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Reductive amination of fusidane triterpenoid ketones

Elena V. Salimova [1,*], Andrey G. Mamaev [1], Elena V. Tretyakova [1], Olga S. Kukovinets [2] and Lyudmila V. Parfenova [1]

[1] Institute of Petrochemistry and Catalysis of Russian Academy of Sciences, Prospect Oktyabrya 141, 450075, Ufa, Russian Federation

[2] Bashkir State University, ul. Zaki Validi 32, 450076, Ufa, Russian Federation

Abstract: New nitrogen-containing analogues of fusidane triterpenoids were synthesized via the reductive amination of 3,11-dioxo derivatives of fusidic acid and its methyl ester by primary and secondary amines (Bu^nNH_2, Pyrrolidine, $NH_2CH_2CH_2NH_2$) in the presence of sodium borohydrides. The reaction proceeds with high chemo- and stereoselectivity and gives 3*β*-amino substituted products with yields of 75-88%.

Key words: reductive amination; fusidane triterpenoids; sodium triacetoxyborohydride; sodium borohydride.

Introduction

Amines are an important class of compounds found in many natural products, pharmaceuticals and other valuable organic molecules, including dyes and chemicals for agriculture [1,2]. Even though there are numerous approaches to the amine preparation [1], the range of methods for their selective synthesis is rather limited [3-5]. The most commonly used method is the reductive amination involving the interaction of aldehydes or ketones with primary or secondary amines in the presence of reducing agents. The reaction proceeds in two stages and includes the formation of iminium ion [6], which subsequent reduction provides amine alkylation product [7]. However, a direct reductive amination reaction implies the treatment of a mixture of a carbonyl compound and amine with suitable reducing agents *in situ*, without isolation the intermediate iminium salt. At this point, the choice of reducing agent is crucial to the success of the reaction, since it should interact with imines selectively without affecting the carbonyl functions of the substrate [8]. Hydrides of various metals and non-metals, sometimes in combination with complexes of transition metals as catalysts, are applied as effective reagents in the mentioned reactions. However, most of these reagents have some limitations. In particular, catalytic amination is often incompatible with the compounds containing additional double or triple carbon-carbon bonds and other reactive functional groups.[9] Cyanoborohydride and tin hydride are highly toxic and generate toxic by-products during the reaction [10,11].

Reductive amination is most important for the synthesis and modification of natural compounds since it provides selective single-step preparation of amines of different degree of substitution. The fusidane triterpenoids is a group of natural compounds produced by fungi, which exhibits antimicrobial activity against staphylococci [12]. A well-known representative is a fusidic acid applied in clinical practice for the treatment of staphylococcal infections resistant to penicillin. The synthesis of novel nitrogen-containing analogues of fusidic acid is an important task since it can expand the range of new agents that have a broad spectrum of antibacterial activity [13]. It should be noted that earlier the authors [14,15] synthesized a series of amino-derivatives in the reaction of 3-keto-fusidic acid with amines in the presence of acetic acid and $NaBH(OAc)_3$. In our research we studied the reductive amination of 3,11-dioxo-derivatives by primary and secondary amines, using sodium hydrides as reducing agents, and also in the presence of a catalyst $(i\text{-}PrO)_4Ti$.

Results and Discussion

The reaction of fusidic acid diketone **1** or its methyl ester **2** with n-butylamine or pyrrolidine was carried out in chloroform in the presence of acetic acid, followed by treatment of reaction media by $NaBH(OAc)_3$ (Scheme 1). This reagent was selected because sodium triacetoxyborohydride is a soft, reducing agent with steric and electron-withdrawing effects of the three acetoxy groups stabilizing the boron-hydrogen bond [16]. Thus, it exhibits high stereoselectivity, particularly for cyclic ketones.[17] Reductive amination of compounds **1** and **2** proceeded with high chemo- and stereoselectivity at the C^3 atom with the formation of derivatives **3-5**,

