ISSN 1070-4280, Russian Journal of Organic Chemistry, 2013, Vol. 49, No. 7, pp. 1047–1054. © Pleiades Publishing, Ltd., 2013.
Original Russian Text © F.A. Gimalova, G.M. Khalikova, V.A. Egorov, I.I. Fatkullina, A.G. Mustafin, M.S. Miftakhov, 2013, published in Zhurnal Organicheskoi Khimii, 2013, Vol. 49, No. 7, pp. 1062–1069.

Effect of the β-Substituent with Respect to the Azido Group on the Reactivity of Methyl (2*E*)-3-[5-(Azidomethyl)-2,2-diethyl-1,3-dioxolan-4-yl]-2-methylprop-2-enoate

F. A. Gimalova[a], G. M. Khalikova[b], V. A. Egorov[a], I. I. Fatkullina[b], A. G. Mustafin[b], and M. S. Miftakhov[a]

[a] *Institute of Organic Chemistry, Ufa Research Center, Russian Academy of Sciences, pr. Oktyabrya 71, Ufa, 450054 Bashkortostan, Russia*
e-mail: bioreg@anrb.ru

[b] *Bashkir State University, Ufa, Bashkortostan, Russia*

Received April 30, 2012

Abstract—Unlike methyl (2*E*)-3-[5-(azidomethyl)-2,2-diethyl-1,3-dioxolan-4-yl]-2--methylprop-2-enoate which is stable on storage, its acyclic derivative, methyl (2*E*,4*S*,5*S*)-6-azido-5-hydroxy-2-methyl-4-(pent-3-yloxy)hex-2-enoate at 20°C undergoes unusual decomposition with formation of *exo*-methylidenepyrrolidine. Analogous transformation was also observed in the epoxide ring opening in methyl (2*E*)-2-methyl-4-[(*S*)-oxiran-2-yl]-4-(pent-3-yloxy)but-2-enoate and in the substitution reaction of ethyl 5,6-bis(methanesulfonyloxy)-2-methyl-4-(pent-3-yloxy)hex-2-enoate with azide ion. Opening of the oxirane ring in the former by the action of azide ion was accompanied by formation of oxazetidine derivative as a minor product. The major intramolecular cyclization products, 4-hydroxy- and 4-mehtanesulfonyloxypyrrolidines were converted into stable pyrrole derivatives via elimination of the leaving groups. The hydrogenation of methyl and ethyl (2*E*)-3-[5-(azidomethyl)-2,2-diethyl-1,3-dioxolan-4-yl]-2-methylprop-2-enoates over palladium catalyst afforded the expected reduction products.

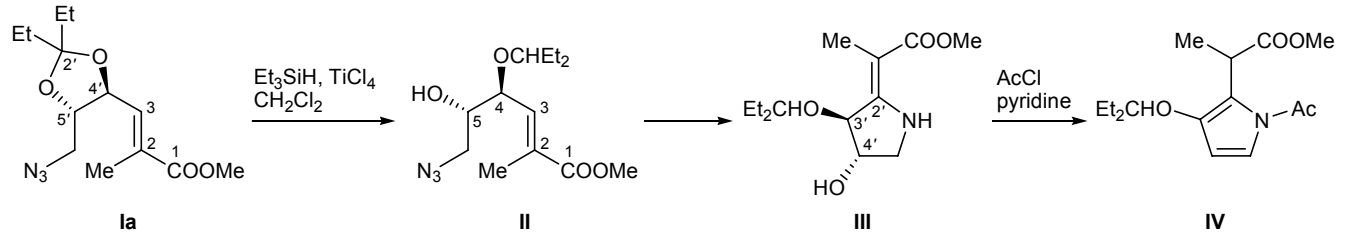
DOI: 10.1134/S1070428013070154

Organic azides are popular synthons in the design of nitrogen-containing compounds; they may be regarded as latent source of amines or nitrenes, may act as 1,3-dipoles in cycloaddition reactions and nucleophiles, undergo rearrangements (e.g., Schmidt and Curtius reactions), etc. [1–5]. The present article describes some reactions of previously synthesized azide **Ia** [6] and structurally related compounds. The functionalization character and topology of structure **Ia** largely determine its synthetic potential and interest in intramolecular transformations promoted by the azido group therein.

Initially, with a view to estimate possible pathways of carbocation binding by internal and external nucleophiles, we examined the reaction of azide **Ia** with $TiCl_4$–Et_3SiH [7] (Scheme 1). It was found that the azido group in **Ia** remained intact under ionic hydrogenation conditions; the only product (compound **II**) was that resulting from the reduction of carbocation with external nucleophile (Et_3SiH).

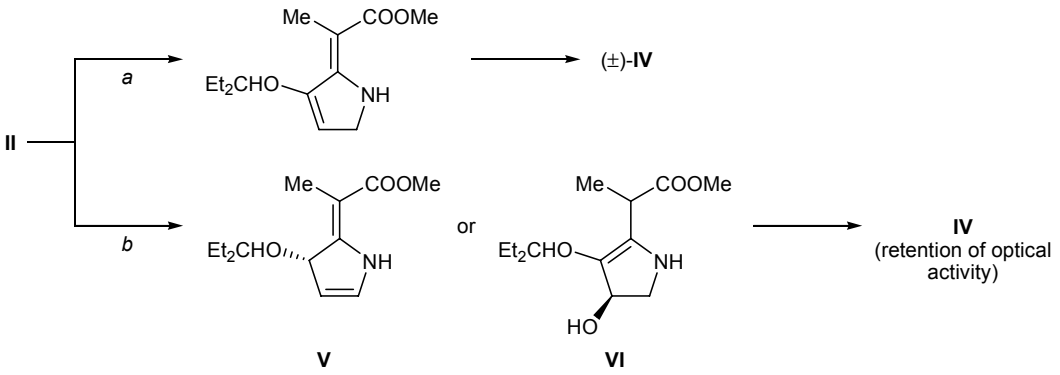
However, unlike initial compound **Ia**, azide **II** in 48 h was completely converted into pyrrolidine **III** having an exocyclic double C=C bond [6]; by treatment of **III** with acetyl chloride in pyridine we ob-

Scheme 1.



Ia **II** **III** **IV**

Scheme 2.

