Supporting Information
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Supplementary Material

Investigations on the [2,3]-Wittig rearrangement of chiral 4-amino-propargyloxy acetates to novel α-hydroxy-γ-amino acids containing an allene unit

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Procedure for synthesis of compounds 7-13:

tert-Butyl [(2S)-4-methyl-1-oxopentan-2-yl]carbamate (7)

Dimethylsulfoxide (41.4 mmol, 3.0 eq.) was added drop wise to a solution of oxalyl chloride (20.7 mmol, 1.5 eq.) in 70 ml dichloromethane cooled to -78°C. After stirring for 15 min, a solution of tert-butyl [(2S)-1-hydroxy-4-methylpentan-2-yl]carbamate (13.8 mmol, 1.0 eq.) in 15 ml DCM was added drop wise. The mixture was stirred at -78°C for 1 h followed by the addition of triethylamine (69.0 mmol, 5 eq.). The mixture was allowed to warm up to room temperature and treated with 1N aq. hydrochloric acid. The mixture was extracted 3 times diethyl ether and the combined organic phases were washed with brine and saturated aq. sodium hydrogen carbonate solution. The organic phase was dried and concentrated to give the target compound which was introduced in the next step without further purification.

tert-Butyl [(3S)-1,1-dibromo-5-methylhex-1-en-3-yl]carbamate (8)

A suspension of zinc dust (3.28 g, 27.7 mmol) and triphenyl phosphine (7.25 g, 27.7 mmol) in 30 ml dry DCM was charged with tetrabromomethane (9.17 g, 27.7 mmol). The mixture was stirred at room temperature for 24 h. Subsequently, tert-butyl [(2S)-4-methyl-1-oxopentan-2-yl]carbamate (3.97 g, 13.8 mmol) in 15 ml DCM was added and the mixture was
stirred for 2 h at room temperature. The reaction mixture was concentrated to approx. 20 ml and quickly flashed on silica gel (eluent: diethyl ether/pentane (v/v) = 1:1).

Yield: 3.14 g (8.5 mmol) 61%.

$^1$H-NMR (200 MHz, CDCl$_3$): $\delta$ / ppm = 0.94 [d, $J$ = 6.6, 3H, CH(CH$_3$)$_2$], 0.95 [d, $J$ = 6.6, 3H, CH(CH$_3$)$_2$], 1.25-1.45 [m, 2H, CH$_2$-CH(CH$_3$)$_2$], 1.45 [s, 9H, C(CH$_3$)$_3$], 1.60-1.70 [m, 1H, CH(CH$_3$)$_2$], 4.25-4.35 (m, 1H, NH-CH), 4.61 (d br, $J$ = 8.4, 1H, NH-CH), 6.30 (d, $J$ = 8.5, 1H, CH=CB$_2$); $^{13}$C-NMR (50 MHz, CDCl$_3$): $\delta$ / ppm = 21.12, 22.98, 24.53, 28.41, 43.40, 51.94, 79.64, 90.50, 139.90, 154.92; MS (EI): m/z = 57 (100.00 %), 371 (0.09 %); MS (Cl, NH$_3$): m/z = 389 [(M+NH$_4^+$)]; CHN Anal. Calcd. for C$_{12}$H$_7$Br$_2$NO$_2$ (371.11 g/mol): C 38.84, H 5.70, N 3.77, Found: C 38.80, H 5.74, N 3.81.

**tert-Butyl [(4S)-1-hydroxy-6-methylhept-2-yn-4-yl]carbamate (9)**

$n$-Butyllithium (9.43 mmol, 5.90 ml of a 1.6 M solution in $n$-hexane) was added drop wise to a solution of tert-butyl [(3S)-1,1-dibromo-5-methylhex-1-en-3-yl]carbamate (1.00 g, 2.70 mmol) in 10 ml dry THF -78°C. The mixture was stirred at -78°C for 1 h and paraformaldehyde (0.50 g, 16.67 mmol) was added subsequently. The mixture was stirred again at -78°C for 1 h. Then, the mixture was warmed to room temperature within 2 h. Saturated aq. ammonium chloride (10 ml) was added and the reaction mixture was extracted with diethyl ether 3 times. The combined organic phases were washed with brine and saturated aq. sodium hydrogen carbonate solution. Subsequently, the organic phase was dried and concentrated. The residue was purified on silica gel (eluent: diethyl ether/pentane (v/v) = 1:1).