**Corresponding author: Elena V. Salimova*
Email address: salimovaev@mail.ru
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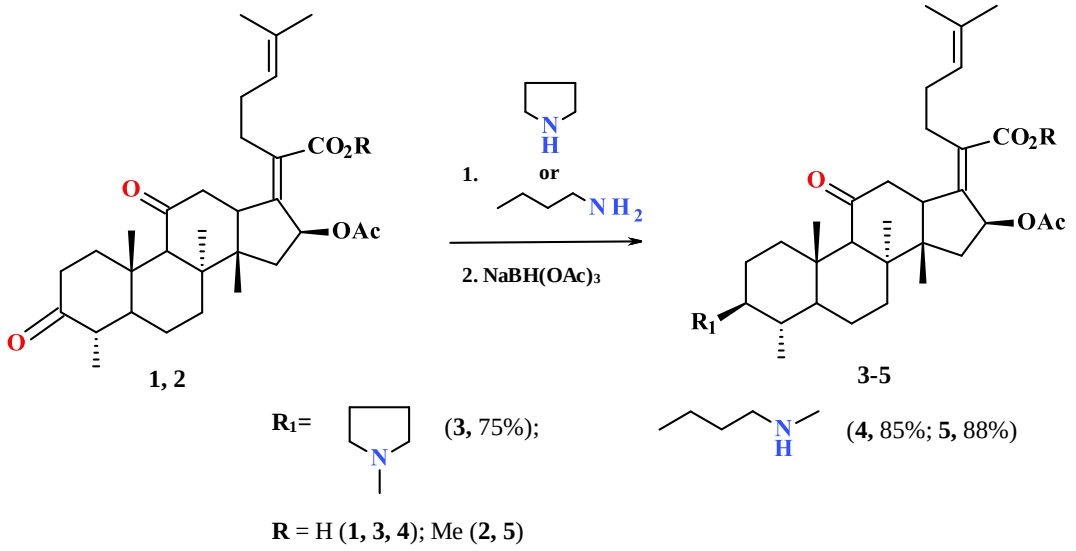
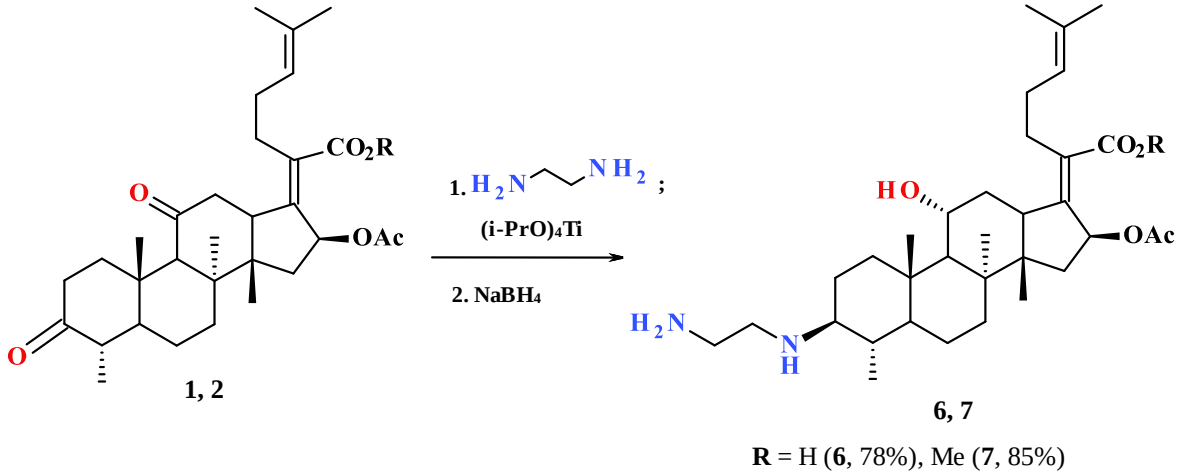
while other functional groups of triterpenoid were not affected.



Scheme 1. Synthesis of 11-oxo-3β-amino-derivatives of fusidane triterpenoids.