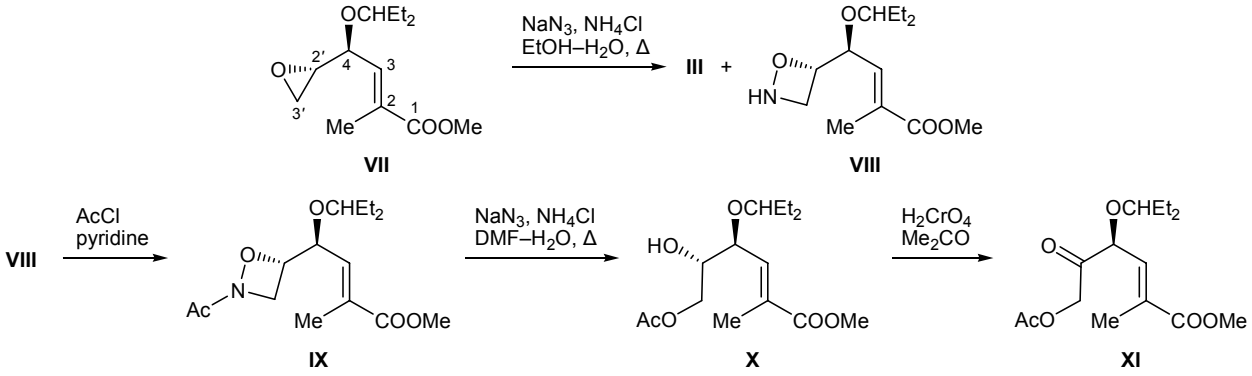


tained functionalized pyrrole **IV**. Compound **IV** turned out to be optically active. The enantiomer ratio determined with the use of europium tris[3-(trifluoromethylhydroxymethylidene)-(−)-camphorate] as chiral shift reagent was 7:6, i.e., one of the enantiomers was formed in excess over the other. It is seen that molecule **II** contains two chiral centers which disappear in the transformation of **III** into **IV**. Dehydration and double bond migration according to path *a* (Scheme 2) should led to complete loss of optical activity. Retention of optical activity is possible if the reaction takes path *b* with allylic rearrangement of intermediate **V** or **VI**. In both cases, the allylic rearrangement (hydrogen atom transfer) is a concerted suprafacial process, which should occur with retention of optical activity.

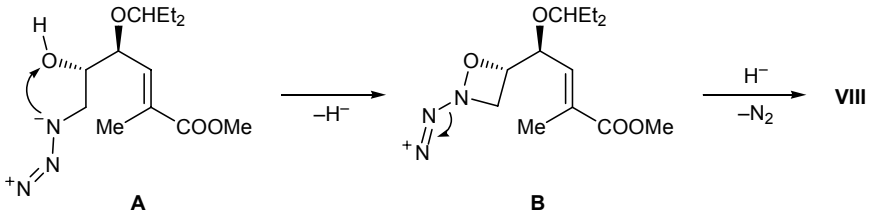
The fact that the amounts of enantiomers **IV** were comparable indicated predominant contribution of path *b* without allylic rearrangement. Thus, the formation of scalemic pyrrole **IV** provides an evidence in favor of path *b*.

The use of azide ion as external nucleophile for carbocations generated from epoxide **VII** (Scheme 3) led to the formation of pyrrolidine **III** together with an unidentified product [6]. More detailed study of this reaction allowed us to identify new compound **VIII** as a 3:2 mixture with initial epoxide **VII**, which cannot be separated by chromatography on silica gel. The acylation of that mixture and subsequent chromatographic purification afforded *N*-acetyloxazetidine derivative **IX**. Opening of the four-membered ring in **IX** on heating in DMF–H_2O (5:1) in the presence of NaN_3 and NH_4Cl produced hydroxy acetate **X** whose structure was also confirmed by oxidation to ketone **XI**. Presumably, oxazetidine **VIII** is formed via partial

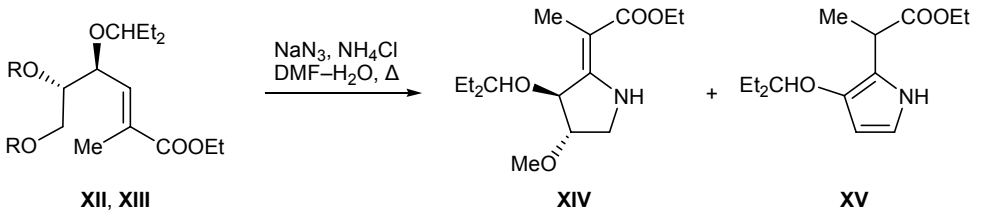
Scheme 3.



Scheme 4.



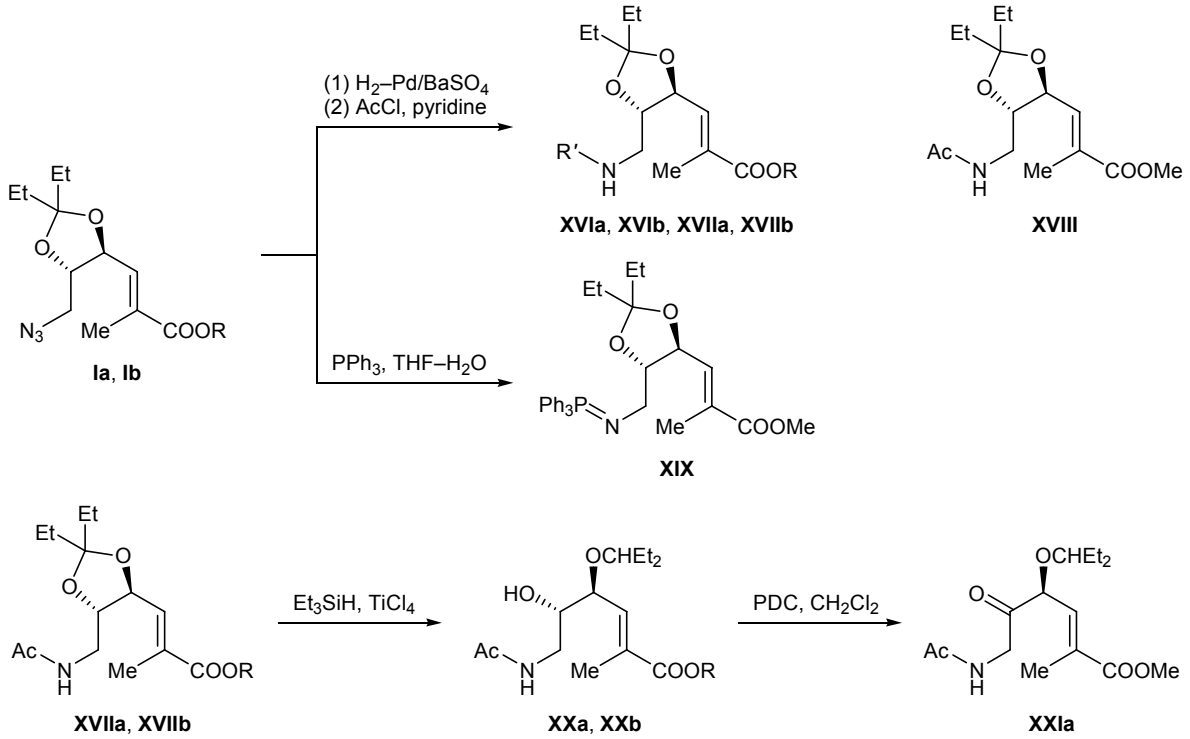
Scheme 5.



XII, **XIII** **XIV** **XV**

XII, R = H; **XIII**, R = Ms.

Scheme 6.



