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3-Allylation of *tert*-Butyl 4-Oxopiperidine-1-carboxylate

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Abstract—Reaction of *tert*-butyl 4-oxopiperidine-1-carboxylate dimethylhydrazone with BuLi in the presence of *N,N'*-dimethylpropylene urea and subsequently with $BrCH_2CH=CRR'$ (R=H, Me, Et; R'=CH_2Ar) afforded in 50–80% yields the corresponding *tert*-butyl 3-alkenyl-4-oxopiperidine-1-carboxylates, promising synthons for preparation of diverse piperidine derivatives.

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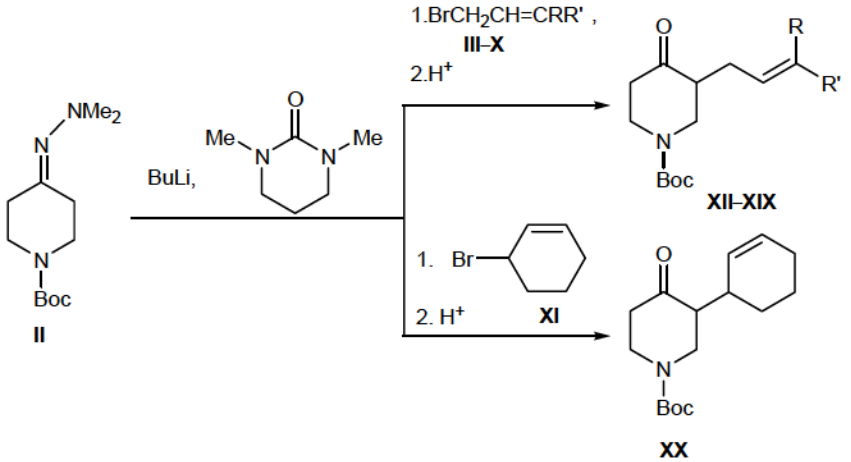
Piperidine derivatives, an important class of heterocyclic compounds [1], possess a wide range of biological action, and their fragments are contained in the composition of numerous drugs [2–4] as pharmacophore groups. Therefore the investigations on the synthesis of new functionally substituted piperidine derivatives is obviously topical for contemporary organic chemistry.

The target of this study was a development of convenient methods of 3-allylation of the commercially available *tert*-butyl 4-oxopiperidine-1-carboxylate (**I**) that were not yet materially investigated. Only two patents [5] contained descriptions of the same allylation method of compound **I** with allyl alcohol at boiling (16 h) of reagents in benzene with a Dean–Stark trap for water removal. However we failed to reproduce this metod and to obtain *tert*-butyl 3-allyl-4-oxopiperidine-1-carboxylate (**XII**), which might be interesting as a multifunctional synthon in the organic synthesis. The other described methods of α-allylation of carbocyclic ketones [6–12] we found to be of low efficiecy with respect to heterocyclic ketone **I**, and the yields of target compound **XII** obtained by reactions [6–12] did not exceed 20%. Besides many among the reactions required expensive palladium (Trost reaction) catalysts.