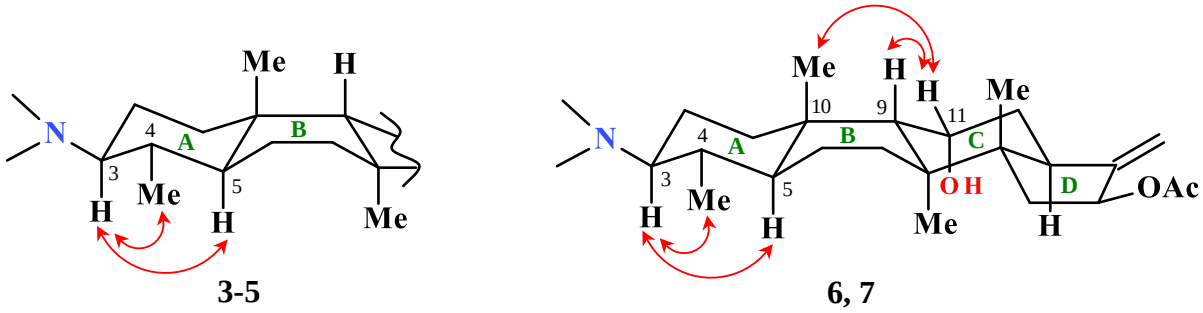
Despite the fact that the reductive amination reactions proceed with sufficiently high chemoselectivity, the synthesis of primary and secondary amines, in comparison with tertiary amines, is complicated by additional alkylation reactions [3]. Moreover, in the case of polyamines, the formation of polymer molecules are most likely in the reaction mixture. The use of system titanium isobutoxide (IV)/sodium borohydrides ($NaBH_4$, $NaBH(OAc)_3$, $NaBH_3CN$) prevents the formation of by-products and substantially improve the chemoselectivity of the reaction [18-22].

Thus, the reaction of compounds **1, 2** with ethylenediamine was carried out in methanol in the presence of $Ti(Oi\text{-}Pr)_4$ catalyst, followed by the reduction of the mixture by $NaBH_4$. As a result, monoamino substituted derivatives **6, 7** at the C^3 atom of the molecule were obtained. The keto group at the C^{11} was not involved in amination, but it was reduced to hydroxyl group (Scheme 2).



Scheme 2. Synthesis of 11α-hydroxy-3β-amino-derivatives of fusidane triterpenoids.

The formation of products **3-7** was accompanied by the disappearance of the sp^2-hybridized C^3-carbonyl atom signal of compounds **1**, **2** at 215 ppm in NMR ^{13}C spectra and the presence of sp^3-hybridized C^3 atom signals for *n*-butylamino-substituted derivatives at 57-59 ppm, pyrrolidine-substituted products at 76 ppm and for ethanediyldiamino-substituted products at 62 ppm. The amino group in the resulting compounds has *β*-configuration, as confirmed by NOESY spectra (Scheme 3). Thus, NOESY spectra of compounds **3-7** exhibited cross-peaks between H^3, H^5 and protons of methyl group at C^4 atom. α-Configuration of hydroxyl-group at C11 position in compounds **6,7** is evidenced from the correlations between H^{11}, H^9 and methyl protons at C^{10} atom.



Scheme 3. Correlations between atoms in NOESY spectra of compounds **3-7**.

Conclusion

Thus, the reaction of reductive amination of 3,11-dioxo derivatives of fusidane triterpenoids was studied, and new nitrogen-containing analogues of fusidic acid were obtained. It was found that the reaction with primary and secondary amines in the presence of sodium borohydrides proceeds with high chemo- and stereoselectivity and provides 3*β*-amino substituted derivatives, whose biological activity will be further investigated.

Acknowledgements

The study was financially supported by the Russian Foundation of Basic Research (research project No. 17-43-020021 r_a). The part of the research was carried out by the federal program № AAAA-A17-117012610057-7. The structural studies of compounds were carried out at the Center for Collective Use "Agidel" at the Institute of Petrochemistry and Catalysis, Russian Academy of Sciences.

Experimental Section

One-dimensional (^{1}H and ^{13}C) and two-dimensional (COSY, NOESY, HSQC and HMBC) NMR spectra of compounds were recorded on *Bruker Avance 400* spectrometer (400.13 MHz for ^{1}H and 100.62 MHz for ^{13}C) and *Bruker Avance II 500 HD Ascend* spectrometer (500.17 MHz for ^{1}H and 125.77 MHz for ^{13}C). All the experiments were set up with standard Bruker pulse sequences. Chemical shifts are given in ppm relative to TMS as the internal standard. Mass-spectra were measured by MALDI TOF/TOF methods on *Bruker Autoflex III* spectrometer with the registration of positive ions; 3-(4-hydroxy-3,5-dimethoxyphenyl)prop-2-enoic acid was used as matrix. The elemental analyses were carried out on a Carlo Erba 1106 analyzer. The melting points were determined on a PHMK 80/2617 apparatus. The reaction progress was monitored by TLC using Sorbfil plates (PTSHAF-V, Sorbopolymer, Russia), visualization by 10% solution of sulfuric acid with subsequent heating at 100–120°C during 2–3 min. Column chromatography was performed on KSK silica gel (100-200 µm, Sorbopolymer, Russia).

