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Synthesis of Dipeptides Based on Valine and Threonine

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Abstract— Val–Val, Val–Thr, and Thr–Val dipeptides were synthesized using trifluoroacetyl protecting group. The optical rotations of the products were similar to those of samples synthesized using Boc protection, which indicated the absence of racemization in the course of introduction and removal of trifluoroacetyl protection.

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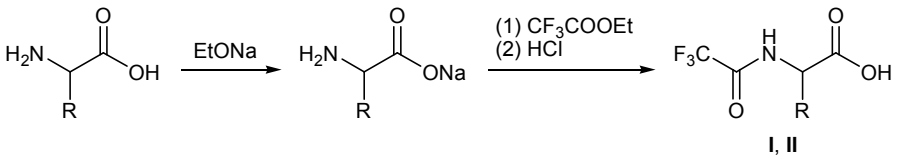
Hydroxy-containing amino acids and peptides occupy a specific place among related compounds due to diversity of radiation-induced reactions with their participation. Water radiolysis products initiate considerably more efficient deamination of threonine and serine as compared to other amino acids [1]. Furthermore, di- and tripeptides having a hydroxy amino acid residue at the C-terminus are known to be characterized by higher radiochemical yields of the corresponding amino acid amides, while dipeptides with a hydroxy amino acid residue at the *N*-terminus undergo deamination with a higher efficiency [2]. Decomposition of hydroxy-substituted peptides via rupture of C–C bond by the action of UV or γ-irradiation was not studied. Dipeptides based on valine and threonine may be convenient model compounds for studying the mechanism of radiation- and photoinduced decomposition of carbon skeleton in hydroxy-containing peptides. The goal of the present work was to develop efficient procedures for the synthesis of L-valyl–L-valine, L-valyl–L-threonine, and L-threonyl–L-valine.

An important problem in peptide synthesis is the choice of an optimal combination of protecting groups. At present, carbamate type groups are used most widely to protect amino groups in amino acids. Although trifluoroacetyl protection has long been known, it has not received wide application in peptide synthesis because of possible racemization. Nevertheless, facile introduction and removal of trifluoroacetyl protecting group makes its use quite promising provided that racemization is impossible. In the present work we synthesized L-valyl–L-valine, L-valyl–L-threonine, and L-threonyl–L-valine using both trifluoroacetyl and *tert*-butoxycarbonyl protecting groups and compared optical rotations of the products, taking into account that peptide synthesis with Boc-protected amino acids is not accompanied by racemization.

N-Trifluoroacetyl derivatives of valine and threonine **I** and **II** were synthesized by reaction of the corresponding amino acid sodium salts with ethyl trifluoroacetate (Scheme 1). Compounds **I** and **II** reacted with valine and threonine methyl esters in tetrahydrofuran in the presence of *N*,*N*′-dicyclohexylcarbodiimide (DCC) as condensing agent to give esters **III**–**V** which were subjected to hydrolysis by the action of aqueous sodium hydroxide; and subsequent acidification afforded target dipeptides **VI**–**VIII** (Scheme 2).

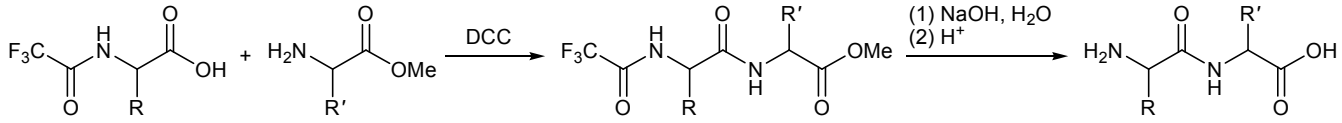
Scheme 1.



I, **II**

I, R = *i*-Pr; **II**, R = MeCH(OH).

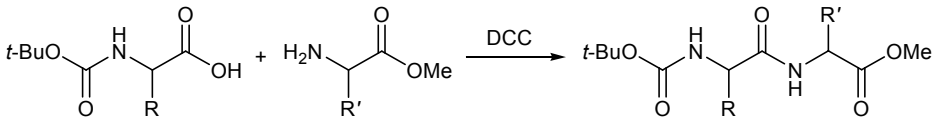
Scheme 2.