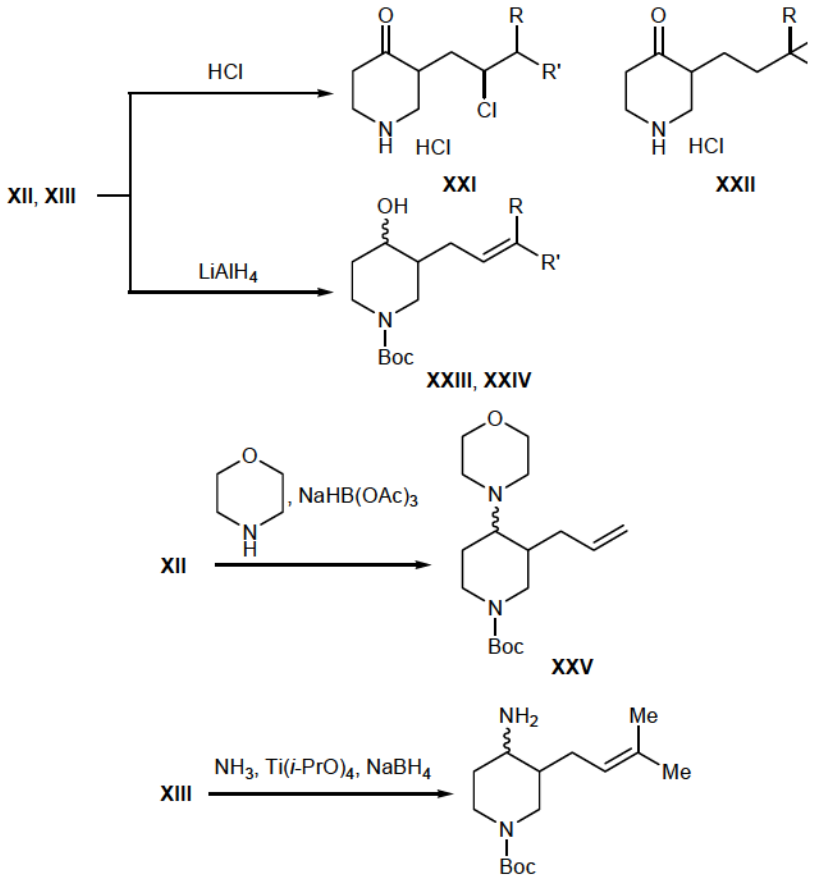
We successfully carried out the 3-allylation of ketone **I** by an indirect process, the reaction of its

Scheme 1.



R = H (**III**, **XII**), Me (**IV**–**IX**, **XIII**–**XVIII**), Et (**X**, **XIX**). R' = H (**III**, **XII**), Me (**IV**, **XIII**), 4-F-Bn (**V**, **XIV**), 4-Cl-Bn (**VI**, **XV**), 3-CF_3-Bn (**VII**, **XVI**), $CH_2CH_2CHMe_2$ (**VIII**, **XVII**), CH_2CH_2Ph (**IX**, **XVIII**), Bn (**X**, **XIX**); Boc = *t*-BuOCO.

Scheme 2.



R= H (**XII**, **XXI**, **XXIII**), Me (**XIII**, **XXII**, **XXIV**).

dimethylhydrazone **II** [13] with BuLi in the presence of *N*,*N*'-dimethylpropylene urea with subsequent treatment with versatile allyl bromides **III**–**XI** [14] followed by the removal of the dimethylhydrazine group by treating with a water solution of oxalic acid. Therewith the yields of the target reaction products, 3-substituted allyl ketones **XII**–**XX**, reached 50–80%. Any difficulties consisting in the possibility of isomerization [15] in the unsaturated compounds **XII**–**XX** we did not observe (Scheme 1).

In contrast to dimethylhydrazone **II** the allylation of ketone **I** in the above described conditions proceeded with difficulty and the yields of target products **XII**–**XX** did not exceed 10%. Therewith after an appropriate treatment 80–85% of initial ketone **I** was recovered from the reaction mixture.

The obtained compounds **XII**–**XX** possessing several reactive sites are promising intermediates for the synthesis of diverse piperidine derivatives, potential biologically active substances. We demonstrated their wide synthetic opportunities by an example of compounds **XII** and **XIII**. Thus at the reaction with excess anhydrous hydrogen chloride in dioxane [16] these compounds underwent debocing with simultaneous addition of HCl to the double bond affording hydrochlorides **XXI** and **XXII**. Owing to the presence of the carbonyl group compounds **XII** and **XIII** entered the reactions of reduction and reductive amination [17] giving respectively alcohols **XXIII** and **XXIV** and amines **XXV** and **XXVI** as stereoisomers mixtures (as shown by HPLC-MS and ^{1}H NMR spectra) (Scheme 2).

The composition and structure of synthesized compounds **XII**–**XXVI** were proved by elemental analysis, IR and ^{1}H NMR spectra, and also by HPLC-MS data presented in EXPERIMENTAL.

In should be noted in conclusion that compounds **XXI**–**XXVI** also possess a considerable synthetic potential owing to the presence in their structures of

various functional groups (double bond, NH, NH_2, OH, etc.). Therefore the compounds obtained by us may be used in creating focus libraries of new substances of piperidine series for screening their biological action.

