Synthesis of methyl (*E*)-2-[(3*S*,4*S*)-4-hydroxy-3-(pent-3-yloxy)-pyrrolidin-2-ylidene]propanoate and its unusual recyclization

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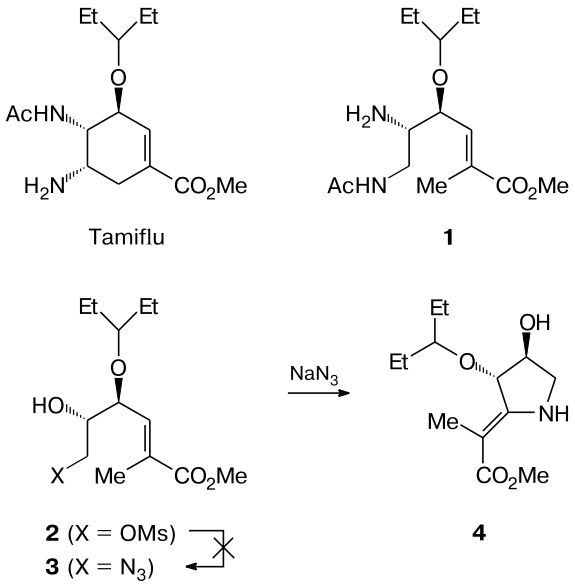
Methyl (2*E*,4*S*,5*S*)-5-hydroxy-6-mesyloxy-2-methyl-4-(pent-3-yloxy)hex-2-enoate was synthesized from L-tartaric acid. Attempted substitution of the mesyloxy group by the reaction with NaN_3 directly led to methyl (*E*)-2-[(3*S*,4*S*)-4-hydroxy-3-(pent-3-yloxy)pyrrolidin-2-ylidene]propanoate. The latter on treatment with CF_3COOH and then NaOH gave methyl (2*E*)-2-methyl-4-[(*S*)-oxiran-2-yl]-4-(pent-3-yloxy)but-2-enoate.

Key words: L-tartaric acid, mesylates, azides, heterocyclization, pyrrolidines, recyclization.

Heterocyclic secondary enamines bearing electron-withdrawing groups at the double bond are important intermediates in the synthesis of natural and heterocyclic compounds.[1—5] The latter can be conveniently synthesized by the intramolecular 1,3-dipolar azide—olefin cyclization reactions.[6—10]

During development of a procedure for the synthesis of seco analog of known antiviral agent Tamiflu, *i.e.*, compound **1** (see Refs 11—14), based on L-tartaric acid, the standard step of the replacement of the OMs group in compound **2** with the N_3 group led, instead of the expected azide **3**, to the pyrrolidine derivative **4** (Scheme 1).

Scheme 1



The synthesis of the starting mesylate **2** is shown in Scheme 2. Ketal **5** obtained from L-tartaric acid[15] was reduced with $LiAlH_4$ to diol **6**. Its oxidation with pyridinium dichromate was fairly selective and stopped at the formation of hemiacetal **7**. The latter reacted with phosphorane **8** stereoselectively giving rise to (*E*)-α,β-unsaturated ester **9**. The reductive opening of the ketal function in compound **9** with the system $Et_3SiH—TiCl_4$ (see Ref. 16) led to diols **10** and **11** in the ratio ~3 : 2. The selectivity of this step was somewhat improved by the use of Si derivative **12**, in this case alcohols **13** and **14** were formed in the ratio 2 : 1. The mesylation of diol **10** was also selective, leading to the primary mesylate **2** in high yield. The more efficient pathway for the synthesis of compound **2** was accomplished by the dioxolane ring opening in mesylate **15** with $Et_3SiH—TiCl_4$, which led to the regioselective formation of single compound **2** in high yield.

The structures of diols **10** and **11** and silyl derivatives **13** and **14** were assigned based on the spectroscopic data, as well as on the results of the TEMPO-catalyzed oxidation of compound **14** with $PhI(OAc)_2$ (see Ref. 17) to the unambiguously spectroscopically identifiable enone **16** (Scheme 3).

Then, mesylate **2** was subjected to the azide substitution, however, no expected azide **3** was obtained. Instead, pyrrolidine derivative **4** was isolated in good yield (Scheme 4). The indicated geometry of the double bond in pyrrolidine **4** was confirmed by the NOE experiment: the nuclear Overhauser effect (2.0%) was observed for the proton C(3′)—H