I, **II** **III–V** **VI–VIII**

III, **VI**, R = R′ = *i*-Pr; **IV**, **VII**, R = *i*-Pr, R′ = MeCH(OH); **V**, **VIII**, R = MeCH(OH), R′ = *i*-Pr.

Scheme 3.



IX–XI

IX, R = R′ = *i*-Pr; **X**, R = *i*-Pr, R′ = MeCH(OH); **XI**, R = MeCH(OH), R′ = *i*-Pr.

Compounds **VI–VIII** were also synthesized using Boc-protected amino acids. By condensation of *N*-*tert*-butoxycarbonylvaline and *N*-*tert*-butoxycarbonylthreonine with valine and threonine methyl esters in the presence of DCC we obtained *N*-Boc-Val–Val, *N*-Boc-Val–Thr, and *N*-Boc-Thr–Val methyl esters (**IX–XI**) (Scheme 3). Methyl esters **IX** and **X** were deprotected using a solution of hydrogen chloride in methanol, and hydrochlorides **XII** and **XIII** thus formed were converted into dipeptides **VI** and **VII** by treatment with aqueous sodium hydroxide, followed by acidification (Scheme 4).

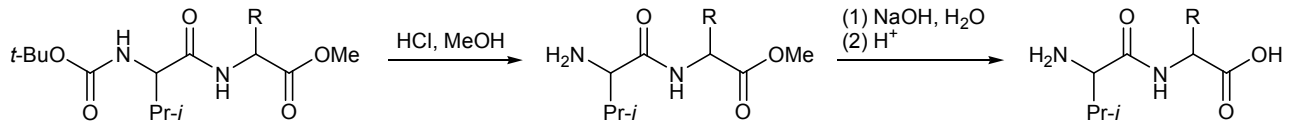
Threonylvaline **VIII** was synthesized from methyl ester **XI** following a different reaction sequence. Hydrolysis of the ester moiety in **XI** in aqueous sodium hydroxide and subsequent acidification with citric acid produced *N*-Boc-threonylvaline **XIV** which was treated with a solution of HCl in dioxane to obtain hydrochloride **XV**, and the latter was converted into target dipeptide **VIII** by reaction with an equimolar amount of sodium ethoxide (Scheme 5).

Samples of dipeptides **VI–VIII** obtained by the two methods were characterized by almost similar optical rotations, which indicated the absence of racemization at all steps of synthesis of these dipeptides with the use of trifluoroacetyl protecting group.

EXPERIMENTAL

Commercial amino acids from Sigma and Aldrich were used. *N*-*tert*-Butoxycarbonyl derivatives of valine and threonine and valine and threonine methyl esters

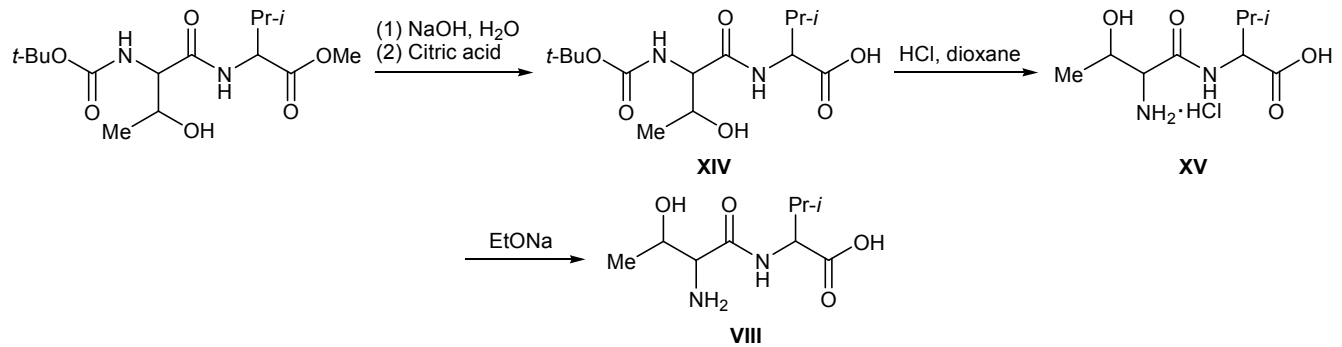
Scheme 4.