I, **XVI**, **XVII**, **XX**, R = Me (**a**), Et (**b**); **XVI**, R′ = H; **XVII**, R′ = Ac.

intramolecular cyclization of primary intermediate (**A**→**B**), followed by elimination of nitrogen molecule (Scheme 4).

The reaction with sodium azide of bis-methanesulfonate **XIII** prepared from diol **XII** [6] gave a mixture of pyrrolidine **XIV** and pyrrole **XV** in 37 and 38% yield, respectively (Scheme 5).

Azides **Ia** and **Ib** were subjected to hydrogenation over $Pd/BaSO_4$ as catalyst. The reduction of **Ib** smoothly afforded amine **XVIb** whose acetylation with acetyl chloride in pyridine gave amide **XVIIb**. Prolonged hydrogenation of **I** may be accompanied by partial reduction of the double bond. For example, a mixture of **XVIIa** and **XVIII** was obtained by hydrogenation of compound **Ia** and subsequent acetylation. The reduction of azide **Ia** with triphenylphosphine with a view to obtain the corresponding amine (**XVIa**) [8] stopped at the step of formation of iminophosphorane **XIX**. Opening of the dioxolane ring in amides **XVIIa** and **XVIIb** under analogous reduction conditions as for **Ia** led to hydroxy amides **XXa** and **XXb** in good yields, whereas no intramolecular cyclization products were detected (Scheme 6). The structure of **XX** was also confirmed by the oxidation of hydroxy ester **XXa** to ketone **XXIa**.

EXPERIMENTAL

The IR spectra were recorded on a Shimadzu IR Prestige-21 spectrometer from thin films. The ^1H and ^{13}C NMR spectra were recorded on Bruker AM-300 (300.13 MHz for ^1H and 75.47 MHz for ^{13}C) and Bruker Avance-500 spectrometers (500.13 MHz for ^1H

and 125.77 MHz for ^{13}C) using tetramethylsilane as internal reference. The optical rotations were measured on a Perkin Elmer-341 polarimeter. The mass spectra (electron impact, 70 eV) were obtained on a Thermo Finnigan MAT 95XP mass spectrometer (ion source temperature 200°C, batch inlet probe temperature programming from 5 to 270°C at a rate of 22 deg/min). The elemental compositions were determined on a Euro EA 2000 CHN analyzer. The progress of reactions was monitored by TLC on Sorbfil plates (Russia); spots were detected by treatment with a solution of 4-methoxybenzaldehyde in ethanol acidified with sulfuric acid, followed by heating to 120–150°C. The products were isolated by column chromatography on silica gel (30–60 g of sorbent per gram of substrate); freshly distilled solvents were used as eluents. All newly synthesized compounds were isolated as oily substances.

Methyl (2*Z*)-2-[(3*S*,4*S*)-4-hydroxy-3-(pent-3-yloxy)pyrrolidin-2-ylidene]propanoate (III). A solution of 0.029 g (0.1 mmol) of compound **Ia** [6] in 5 ml of anhydrous methylene chloride was cooled to –35 to –40°C, 0.02 ml (0.14 mmol) of triethylsilane was added, and a solution of 0.01 ml (0.11 mmol) of $TiCl_4$ in 0.5 ml of methylene chloride was added dropwise under stirring, maintaining the temperature not exceeding –30°C. The mixture was stirred at that temperature until the initial compound disappeared (TLC), ice water was quickly added, the mixture was allowed to warm up to –5°C, the organic phase was separated, and the aqueous phase was extracted with methylene chloride (3×10 ml). The extracts were combined with the organic phase, washed with brine, and dried over $MgSO_4$, the solvent was distilled off on a rotary evaporator, and the residue was purified by flash chromatography on silica gel using ethyl acetate–petroleum ether (1:2) as eluent to isolate 0.017 g (60%) of unstable methyl (2*E*,4*S*,5*S*)-6-azido-5-hydroxy-2-methyl-4-(pent-3-yloxy)hex-2-enoate (**II**). ^1H NMR spectrum (acetone-d_6), δ, ppm: 0.85 t (3H, CH_3, *J* = 7.3 Hz), 0.88 t (3H, CH_3, *J* = 7.4 Hz), 1.37–1.46 m (2H, CH_2, *J* = 7.3 Hz), 1.48–1.56 m (2H, CH_2), 1.92 d (3H, CH_3, *J* = 1.2 Hz), 3.19 quint (1H, 3′-H, *J* = 6.1, 6.7 Hz), 3.30 d.d (1H, NCH_2, *J* = 7.3, 12.8 Hz), 3.38 d.d (1H, NCH_2, *J* = 3.5, 12.8 Hz), 3.72 s (3H, OCH_3), 3.83 m (1H, OH), 4.27 d (1H, 5-H, *J* = 5.5 Hz), 4.38 d.d (1H, 4-H, *J* = 5.5, 9.5 Hz), 6.60 d.d (1H, =CH, *J* = 9.4, 1.5 Hz).

Compound **IIa** on storage in acetone-d_6 solution was completely converted into pyrrolidine **III**. $[\alpha]_D^{20}$ = +39.3° (*c* = 1.921, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3360, 2960, 2880, 1695, 1655, 1603, 1460, 1319, 1278, 1232, 1190, 1132, 1070, 957, 760. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.89 t (3H, CH_3, *J* = 7.3 Hz), 0.91 t (3H, CH_3, *J* = 7.3 Hz), 1.49–1.66 m (4H, CH_2), 1.84 s (3H, CH_3), 3.39 m (2H, 3″-H, NCH_2), 3.68 s (3H, OCH_3), 3.84 d.d (1H, NCH_2, *J* = 3.7, 11.1 Hz), 4.24 d (1H, 4′-H, *J* = 3.9 Hz), 4.40 s (1H, 3′-H), 7.87 br.s (1H, NH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 9.17 and 10.08 (CH_3), 12.69 (CH_3), 25.45 and 26.15 (CH_2), 50.80 (OCH_3), 53.85 (NCH_2), 72.29 and 81.44 ($C^{3'}$, $C^{4'}$), 82.85 ($C^{3''}$), 88.24 (=CMe), 158.84 ($C^{2'}$), 171.47 (C=O). Found: *m*/*z* 257.161 $[M]^+$. $C_{13}H_{22}O_5$. Calculated: *M* 257.1622.