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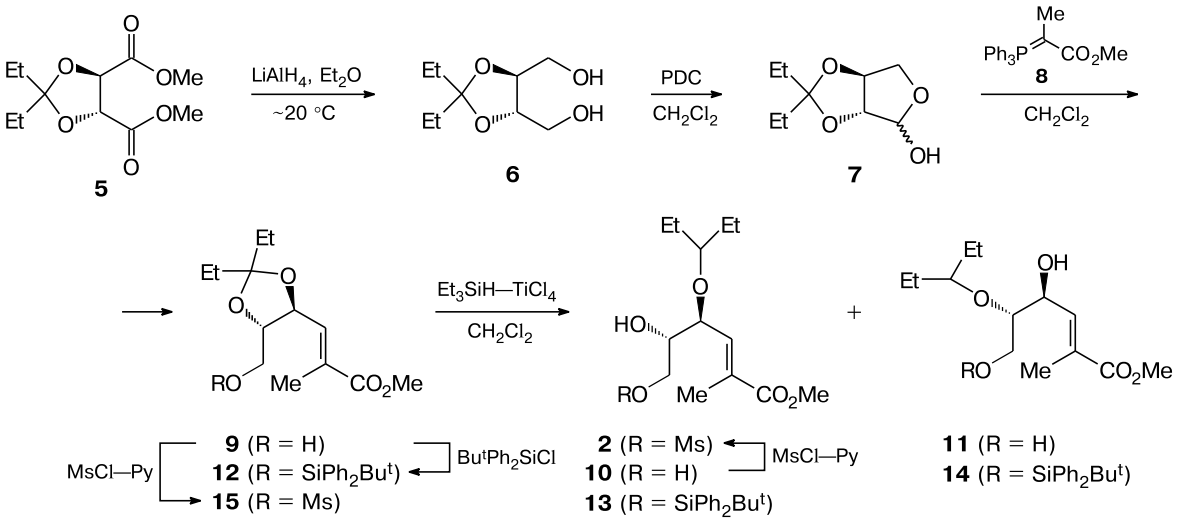
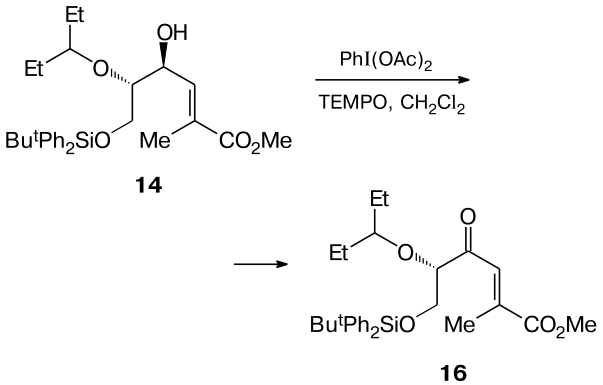
Scheme 2



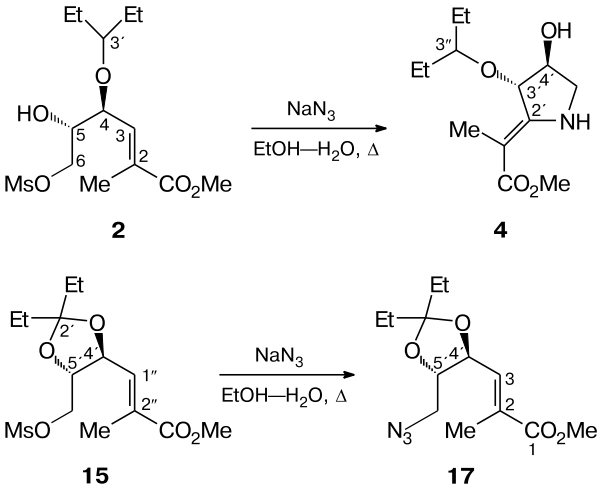
upon irradiation of the protons of the CH_3—C=C group. Unlike compound **2**, mesylate **15** in the reaction with NaN_3 gave the expected azide **17**, which seems more promising building block on the way to seco analog **1** (see Scheme 4).

Pyrrolidine derivatives **4** cannot be used in the synthesis of compound **1**. However, the unusual recyclization of this compound in CF_3COOH—THF discovered herein is of undoubted interest (Scheme 5). The TLC monitoring showed that the dropwise addition of a solution of compound **4** in THF to the mixture of CF_3COOH—THF (1 : 10) at 0 °C rapidly led to a new product, which in the course of neutralization with aqueous NaOH (pH > 8) was converted to the low polar epoxide **18**. Its spectroscopic characteristics and the R_f values agree with those for the authentic sample **18** obtained by treatment of mesylate **2** with $NaHCO_3$ in aqueous ethanol. Additional studies are required to establish the mechanism of the formation of compound **18**.

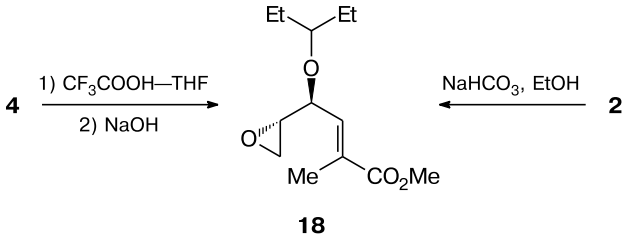
Scheme 3



Scheme 4



Scheme 5



In conclusion, optically active methyl (*E*)-2-[(3*S*,4*S*)-4-hydroxy-3-(pent-3-yloxy)pyrrolidin-2-ylidene]propanoate (**4**) was synthesized from L-tartaric acid in nine steps and its unusual recyclization to epoxide **18** was discovered.

Experimental

IR spectra were obtained on a Prestige-21 Shimadzu IR spectrometer for neat samples. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AM-300 (300.13 and 75.47 MHz, respectively) and Bruker AVANCE-500 spectrometers (500.13 and 125.77 MHz, respectively), using Me_4Si as an internal standard. Angles of optical rotation were measured on a Perkin—Elmer-341 instrument. Mass spectra were obtained on a Thermo Finnigan MAT 95XP instrument (70 eV). Reaction progress was monitored by TLC on Sorbfil plates (Russia), with visualization by the moisturizing the plates with a solution of anisaldehyde and sulfuric acid in ethanol with subsequent heating at 120—150 °C. Reaction products were isolated by column chromatography on silica gel (30—60 g of the adsorbent per 1 g of compound), using freshly distilled solvents as eluents. L-Tartaric acid used in the work was purchased from Aldrich.