IX, **X** **XII**, **XIII** **VI**, **VII**

VI, **XII**, R = *i*-Pr; **VII**, **XIII**, R = MeCH(OH).

Scheme 5.



XIV **XV** **VIII**

were synthesized according to standard procedures [3]. Methanol and ethanol were purified by distillation over calcium hydride. Diethyl ether, tetrahydrofuran, and hexane were purified by distillation over metallic sodium.

The IR spectra were recorded in KBr on a Nicolet Protégé-460 spectrometer with Fourier transform. The NMR spectra were run at 20°C on Bruker Avance-400 and Tesla BS-567A spectrometers; the chemical shifts were measured relative to the residual proton signal of the corresponding deuterated solvent. The optical rotations were measured on a Polamat A polarimeter (DDR).

***N*-Trifluoroacetyl-L-valine (I).** L-Valine, 11.7 g (100 mmol), was dissolved in a solution of sodium methoxide prepared from 2.3 g (100 mmol) of sodium and 100 ml of methanol, 21.3 g (150 mmol) of ethyl trifluoroacetate was added dropwise, and the mixture was stirred for 42 h, acidified with 21 ml of a 4.8 N solution of hydrogen chloride in methanol, stirred for 2 h, and filtered. The filtrate was evaporated under reduced pressure, the residue was extracted with diethyl ether (3×100 ml), the extracts were filtered and evaporated under reduced pressure, and the residue was purified by reprecipitation from diethyl ether with hexane. Yield 18.37 g (86%), $[\alpha]_D^{20}$ = –15.3 (*c* = 3, H_2O); published data [4]: $[\alpha]_D^{20}$ = –15.2. Found, %: C 39.62; H 4.98; N 6.35. $C_7H_{10}F_3NO_3$. Calculated, %: C 39.44; H 4.73; N 6.57.

***N*-Trifluoroacetyl-L-threonine (II)** was synthesized in a similar way from 11.9 g (100 mmol) of L-threonine. Yield 17.2 g (80%), $[\alpha]_D^{20}$ = –5.72 (*c* = 3, MeOH); published data [5]: $[\alpha]_D^{20}$ = –5.6. Found, %: C 33.64; H 3.91; N 6.67. $C_6H_8F_3NO_4$. Calculated, %: C 33.50; H 3.75; N 6.51.

***N*-Trifluoroacetyl-L-valyl-L-valine methyl ester (III).** A solution of 12.14 g (57 mmol) of *N*-trifluoroacetyl-L-valine (**I**) in 25 ml of THF was cooled to 0–5°C, a solution of 11.74 g (57 mmol) of DCC in 25 ml of THF was added, the mixture was stirred for 5 min, and a solution of 7.47 g (57 mmol) of L-valine methyl ester in 25 ml of THF was added. The mixture was stirred for 40 h, the precipitate was filtered off, the filtrate was evaporated under reduced pressure, and the residue was washed with hexane, dried under reduced pressure, and reprecipitated from methylene chloride with hexane. Yield 12.61 g (68%), mp 92–94°C, $[\alpha]_D^{20}$ = –55.6 (*c* = 3.0, MeOH). IR spectrum, ν, cm^{-1}: 1750, 1713, 1656 (C=O), 1557 (δNH). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.85 d (3H, CH_3, *J* = 6.5 Hz), 0.89 d (3H, CH_3, *J* = 6.4 Hz), 0.94 d (3H, CH_3, *J* = 6.4 Hz), 0.99 d (3H, CH_3, *J* = 6.4 Hz), 2.08–2.19 m (2H, CH), 3.73 s (3H, OCH_3), 4.48–4.52 m (1H, CH), 4.56 t (1H, CH, *J* = 6.5 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 18.33, 18.83, 19.38, 19.43, 31.53, 32.08, 52.77, 58.21, 59.50, 116.48 q, 157.99 q, 170.83, 172.63. Found, %: C 47.99; H 6.64; N 8.43. $C_{13}H_{21}F_3N_2O_4$. Calculated, %: C 47.85; H 6.49; N 8.58.