EXPERIMENTAL

IR spectra of compounds synthesized were recorded on a spectrophotometer Specord 75 IR from thin film or pellets with KBr. ^{1}H NMR spectra were registered on a spectrometer Mercury Plus-400 Varian (400 MHz) in $CDCl_3$ for compounds **XII**–**XX** and **XXIII**–**XXVI**, in DMSO-d_6 for compounds **XXI** and **XXII** (internal reference HMDS). HPLC-MS data were obtained on an instrument Surveyor MSQ Thermo Finnigan equipped with a column Phenomenex Onyx Monoliythic C18 25 × 4.6 mm; solvent for the samples DMSO–acetonitrile, 1 : 1. Eluent 0.1% water solution of formic acid – acetonitrile with varying in time concentration gradient within 4 min. Column temperature 25°C, eluent flow rate 1.5 mL/min. Detectors: diode matrix (200–800 nm); mass detector using ionization APCI and registering positive and negative ions; detector of light scattering (ELSD). The volume of the probe 2 μL; analysis time 4.5 min. The reaction progress was monitored by TLC on Silufol UV-254 plates, eluent hexane–ethyl acetate, 3 : 1, development with ninhydrin solution in 2-propanol with subsequent heating. Silica gel 60 Merck was used for column chromatography.

Initial compounds **II**–**XI** were prepared by procedures [13, 14].

***tert*-Butyl 3-allyl-4-oxopiperidine-1-carboxylate (XII)**. To a solution of 7.0 g (29 mmol) of dimethylhydrazone **II** [13] and 3.71 g (29 mmol) of *N*,*N*'-dimethylpropylene urea in 60 mL of anhydrous THF was added at –78°C 20 mL (32 mmol) of 1.6 M BuLi solution in hexane, and the mixture was stirred for 2 h under an argon atmosphere at –70°C. Then at the same temperature was added a solution of 3.63 g (30 mmol) of allyl bromide in 20 mL of THF, the mixture was stirred for 1.5 h at –70°C and left overnight at room temperature. The reaction mixture was evaporated on a rotary evaporator, to the residue was added 150 mL of ethyl acetate and 150 mL of saturated water solution of oxalic acid, the mixture was stirred for 1.5 h, the organic layer was separated, the water layer was extracted with 150 mL of ethyl acetate. The combined organic solutions were washed in succession with $NaHCO_3$ solution, with water, with brine, dried with anhydrous Na_2SO_4, and concentrated. Reaction product **XII** was isolated by column chromatography on silica gel, elution with a mixture ethyl acetate–hexane, 1 : 3, compound **XII** R_f 0.52, initial ketone **I** R_f 0.26. Yield 5.58 g (80%), colorless oily substance. IR spectrum, ν, cm^{-1}: 1718, 1686 (C=O), 1631 (C=C). ^{1}H NMR spectrum, δ, ppm: 1.49 s (9H, CMe_3), 2.02–2.11 m (1H, CHC=O), 2.40–2.55 m (4H, CH_2C=O, CH_2), 3.02 t (1H, CHN, *J* 8.4 Hz), 3.32–3.41 m (1H, CHN), 4.04–4.16 m (2H, CH_2N), 5.04–5.11 m (2H, CH_2=C), 5.73–5.83 m (1H, CH=C). Mass spectrum, *m/z* (I_{rel}, %): 240.15 (28) $[M + H]^+$, 184.18 (100) $[M - 57 + 2H]^+$, 140.34 (31) $[M - 101 + 2H]^+$. Found, %: C 65.18; H 8.57; N 5.73. $C_{13}H_{21}NO_3$. Calculated, %: C 65.24; H 8.86; N 5.96. *M* 239.32.

Compounds **XIII**–**XX** were similarly prepared.