Yield 0.191 g (0.79 mmol) 29%.

$^1$H-NMR (200 MHz, CDCl$_3$): $\delta$ / ppm = 0.93 [d, $J$ = 6.5, 3H, CH$_2$-CH(CH$_3$)$_2$], 0.94 [d, $J$ = 6.6, 3H, CH$_2$-CH(CH$_3$)$_2$], 1.45 [s, 9H, C(CH$_3$)$_3$], 1.47-1.55 [m, 2H, CH$_2$-CH(CH$_3$)$_2$], 1.68-1.86 [m, 1H, CH$_2$-CH(CH$_3$)$_2$], 3.25 (s, 1H, CH$_2$-OH), 4.26 (s br, 2H, CH$_2$-OH), 4.35-4.48 (m, 1H, NH-CH), 4.76-4.97 (m, 1H, NH-CH); $^{13}$C-NMR (50 MHz, CDCl$_3$): $\delta$ / ppm = 21.85, 22.54, 24.82, 28.23, 41.38, 45.10, 50.58, 79.78, 81.06, 85.03, 154.95.
**tert-Butyl ([(4S)-4-[(tert-butoxycarbonyl)amino]-6-methylhept-2-yn-1-yl]oxy)acetate (10)**

![Chemical Structure](image)

**tert-Butyl [(4S)-1-hydroxy-6-methylhept-2-yn-4-yl]carbamate** (0.158 g, 0.66 mmol) was dissolved in toluene (5.2 ml). An aq. potassium hydroxide solution (5.2 ml, c = 8.91 mol/l) was added and tetra-n-butylammonium bromide (42 mg, 0.13 mmol, 0.2 eq.). Then, tert-butyl bromoacetate (192 mg, 0.98 mmol, 160 μl) was added drop wise and the mixture was stirred intensively at room temperature for 1 h. Water (10 ml) was added and the mixture was extracted 3 times with diethyl ether. The combined organic phases were washed with brine and saturated aq. sodium hydrogen carbonate solution. Subsequently, the organic phase was dried and concentrated. The residue was purified on silica gel (eluent: diethyl ether/pentane (v/v) = 1:2).

Yield: 0.206 g (0.58 mmol) 89%.

**1H-NMR** (200 MHz, CDCl3): δ / ppm = 0.93 [d, J = 6.6, 3H, CH2-CH(CH3)2], 0.94 [d, J = 6.6, 3H, CH2-CH(CH3)2], 1.39-1.58 [m, 2H, CH2-CH(CH3)2], 1.45 [s, 9H, C(CH3)3], 1.49 [s, 9H, C(CH3)3], 1.68-1.85 [m, 1H, CH2-CH(CCH3)2], 4.04 (s, 2H, O-CH2-CO-O), 4.29 (d, J = 1.8, 2H, alkyne-CH2-O), 4.40-4.55 (m, 1H, NH-CH), 4.75-4.87 (m, 1H, NH-CH), 13C-NMR (50 MHz, CDCl3): δ / ppm = 21.75, 22.45, 24.79, 27.879, 28.15, 41.27, 45.03, 58.15, 66.31, 77.29, 79.49, 81.51, 87.04, 154.61, 168.89.

