169,0	168,4	169,1
	C_α	50,6	50,7	51,4	50,7	50,7	51,2
	C_β	35,0	32,5	29,8	32,3	32,6	32,1
Pro	C_o	(171,8)	(171,4)	(171,9)	(171,6)	171,4	(171,6)
	C_α	60,2	59,9	60,0	60,0	59,6	60,0
	C_β	29,0	28,8	29,0	29,0	28,5	29,0
	C_γ	24,5	24,4	24,5	24,5	24,4	24,5
	C_δ	47,1	46,8	47,1	46,9	46,6	47,1
Leu	C_o	172,3	172,0	172,3	172,0	172,2	172,0
	C_α	51,6	51,5	51,6	51,5	51,5	51,6
	C_β	40,2	40,2	40,1	***	40,3	***
	C_γ	24,4	24,2	24,3	24,3	24,2	24,2
	C_{δ_1}	23,1	22,9	23,1	23,0	22,9	23,0
	C_{δ_2}	21,6	21,6	21,6	21,6	21,7	21,5
Gly	C_o	[170,9]	[170,9]	(171,1)	[170,8]	171,0	[170,9]
	C_α	42,1	42,0	42,2	42,0	42,0	42,0
BOC	C=O	155,6	155 3	155,5	155,3	155,5	155,3
	$-\overset{\vert}{C}-$	78,4	78,2	78,3	78,2	78,3	78,2
	CH_3	28,3	28,2	28,3	28,2	28,2	28,2

* For the groups of signals in square brackets and parentheses, see the explanation in the text. Signals for which the opposite assignment is possible are marked by letters.
**Signals masked by the powerful singlet of the CH_3 of the BOC group.
***Signal masked by a multiplet of the solvent.

mmole each of pyridine and triethylamine (TEA) cooled to −30°C. The mixture was kept at −20 ±2°C for 15 min, and then a solution of 10 mmole of the hydrochloride of a penta- or tetrapeptide amine in 50 ml of DMFA and 10 mmole of TEA was added. The mixture was carefully stirred at −10 ±5°C for 60 min and then at 2 ±2°C for 18 h. The method of isolating the peptide depended on its structure.

Isolation of the Peptides BOCAsnCys(X)ProLeuGlyNH$_2$. The reaction mixture was treated with 10 ml of chloroform and 50 ml of ether. The mixture was kept at 2 ±2°C for 18 h. The precipitate that had deposited was filtered off and was washed on the filter with 80 ml of chloroform, 40 ml of ether, 100 ml of H_2O, and 60 ml of ether. The product was dried to constant weight in a vacuum drying cabinet.

Isolation of BOCGlnAsnCys(X)ProLeuGlyNH$_2$. X = Bzl. The reaction mixture was treated with 154 ml of dry ether. The mixture was kept at 2 ±2°C for 2 h. The precipitate that had deposited was filtered off and was washed with 22 ml of ether. The product was dried

TABLE 6. Chemical Shifts in the ^{13}C NMR Spectra for the Carbon Nuclei Present in the Protective Groups of the Thiol Function of Cysteine

Protective group	Nucleus	Compound II	Compound VIII	Compound XII	Protective group	Nucleus	Compound III	Compound XIII
Bzl	CH_2	35,7	35,7	35,7	Bz	C=O	202,1	200,6
	C_1	138,4	138,6	138,4		C_1	133,6	133,7
	C_2	129,0	129,0	128,9		C_2	127,5	127,5
	C_3	128,3	128,4	128,3		C_3	128,3	128,4
	C_4	126,8	126,8	126,7		C_4	131,5	131,6
		I	VII	XI			IV	XIV
Me	CH_3	15,4	15,5	15,5				
		IX	XVI		Pym*	CH_2	44,4	44,3
						C=O	174,8	174,7
						C_1	30,5	30,5
						C_2	17,2	17,2
						C_3	45,4	**
	CH_2	***	***				V	XV
Bzm	C=O	166,3	166,1					
	C_1	134,0	133,9					
	C_2	127,4	127,2		Trit	$-\overset{1}{C}-$	66,4	66,4
	C_3	128,4	128,3			C_1	144,4	144,4
	C_4	131,6	131,4			C_2	129,3	129,3
						C_3	128,1	128,1
						C_4	126,8	126,8

* The positions of the carbon atoms in the pyrrolidone are shown relative to the carbonyl group.
**Signal masked by the strong signal of a triethylamine impurity (45.6 ppm).
***Signal masked by a multiplet of the solvent.

in a vacuum drying cabinet. Then it was dissolved in 66 ml of DMFA, and the solution was treated with 200 ml of chloroform and kept at 2 ±2°C for 8 h. The precipitate was filtered off and washed on the filter with 66 ml of chloroform and 62 ml of ether. The product was dried in a vacuum drying cabinet to constant weight.

X = Bzm. The reaction mixture was evaporated to incipient turbidity of the solution. The oily precipitate was treated with 2 × 60 ml of ether, and then 60 ml of chloroform was added to the residue and the mixture was kept at 2 ±2°C for 8 h. The resulting precipitate was filtered off and was washed on the filter with 150 ml of ether, 150 ml of H_2O, and 70 ml of ether. The product was dried in a vacuum drying cabinet to constant weight.