***tert*-Butyl 3-(3-methylbut-2-enyl)-4-oxopiperidine-1-carboxylate (XIII)**. Yield 75%, colorless oily substance, R_f 0.64. IR spectrum, ν, cm^{-1}: 1716, 1685 (C=O), 1626 (C=C). ^{1}H NMR spectrum, δ, ppm: 1.48 s (9H, CMe_3), 1.62 c (3H, CH_3), 1.70 s (3H, CH_3), 2.00–2.09 m (1H, CHC=O), 2.38–2.46 m (4H, CH_2C=O, CH_2), 3.01 t (1H, CHN, *J* 8.2 Hz), 3.35–3.44 m (1H, CHN), 4.00–4.13 m (2H, CH_2N), 5.11 t (1H, CH=C, *J* 6.7 Hz). Mass spectrum, *m/z* (I_{rel}, %): 268.13 (2.5) $[M + H]^+$, 211.71 (100) $[M - 57 + 2H]^+$, 168.22 (10) $[M - 101 + 2H]^+$. Found, %: C 67.25; H 9.32; N 5.18. $C_{15}H_{25}NO_3$. Calculated, %: C 67.46; H 9.48; N 5.23. *M* 267.36.

***tert*-Butyl 3-[(*E*,*Z*)-3-methyl-4-(4-fluorophenyl)-but-2-enyl]-4-oxopiperidine-1-carboxylate (XIV)**. Yield 62%, light yellow oily substance, R_f 0.68. IR spectrum, ν, cm^{-1}: 1712, 1686 (C=O), 1628 (C=C). ^{1}H NMR spectrum, δ, ppm: 1.48 s (9H, CMe_3), 1.53 s (3H, CH_3), 2.04–2.15 m (1H, CHC=O), 2.41–2.50 m (4H, CH_2C=O, CH_2C=C), 3.01 t (1H, CHN, *J* 8.5 Hz), 3.25 s (2H, CH_2Ar), 3.31–3.42 m (1H, CHN), 4.01–4.15 m (2H, CH_2N), 5.23 t (0.75H, CH=C, *J* 6.8 Hz), 5.29 t (0.25H, CH=C, *J* 6.8 Hz), 6.93–6.98 m ($2H_{Ar}$), 7.07–7.12 m ($2H_{Ar}$). Mass spectrum, *m/z* (I_{rel}, %): 362.17 (6.2) $[M + H]^+$, 306.17 (100) $[M - 57 + 2H]^+$, 262.14 (25) $[M - 101 + 2H]^+$. Found, %: C 69.63; H 7.83; N 4.06. $C_{21}H_{28}FNO_3$. Calculated, %: C 69.84; H 7.86; N 3.96. *M* 361.45.

***tert*-Butyl 3-[(*E*,*Z*)-3-methyl-4-(4-chlorophenyl)-but-2-enyl]-4-oxopiperidine-1-carboxylate (XV)**. Yield 53%, light yellow oily substance, R_f 0.61. IR spectrum, ν, cm^{-1}: 1714, 1686 (C=O), 1630 (C=C). ^{1}H

NMR spectrum, δ, ppm: 1.48 s (9H, CMe_3), 1.52 s (3H, CH_3), 2.06–2.12 m (1H, CHC=O), 2.40–2.51 m (4H, CH_2C=O, CH_2C=C), 3.01 t (1H, CHN, *J* 8.5 Hz), 3.25 s (2H, C$\underline{H}_2$Ar), 3.31–3.41 m (1H, CHN), 4.01–4.13 m (2H, CH_2N), 5.22 t (0.8H, CH=C, *J* 6.6 Hz), 5.30 t (0.2H, CH=C, *J* 6.6 Hz), 7.08 d ($2H_{Ar}$, *J* 12.2 Hz), 7.23 d ($2H_{Ar}$, *J* 12.2 Hz). Mass spectrum, *m/z* (I_{rel}, %): 379.20 (10) $[M + H]^+$, 323.15 (100) $[M - 57 + 2H]^+$, 279.12 (10.8) $[M - 101 + 2H]^+$. Found, %: C 66.54; H 7.42; N 3.88. $C_{21}H_{28}ClNO_3$. Calculated, %: C 66.73; H 7.58; N 3.75. *M* 377.92.