Methyl 2-[1-acetyl-3-(pent-3-yloxy)-1*H*-pyrrol-2-yl]propanoate (IV). A solution of 0.080 g (0.31 mmol) of compound **III** in 5 ml of methylene chloride was cooled to 0°C, 0.23 ml (2.82 mmol) of pyridine was added, and 0.1 ml (1.40 mmol) of acetyl chloride was added dropwise. The mixture was stirred for 1 h and diluted with 10 ml of ethyl acetate. The organic phase was washed with water and brine, dried over $MgSO_4$, and evaporated, and the residue was subjected to column chromatography on silica gel using ethyl acetate–petroleum ether (1:1) as eluent. Yield 0.044 g (50%), oily substance, $[\alpha]_D^{20}$ = –13° (*c* = 0.1932, $CHCl_3$). IR spectrum, ν, cm^{-1}: 2967, 2939, 2878, 1739, 1715, 1603, 1501, 1462, 1435, 1373, 1331, 1290, 1205, 1092, 1055, 1034, 966, 943, 719, 681, 648. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.92 t (3H, CH_3, *J* = 7.4 Hz), 0.93 t (3H, CH_3, *J* = 7.4 Hz), 1.43 d (3H, CH_3, *J* = 7.0 Hz), 1.60 m (4H, CH_2, *J* = 7.4, 1.6 Hz), 2.47 s (3H, CH_3CO), 3.63 s (3H, OCH_3), 3.81 quint (1H, 3″-H, *J* = 5.8 Hz), 4.24 q (1H, 2-H, *J* = 7.1 Hz), 6.07 d (1H, =CH, *J* = 3.9 Hz), 6.89 d (1H, =CH, *J* = 3.9 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 9.48 (CH_3), 16.17 (CH_3), 23.07 (**C**H_3CO), 26.02 (CH_2), 35.76 (C^2), 51.83 (OCH_3), 83.52 ($C^{3''}$), 104.34 ($C^{4'}$), 118.34 ($C^{5'}$), 118.90 ($C^{2'}$), 146.17 ($C^{3'}$), 168.40 (CH_3CO), 173.79 (**C**O_2Me). Mass spectrum, *m*/*z* (I_{rel}, %): 266 (0.3) $[M - CH_3]^+$, 239 (3) $[M - H - CH_3CO]^+$, 222 (0.3) $[M - CO_2Me]^+$, 211 (6) $[M - C_5H_{10}]^+$, 179 (4), 169 (78), 110 (100), 83 (22), 70 (4), 55 (9). Found, %: C 64.34; H 8.02; N 5.36. $C_{15}H_{23}NO_4$. Calculated, %: C 64.03; H 8.24; N 4.98.

Methyl (2*E*,4*S*)-2-methyl-4-(1,2-oxazetidin-4-yl)-4-(pent-3-yloxy)but-2-enoate (VIII). Epoxide **VII**, 0.040 g (0.14 mmol), was dissolved in 5 ml of ethanol–water (5:1), 92 mg (0.16 mmol) of ammonium chloride and 112 mg (0.16 mmol) of sodium azide were added, and the mixture was heated for 3 h under

reflux (TLC). The mixture was cooled, diluted with 10 ml of a 5% solution of $NaHCO_3$, ethanol was distilled off, and the residue was extracted with ethyl acetate (3 × 10 ml). The extracts were combined, washed with brine, dried over $MgSO_4$, and evaporated, and the residue was subjected to column chromatography on silica gel using ethyl acetate–petroleum ether (1:5) as eluent to isolate 0.018 g (44%) of pyrrolidine **III** [6] and 0.012 g of an inseparable mixture of compounds **VII** and **VIII**. IR spectrum, ν, cm^{-1}: 3487, 2965, 2936, 2876, 2043, 1718, 1651, 1456, 1437, 1385, 1300, 1248, 1134, 1089, 1059, 959, 935, 744.

Compound **VIII** (in a mixture with **VII**). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.88 t (3H, CH_3, J = 7.5 Hz), 0.89 t (3H, CH_3, J = 7.5 Hz), 1.38–1.57 m (4H, CH_2), 1.93 d (3H, CH_3, J = 1.3 Hz), 3.20 m (1H, 3″-H), 3.53 m and 3.78 m (1H each, NCH_2), 3.72 s (3H, OCH_3), 4.18 m (1H, 4′-H), 4.49 d.d (1H, 4-H, J = 3.9, 9.3 Hz), 6.68 d.d (1H, =CH, J = 1.2, 9.4 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 9.39 and 10.15 (CH_3), 13.42 (CH_3), 26.06 and 27.13 (CH_2), 46.49 (NCH_2), 52.15 (OCH_3), 54.18 (NCH), 74.79 (C^4), 74.88 ($C^{4'}$), 80.57 ($C^{3''}$), 131.38 (C^2), 140.34 (C^3), 168.14 (C=O). Mass spectrum, m/z (I_{rel}, %): 199 (29) $[M - CH_2NHOCH]^+$, 155 (47), 129 (100), 113 (15), 95 (45), 67 (16), 59 (12), 43 (38).

Methyl (2*E*)-4-[(*S*)-2-acetyl-1,2-oxazetidin-4-yl]-2-methyl-4-(pent-3-yloxy)but-2-enoate (IX) was synthesized as described above for compound **IV** by acetylation of a mixture of **VII** with **VIII** and was isolated by column chromatography on silica gel. Yield ~75%. IR spectrum, ν, cm^{-1}: 2965, 2936, 2878, 2043, 1747, 1717, 1653, 1456, 1435, 1373, 1238, 1204, 1136, 1088, 1067, 1043, 984, 962, 941, 750. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.85 t (3H, CH_3, J = 7.5 Hz), 0.89 t (3H, CH_3, J = 7.5 Hz), 1.39–1.56 m (4H, CH_2), 1.93 d (3H, CH_3, J = 1.5 Hz), 2.06 s (3H, CH_3CO), 3.22 quint (1H, 3″-H, J = 5.4, 6.2 Hz), 3.67 d.d (1H, NCH_2, J = 7.3, 11.9 Hz), 3.72 s (3H, OCH_3), 3.88 d.d (1H, NCH_2, J = 4.0, 11.9 Hz), 4.59 d.d (1H, 4-H, J = 5.2, 9.3 Hz), 5.15 m (1H, 4′-H), 6.59 d.d (1H, =CH, J = 9.3, 1.6 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 9.35 and 10.04 (CH_3), 13.55 (CH_3), 20.70 (CH_3CO), 26.07 and 27.05 (CH_2), 43.71 (NCH_2), 52.26 (OCH_3), 73.42 ($C^{4'}$), 75.15 (C^4), 81.03 ($C^{3''}$), 132.49 (C^2), 138.15 (=CH), 167.93 ($CH_3\mathbf{C}O$), 170.32 ($\mathbf{C}O_2Me$). Mass spectrum, m/z (I_{rel}, %): 283 (0.05) $[M - H - CH_3]^+$, 233 (14), 199 (20), 159 (22), 129 (100), 97 (21), 83 (48).