Methyl (2*E*,4*S*,5*S*)-5-hydroxy-6-mesyloxy-2-methyl-4-(pent-3-yloxy)hex-2-enoate (2). Triethylsilane (55 mg, 0.47 mmol) was added to a solution of compound **15** (0.109 g, 0.32 mmol) in anhydrous CH_2Cl_2 (5 mL) cooled to −30——40 °C with stirring, followed by a dropwise addition of a solution of $TiCl_4$ (74 mg, 0.39 mmol) in CH_2Cl_2 (1 mL) at such a rate that to keep the temperature below −30 °C. The reaction mixture was stirred at this temperature until the starting compound was consumed (TLC), then, an ice-cold water was rapidly added and the temperature was raised to −5 °C. The organic layer was separated, the aqueous layer was extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were washed with brine and dried with $MgSO_4$. The solvent was evaporated and the residue was subjected to column chromatography with SiO_2 (eluent AcOEt—light petroleum, 1 : 5) to obtain compound **2** (0.105 g, 95%). $[\alpha]_D^{20}$ +7.0 (*c* 0.252, $CHCl_3$). MS, *m*/*z* (I_{rel} (%)): 467 $[M - C_2H_5]^+$ (14), 353 (100), 323 (12), 269 (10), 213 (61), 199 (50), 135 (25), 112 (16), 69 (37). IR, ν/cm^{-1}: 3520, 2964, 2936, 2883, 1716, 1645, 1460, 1437, 1358, 1248, 1176, 1136, 1101, 1061, 1034, 964, 935, 831, 796, 528. ^{1}H NMR ($CDCl_3$), δ: 0.83 (t, 3 H, CH_3, *J* = 7.3 Hz); 0.85 (t, 3 H, CH_3, *J* = 7.3 Hz); 1.41 (m, 2 H, CH_2, *J* = 7.4 Hz); 1.48 (m, 2 H, CH_2, *J* = 7.4 Hz); 1.90 (d, 3 H, CH_3, *J* = 1.3 Hz); 2.98 (d, 1 H, OH, *J* = 4.4 Hz); 3.07 (s, 3 H, CH_3SO_2); 3.19 (m, 1 H, H(3′), *J* = 5.3 Hz, *J* = 5.9 Hz); 3.77 (s, 3 H, OCH_3); 3.84 (m, 1 H, OCH_2); 4.17 (dd, 1 H, OCH_2, *J* = 5.0 Hz, *J* = 11.4 Hz); 4.33 (m, 2 H, H(4), H(5)); 6.58 (dq, 1 H, =CH, *J* = 1.3 Hz, *J* = 9.6 Hz). ^{13}C NMR ($CDCl_3$), δ: 9.14, 9.87 (CH_3); 13.33 (CH_3); 25.28, 26.45 (CH_2); 37.55 (CH_3SO_2); 52.19 (OCH_3); 69.80 (OCH_2); 71.78, 73.05 (C(5), C(4)); 80.09 (C(3′)); 132.42 (C(2)); 137.75 (C(3)); 167.62 (CO_2). Found (%): C, 50.02; H, 7.56; S, 9.82. $C_{14}H_{26}O_7S$. Calculated (%): C, 49.69; H, 7.74; S, 9.48.

Methyl (*E*)-2-[(3*S*,4*S*)-4-hydroxy-3-(pent-3-yloxy)pyrrolidin-2-ylidene]propanoate (4). Sodium azide (10 mg, 0.16 mmol) was added to a solution of mesylate **2** (26 mg, 0.08 mmol) in a mixture of EtOH—H_2O (5 : 1) (8 mL), and the reaction mixture was refluxed for 4 h (TLC monitoring), then it was treated with water and ethyl acetate (10 mL). The organic layer was separated, the aqueous layer was extracted with AcOEt (3×10 mL). The combined organic layers were washed with brine and dried with $MgSO_4$. The solvent was evaporated, the residue was subjected to column chromatography on SiO_2 (AcOEt—light petroleum, 1 : 5) to obtain product **4** (19 mg, 95%). $[\alpha]_D^{20}$ +39.3 (*c* 1.921, $CHCl_3$). HRMS, found: *m*/*z* 257.1618 $[M]^+$. $C_{13}H_{22}NO_4$. Calculated: M = 257.1622. MS, *m*/*z* (I_{rel} (%)): 257 $[M]^+$ (3), 239 $[M - H_2O]^+$ (0.5), 228 $[M - C_2H_5]^+$ (0.5), 186 $[M - C_5H_{11}]^+$ (18), 171 (19), 154 (100), 138 (45), 126 (14), 110 (31), 94 (27), 82 (19), 74 (40), 56 (13), 43 (27). IR, ν/cm^{-1}: 3360, 2960, 2880, 1695, 1655, 1603, 1460, 1319, 1278, 1232, 1190, 1132, 1070, 957, 760. ^{1}H NMR ($CDCl_3$), δ: 0.89 (t, 3 H, CH_3, *J* = 7.3 Hz); 0.91 (t, 3 H, CH_3, *J* = 7.3 Hz); 1.49—1.66 (m, 4 H, CH_2); 1.84 (s, 3 H, CH_3); 3.39 (m, 2 H, NCH_2, H(3″)); 3.68 (s, 3 H, OCH_3); 3.84 (dd, 1 H, NCH_2, *J* = 3.7 Hz, *J* = 11.1 Hz); 4.24 (d, H(4′), *J* = 3.9 Hz); 4.40 (s, H(3′)); 7.87 (br.s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 9.17, 10.08 (CH_3); 12.69 (CH_3); 25.45, 26.15 (CH_2); 50.80 (OCH_3); 53.85 (NCH_2); 72.29, 81.44 (C(3′), C(4′)); 82.85 (C(3″)); 88.24 (=C̲Me); 158.84 (C(2′)); 171.47 (CO_2).