***tert*-Butyl 3-{(*E,Z*)-3-methyl-4-[3-(trifluoromethyl)phenyl]but-2-enyl}-4-oxopiperidine-1-carboxylate (XVI)**. Yield 59%, light yellow oily substance, R_f 0.58. IR spectrum, ν, cm^{-1}: 1715, 1686 (C=O), 1636 (C=C). ^1H NMR spectrum, δ, ppm: 1.48 s (9H, CMe_3), 1.52 s (0.85·3H, CH_3), 1.63 s (0.15·3H, CH_3), 2.08–2.20 m (1H, CHC=O), 2.41–2.50 m (4H, CH_2C=O, CH_2C=C), 3.03 t (1H, CHN, *J* 8.8 Hz), 3.35 s (2H, C$\underline{H}_2$Ar), 3.36–3.46 m (1H, CHN), 4.01–4.09 m (2H, CH_2N), 5.28 t (0.85H, CH=C, *J* 7.1 Hz), 5.35 t (0.15H, CH=C, *J* 7.1 Hz), 7.27–7.48 m ($2H_{Ar}$). Mass spectrum, *m/z* (I_{rel}, %): 412.22 (39) $[M + H]^+$, 355.84 (100) $[M - 57 + 2H]^+$, 312.20 (31) $[M - 101 + 2H]^+$. Found, %: C 64.18; H 6.83; N 3.28. $C_{22}H_{28}F_3NO_3$. Calculated, %: C 64.23; H 6.95; N 3.47. *M* 411.46.

***tert*-Butyl 3-[(*E,Z*)-3,6-dimethylhept-2-enyl]-4-oxopiperidine-1-carboxylate (XVII)**. Yield 62%, colorless oily substance, R_f 0.77. IR spectrum, ν, cm^{-1}: 1716, 1684 (C=O), 1624 (C=C). ^1H NMR spectrum, δ, ppm: 0.82–0.96 m (6H, $2CH_3$), 1.21–1.30 m (2H, CH_2), 1.48 s (9H, CMe_3), 1.55 s (0.86·3H, CH_3C=C), 1.63 s (0.14·3H, CH_3C=C), 1.96 t (2H, CH_2C=C, *J* 5.8 Hz), 2.02–2.08 m (1H, CHC=O), 2.38–2.49 m (4H, CH_2C=O, CH_2C=C), 3.01 t (1H, CHN, *J* 8.9 Hz), 3.33–3.43 m (1H, CHN), 3.98–4.11 m (2H, CH_2N), 5.05–5.15 m (1H, CH=C). Mass spectrum, *m/z* (I_{rel}, %): 324.10 (5.4) $[M + H]^+$, 268.15 (100) $[M - 57 + 2H]^+$, 224.19 (78) $[M - 101 + 2H]^+$. Found, %: C 70.41; H 10.17; N 4.38. $C_{19}H_{33}NO_3$. Calculated, %: C 70.52; H 10.36; N 4.36. *M* 323.47.

***tert*-Butyl 3-[(*E,Z*)-3-methyl-5-phenylpent-2-enyl]-4-oxopiperidine-1-carboxylate (XVIII)**. Yield 65%, light yellow oily substance, R_f 0.65. IR spectrum, ν, cm^{-1}: 1713, 1685 (C=O), 1638 (C=C). ^1H NMR spectrum, δ, ppm: 1.50 s (9H, CMe_3), 1.67 s (0.84·3H, CH_3C=C), 1.73 s (0.16·3H, CH_3C=C), 2.02–2.12 m (1H, CHC=O), 2.30 t (2H, CH_2C=C, *J* 5.8 Hz), 2.38–2.46 m (4H, CH_2C=O, CH_2C=C), 2.97 t (1H, CHN, *J* 7.8 Hz), 3.32–3.41 m (1H, CHN), 3.95–4.09 m (2H, CH_2N), 5.12 t (1H, CH=C, *J* 6.8 Hz), 7.13–7.18 m ($3H_{Ar}$), 7.23–7.27 m ($2H_{Ar}$). Mass spectrum, *m/z* (I_{rel}, %): 358.28 (10) $[M + H]^+$, 302.19 (100) $[M - 57 + 2H]^+$, 258.19 (12) $[M - 101 + 2H]^+$. Found, %: C 73.64; H 8.71; N 4.06. $C_{22}H_{31}NO_3$. Calculated, %: C 73.96; H 8.74; N 3.97. *M* 357.49.