Methyl (2*E*)-(4*S*,5*S*)-6-acetoxy-5-hydroxy-2-methyl-4-(pent-3-yloxy)hex-2-enoate (X). A mixture of 0.05 g (0.08 mmol) of compound **IX**, 0.058 g (0.88 mmol) of sodium azide, and 0.038 g (0.70 mmol) of ammonium chloride in 5 ml of a 5:1 DMF–H_2O mixture was stirred for 14 h at room temperature. The mixture was diluted with ethyl acetate, the organic phase was separated, washed with water and brine, dried over $MgSO_4$, and evaporated, and the residue was subjected to column chromatography on silica gel using ethyl acetate–petroleum ether (1:5 to 1:2) as eluent. Yield 0.014 g (26%), $[\alpha]_D^{20}$ = +14° (c = 0.3434, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3487, 2965, 2936, 2878, 1744, 1717, 1651, 1480, 1437, 1381, 1315, 1240, 1136, 1101, 1059, 1043, 937, 750. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.85 t (3H, CH_3, J = 7.3 Hz), 0.88 t (3H, CH_3, J = 7.5 Hz), 1.37–1.46 m (2H, CH_2), 1.51–1.55 m (2H, CH_2), 1.91 d (3H, CH_3, J = 1.3 Hz), 2.00 s (3H, CH_3CO), 2.86 br.s (1H, OH), 3.19 quint (1H, 3′-H, J = 5.2, 6.0 Hz), 3.72 s (3H, OCH_3), 3.87 quint (1H, 5-H, J = 5.5 Hz), 4.03 d.d (1H, OCH_2, J = 6.7, 11.2 Hz), 4.17 d.d (1H, OCH_2, J = 4.3, 11.3 Hz), 4.41 d.d (1H, 4-H, J = 5.2, 9.4 Hz), 6.66 d.d (1H, =CH, J = 9.4, 1.5 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 6.96 and 7.76 (CH_3), 10.98 (CH_3), 18.30 ($\mathbf{C}H_3CO$), 23.66 and 24.75 (CH_2), 49.69 (OCH_3), 63.38 (OCH_2), 70.12 (C^5), 72.76 (C^4), 78.07 ($C^{3'}$), 128.79 (C^2), 138.00 (=CH), 165.77 ($\mathbf{C}O_2Me$), 168.50 ($CH_3\mathbf{C}O$). Mass spectrum, m/z (I_{rel}, %): 284 (0.5) $[M - H_2O]^+$, 215 (5) $[M - C_5H_{11}O]^+$, 199 (9), 183 (7), 141 (15), 129 (100), 123 (14), 97 (27), 71 (5). Found, %: C 60.05; H 8.33. $C_{15}H_{26}O_6$. Calculated, %: C 59.58; H 8.67.

Methyl (2*E*,4*S*)-6-acetoxy-2-methyl-5-oxo-4-(pent-3-yloxy)hex-2-enoate (XI). A solution of 0.020 g (0.066 mmol) of compound **X** in 5 ml of acetone was cooled to 0°C, and 0.13 ml (0.33 mmol) of a 2.67 M solution of the Jones reagent was added dropwise under stirring. The mixture was stirred until the initial compound disappeared (TLC), and isopropyl alcohol was added dropwise until the mixture turned green. The mixture was filtered through a thin layer of silica gel and evaporated, and the residue was subjected to column chromatography on silica gel using ethyl acetate–petroleum ether (1:5) as eluent. Yield 0.011 g (56%). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.90 t (3H, CH_3, J = 7.3 Hz), 0.92 t (3H, CH_3, J = 7.3 Hz), 1.50–1.57 m (4H, CH_2), 1.96 d (3H, CH_3, J = 1.2 Hz), 2.16 s (3H, CH_3CO), 3.29 quint (1H, 3′-H, J = 5.8 Hz), 3.77 s (3H, OCH_3), 4.80 d (1H, 4-H, J = 8.2 Hz), 4.94 d (1H, OCH_2, J = 18.0 Hz), 5.07 d (1H, OCH_2, J = 18.0 Hz), 6.58 d.d (1H, =CH, J = 8.2, 1.2 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 7.01 and 7.82 (CH_3), 11.02 (CH_3), 18.44 ($\mathbf{C}H_3CO$), 23.77 and 24.86

(CH_2), 50.71 (OCH_3), 65.22 (OCH_2), 78.69 (C^4), 82.02 ($C^{3'}$), 143.88 (C^2), 137.02 (=CH), 164.56 (**C**O_2Me), 169.03 (CH_3**C**O), 206.00 (C^5). Found, %: C 60.38; H 8.25. $C_{15}H_{24}O_6$. Calculated, %: C 59.98; H 8.05.

Ethyl (2*E*,4*S*,5*S*)-2-methyl-4-(pent-3-yloxy)-5,6-bis(methanesulfonyloxy)hex-2-enoate (XIII). A solution of 0.1479 (0.43 mmol) of compound **XII** [6] in 5 ml of methylene chloride was cooled to 0°C, 0.12 ml (0.87 mmol) of triethylamine and 0.07 ml (0.87 mmol) of methanesulfonyl chloride were added, and the mixture was stirred for 30 min at room temperature. The organic phase was washed with water and brine, dried over $MgSO_4$, and evaporated, and the residue was purified by column chromatography on silica gel using ethyl acetate–petroleum ether (1:2) as eluent. Yield 0.142 g (78%), $[\alpha]_D^{20}$ = –4.3° (*c* = 1.524, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3026, 2968, 2939, 2878, 1713, 1657, 1462, 1454, 1414, 1359, 1236, 1177, 1144, 1099, 1067, 972, 953, 833, 810, 752, 528. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.85 t (3H, CH_3, *J* = 7.3 Hz), 0.89 t (3H, CH_3, *J* = 7.3 Hz), 1.31 t (3H, CH_3, *J* = 7.4 Hz), 1.45–1.55 m (4H, CH_2), 1.97 s (3H, CH_3), 3.08 s (3H, SO_2CH_3), 3.11 s (3H, SO_2CH_3), 3.17 quint (1H, 3′-H, *J* = 5.8 Hz), 4.22 m (2H, OCH_2), 4.30 d.d (1H, OCH_2, *J* = 6.3, 11.3 Hz), 4.52 d.d (1H, OCH_2, *J* = 1.2, 11.3 Hz), 4.57 d.d (1H, 4-H, *J* = 6.4, 9.8 Hz), 4.83 m (1H, 5-H), 6.46 d (1H, =CH, *J* = 9.4 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 9.21 and 9.82 (CH_3), 13.48 (CH_3), 14.19 (CH_3), 25.36 and 26.45 (CH_2), 37.62 and 38.49 (SO_2CH_3), 61.23 (OCH_2), 67.77 (C^6), 71.91 (C^4), 80.09 (C^5), 80.44 ($C^{3'}$), 134.27 (C^2), 134.83 (C^3), 166.80 (C=O). Mass spectrum, *m*/*z* (I_{rel}, %): 385 (1) $[M - OEt]^+$, 343 (9) $[M - C_5H_{11}O]^+$, 283 (4), 247 (10), 233 (10), 216 (22), 189 (10), 159 (8), 143 (100), 123 (21), 97 (23), 79 (8), 59 (13).