(4*S*,5*S*)-2,2-Diethyl-4,5-bis(hydroxymethyl)-1,3-dioxolane (6). The ketalized dimethyl tartrate **5** (1.0 g, 3.87 mmol) was added dropwise to a suspension of $LiAlH_4$ (0.3 g, 7.75 mmol) in anhydrous diethyl ether (15 mL) under argon at room temperature. The reaction mixture was stirred for 4 h, then saturated aqueous Na_2SO_4 was added, the organic layer was separated, Et_2O was evaporated, and the residue was extracted with $CHCl_3$ (5×10 mL). The combined organic exstracts were washed with brine, dried with $MgSO_4$, and concentrated to obtain diol **6** (0.63 g, 85%). $[\alpha]_D^{20}$ −1.4 (*c* 1.202, $CHCl_3$). MS, *m*/*z* (I_{rel} (%)): 161 $[M - C_2H_5]^+$ (100), 99 (4), 87 (41), 75 (16), 69 (29), 57 (58). IR, ν/cm^{-1}: 3458, 3439, 3419, 3400, 3361, 3014, 2974, 2941, 2884, 1792, 1749, 1464, 1445, 1379, 1356, 1339, 1273, 1217, 1204, 1173, 1139, 1084, 1055, 1042, 979, 934, 891, 756, 667. ^{1}H NMR ($CDCl_3$), δ: 0.85 (t, 6 H, *J* = 7.4 Hz); 1.60 (q, 4 H, CH_2, *J* = 7.3 Hz); 3.33 (br.s, 2 H, OH); 3.68 (br.s, 4 H, OCH_2); 3.86 (s, 2 H, H(4′), H(5′)). ^{13}C NMR ($CDCl_3$), δ: 8.02 (CH_3); 30.34 (CH_2); 62.60 (OCH_2); 79.03 (C(4′), C(5′)); 113.03 (C(2′)).

Methyl (*E*)-3-[(4*S*,5*S*)-2,2-diethyl-5-hydroxymethyl-1,3-dioxolan-4-yl]-2-methylacrylate (9). Pyridinium dichromate (PDC) (1.52 g, 4.05 mmol) was added in one portion to a solution of diol **6** (0.6 g, 3.11 mmol) in anhydrous CH_2Cl_2 (10 mL) at room temperature with stirring. The reaction mixture was stirred for 3 h, then filtered through a short layer of SiO_2, the solvent was evaporated. The crude lactol **7** (0.56 g) was dissolved in CH_2Cl_2 (10 mL), followed by the addition of phosphorane **8** (2.12 g, 5.60 mmol). The reaction mixture was stirred for 5 h at room temperature (TLC monitoring) and concentrated, the residue was purified by column chromatography on SiO_2 (eluent AcOEt—light petroleum, 1 : 2) to obtain compound **9** (0.37 g, 45%). $[\alpha]_D^{20}$ −32.0 (*c* 0.881, $CHCl_3$). HRMS, found: *m*/*z* 257.1 $[M - H]^+$. $C_{13}H_{22}O_5$. Calculated: $[M - H]^+$ = 257.139. MS, *m*/*z* (I_{rel} (%)): 257 $[M - H]^+$ (6), 229 $[M - C_2H_5]^+$ (65), 198 (9), 167 (10), 155 (34), 141 (35), 123 (28), 112 (40), 97 (15), 87 (19), 58 (100). IR, ν/cm^{-1}: 3440, 2974, 2941, 1721, 1690, 1462, 1439, 1379, 1336, 1317, 1265, 1225, 1198, 1173, 1138, 1115, 1082, 1057, 970, 941, 746. ^{1}H NMR ($CDCl_3$), δ: 0.95 (t, 6 H, CH_3, *J* = 7.4 Hz); 1.71 (q, 4 H, CH_2, *J* = 7.4 Hz); 1.94 (d, 3 H, CH_3, *J* = 1.3 Hz); 2.00 (m, 1 H, OH); 3.55 (m, 1 H, OCH_2); 3.76 (s, 3 H, OCH_3); 3.85 (m, 1 H, OCH_2, *J* = 3.7 Hz); 3.90 (m, 1 H, H(5′)); 4.77 (d, 1 H, H(4′), *J* = 8.5 Hz); 6.66 (dq, 1 H, =CH, *J* = 1.3 Hz, *J* = 8.4 Hz). ^{13}C NMR ($CDCl_3$), δ: 8.19 (CH_3); 13.28 (CH_3); 30.44 (CH_2); 52.17 (OCH_3); 60.49 (OCH_2); 73.31 (C(5′)); 81.22 (C(4′)); 113.79 (C(2′)); 132.14 (C(2)); 137.10 (C(3)); 167.85 (CO_2).

Methyl (2*E*,4*S*,5*S*)-5,6-dihydroxy-2-methyl-4-(pent-3-yloxy)hex-2-enoate (10) and methyl (2*E*,4*S*,5*S*)-4,6-dihydroxy-2-methyl-5-(pent-3-yloxy)hex-2-enoate (11) were obtained simi-