***tert*-Butyl 3-[(*E,Z*)-3-benzylpent-2-enyl]-4-oxopiperidine-1-carboxylate (XIX)**. Yield 45%, light yellow oily substance, R_f 0.62. IR spectrum, ν, cm^{-1}: 1715, 1686 (C=O), 1625 (C=C). ^1H NMR spectrum, δ, ppm: 0.90–1.04 m (3H, CH_3), 1.50 s (9H, CMe_3), 1.97 q (2H, CH_2, *J* 6.2 Hz), 2.05–2.20 m (1H, CHC=O), 2.40–2.70 m (4H, CH_2C=O, CH_2C=C), 3.01 t (1H, CHN, *J* 8.4 Hz), 3.24 s (2H, CH_2Ar), 3.26–3.40 m (1H, CHN), 4.01–4.12 m (2H, CH_2N), 5.13 t (0.55H, CH=C, *J* 6.4 Hz), 5.30 t (0.45H, CH=C, *J* 6.4 Hz), 7.11–7.28 m ($5H_{Ar}$). Mass spectrum, *m/z* (I_{rel}, %): 358.26 (5.4) $[M + H]^+$, 302.15 (100) $[M - 57 + 2H]^+$, 258.17 (1.8) $[M - 101 + 2H]^+$. Found, %: C 73.70; H 8.63; N 3.84. $C_{22}H_{31}NO_3$. Calculated, %: C 73.96; H 8.74; N 3.97. *M* 357.49.

***tert*-Butyl 4-oxo-3-(cyclohex-2-en-1-yl)-piperidine-1-carboxylate (XX)**. Yield 54%, light yellow oily substance, R_f 0.58. IR spectrum, ν, cm^{-1}: 1714, 1686 (C=O), 1622 (C=C). ^1H NMR spectrum, δ, ppm: 1.49 s (9H, CMe_3), 1.54–1.90 m (4H, CH_2CH_2), 1.97 t (2H, CH_2C=C, *J* 5.2 Hz), 2.30 t (1H, CHC=C, *J* 6.0 Hz), 2.36–2.50 m (2H, CH_2C=O), 2.61–2.73 m (1H, CHC=O), 3.41–3.85 m (4H, $2CH_2N$), 5.44 d (1H, CH=C, *J* 6.8 Hz), 5.60 d (1H, CH=C, *J* 6.8 Hz), 5.73–5.80 m (1H, CH=C). Mass spectrum, *m/z* (I_{rel}, %): 280.23 (36) $[M + H]^+$, 224.20 (100) $[M - 57 + 2H]^+$, 179.81 (39) $[M - 101 + 2H]^+$. Found, %: C 68.71; H 8.93; N 5.17. $C_{16}H_{25}NO_3$. Calculated, %: C 68.84; H 9.06; N 5.07. *M* 279.38.

3-(2-Chloropropyl)piperidin-4-one hydrochloride (XXI). To a solution of 1.20 g (5 mmol) of compound **XII** in 8 mL of anhydrous dioxane was added 20 mL of dioxane saturated with HCl, the mixture was stirred for 20 h at room temperature, evaporated in a vacuum, 50 mL of anhydrous ethyl ether was added, and the solution was left standing for 24 h. The precipitated white crystals were separated, washed with ether, and dried in a vacuum over $CaCl_2$. Yield 0.98 g (92%), mp 198–200°C. IR spectrum, ν, cm^{-1}: 3476–3287 (NH_2^+), 1722 (C=O). ^1H NMR spectrum, δ, ppm: 1.57 d (3H, CH_3, *J* 8.4 Hz), 1.95–2.03 m (2H, CH_2), 2.13–2.18 m (1H, CHC=O), 2.92–

2.97 m (2H, CH_2C=O), 3.15–3.42 m (2H, CH_2N), 3.64–3.95 m (2H, CH_2N), 4.45–4.52 m (1H, HCCl), 11.18 br.s (2H, NH_2^+). Mass spectrum, *m/z* (I_{rel}, %): 176.24 (100) $[M - 35.5]^+$. Found, %: C 45.43; H 6.85; Cl 33.16; N 6.73. $C_8H_{15}Cl_2NO$. Calculated, %: C 45.25; H 7.07; Cl 33.47; N 6.60. *M* 212.16.