Reaction of bis-methanesulfonate XIII with sodium azide. Compound **XIII**, 0.281 g (0.67 mmol), was dissolved in 6 ml of DMF–H_2O (3:1), 0.145 g (2.7 mmol) of ammonium chloride and 0.22 g (3.38 mmol) of sodium azide were added, and the mixture was heated for 3 h under reflux (TLC). The mixture was cooled, diluted with water, and extracted with ethyl acetate (3 × 10 ml). The extracts were combined, washed with brine, dried over $MgSO_4$, and evaporated, and the residue was purified by column chromatography on silica gel using ethyl acetate–petroleum ether (1:3, 1:2, and 1:1) as eluent to isolate 0.064 g (37%) of pyrrolidine **XIV** and 0.062 g (38%) of compound **XV**.

Ethyl (2*Z*)-2-[(3*S*,4*S*)-4-methanesulfonyloxy-3-(pent-3-yloxy)pyrrolidin-2-ylidene]propanoate (XIV). IR spectrum, ν, cm^{-1}: 3360, 2960, 2880, 1695, 1655, 1603, 1460, 1319, 1278, 1232, 1190, 1132, 1070, 957, 760. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.91 t (3H, CH_3, *J* = 7.3 Hz), 0.93 t (3H, CH_3, *J* = 7.3 Hz), 1.27 t (3H, CH_3, *J* = 6.7 Hz), 1.48–1.64 m (4H, CH_2), 1.83 s (3H, CH_3), 3.07 s (3H, SO_2CH_3), 3.50 m (1H, 3″-H), 3.67 d.d (1H, NCH_2, *J* = 12.2 Hz), 3.93 d.d (1H, NCH_2, *J* = 3.9, 12.2 Hz), 4.69 s (1H, 3′-H), 5.09 d (1H, 4′-H, *J* = 3.3 Hz), 7.89 br.s (1H, NH).

Ethyl 2-[3-(pent-3-yloxy)-1*H*-pyrrol-2-yl]propanoate (XV). $[\alpha]_D^{20}$ = +5.2° (*c* = 0.3893, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3350, 2966, 2936, 2130, 1718, 1690, 1600, 1458, 1369, 1330, 1308, 1252, 1179, 1143, 1128, 1103, 1063, 1051, 950, 750, 690. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.96 t (3H, CH_3, *J* = 7.3 Hz), 0.97 t (3H, CH_3, *J* = 7.3 Hz), 1.26 t (3H, CH_3, *J* = 7.1 Hz), 1.45 d (3H, CH_3, *J* = 7.3 Hz), 1.63 m (4H, CH_2), 3.74 quint (1H, 3″-H, *J* = 5.8 Hz), 3.95 q (1H, 2-H, *J* = 7.1 Hz), 4.15 m (2H, OCH_2), 5.86 t (1H, =CH, *J* = 2.8 Hz), 6.52 t (1H, =CH, *J* = 2.8 Hz), 8.15 br.s (1H, NH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 9.52 (CH_3), 14.13 (CH_3), 19.10 (CH_3), 25.99 and 26.04 (CH_2), 35.19 (C^2), 60.77 (OCH_2), 84.19 ($C^{3''}$), 99.11 ($C^{4'}$), 114.45 ($C^{5'}$), 115.26 ($C^{2'}$), 141.98 ($C^{3'}$), 175.08 (C=O). Mass spectrum, *m*/*z* (I_{rel}, %): 254 (0.3) $[M + H]^+$, 213 (11) $[M + H - OEt]^+$, 143 (100), 115 (5), 97 (36), 71 (13). Found: *m*/*z* 254.201 $[M + H]^+$. $C_{14}H_{23}NO_3$. Calculated: $[M + H]^+$ 254.1672.

Reduction of compounds Ia and Ib with hydrogen. *a*. Compound **Ib**, 0.112 g (0.38 mmol), was dissolved in 5 ml of ethanol, 0.112 g of the Lindlar catalyst was added, and the mixture was stirred for 2 h under a hydrogen pressure of 1 atm. The mixture was filtered through a thin layer of silica gel, the sorbent was washed with ethyl acetate, and the solvent was evaporated. The residue was purified by column chromatography on silica gel using ethyl acetate–petroleum ether (1:2) as eluent to isolate 0.079 g (78%) of ethyl (2*E*)-3-(5-aminomethyl-2,2-diethyl-1,3-dioxolan-4-yl)-2-methylprop-2-enoate (**XVIb**). $[\alpha]_D^{20}$ = –26.0° (*c* = 0.773, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3282, 2974, 2939, 2882, 1715, 1661, 1464, 1447, 1368, 1312, 1300, 1258, 1227, 1202, 1173, 1136, 1076, 1057, 1032, 975, 935, 746. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.90 t (3H, CH_3, *J* = 7.3 Hz), 0.91 t (3H, CH_3, *J* = 7.3 Hz), 1.26 t (3H, CH_3, *J* = 7.3 Hz), 1.63–1.67 m (4H, CH_2), 1.88 d (3H, CH_3, *J* = 1.2 Hz), 2.72 d.d (1H, NCH_2, *J* = 6.1, 13.15 Hz), 2.92 d.d (1H, NCH_2, *J* = 3.05, 13.15 Hz), 3.75 m (1H, 5′-H), 4.18 m (2H, OCH_2), 4.57 t (1H, 4′-H, *J* = 8.9 Hz), 6.61 d.d (1H, =CH, *J* = 1.2, 8.9 Hz). ^{13}C NMR spectrum ($CDCl_3$),

δ_C, ppm: 8.03 and 8.16 (CH_3), 13.23 (CH_3), 14.21 (CH_3), 30.43 and 30.50 (CH_2), 42.55 (NCH_2), 60.91 (OCH_2), 74.75 ($C^{4'}$), 82.36 ($C^{5'}$), 113.48 ($C^{2'}$), 132 06 (C^2), 137.02 (C^3), 167.31 (C=O). Mass spectrum, *m*/*z* (I_{rel}, %): 242 (46) $[M - Et]^+$, 226 (23) $[M - OEt]^+$, 213 (100) $[M - 2Et]^+$, 185 (14), 169 (25), 157 (44), 126 (37), 111 (23), 98 (28), 83 (35), 70 (16), 57 (20). Found, %: C 64.34; H 8.02; N 5.36. $C_{15}H_{23}NO_4$. Calculated, %: C 64.03; H 8.24; N 4.98.

b. Compound **Ia**, 0.046 g (0.16 mmol), was dissolved in ethanol, 0.065 g of the Lindlar catalyst was added, and the mixture was stirred for 16 h under a hydrogen pressure of 1 atm. The mixture was filtered through a thin layer of silica gel, the sorbent was washed with ethyl acetate, and the solvent was evaporated. The residue (0.041 g) was dissolved in 5 ml of methylene chloride, the solution was cooled to 0°C, 0.11 ml (1.42 mmol) of pyridine was added, and 0.05 ml (0.71 mmol) of acetyl chloride was added dropwise. The mixture was stirred for 1 h and diluted with ethyl acetate, the organic phase was washed with water and brine, dried over $MgSO_4$, and evaporated, and the residue was subjected to column chromatography on silica gel using ethyl acetate–petroleum ether (1:2) to isolate 0.034 g (72%) of a mixture of compounds **XVIIa** and **XVIII**. IR spectrum, ν, cm^{-1}: 2963, 2930, 2880, 1718, 1653, 1456, 1437, 1385, 1298, 1273, 1238, 1192, 1157, 1136, 1111, 1059, 1032, 959, 914, 852, 813, 744.