larly to compound **2** from alcohol **9** (0.30 g, 1.15 mmol), Et_3SiH (0.18 g, 1.55 mmol), and $TiCl_4$ (0.24 g, 1.29 mmol). Chromatographic purification on a column with SiO_2 (eluent AcOEt—light petroleum, 1 : 2) gave compound **10** (97 mg) and compound **11** (63 mg) (54% total yield). Compound **10**. $[\alpha]_D^{20}$ −32.4 (*c* 2.785, $CHCl_3$). MS, *m/z* (I_{rel} (%)): 243 $[M - OH]^+$ (0.3), 231 $[M - C_2H_5]^+$ (0.4), 213 $[M - C_2H_5 - H_2O]^+$ (6), 183 (6), 155 $[M - C_5H_{11}O - H_2O]^+$ (7), 141 (9), 130 (100), 123 (28), 111 (10), 97 (30), 71 (22), 61 (8). IR, ν/cm^{-1}: 3441, 3426, 2965, 2936, 2876, 1719, 1715, 1697, 1651, 1470, 1435, 1384, 1246, 1132, 1089, 1043, 937, 750. ^{1}H NMR ($CDCl_3$), δ: 0.83 (t, 3 H, CH_3, *J* = 7.3 Hz); 0.85 (t, 3 H, CH_3, *J* = 7.3 Hz); 1.38—1.52 (m, 4 H, CH_2); 1.89 (d, 3 H, CH_3, *J* = 1.3 Hz); 2.74 (m, 1 H, OH); 3.13 (m, 1 H, H(3′)); 3.19 (br.s, 1 H, OH); 3.45 (m, 1 H, OCH_2); 3.54—3.64 (m, 2 H, H(5), OCH_2); 3.72 (s, 3 H, OCH_3); 4.28 (dd, 1 H, H(4), *J* = 7.0 Hz, *J* = 9.5 Hz); 6.54 (dq, 1 H, =CH, *J* = 1.3 Hz, *J* = 9.6 Hz). ^{13}C NMR ($CDCl_3$), δ: 9.50, 9.90 (CH_3); 13.24 (CH_3); 25.33, 26.55 (CH_2); 52.11 (OCH_3); 62.60 (OCH_2); 73.61, 74.18 (C(4), C(5)); 80.00 (C(3′)); 131.77 (C(2)); 138.94 (C(3)); 167.87 (CO_2). Found (%): C, 60.23; H, 9.38. $C_{13}H_{24}O_5$. Calculated (%): C, 59.98; H, 9.29. Compound **11**. $[\alpha]_D^{20}$ −25.85 (*c* 0.928, $CHCl_3$). ^{1}H NMR ($CDCl_3$), δ: 0.86 (t, 3 H, CH_3, *J* = 7.3 Hz); 0.87 (t, 3 H, CH_3, *J* = 7.6 Hz); 1.46 (m, 4 H, CH_2, *J* = 7.3); 1.89 (d, 3 H, CH_3, *J* = 1.3 Hz); 2.96 (d, 1 H, OH, *J* = 5.9 Hz); 3.14—3.17 (m, 2 H, OH, H(3′)); 3.46 (dd, OCH_2, 1 H, *J* = 5.0 Hz, *J* = 9.6 Hz); 3.53 (dd, 1 H, OCH_2, *J* = 4.0 Hz, *J* = 9.7 Hz); 3.65 (m, 1 H, H(5), *J* = 5.0 Hz, *J* = 5.3 Hz); 3.73 (s, 3 H, OCH_3); 4.49 (m, 1 H, H(4)); 6.69 (dq, 1 H, =CH, *J* = 1.3 Hz, *J* = 9.0 Hz). ^{13}C NMR ($CDCl_3$), δ: 9.47 (CH_3); 13.28 (CH_3); 25.64 (CH_2); 52.06 (OCH_3); 69.77 (OCH_2); 69.53, 72.89 (C(4), C(5)); 82.92 (C(3′)); 130.73 (C(2)); 139.18 (C(3)); 168.18 (CO_2).

Methyl (*E*)-3-[(4*S*,5*S*)-2,2-diethyl-5-(*tert*-butyldiphenylsilyloxymethyl)-1,3-dioxolan-4-yl]-2-methylacrylate (12). Imidazole (50 mg, 0.77 mmol) and Bu^tPh_2SiCl (0.17 g, 0.60 mmol) were added to a solution of compound **9** (0.14 g, 0.55 mmol) in anhydrous CH_2Cl_2 (10 mL). The reaction mixture was stirred until the starting alcohol was consumed (TLC monitoring), then diluted with CH_2Cl_2 (10 mL) and saturated aqueous NH_4Cl (5 mL), the organic layer was separated, washed with brine, and dried with $MgSO_4$, the solvent was evaporated. The residue was subjected to column chromatography on SiO_2 (eluent AcOEt—light petroleum, 1 : 5) to obtain silyl ether **12** (0.27 g, 98%). $[\alpha]_D^{20}$ −6.5 (*c* 2.114, $CHCl_3$). MS, *m/z* (I_{rel} (%)): 467 $[M - C_2H_5]^+$ (14), 353 (100), 323 (12), 269 (10), 213 (61), 199 (50), 135 (25), 112 (16), 69 (37). IR, ν/cm^{-1}: 3440, 2957, 2930, 2887, 1720, 1710, 1470, 1420, 1390, 1330, 1230, 1113, 1040, 1001, 960, 822, 741, 702, 505, 489. ^{1}H NMR ($CDCl_3$), δ: 0.97 (t, 3 H, CH_3, *J* = 7.3 Hz); 0.98 (t, 3 H, CH_3, *J* = 7.3 Hz); 1.10 (s, 9 H, CMe_3); 1.75 (m, 4 H, CH_2); 1.92 (d, 3 H, CH_3, *J* = 1.3 Hz); 3.69 (dd, 1 H, OCH_2, *J* = 3.3 Hz, *J* = 11.3 Hz); 3.77 (s, 3 H, OCH_3); 3.87 (m, 2 H, OCH_2, H(5′)); 4.89 (t, 1 H, H(4′), *J* = 8.4 Hz); 6.70 (dq, 1 H, =CH, *J* = 1.3 Hz, *J* = 8.4 Hz); 7.42 (m, 6 H, Ph); 7.75 (m, 4 H, Ph). ^{13}C NMR ($CDCl_3$), δ: 8.06, 8.24 (CH_3); 13.20 (CH_3); 19.10 ($\underline{C}Me_3$); 26.78 (3 CH_3); 30.23, 30.50 (CH_2); 52.03 (OCH_3); 62.19 (OCH_2); 73.91 (C(5′)); 81.55 (C(4′)); 113.67 (C(2′)); 127.72, 129.65, 134.81, 135.18 (Ph); 133.00 (C(2)); 137.59 (C(3)); 168.10 (CO_2).