Compound **XXII** was synthesized similarly.

3-(3-Methyl-3-chlorobutyl)piperidin-4-one hydrochloride (XXII). Yield 93%, mp 178–179°C. IR spectrum, ν, cm^{-1}: 3468–3273 (NH_2^+), 1721 (C=O). ^1H NMR spectrum, δ, ppm: 1.51–1.61 m (2H, CH_2), 1.67 s (6H, $2CH_3$), 1.74 t (2H, CH_2CCl), 1.97–2.02 m (1H, CHC=O), 2.94 t (2H, CH_2C=O, *J* 7.8 Hz), 3.12–3.87 m (4H, $2CH_2N$), 10.93 br.s (2H, NH_2^+). Mass spectrum, *m/z* (I_{rel}, %): 205.12 (12) $[M - 35.5]^+$, 168.21 (100) $[M - 71 - H]^+$. Found, %: C 49.68; H 7.84; Cl 28.93; N 5.53. $C_{10}H_{19}Cl_2NO$. Calculated, %: C 49.96; H 7.91; Cl 29.56; N 5.83. *M* 240.21.

***tert*-Butyl 3-allyl-4-hydroxypiperidine-1-carboxylate (XXIII)**. To a solution of 0.68 g (2.85 mmol) of compound **XII** in 10 mL of anhydrous THF in an argon atmosphere at 0°C was added 0.10 g (2.85 mmol) of $LiAlH_4$, and the reaction mixture was stirred for 6 h at 20°C (TLC monitoring). Then was added in succession 2 mL of methanol, 4 mL of 20% water solution of NaOH, 8 mL of 40% aqueous ammonia, the precipitate was filtered off, washed with 20 mL of THF, the filtrate was evaporated, the residue was dissolved in 30 mL of dichloromethane, the solution was washed with water and dried with anhydrous Na_2SO_4. The solution was evaporated in a vacuum. Yield 0.557 g (81%). IR spectrum, ν, cm^{-1}: 3493 (OH), 1684 (C=O), 1630 (C=C). ^1H NMR spectrum, δ, ppm: 1.47–1.52 m (9H, CMe_3), 1.67–1.73 m (2H, CH_2), 1.81–1.86 m (1H, CH), 2.32–2.51 m (2H, CH_2C=C), 2.82–3.32 m (2H, CH_2N), 3.49–3.98 m (3H, CH_2N, HCO), 5.01–5.11 m (2H, CH_2=C), 5.75–5.84 m (1H, CH=C). Mass spectrum, *m/z* (I_{rel}, %): 186.26 (1.5) $[M - 57 + 2H]^+$, 141.96 (11.2) $[M - 101 + 2H]^+$, 124.32 (100) $[M - 101 - 18 + 2H]^+$. Found, %: C 64.58; H 9.63; N 5.78. $C_{13}H_{23}NO_3$. Calculated, %: C 64.73; H 9.65; N 5.87. *M* 241.33.

Compound **XXIV** was synthesized similarly.

***tert*-Butyl 4-hydroxy-3-(3-methylbut-2-enyl)piperidine-1-carboxylate (XXIV)**. Yield 72%. IR spectrum, ν, cm^{-1}: 3487 (OH), 1685 (C=O), 1621 (C=C). ^1H NMR spectrum, δ, ppm: 1.43–1.49 m (9H, CMe_3), 1.61–1.72 m (6H, $2CH_3$), 1.77–1.91 m (2H, CH_2), 1.95–1.99 m (1H, CH), 2.21–2.32 m (2H, CH_2C=C), 2.52–2.84 m (2H, CH_2N), 3.25–3.98 m (3H, CH_2N, HCO), 5.18–5.24 m (1H, CH=C). Mass spectrum, *m/z* (I_{rel}, %): 270.19 (22) $[M + H]^+$, 214.18 (100) $[M - 57 + 2H]^+$, 170.25 (21) $[M - 101 + 2H]^+$. Found, %: C 66.71; H 9.84; N 5.36. $C_{15}H_{27}NO_3$. Calculated, %: C 66.82; H 10.02; N 5.20. *M* 269.38.