**tert-Butyl [(4S)-7-hydroxy-2,7-dimethyloct-5-yn-4-yl]carbamate (11)**

![Chemical Structure](image)

n-Butyllithium (9.43 mmol, 5.90 ml of a 1.6 M solution in n-hexane) was added drop wise to a solution of tert-butyl [(3S)-1,1-dibromo-5-methylhex-1-en-3-yl]carbamate (2.00 g, 5.39 mmol) in 20 ml dry THF at -78°C. The mixture was stirred at -78°C for 1 h and acetone (3.13 g, 53.91 mmol) was added subsequently. The mixture was stirred again at -78°C for 1 h and then at -40°C for 12 h. The mixture was warmed to room temperature and saturated aq. ammonium chloride (10 ml) and water (5 ml) were added and the reaction mixture was extracted with diethyl ether 3 times. The combined organic phases were washed with brine
and saturated aq. sodium hydrogen carbonate solution. Subsequently, the organic phase was dried and concentrated. The residue was purified on silica gel (eluent: diethyl ether/pentane (v/v) = 2:1).

Yield 0.78 g (2.90 mmol) 54%.

\(^1\)H-NMR (200 MHz, CDCl\(_3\)): \(\delta / \text{ppm} = 0.93 \ [d, J = 6.6, 3H, CH\(_2\)-CH(CH\(_3\))\(_2\)], 0.94 \ [d, J = 6.6, 3H, CH\(_2\)-CH(CH\(_3\))\(_2\)], 1.23-1.42 \ [m, 2H, CH\(_2\)-CH(CH\(_3\))\(_2\)], 1.45 \ [s, 9H, C(CH\(_3\))\(_3\)], 1.49 \ [s, 6H, C(CH\(_3\))\(_2\)-OH], 1.66-1.83 \ [m, 1H, CH\(_2\)-CH(CH\(_3\))\(_2\)], 2.13 \ (s br, 1H, CH\(_2\)-OH)], 4.30-4.48 \ (m, 1H, NH-CH), 4.66-4.80 \ (m, 1H, NH-CH); \(^{13}\)C-NMR (50 MHz, CDCl\(_3\)): \(\delta / \text{ppm} = 21.94, 22.64, 24.97, 28.31, 31.37, 41.10, 45.36, 69.95, 79.76, 81.74, 87.48, 154.80;\) CHN Anal. Calcd. for C\(_{15}\)H\(_{27}\)NO\(_3\) (269.38 g/mol): C 66.88, H 10.10, N 5.20, Found: C 66.75, H 10.17, N 5.10.

**tert-Butyl (\{(5S)-5-[(tert-butoxycarbonyl)amino]-2,7-dimethyloct-3-yn-2-yl\}oxy)acetate (12)**

\[\text{\begin{align*}
\text{O} & \text{H} \\
\text{N} & \text{O} \\
\text{\_} & \text{\_} \\
\end{align*}}\]

**tert-Butyl [(4S)-7-hydroxy-2,7-dimethyloct-5-yn-4-yl]carbamate (0. 468 g, 1.74 mmol) was dissolved in toluene (13.8 ml). To the solution was added an aq. potassium hydroxide solution (13.8 ml, c = 8.91 mol/l) and tetra-n-butylammonium bromide (112 mg, 0.348 mmol, 0.2 eq.). Then, tert-butyl bromoacetate (443 mg, 2.26 mmol, 333 \(\mu\)l) was added drop wise and the mixture was stirred intensively at room temperature for 1 h. Water (30 ml) was added and the mixture was extracted 3 times with diethyl ether. The combined organic phases were washed with brine and saturated aq. sodium hydrogen carbonate solution. Subsequently, the organic phase was dried and concentrated. The residue was purified on silica gel (eluent: diethyl ether/pentane (v/v) = 1:3 to 2:1).

Yield: 0.285 g (0.74 mmol) 43%.