Methyl (2*E*,4*S*,5*S*)-6-(*tert*-butyldiphenylsilyloxy)-5-hydroxy-2-methyl-4-(pent-3-yloxy)hex-2-enoate (13) and methyl (2*E*,4*S*,5*S*)-6-(*tert*-butyldiphenylsilyloxy)-4-hydroxy-2-methyl-5-(pent-3-yloxy)hex-2-enoate (14) were obtained similarly to diols **10** and **11** from compound **12** (0.11 g, 0.22 mmol), Et_3SiH (40 mg, 0.3 mmol), and $TiCl_4$ (50 mg, 0.25 mmol). The products were isolated by column chromatography on SiO_2 (eluent AcOEt—light petroleum, 1 : 5) to obtain compound **13** (50 mg) and compound **14** (20 mg) (60% total yield). Compound **13**. $[\alpha]_D^{20}$ +32.4 (*c* 2.554, $CHCl_3$). MS, *m/z* (I_{rel} (%)): 454 (3), 431 (0.5), 441 $[M - C_4H_9]^+$ (0.5), 353 (56), 277 (17), 241 (9), 213 (36), 199 (100), 169 (18), 119 (15), 77 (7). IR, ν/cm^{-1}: 3520, 2961, 2932, 2876, 1719, 1645, 1462, 1427, 1389, 1362, 1317, 1248, 1219, 1134, 1113, 1063, 1009, 937, 824, 743, 702, 505. ^{1}H NMR ($CDCl_3$), δ: 0.87 (t, 3 H, CH_3, *J* = 7.4 Hz); 0.88 (t, 3 H, CH_3, *J* = 7.4 Hz); 1.08 (s, 9 H, CMe_3); 1.44—1.56 (m, 4 H, CH_2); 1.93 (d, 3 H, CH_3, *J* = 1.3 Hz); 2.67 (d, 1 H, OH, *J* = 7.4 Hz); 3.20 (quint, 1 H, H(3′), *J* = 5.3 Hz, *J* = 6.0 Hz); 3.64 (m, 1 H, H(5)); 3.69 (m, 2 H, OCH_2); 3.76 (s, 3 H, OCH_3); 4.52 (dd, 1 H, H(4), *J* = 4.3 Hz, *J* = 9.3 Hz); 6.74 (dq, 1 H, =CH, *J* = 1.3 Hz, *J* = 9.3 Hz); 7.41 (m, 6 H, Ph); 7.68 (m, 4 H, Ph). ^{13}C NMR ($CDCl_3$), δ: 9.21, 9.96 (CH_3); 13.25 (CH_3); 25.47, 26.54 (CH_2); 26.86 (3 CH_3); 52.02 (OCH_3); 63.79 (OCH_2); 72.76, 74.20 (C(4), C(5)); 79.99 (C(3′)); 127.74, 127.79, 129.69, 129.81, 133.18, 133.32, 135.57, 135.71 (Ph); 130.28 (C(2)); 140.03 (C(3)); 168.03 (CO_2). Compound **14**. ^{1}H NMR ($CDCl_3$), δ: 0.74 (t, 3 H, CH_3, *J* = 7.4 Hz); 0.85 (t, 3 H, CH_3, *J* = 7.4 Hz); 1.07 (s, 9 H, CMe_3); 1.27—1.45 (m, 4 H, CH_2); 1.91 (d, 3 H, CH_3, *J* = 1.3 Hz); 2.66 (d, 1 H, OH, *J* = 7.0 Hz); 3.14 (quint, 1 H, H(3′), *J* = 5.6 Hz, *J* = 6.0 Hz); 3.36 (m, 1 H, H(5), *J* = 4.3 Hz, *J* = 3.6 Hz); 3.62 (dd, 1 H, OCH_2, *J* = 4.3 Hz, *J* = 10.6 Hz); 3.76 (s, 3 H, OCH_3); 3.79 (m, 1 H, OCH_2); 4.64 (ddd, 1 H, H(4), *J* = 3.6 Hz, *J* = 5.0 Hz, *J* = 8.6 Hz); 6.82 (dq, 1 H, =CH, *J* = 1.3 Hz, *J* = 8.6 Hz); 7.42 (m, 6 H, Ph); 7.68 (dt, 4 H, Ph, *J* = 1.7 Hz, *J* = 7.6 Hz).