***N*-Trifluoroacetyl-L-valyl-L-threonine methyl ester (IV).** A solution of 18.32 g (86 mmol) of compound **I** in 75 ml of THF was cooled to 0–5°C, a solution of 17.72 g (86 mmol) of DCC in 75 ml of THF was added, the mixture was stirred for 5 min, and a solution of 11.44 g (86 mmol) of L-threonine methyl ester in 100 ml of THF was added. The mixture was stirred for 30 h, the precipitate was filtered off, the solvent was removed from the filtrate under reduced pressure, the residue was dried under reduced pressure and extracted with methylene chloride, the extract was filtered and evaporated under reduced pressure, and the residue was washed with diethyl ether, dried under reduced pressure, and purified by reprecipitation from methylene chloride with hexane. Yield 18.35 g (65%), mp 148–149°C, $[\alpha]_D^{20}$ = –21.9 (*c* 3.0, MeOH). IR spectrum, ν, cm^{-1}: 1731, 1709, 1655 (C=O), 1561 (NH). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.01 d (3H, CH_3, *J* = 7 Hz), 1.03 d (3H, CH_3, *J* = 7 Hz), 1.22 d (3H, CH_3, *J* = 6.5 Hz), 2.18–2.23 m (1H, CH), 3.80 s (3H, CH_3), 4.41–4.44 m (2H, CH), 4.61 d (1H, CH, *J* = 6.7 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 18.61, 19.47, 20.66, 32.35, 53.39, 58.12, 59.48, 68.52, 170.79, 171.65. Found, %: C 43.95; H 5.94; N 8.41. $C_{12}H_{19}F_3N_2O_5$. Calculated, %: C 43.90; H 5.82; N 8.53.

***N*-Trifluoroacetyl-L-threonyl-L-valine methyl ester (V)** was synthesized in a similar way from 16.56 g (77 mmol) of *N*-trifluoroacetyl-L-threonine (**II**) and 10.09 g (77 mmol) of L-valine methyl ester using 15.86 g (77 mmol) of DCC. Yield 18.45 g (73%), mp 106–108°C, $[\alpha]_D^{20}$ = –6.8 (*c* = 2.0, MeOH). IR spectrum, ν, cm^{-1}: 1740, 1708, 1653 (C=O), 1553 (NH). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.89 d (3H, CH_3, *J* = 7 Hz), 0.93 d (3H, CH_3, *J* = 7 Hz), 1.18 d (3H, CH_3, *J* = 6.5 Hz), 2.19–2.22 m (1H, CH), 3.74 s (3H, CH_3), 4.22–4.31 m (1H, CH), 4.40–4.49 m (1H, CH), 4.62 br.s (1H, CH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 18.12, 18.30, 19.58, 31.20, 52.97, 58.04, 58.42, 67.28, 116.25 q, 158.29 q, 169.63, 172.72. Found, %: C 44.05; H 5.63; N 8.32. $C_{12}H_{19}F_3N_2O_5$. Calculated, %: C 43.90; H 5.82; N 8.53.

***N*-Boc-L-valyl-L-valine methyl ester (IX).** A solution of 12.36 g (60 mmol) of DCC in 35 ml of THF

was added to a solution of 13.02 g (60 mmol) of Boc-L-valine in 50 ml of THF, cooled to 0–5°C. The mixture was stirred for 5 min, a solution of 7.86 g (60 mmol) of L-valine methyl ester in 50 ml of THF was added, and the mixture was stirred for 40 h. The precipitate was filtered off, the solvent was removed from the filtrate under reduced pressure, the residue was washed with hexane, dried under reduced pressure, and extracted with diethyl ether, the extract was filtered and evaporated under reduced pressure, and the residue was washed with hexane and dried under reduced pressure. Yield 13.86 g (70%), mp 149–150°C, $[\alpha]_D^{20}$ = +8,2 (*c* = 3.0, THF). IR spectrum, ν, cm^{-1}: 1746, 1717, 1665 (C=O), 1545 (NH). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.83 br.s (6H, CH_3), 0.92 br.s (6H, CH_3), 1.37 s (9H, *t*-Bu), 1.90–2.20 m (2H, CH), 3.61 s (3H, OCH_3), 3.85–4.00 m (1H, CH), 4.35–4.50 m (1H, CH).