Methyl (2*E*)-3-[(4*S*,5*S*)-5-acetamidomethyl-2,2-diethyl-1,3-dioxolan-4-yl]-2-methylprop-2-enoate (XVIIa). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.94 t (3H, CH_3, *J* = 7.3 Hz), 0.92 t (3H, CH_3, *J* = 7.1 Hz), 1.59 q (4H, CH_2, *J* = 7.3 Hz), 1.93 d (3H, CH_3, *J* = 1.0 Hz), 2.00 s (3H, CH_3CO), 3.29 d.t (1H, NCH_2, *J* = 5.8, 14.0 Hz), 3.38 d.t (1H, NCH_2, *J* = 5.9, 14.1 Hz), 3.76 s (3H, OCH_3), 3.87 m (1H, 5-H), 4.47 t (1H, 4-H, *J* = 8.6 Hz), 5.90 br.s (1H, NH), 6.59 d.d (1H, =CH, *J* = 8.8, 1.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 8.00 and 8.21 (CH_3), 13.25 (CH_3), 23.30 (**C**H_3CO), 30.36 and 30.55 (CH_2), 39.62 (NCH_2), 51.76 (OCH_3), 74.98 ($C^{4'}$), 79.52 ($C^{5'}$), 112.85 ($C^{2'}$), 132.81 (C^2), 136.27 (=CH), 167.75 (CH_3**C**O), 170.02 (**C**O_2Me).

Methyl 3-[(4*S*,5*S*)-5-acetamidomethyl-2,2-diethyl-1,3-dioxolan-4-yl)]-2-methylpropanoate (XVIII). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.87 t (6H, CH_3, *J* = 7.3 Hz), 1.22 d (3H, CH_3, *J* = 7.1 Hz), 1.68 m (4H, CH_2), 1.96 m (2H, CH_2), 1.99 s (3H, CH_3CO), 2.72 m (1H, CH, *J* = 7.2 Hz), 3.53–3.59 m (2H, NCH_2), 3.68 s (3H, OCH_3), 3.87 m (1H, 5′-H), 4.12 q (1H, 4′-H, *J* = 7.1 Hz), 5.99 br.s (1H, NH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 8.06 and 8.13 (CH_3), 18.07 (CH_3), 23.27 (**C**H_3CO), 30.56 and 30.65 (CH_2), 36.64 (CH), 37.07 (C^3), 40.79 (NCH_2), 52.14 (OCH_3), 77.32 ($C^{4'}$), 79.98 ($C^{5'}$), 113.94 ($C^{2'}$), 170.08 (CH_3**C**O), 176.65 (**C**O_2Me).

Ethyl (2*E*)-3-[(4*S*,5*S*)-5-(acetamidomethyl)-2,2-diethyl-1,3-dioxolan-4-yl]-2-methylprop-2-enoate (XVIIb) was synthesized as described above for compound **IV** from 0.045 g (0.17 mmol) of amine **XVIb** and 0.06 ml (0.75 mmol) of acetyl chloride in 0.14 ml (1.5 mmol) of pyridine. Yield 0.074 g (96%), $[\alpha]_D^{20}$ = –27.0° (*c* = 0.301, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3289, 3082, 2974, 2939, 2882, 1722, 1651, 1556, 1537, 1462, 1435, 1371, 1269, 1229, 1199, 1175, 1138, 1085, 1057, 1039, 997, 932, 749. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.93 t (3H, CH_3, *J* = 7.1 Hz), 0.95 t (3H, CH_3, *J* = 7.3 Hz), 1.30 t (3H, CH_3, *J* = 7.3 Hz), 1.63–1.67 m (4H, CH_2), 1.93 d (3H, CH_3, *J* = 1.2 Hz), 2.01 s (3H, CH_3CO), 3.37 d.t (1H, NCH_2, *J* = 5.8, 14.0 Hz), 3.58 d.d.d (1H, NCH_2, *J* = 3.6, 5.8, 14.04 Hz), 3.87 m (1H, 5′-H, *J* = 2.8 Hz), 4.18 q (2H, OCH_2, *J* = 7.0 Hz), 4.47 t (1H, 4′-H, *J* = 8.5 Hz), 5.82 br.s (1H, NH), 6.61 d.d (1H, =CH, *J* = 1.2, 8.5 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 8.01 and 8.13 (CH_3), 13.17 (CH_3), 14.19 (CH_3), 23.22 (**C**H_3CO), 30.32 and 30.46 (CH_2), 39.59 (NCH_2), 60.95 (OCH_2), 74.96 ($C^{4'}$), 79.41 ($C^{5'}$), 112.85 ($C^{2'}$), 133.15 (C^2), 135.73 (=CH), 169.95 (CH_3**C**O), 176.21 (**C**O_2Et). Mass spectrum, *m*/*z* (I_{rel}, %): 312 (0.5) $[M - H]^+$, 284 (100) $[M - Et]^+$, 213 (42), 182 (33), 157 (23), 140 (21), 126 (20), 98 (15), 57 (12). Found: *m*/*z* 312.178 $[M - H]^+$. $C_{14}H_{22}NO_5$. Calculated: $[M - H]$ 312.189.

Methyl (2*E*)-3-[(4*S*,5*S*)-5-(triphenylphosphanylideneaminomethyl)-2,2-diethyl-1,3-dioxolan-4-yl]-2-methylprop-2-enoate (XIX). Compound **Ia**, 0.16 g (0.57 mmol), was dissolved in 5 ml of THF–H_2O (5:1), 0.223 g (0.86 mmol) of triphenylphosphine was added, and the mixture was stirred for 4 h at 50°C. Tetrahydrofuran was distilled off, the residue was treated with ethyl acetate, the organic phase was washed with brine, dried over $MgSO_4$, and evaporated, and the residue was purified by column chromatography on silica gel using ethyl acetate–petroleum ether (1:2, 1:1, 2:1) as eluent. Yield 0.15 g (52%), $[\alpha]_D^{20}$ = –27.2° (*c* = 3.745, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3053, 2972, 2939, 2882, 1718, 1680, 1460, 1437, 1375, 1354, 1313, 1259, 1227, 1190, 1176, 1163, 1121, 1078, 1057, 1026, 939, 746, 721, 696, 542. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.89 t (3H, CH_3, *J* = 7.2 Hz),

0.92 t (3H, CH_3, J = 7.3 Hz), 1.61–1.69 m (4H, CH_2), 1.89 s (3H, CH_3), 3.34 t (2H, NCH_2, J = 4.3 Hz), 3.72 s (3H, OCH_3), 4.01 m (1H, 5′-H), 4.85 t (1H, 4′-H, J = 8.5 Hz), 6.67 d (1H, =CH, J = 8.6 Hz), 7.54–7.63 m (9H, Ph), 7.70 d.d (6H, Ph, J = 7.7, 11.7 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 12.66 and 12.76 (CH_3), 17.79 (CH_3), 35.50 and 35.55 (CH_2), 57.02 (NCH_2), 56.44 (OCH_3), 81.01 ($C^{4'}$), 86.56 ($C^{5'}$), 117.97 ($C^{2'}$); 133.66, 133.82, 137.09, 138.25 (C_6H_5); 136.97 (=CH), 143.41 (C^2), 171.0 (**C**O_2Me). Found, %: C 71.75; H 6.98; N 2.55; P 5.77. $C_{31}H_{36}NO_4P$. Calculated, %: C 71.93; H 7.01; N 2.71; P 5.98.