(4*S*,5*S*)-2,2-Diethyl-4-mesyloxymethyl-5-(3-methoxy-2-methyl-3-oxoprop-1*E*-enyl)-1,3-dioxolane (15). Triethylamine (0.41 mL, 2.93 mmol) and methanesulfonyl chloride (0.335 g, 2.93 mmol) were added to a solution of compound **9** (0.377 g, 1.46 mmol) in CH_2Cl_2 (10 mL) at 0 °C, and the reaction mixture was stirred for 3 h at room temperature. Then, saturated aqueous NH_4Cl was added, the organic layer was separated, the aqueous layer was extracted with CH_2Cl_2 (3×5 mL). The combined organic layers were washed with brine and dried with $MgSO_4$. The solvent was evaporated, the residue was subjected to column chromatography on SiO_2 (eluent AcOEt—light petroleum, 1 : 5) to obtain compound **15** (0.40 g, 82%). $[\alpha]_D^{20}$ −32.6 (*c* 1.819, $CHCl_3$). MS, *m/z* (I_{rel} (%)): 307 $[M - C_2H_5]^+$ (100), 267 (14), 219 (18), 155 (54), 112 (40), 95 (12). IR, ν/cm^{-1}: 2974, 2943, 2884, 1763, 1717, 1661, 1456, 1437, 1359, 1263, 1236, 1198, 1177, 1144, 1109, 1057, 1016, 966, 941, 831, 752, 528. ^{1}H NMR ($CDCl_3$), δ: 0.83 (t, 3 H, CH_3, *J* = 7.4 Hz); 0.85 (t, 3 H, CH_3, *J* = 7.3 Hz); 1.61 (q, 4 H, CH_2, *J* = 7.3 Hz); 1.83 (d, 3 H, CH_3, *J* = 1.3 Hz); 2.99 (s, 3 H, SO_2CH_3); 3.68 (s, 3 H, OCH_3); 3.89 (m, 1 H, OCH_2, *J* = 4.4 Hz); 4.14 (dd, 1 H, OCH_2, *J* = 4.6 Hz, *J* = 11.4 Hz); 4.28 (m, 1 H, H(5′), *J* = 3.0 Hz, *J* = 7.2 Hz); 4.59 (t, 1 H, H(4′), *J* = 8.8 Hz); 6.58 (dq, 1 H, =CH, *J* = 1.3 Hz, *J* = 8.8 Hz). ^{13}C NMR ($CDCl_3$), δ: 7.96, 8.09 (CH_3); 13.30 (CH_3); 30.28, 30.37 (CH_2); 37.67 (SO_2CH_3); 52.21 (OCH_3); 67.11 (OCH_2); 73.72 (C(4′)); 78.48 (C(5′)); 114.69 (C(2′)); 133.04 (C(2″)); 135.61 (C(1″)); 167.53 (CO_2). Found (%): C, 50.31; H, 7.24; S, 9.35. $C_{14}H_{24}O_7S$. Calculated (%): C, 49.98; H, 7.19; S, 9.53.

Methyl (2*E*,5*S*)-6-(*tert*-butyldiphenylsilyloxy)-2-methyl-4-oxo-5-(pent-3-yloxy)hex-2-enoate (16). The reagents $PhI(OAc)_2$ (54 mg, 0.17 mmol) and TEMPO (1 mg, 0.006 mmol) were added to a solution of silyl ether **14** (20 mg, 0.04 mmol) in

CH_2Cl_2 (5 mL) under argon, and the reaction mixture was stirred for 3 h at room temperature (TLC monitoring). Then the solvent was evaporated, the residue was purified by column chromatography on SiO_2 (eluent AcOEt—light petroleum, 1 : 5) to obtain compound **16** (10 mg, 66%). $[\alpha]_D^{20}$ –29.6 (*c* 0.7191, $CHCl_3$). MS, *m/z* (I_{rel} (%)): 439 $[M - C_4H_9]^+$ (0.2), 337 (9), 291 (100), 261 (22), 199 (43), 163 (21), 91 (6). IR, ν/cm^{-1}: 2974, 2941, 2880, 2106, 1718, 1655, 1464, 1437, 1377, 1354, 1315, 1265, 1245, 1225, 1198, 1173, 1140, 1086, 1057, 1030, 970, 941, 850, 758, 680. ^{1}H NMR ($CDCl_3$), δ: 0.83 (t, 3 H, CH_3, *J* = 7.4 Hz); 0.89 (t, 3 H, CH_3, *J* = 7.4 Hz); 1.02 (s, 9 H, CMe_3); 1.49 (q, 4 H, CH_2, *J* = 6.6 Hz, *J* = 7.6 Hz); 2.28 (d, 3 H, CH_3, *J* = 1.7 Hz); 3.19 (t, 1 H, H(3′), *J* = 5.6 Hz); 3.81 (s, 3 H, OCH_3); 3.87 (t, 2 H, OCH_2, *J* = 4.3 Hz, *J* = 5.3 Hz); 3.94 (dd, 1 H, H(5), *J* = 4.6 Hz, *J* = 5.3 Hz); 7.54 (dq, 1 H, =CH, *J* = 1.3 Hz, *J* = 1.7 Hz); 7.42 (m, 6 H, Ph); 7.66 (dd, 2 H, Ph, *J* = 1.3 Hz, *J* = 7.6 Hz); 7.69 (dd, 2 H, Ph, *J* = 1.3 Hz, *J* = 7.6 Hz). ^{13}C NMR ($CDCl_3$), δ: 9.05, 9.69 (CH_3); 14.64 (CH_3); 19.19 ($\underline{C}Me_3$); 25.10, 26.19 (CH_2); 26.64 (3 CH_3); 52.52 (OCH_3); 65.05 (OCH_2); 82.07, 84.15 (C(5), C(3′)); 127.71, 127.75, 129.77 (2 C), 132.93, 133.09, 135.65, 135.76 (Ph); 130.81 (C(2)); 141.56 (C(3)); 168.24 (CO_2); 203.38 (C(4)). Found (%): C, 70.55; H, 7.98; Si, 5.97. $C_{29}H_{40}O_5Si$. Calculated (%): C, 70.12; H, 8.12; Si, 5.65.