***N*-Boc-L-valyl-L-threonine methyl ester (X)** was synthesized in a similar way from 19.53 g (90 mmol) of Boc-L-valine and 11.97 g (90 mmol) of threonine methyl ester using 18.54 g (90 mmol) of DCC. Yield 19.44 g (65%), $[\alpha]_D^{20}$ = –22.6 (*c* = 3.0, MeOH). IR spectrum, ν, cm^{-1}: 1745, 1715, 1683 (C=O), 1542 (NH). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.90–0.95 m (6H, CH_3), 1.15 d (3H, CH_3, *J* = 6.5 Hz), 1.38 s (9H, *t*-Bu), 1.98–2.06 m (1H, CH), 3.71 s (3H, OCH_3), 3.92–3.96 m (1H, CH), 4.29–4.34 m (1H, CH), 4.55–4.60 m (1H, CH). Found, %: C 54.36; H 8.74; N 8.63. $C_{15}H_{28}N_2O_6$. Calculated, %: C 54.20; H 8.49; N 8.43.

***N*-Boc-L-threonyl-L-valine methyl ester (XI)** was synthesized from 13.14 g (60 mmol) of Boc-L-threonine and 7.86 g (60 mmol) of valine methyl ester using 12.36 g (60 mmol) of DCC. Yield 15.96 g (80%), mp 71.5–73°C, $[\alpha]_D^{20}$ = –18.0 (*c* = 3.0, MeOH). IR spectrum, ν, cm^{-1}: 1740, 1716, 1681 (C=O), 1525 (NH). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.81–0.86 m (6H, CH_3), 1.11 d (3H, CH_3, *J* = 6.5 Hz), 1.35 s (9H, *t*-Bu), 2.06–2.14 m (1H, CH), 3.72 s (3H, CH_3), 4.05–4.10 m (1H, CH), 4.18–4.24 m (1H, CH), 4.38–4.43 m (1H, CH). Found, %: C 54.32; H 8.61; N 8.27. $C_{15}H_{28}N_2O_6$. Calculated, %: C 54.20; H 8.49; N 8.43.

L-Valyl-L-valine (VI). *a*. A solution of 3.6 g (90 mmol) of sodium hydroxide in 20 ml of water was added dropwise to a solution of 13.05 g (40 mmol) of ester **III** in 40 ml of ethanol, and the mixture was stirred for 5 h and acidified with 5.7 g (50 mmol) of trifluoroacetic acid. The mixture was stirred for 1 h and evaporated under reduced pressure, and the residue was washed with acetone, dried under reduced pressure, and reprecipitated from water with acetone. Yield 6.06 g (70%), mp 186–188°C, $[\alpha]_D^{20}$ = +13.3 (*c* = 3.0, H_2O). IR spectrum, ν, cm^{-1}: 1665, 1585 (C=O), 1554 (NH). ^1H NMR spectrum (D_2O), δ, ppm: 0.86–0.93 d.d (6H, CH_3), 0.97–1.02 d.d (6H, CH_3), 1.97–2.04 m (1H, CH), 2.18–2.24 m (1H, CH), 3.84 d (1H, CH, *J* = 6 Hz), 4.0 d (1H, CH, *J* = 6.5 Hz). ^{13}C NMR spectrum (D_2O), δ_C, ppm: 16.86, 17.69, 17.81, 18.81, 30.16, 30.30, 58.58, 61.57, 168.86, 177.99. Found, %: C 55.68; H 9.54; N 12.73. $C_{10}H_{20}N_2O_3$. Calculated, %: C 55.53; H 9.32; N 12.95.