Ethyl (2*E*)-6-acetamido-5-hydroxy-2-methyl-4-(pent-3-yloxy)hex-2-enoate (XXb) was synthesized as described above for compound **II** from 0.148 g (0.47 mmol) of **XVIIb** using 0.11 ml (0.68 mmol) of Et_3SiH and 0.06 ml (0.57 mmol) of $TiCl_4$. Yield 0.121 g (80%), $[\alpha]_D^{20}$ = +17.1° (c = 0.381, $CHCl_3$). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.85 t (3H, CH_3, J = 7.3 Hz), 0.88 t (3H, CH_3, J = 7.6 Hz), 1.29 t (3H, CH_3, J = 7.1 Hz), 1.39–1.53 m (4H, CH_2), 1.89 d (3H, CH_3, J = 1.3 Hz), 1.99 s (3H, CH_3CO), 3.09–3.16 m (3H, 3′-H, NCH_2, OH), 3.51 d.d.d (1H, NCH_2, J = 3.2, 6.6, 13.7 Hz), 3.67 m (1H, 5-H, J = 7.3 Hz), 4.12 d.d (1H, 4′-H, J = 6.4, 9.6 Hz), 4.19 m (2H, OCH_2, J = 7.1 Hz), 6.03 br.s (1H, NH), 6.55 d.d (1H, =CH, J = 1.2, 9.6 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 9.12 and 9.80 (CH_3), 13.23 (CH_3), 14.13 (CH_3), 23.17 (**C**H_3CO), 25.32 and 26.46 (CH_2), 41.58 (NCH_2), 60.90 (OCH_2), 72.57 (C^5), 74.87 (C^4), 79.75 ($C^{3'}$), 132.31 (C^2), 137.73 (C^3), 167.16 (**C**O_2Et), 170.42 (CH_3**C**O). Mass spectrum, m/z (I_{rel}, %): 315 (0.5) $[M]^+$, 297 (0.5) $[M - H_2O]^+$, 270 (1) $[M - OEt]^+$, 228 (15) $[M - C_5H_{10}O]^+$, 214 (82) $[M - 2Et - Ac]^+$, 200 (6) $[M - C_5H_{10} - OEt]^+$, 182 (7), 157 (23), 143 (100), 115 (21), 102 (26), 97 (34), 83 (14), 73 (9). Found: m/z 315.200 $[M]^+$. $C_{16}H_{29}NO_5$. Calculated: M 315.205.

Methyl (2*E*)-6-acetamido-2-methyl-5-oxo-4-(pent-3-yloxy)hex-2-enoate (XXIa). Pyridinium dichromate (PDC), 0.028 g (0.074 mmol), was added to a solution of 0.016 g (0.049 mmol) of compound **XXa** (prepared as described above for **XXb**) in 20 ml of methylene chloride, and the mixture was stirred for 6 h. The mixture was filtered through a thin layer of silica gel, the filtrate was evaporated, and the residue was subjected to column chromatography on silica gel using ethyl acetate–petroleum ether (1 : 1) as eluent to isolate 0.008 g of unreacted compound **XXa** and 0.005 g (31%) of **XXIa**, $[\alpha]_D^{20}$ = +32.3° (c = 0.306, $CHCl_3$). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.89 t (6H, CH_3, J = 7.5 Hz), 1.50–1.56 m (4H, CH_2), 1.96 d (3H, CH_3, J = 0.8 Hz), 2.04 s (3H, CH_3CO), 3.25 quint (2H, 3′-H, J = 5.7 Hz), 3.96 s (3H, OMe), 4.33 d.d (1H, NCH_2, J = 4.4, 21.1 Hz), 4.49 d.d (1H, NCH_2, J = 4.6, 21.0 Hz), 4.78 d (1H, 4-H, J = 8.4 Hz), 6.14 br.s (1H, NH), 6.55 d.d (1H, =CH, J = 1.2, 8.4 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 9.26 and 9.61 (CH_3), 13.58 (CH_3), 23.02 (**C**H_3CO), 25.29 and 25.96 (CH_2), 46.89 (NCH_2), 52.22 (OCH_3), 79.60 (C^4), 81.22 ($C^{3'}$), 135.93 (C^3), 152.20 (C^2), 162.0 (**C**O_2Me), 172.80 (CH_3**C**O), 215.05 (C^5). Mass spectrum, m/z (I_{rel}, %): 268 (1) $[M - OMe]^+$, 238 (6), 229 (11) $[M - C_5H_{10}]^+$, 197 (18), 185 (50), 170 (40), 155 (44), 126 (100), 102 (84), 73 (48), 60 (9). Found, %: C 60.42; H 8.28; N 4.55. $C_{15}H_{25}NO_5$. Calculated, %: C 60.18; H 8.42; N 4.68.

This study was performed under financial support by the Russian Foundation for Basic Research (project no. 11-03-97013-r_a-povolzh'e) and by the Ministry of Education and Science of the Russian Federation (state contract no. 14.740.11.0367).

REFERENCES

1. L'Abbe, G.L., *Chem. Rev*., 1969, vol. 69, p. 345.
2. Scriven, E.F.V. and Turnbull, K., *Chem. Rev*., 1988, vol. 88, p. 297.
3. Lang, S. and Murphy, J.A., *Chem. Soc. Rev*., 2006, vol. 35, p. 146.
4. Reichen, W., *Chem. Rev*., 1978, vol. 78, p. 569.
5. Bräse, S., Gil, C., Knepper, K., and Zimmerman, V., *Angew. Chem., Int. Ed*., 2005, vol. 44, p. 5188.
6. Gimalova, F.A., Khalikova, G.M., Egorov, V.A., Mustafin, A.G., and Miftakhov, M.S., *Izv. Akad. Nauk, Ser. Khim*., 2012, p. 1227.
7. Mori, A., Ishihara, K., and Yamamoto, H., *Tetrahedron Lett*., 1986, vol. 27, p. 987.
8. Gololobov, Y.G. and Kasukhin, L.F., *Tetrahedron*, 1992, vol. 48, p. 1353.