General procedure of reductive amination of ketones 1 or 2 with sodium triacetoxyborohydride.

Diketone (**1** or **2**) (0.5 mmol) and pyrrolidine or *n*-butylamine (3.0 mmol) were mixed in dry chloroform (5 mL), then treated with sodium triacetoxyborohydride (0.3 g, 1.5 mmol) and AcOH (60 mg, 1.0 mmol) and the mixture was stirred under argon at room temperature for 12 hours (TLC control; chloroform - methanol, 10:1). The reaction mixture was quenched by adding 10% $NaHCO_3$ and the product was extracted with chloroform. The organic extract was washed with brine and dried $MgSO_4$. The solvent was evaporated to give the crude amine which was purified by column chromatography on silica gel.

(2Z)-2-[(3b,4a,5a,8a,9b,13a,14b,16b)-16-(Acetyloxy)-4,8,10,14-tetramethyl-11-oxo-3-pyrrolidin-1-ylgonan-17-ylidene]-6-methylhept-5-enoic acid (3).

Purification by column chromatography (silica gel; chloroform / methanol, 4:1). Yield: 75%, yellow crystals, m.p. 240-242°C, $[\alpha]_D^{20}$ +52.0° (*c* 0.77, $CHCl_3$).

^{1}H NMR (MeOD, δ): 5.86 (1H, d, *J* = 8.4 Hz; H-16); 5.05 (1H, t, *J* = 7.3 Hz; H-24); 3.42 (2H, t, *J* = 6.9 Hz; H-33); 3.40 (2H, t, *J* = 6.9 Hz; H-34); 3.07 (1H, td, *J* = 5.7 Hz, 10.0 Hz; H-3); 2.79-2.88 (1H, m, H-13); 2.74-2.83 (1H, m, H-12a); 2.60 (1H, s, H-9); 2.59-2.69 (1H, m, H-12b); 2.33-2.42 (1H, m, H-1a); 2.24-2.44 (2H, m, H-22); 2.03-2.15 (1H, m, H-15b); 1.98 (3H, s, $COCH_3$); 1.98-2.19 (2H, m, H-23); 1.93 (2H, d, *J* = 6.9 Hz; H-35); 1.89-1.99 (1H, m, H-7b); 1.84 (3H, d, *J* = 6.9 Hz; H-36); 1.79-1.85 (1H, m, H-2a); 1.66-1.76 (1H, m, H-1b); 1.63 (3H, s, H-26); 1.56 (3H, s, H-27); 1.55-1.66 (1H, m, H-6a); 1.53-1.66 (1H, m, H-2b); 1.34-1.48 (1H, m, H-4); 1.29-1.38 (1H, m, H-15a); 1.23-1.32 (1H, m, H-5); 1.15 (3H, s, H-18); 1.09-1.21 (1H, m, H-7a); 1.06 (3H, s, H-30); 1.01 (3H, s, H-19); 0.98-1.10 (1H, m, H-6b); 0.92 (3H, d, *J* = 6.2 Hz; H-28).

^{13}C NMR (MeOD, δ): 210.74 (C-11); 173.01 (C-21); 171.01 ($\underline{C}OCH_3$); 143.71 (C-17); 132.68 (C-20); 132.60 (C-25); 122.92 (CH-24); 76.65 (C-3); 74.19

(C-16); 58.48 (C-9); 48.70 (C-14); 47.48 (C-34); 47.29 (C-13); 45.62 (C-33); 45.14 (C-5); 44.93 (C-12); 41.28 (C-8); 38.12 (C-4); 38.09 (C-15); 37.10 (C-10); 32.59 (C-7); 32.20 (C-1); 31.46 (C-2); 28.93 (C-22); 27.85 (CH_2-23); 26.04 (CH_3-26); 24.28 (C-36); 24.14 (C-35); 22.91 (C-30); 22.28 (C-19); 20.65 (C-6); 20.61 (CO<u>C</u>H_3); 17.74 (CH_3-27); 16.90 (C-18); 15.50 (C-28).
MALDI TOF/TOF: m/z $[M+H]^+$ calculated for $C_{35}H_{53}NO_5$: 567.80; found 568.40;
Anal. Calcd for $C_{35}H_{53}NO_5$: C, 74.04; H, 9.41; N, 2.47; O, 14.09. Found C, 73.92; H, 9.39; N, 2.50.