Methyl (*E*)-3-[(4*S*,5*S*)-5-azidomethyl-2,2-diethyl-1,3-dioxolan-4-yl]-2-methylacrylate (17) was obtained similarly to the preparation of compound **4** from mesylate **15** (0.2 g, 0.60 mmol) and NaN_3 (0.15 g, 2.38 mmol). The yield was 0.16 g (95%). $[\alpha]_D^{20}$ –97.3 (*c* 2.731, $CHCl_3$). MS, *m/z* (I_{rel} (%)): 268 $[M - CH_3]^+$ (0.2), 254 $[M - Et]^+$ (100), 198 (8), 155 (12), 112 (35), 97 (11). IR, ν/cm^{-1}: 2974, 2941, 2880, 2106, 1718, 1655, 1464, 1437, 1377, 1354, 1315, 1265, 1245, 1225, 1198, 1173, 1140, 1086, 1057, 1030, 970, 941, 850, 758, 680. ^{1}H NMR ($CDCl_3$), δ: 0.91 (t, 3 H, CH_3, *J* = 7.4 Hz); 0.93 (t, 3 H, CH_3, *J* = 7.4 Hz); 1.63—1.74 (m, 4 H, CH_2); 1.88 (d, 3 H, CH_3, *J* = 1.3 Hz); 3.15 (dd, 1 H, NCH_2, *J* = 4.3 Hz, *J* = 13.6 Hz); 3.56 (dd, 1 H, NCH_2, *J* = 3.5 Hz, *J* = 13.6 Hz); 3.85 (s, 3 H, OCH_3); 3.87 (m, 1 H, H(5′)); 4.67 (t, 1 H, H(4′), *J* = 8.6 Hz); 6.58 (dq, 1 H, =CH, *J* = 1.3 Hz, *J* = 8.6 Hz). ^{13}C NMR ($CDCl_3$), δ: 7.77, 7.86 (CH_3); 13.01 (CH_3); 30.09, 30.20 (CH_2); 50.19 (NCH_2); 51.84 (OCH_3); 74.21 (C(4′)); 79.55 (C(5′)); 114.12 (C(2′)); 132.24 (C(2)); 136.15 (C(3)); 167.38 (CO_2).

Methyl (2*E*,4*S*,5*S*)-5,6-epoxy-2-methyl-4-(pent-3-yloxy)-hex-2-enoate (18). ***A.*** Sodium hydrogen carbonate (60 mg, 0.69 mmol) was added to a solution of mesylate **2** (0.15 g, 0.43 mmol) in a mixture of EtOH—H_2O (2 : 1) (10 mL), and the mixture was heated for 1 h at 55—60 °C. Then ethanol was evaporated, the reaction mixture was diluted with water and extracted with AcOEt (3×10 mL). The combined organic extracts were washed with water and dried with $MgSO_4$, the solvent was evaporated. Column chromatography of the product on silica gel (eluent AcOEt—light petroleum, 1 : 2) gave epoxide **18** (90 mg, 90%). $[\alpha]_D^{20}$ –27.17 (*c* 3.746, $CHCl_3$). MS, *m/z* (I_{rel} (%)): 242 $[M]^+$ (1), 213 $[M - C_2H_5]^+$ (5), 199 $[M - C_5H_{11}]^+$ (22), 155 (48), 129 (100), 110 (17), 95 (34), 82 (13), 43 (24). IR, 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. ^{1}H NMR ($CDCl_3$), δ: 0.88 (t, 3 H, CH_3, *J* = 7.4 Hz); 0.94 (t, 3 H, CH_3, *J* = 7.4 Hz); 1.48 (dq, 2 H, CH_2, *J* = 7.4 Hz, *J* = 1.4 Hz); 1.52—1.56 (m, 2 H, CH_2); 1.89 (d, 3 H, CH_3, *J* = 1.3 Hz); 2.57 (dd, 1 H, OCH_2, *J* = 2.8 Hz, *J* = 4.8 Hz); 2.75 (t, 1 H, OCH_2, *J* = 4.5 Hz); 3.12 (m, 1 H, H(5)); 3.31 (q, 1 H, H(3′), *J* = 5.7 Hz); 3.76 (s, 3 H, OCH_3); 4.04 (dd, 1 H, H(4), *J* = 6.0 Hz, *J* = 9.2 Hz); 6.65 (dq, 1 H, =CH, *J* = 1.3 Hz, *J* = 9.2 Hz). ^{13}C NMR ($CDCl_3$), δ: 9.42, 9.76 (CH_3); 13.30 (CH_3); 26.05, 26.37 (CH_2); 43.64 (OCH_2); 52.09 (OCH_3); 53.80 (C(5)); 75.34 (C(4)); 80.54 (C(3′)); 130.58 (C(2)); 137.37 (C(3)); 167.96 (CO_2). Found (%): C, 64.80; H, 9.08. $C_{13}H_{22}O_4$. Calculated (%): C, 64.44; H, 9.15.

B. A solution of pyrrolidine derivative **4** (83.4 mg, 0.32 mmol) in THF (2 mL) was added dropwise to a solution of CF_3COOH (0.12 mL, 1.62 mmol) in THF (3 mL) at 0 °C. The mixture was stirred for 30 min at this temperature, followed by the addition of 10% aqueous NaOH to pH ~8. Then, THF was evaporated on a rotary evaporator, the residue was extracted with $CHCl_3$ (3×5 mL), The combined organic exstracts were washed with brine, dried with $MgSO_4$, and the solvent was evaporated. Column chromatography of the product on silica gel (eluent AcOEt—light petroleum, 1 : 2) gave compound **18** (30 mg, 38%), whose spectroscopic characteristics agreed with those obtained for compound **18** synthesized by the preceding procedure.

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