b. Compound **IX**, 13.2 g (40 mmol), was added under continuous stirring to 30 ml of a 3.5 N solution of HCl in methanol. The mixture was stirred for 5 h and evaporated under reduced pressure, and the residue was washed with diethyl ether and dried under reduced pressure. A solution of sodium ethoxide prepared from 0.92 g (40 mmol) of sodium and 70 ml of ethanol was added to the residue, the mixture was stirred for 1 h, and the precipitate was filtered off. A solution of 2 g (50 mmol) of sodium hydroxide in 20 ml of water was added dropwise to the filtrate, and the mixture was stirred for 10 h and acidified with trifluoroacetic acid to pH ~6. The solvent was removed under reduced pressure, and the residue was washed with acetone and diethyl ether, dried under reduced pressure, and reprecipitated from water with acetone. Yield 4.58 g (53%), mp 187–188°C, $[\alpha]_D^{20}$ = +13.5 (*c* = 3.5, H_2O). Found, %: C 55.62; H 9.43; N 12.81. $C_{10}H_{20}N_2O_3$. Calculated, %: C 55.53; H 9.32; N 12.95.

L-Valyl-L-threonine (VII). *a*. A solution of 3.6 g (90 mmol) of sodium hydroxide in 20 ml of water was added dropwise to a solution of 13.13 g (40 mmol) of *N*-trifluoroacetyl-L-valyl-L-threonine methyl ester (**IV**) in 40 ml of ethanol. The mixture was stirred for 20 h and acidified with trifluoroacetic acid to pH ~6. The solvent was removed under reduced pressure, and the residue was washed with acetone and diethyl ether, dried under reduced pressure, and reprecipitated from water with acetone. Yield 4.63 g (53%), mp 158–159°C, $[\alpha]_D^{20}$ = +16.5 (*c* = 4.0, H_2O). IR spectrum, ν, cm^{-1}: 1667, 1582 (C=O), 1525 (NH). ^1H NMR spectrum (D_2O), δ, ppm: 1.01 d (3H, CH_3, *J* = 7 Hz), 1.03 d (3H, CH_3, *J* = 7 Hz), 1.19 d (3H, CH_3, *J* = 6 Hz), 2.19–2.26 m (1H, CH), 3.89 d (1H, CH, *J* = 6 Hz), 4.11–4.16 m (2H, CH). ^{13}C NMR spectrum (D_2O), δ_C, ppm: 16.86, 17.83, 19.40, 30.10, 58.72, 61.28, 67.82, 169.16, 176.14. Found, %: C 49.69; H 8.54; N 12.75. $C_9H_{18}N_2O_4$. Calculated, %: C 49.53; H 8.31; N 12.84.

b. Ester **X**, 18.28 g (55 mmol), was added under vigorous stirring to 35 ml of a 3.4 N solution of HCl in methanol, the mixture was stirred for 7 h, the solvent

was removed under reduced pressure, and the residue was washed with diethyl ether and dried under reduced pressure. The dry residue was dissolved in 30 ml of ethanol, a solution of 4.4 g (110 mmol) of sodium hydroxide in 30 ml of water was added dropwise, and the mixture was stirred for 15 h and acidified with hydrochloric acid to pH ~6. The solvent was removed under reduced pressure, the residue was washed with acetone, dried under reduced pressure, and extracted with anhydrous ethanol (2×50 ml), the extract was filtered, the filtrate was evaporated under reduced pressure, and the residue was washed in succession with acetone and diethyl ether, and reprecipitated from water with acetone. Yield 5.4 g (45%), mp 157–158°C, $[\alpha]_D^{20}$ = +16.6 (*c* = 3.0, H_2O). Found, %: C 49.40; H 8.18; N 12.61. $C_9H_{18}N_2O_4$. Calculated, %: C 49.53; H 8.31; N 12.84.