\(^1\)H-NMR (200 MHz, CDCl\(_3\)): \(\delta / \text{ppm} = 0.93 \ [d, J = 6.6, 3H, CH\(_2\)-CH(CH\(_3\))\(_2\)], 0.94 \ [d, J = 6.6, 3H, CH\(_2\)-CH(CH\(_3\))\(_2\)], 1.34-1.54 \ [m, 2H, CH\(_2\)-CH(CH\(_3\))\(_2\)], 1.45, 1.47 and 1.48 \ [3 s, 24H, C(CH\(_3\))\(_3\), C(CH\(_3\))\(_2\)-O], 1.66-1.83 \ [m, 1H, CH\(_2\)-CH(CH\(_3\))\(_2\)], 4.07 \ (s, 2H, O-CH\(_2\)-CO-O), 4.42-4.47 \ (m, 1H, NH-CH), 4.73-4.83 \ (m, 1H, NH-CH); \(^{13}\)C-NMR (50 MHz, CDCl\(_3\)): \(\delta / \text{ppm} = 21.75, 22.47, 24.85, 27.83, 28.12, 28.51, 41.20, 45.13, 62.78, 71.01, 79.40, 80.94, 83.56, 84.61, 154.57, 169.57;\) CHN Anal. Calcd. for C\(_{21}\)H\(_{37}\)NO\(_5\) (383.53 g/mol): C 65.77, H 9.72, N 3.65, Found: C 66.08, H 9.78, N 3.78.
**tert-Butyl (2R,4S)-4-[(tert-butoxycarbonyl)amino]-2-hydroxy-6-methyl-3-(2-methylprop-1-en-1-ylidene)heptanoate (13)**

Under an atmosphere of argon, diisopropylamine (230 mg, 2.27 mmol) was dissolved in dry THF (2 ml) and charged with n-butyllithium (2.16 mmol, 1.33 ml of a 1.6 M solution in n-hexane) at -78°C. The solution was stirred at -78°C for 1 h followed by the drop wise addition of tert-butyl ({{5S}-5-[(tert-butoxycarbonyl)amino]-2,7-dimethyloct-3-yn-2-yl}oxy)acetate (210 mg, 0.55 mmol) dissolved in dry THF (3 ml). The mixture was stirred at -78°C for 1 h and at -70°C for 3 d. The mixture was quenched with saturated aq. ammonium chloride solution (5 ml). Water (2 ml) was added and the mixture was extracted 3 times with diethyl ether. The combined organic phases were washed with brine and saturated aq. sodium hydrogen carbonate solution. Subsequently, the organic phase was dried and concentrated. The raw product was analyzed by 1H-NMR and 13C-NMR. The spectra showed only signals of compounds 12 and 13. The corresponding stereoisomer of 13 was not observed. Finally, the residue was purified on silica gel (eluent: diethyl ether/pentane (v/v) = 1:4).

Yield: 21 mg (0.05 mmol) 14% (based on recovered starting material).

**1H-NMR** (200 MHz, CDCl3): δ / ppm = 0.91 [d, J = 6.8, 3H, CH2-CH(CH3)2], 0.93 [d, J = 6.8, 3H, CH2-CH(CH3)2], 1.30-1.49 [m, 2H, CH2-CH(CH3)2], 1.44 [s br, 9H, C(CH3)3], 1.48 [s, 9H, C(CH3)3], 1.59-1.67 [m, 1H, CH2-CH(CH3)2], 1.71 and 1.72 [2 s, 6H, C=C=C(CH3)2], 3.54 (d, J = 7.6, 1H, CH-OH), 4.27-4.33 (m, 1H, NH-CH), 4.42 (d, J = 9.6, 1H, NH-CH), 4.46 (d, J = 7.6, 1H, CH-OH); **13C-NMR** (50 MHz, CDCl3): δ / ppm = 20.04, 20.36, 22.36, 22.83, 24.99, 28.09, 28.41, 43.97, 48.17, 71.12, 79.36, 81.99, 101.20, 104.57, 155.40, 172.58, 199.06; **MS (EI)**: m/z = 29 (17.25 %), 41 (27.93 %), 57 (100.00 %), 86 (59.50 %), 124 (11.85%), 130 (42.03 %), 136 (12.08 %), 226 (10.12 %), 253 (22.69 %); **MS (Cl, NH3)**: m/z = 384 [(M+H)+]; **CHN** Anal. Calcd. for C21H37NO5 (384.53 g/mol): C 65.77, H 9.72, N 3.65, Found: C 65.80, H 9.66, N 3.66.