***tert*-Butyl 3-allyl-4-morpholinopiperidine-1-carboxylate (XXV)**. To a solution of 0.6 g (2.5 mmol) of compound **XII** in 10 mL of anhydrous dichloromethane was added 0.22 g (2.5 mmol) of morpholine and 0.1 mL of glacial acetic acid. The mixture was boiled at stirring for 0.5 h, cooled, 1.7 g (8 mmol) of $NaHB(OAc)_3$ was added, the mixture was stirred for 24 h, then 10 mL of 20% water solution of potassium carbonate and 15 mL of water was added, the organic layer was separated, and the water layer was extracted with CH_2Cl_2 (2 × 15 mL). The combined organic solutions were dried with anhydrous Na_2SO_4, the solvent was distilled off in a vacuum, the residue was chromatographed on silica gel eluting with a mixture ethyl acetate–hexane, 1 : 3, saturated with ammonia. Yield 0.58 g (75%), colorless oily substance. IR spectrum, ν, cm^{-1}: 1686 (C=O), 1628 (C=C). ^1H NMR spectrum, δ, ppm: 1.42–1.48 m (9H, CMe_3), 1.54–1.57 m (1H, CH), 1.78–1.83 m (2H, CH_2), 2.15–2.19 m (2H, CH_2C=C), 2.31–3.48 m (4H, $2CH_2N$), 2.68–2.74 m (1H, CHN), 2.85–3.32 m (2H, CH_2NC=O), 3.52–3.91 m (6H, CH_2NC=O, $2CH_2O$), 5.08–5.13 m (2H, CH_2=C), 5.38–5.42 m (1H, CH=C). Mass spectrum, *m/z* (I_{rel}, %): 311.18 (15) $[M + H]^+$, 255.26 (100) $[M - 57 + 2H]^+$, 211.23 (24) $[M - 101 + 2H]^+$. Found, %: C 65.68; H 9.71; N 8.96. $C_{17}H_{30}N_2O_3$. Calculated, %: C 65.86; H 9.78; N 9.04. *M* 310.43.

***tert*-Butyl 4-amino-3-(3-methylbut-2-enyl)piperidine-1-carboxylate (XXVI)**. A mixture of 1.34 g (5 mmol) of compound **XIII**, 2.85 g (10 mmol) of $Ti(i\text{-}PrO)_4$, 15 mL of ethanol saturated with ammonia was stirred for 20 h in a closed flask, 0.3 g (7.9 mmol) of $NaBH_4$ was added, and the stirring was continued for 4 h (TLC monitoring). Then the reaction mixture was partially evaporated on a rotary evaporator, 30 mL of 5% hydrochloric acid was added, the mixture was washed with 50 mL of ethyl ether, the water layer was separated, 1.75 g of NaOH in 30 mL of water was added to pH 10–11, and the water layer was extracted with dichloromethane (3 × 50 mL). The combined organic solutions were dried with anhydrous Na_2SO_4, the solvent was distilled off in a vacuum. Yield 0.66 g (49%), colorless oily substance. IR spectrum, ν, cm^{-1}: 3354, 3348 (NH), 1685 (C=O), 1624 (C=C). ^1H NMR

spectrum, δ, ppm: 1.15–1.30 m (3H, CH, CH_2), 1.44–1.48 m (9H, CMe_3), 1.62 s (3H, CH_3), 1.71 s (3H, CH_3), 1.89–2.01 m (2H, $CH_2C{=}C$), 2.98–3.02 m (1H, CHN), 3.22–4.02 m (4H, $2CH_2N$), 5.16 t (1H, CH=C, *J* 5.8 Hz). Mass spectrum, *m/z* (I_{rel}, %): 269.27 (100) $[M + H]^+$. Found, %: C 67.26; H 10.43; N 10.51. $C_{15}H_{28}N_2O_2$. Calculated, %: C 67.14; H 10.55; N 10.46. *M* 268.40.

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