L-Threonyl-L-valine (VIII). *a*. A solution of 3.6 g (90 mmol) of sodium hydroxide in 30 ml of water was added dropwise to a solution of 13.13 g (40 mmol) of *N*-trifluoroacetyl-L-threonyl-L-valine methyl ester (**V**) in 35 ml of ethanol, the mixture was stirred for 28 h, 1.14 g (10 mmol) of trifluoroacetic acid was added, the mixture was stirred for 1 h and filtered, and solvent was removed from the filtrate under reduced pressure. The residue was washed with acetone and diethyl ether, dried under reduced pressure, and dissolved in 35 ml of water. The solution was acidified with hydrochloric acid to pH ~6 and evaporated under reduced pressure, the residue was extracted with anhydrous ethanol (2×50 ml), and the combined extracts were filtered and concentrated to a volume of 15 ml. Diethyl ether, 100 ml, was added, and the precipitate was filtered off, washed with diethyl ether, dried under reduced pressure, and reprecipitated from ethanol with diethyl ether. Yield 3.93 g (45%), mp 152–154°C, $[\alpha]_D^{20}$ = –10.8 (*c* = 2.0, H_2O). IR spectrum, ν, cm^{-1}: 1674, 1580 (C=O), 1539 (NH). ^1H NMR spectrum (D_2O), δ, ppm: 0.89 d (3H, CH_3, *J* = 7 Hz), 0.92 d (3H, CH_3, *J* = 7 Hz), 1.29 d (3H, CH_3, *J* = 6.5 Hz), 2.05–2.15 m (1H, CH), 3.86 d (1H, CH, *J* = 6 Hz), 4.04 d (1H, CH, *J* = 6 Hz), 4.10–4.18 m (1H, CH). ^{13}C NMR spectrum (D_2O), δ_C, ppm: 17.53, 18.77, 18.86, 30.27, 58.88, 61.49, 66.67, 168.21, 178.03. Found, %: C 49.67; H 8.53; N 12.66. $C_9H_{18}N_2O_4$. Calculated, %: C 49.53; H 8.31; N 12.84

b. A solution of 2.0 g (50 mmol) of sodium hydroxide in 30 ml of water was added dropwise to a solution of 13.3 g (40 mmol) of *N*-Boc-L-threonyl-L-valine methyl ester (**XI**) in 50 ml of ethanol, and the mixture was stirred for 15 h and acidified with citric acid to pH ~6. The solvent was removed under reduced pressure, the residue was extracted with ethyl acetate (4×50 ml), the combined extracts were washed with a saturated solution of sodium chloride, dried over sodium sulfate, filtered, and evaporated, and the residue was reprecipitated from diethyl ether with hexane, dried under reduced pressure, and dissolved in 40 ml of a 3.5 N solution of HCl in dioxane. The mixture was stirred for 7 h, the solvent was removed under reduced pressure, and the residue was washed with diethyl ether and dried under reduced pressure. A 7.64-g portion of the product was dissolved in 50 ml ethanol, a solution of sodium ethoxide prepared from 0.69 g (30 mmol) of sodium and 50 ml of ethanol was added dropwise, the mixture was stirred for 2 h and filtered, the solvent was removed under reduced pressure, and the residue was reprecipitated from ethanol with diethyl ether. Yield 5.23 g (60%), mp 153–156°C, $[\alpha]_D^{20}$ = –10.7 (*c* = 2.0, H_2O). Found, %: C 49.78; H 8.47; N 12.69. $C_9H_{18}N_2O_4$. Calculated, %: C 49.53; H 8.31; N 12.84.

REFERENCES

1. Shadyro, O.I., Sosnovskaya, A.A., and Vrublevskaya, O.N., *Khim. Vys. Energ*., 1999, vol. 33, no. 2, p. 94.
2. Shadyro, O.I., Sosnovskaya, A.A., and Vrublevskaya, O.N., *J. Radiat. Biol*., 2003, vol. 79, no. 4, p. 269.
3. Gershkovich, A.A. and Kibirev, V.K., *Sintez peptidov. Reagenty i metody* (Synthesis of Peptides. Reagents and Methods), Kiev: Naukova Dumka, 1987.
4. Curphey, T.J., *J. Org. Chem*., 1979, vol. 44, p. 2885.
5. Cherevin, M.S., Gulevich, T.G., Yurashevich, N.Ya., Zubreichuk, Z.P., and Knizhnikov, V.A., *Vestsi Nats. Akad. Navuk Belarusi, Ser. Khim. Navuk*, 2008, no. 2, p. 55.