2. Synthesis of the Peptides by the Activated-Ester Method. A. With stirring, 15 mmole of an activated ester of BOC-asparagine or BOC-glutamine was added to a solution of 10 mmole of a hydrochloride of a tetra- or pentapeptide amide in 40 ml of DMFA and 11 mmole of TEA. The mixture was kept at 17 ±5°C for 40 h in the case of PNPEs and 24 h in the case of PFPEs. Then, 500 ml of H_2O was added to the reaction mixture. The precipitate was filtered off and was washed successively with 100 ml of H_2O, 150 ml of saturated $NaHCO_3$ solution, 50 ml of H_2O, and 100 ml of methanol (in the production of a pentapeptide) or 100 ml of acetone–ether (1:1) (in the case of a hexapeptide).

In the case of the methyl derivatives of cysteine, the pentapeptide precipitate was not washed with methanol; in view of its high degree of contamination, the hexapeptide was isolated as described below with the use of additional recrystallization.

B. With stirring, 10 mmole of the hydrochloride of a tri- or pentapeptide amide, 13 mmole of a BOC-dipeptide, and 14 mmole of N-hydroxybenzothiazole (HBT) were dissolved in 50 ml of DMFA and 11 mmole of TEA. The solution was cooled to −5 ±2°C, and 14 mmole of DCHC was added. The reaction mixture was kept at room temperature for 48 h, and the precipitate that had formed was filtered off. The reaction mixture was treated with ether until a turbidity appeared (120 ml) and was then kept at 2 ±2°C for 24 h. The precipitate was filtered off and was washed with 120 ml of ether. In the case of methyl and benzoyl protections for the mercapto function of cysteine, where necessary the product was additionally recrystallized from 500 ml of ethanol–DMFA (4:1) with the addition of about 330 ml of ether for a turbidity to appear. The mixture was kept in the refrigerator at 2 ±2°C for 18 h. The

precipitate that had deposited was filtered off and was washed on the filter with 66 ml of cooled ethanol. In the case of trityl protection of the mercapto function of cysteine, the crystallization was carried out from 65 ml of hot ethyl acetate.

3. Preparation of the Hydrochlorides of the Tetra-, Penta-, and Hexapeptides. A. A solution of 10 mmole of a tetra- or pentapeptide in 20 ml of acetic acid was treated with 6 ml (40 mmole of HCl) of a solution of HCl in dioxane (c = 0.25 g/ml). The mixture was kept at 17 ±5°C for 30 min, and then the peptide was precipitated by the addition of 50 ml of dry ether. The solution was decanted off and the precipitate was treated with 20 ml of dry ether, transferred to a filter, and washed on the filter with 20 ml of dry ether. The dry powder was dried further in a vacuum drying cabinet over KOH to constant weight. This gave 10 mmole of the tetra- or pentapeptide hydrochloride. Yield 100%.

B. The hexapeptide hydrochloride was obtained similarly, but 14 ml of methanol was used in place of acetic acid and 8.5 ml of HCl in dioxane instead of 6 ml. The mixture was allowed to stand for 15 min and the peptide was precipitated by the addition of 18 ml of ethyl acetate. The subsequent operations were as in paragraph A. this gave 10 mmole of the hexapeptide hydrochloride. Yield 100%.

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SYNTHESIS OF ω-AMINO- AND ω-CARBOXYALKYLAMIDES OF N-ACETYLMURAMOYL-L-ALANYL-D-ISOGLUTAMINE

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The synthesis has been effected of derivatives of MDP having a spacer with an amino or carboxy group. The final stage of the synthesis was the condensation of Boc-L-Ala-D-iGln with 6-aminohexanol (followed by the two-stage replacement of the hydroxy by an azido group) or with benzyl 6-aminohexanoate.

Derivatives of N-acetylmuramoyl-L-alanyl-D-isoglutamine (muramoyldipeptide, MDP) having a spacer with active functional groups are widely used to obtain highly active "macromolecular" glycopeptides [1], conjugates with proteins, peptides, and polysaccharides [2, 4], and new immunomodulators [5, 6]. Spacers have been described which are attached to the MDP molecule at the glycosidic center [1, 4], at the primary hydroxyl [3, 5, 6], and in the dipeptide fragment [2, 7].

We have previously reported the synthesis of β-(ω-aminoalkyl)glycosides of MDP [8]. In continuation of work on the synthesis and study of the biological activity of muramoyldipeptide derivatives, we have obtained derivatives of MDP having an alkyl spacer with an amino or carboxy group at the end (I, a, b). In investigations published previously, amino acids (L-lysine, L-alanine, etc.) have usually been used as spacers [2, 7]. Thr 6-N-acryloylhexamethylenediamide of MDP synthesized by Khorlin et al. [9] can be used only for obtaining copolymers [9, 10]. The ω-amino- and ω-carboxyalkamides of MDP that we have ob-

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