(2Z)-2-[(3b,4a,5a,8a,9b,13a,14b,16b)-16-(Acetyloxy)-3-(butylamino)-4,8,10,14-tetramethyl-11-oxogonan-17-ylidene]-6-methylhept-5-enoic acid (4).
Purification by column chromatography (silica gel; chloroform / methanol, 4:1).
Yield: 85%, yellow crystals, m.p. 176-178°C, $[\alpha]_D^{20}$ +71.8° (*c* 0.86, $CHCl_3$).
^{1}H NMR (MeOD, δ): 5.84 (1H, d, *J* = 7.5 Hz; H-16); 5.03 (1H, t, *J* = 6.5 Hz; H-24); 3.05-3.12 (1H, m, H-3); 2.77-2.86 (1H, m, H-13); 2.72-2.86 (1H, m, H-12a); 2.88-2.98 (1H, m, H-33a); 2.72-2.86 (1H, m, H-33b); 2.54-2.66 (1H, m, H-12b); 2.61 (1H, s, H-9); 2.16-2.35 (2H, m, H-22); 2.15-2.25 (1H, m, H-1a); 1.98-2.09 (1H, m, H-15b); 1.96 (3H, s, $COCH_3$); 1.95-2.08 (2H, m, H-23); 1.87-1.93 (1H, m, H-7b); 1.86-1.93 (1H, m, H-4); 1.86-1.99 (1H, m, H-1b); 1.73-1.90 (2H, m, H-2); 1.69-1.78 (1H, m, H-5); 1.61 (3H, s, H-26); 1.56-1.69 (2H, m, H-34); 1.54 (3H, s, H-27); 1.48-1.56 (1H, m, H-6a); 1.27-1.35 (1H, m, H-15a); 1.26-1.40 (2H, m, H-35); 1.17-1.26 (1H, m, H-7a); 1.14 (3H, s, H-18); 1.10 (3H, s, H-30); 0.99 (3H, s, H-19); 0.98 (3H, d, *J* = 7.0 Hz; H-28); 0.94-1.02 (1H, m, H-6b); 0.90 (3H, t, *J* = 7.3 Hz; H-36).
^{13}C NMR (MeOD, δ): 211.07 (C-11); 175.49 (C-21); 171.03 (<u>C</u>OCH_3); 138.00 (C-17); 137.18 (C-20); 132.02 (C-25); 123.47 (CH-24); 74.42 (C-16); 58.63 (C-9); 57.95 (C-3); 48.70 (C-14); 46.83 (C-13); 46.22 (C-34); 45.05 (C-12); 41.27 (C-8); 39.93 (C-5); 38.16 (C-15); 36.75 (C-10); 32.64 (C-4); 31.72 (C-7); 29.54 (C-22); 29.05 (C-1); 27.74 (CH_2-23); 27.55 (C-35); 25.56 (CH_3-26); 23.28 (C-2); 22.39 (C-19); 22.26 (C-30); 20.81 (CO<u>C</u>H_3); 20.61 (C-6); 20.04 (C-36); 17.68 (CH_3-27); 16.89 (C-18); 14.90 (C-28); 13.54 (C-37).
MALDI TOF/TOF: m/z $[M+H]^+$ calculated for $C_{35}H_{55}NO_5$: 569.81; found 570.40;
Anal. Calcd for $C_{35}H_{55}NO_5$: C, 73.77; H, 9.73; N, 2.46; O, 14.04. Found C, 73.62; H, 9.71; N, 2.49.

Methyl(2Z)-2-[(3b,4a,5a,8a,9b,11a,13a,14b,16b)-16-(acetyloxy)-3-(butylamino)-11-hydroxy-4,8,10,14-tetramethylgonan-17-ylidene]-6-methylhept-5-enoate (5).
Purification by column chromatography (silica gel; chloroform / methanol, 20:1).
Yield: 88%, yellow crystals, m.p. 140-142°C, $[\alpha]_D^{20}$ +32.1° (*c* 1.23, $CHCl_3$).
^{1}H NMR ($CDCl_3$, δ): 5.76 (1H, d, *J* = 8.1 Hz; H-16); 4.95 (1H, t, *J* = 7.1 Hz; H-24); 3.54 (3H, s, $COOCH_3$); 3.03-3.09 (1H, m, H-3); 2.90-3.02 (1H, m, H-34a); 2.77-2.86 (1H, m, H-13); 2.71-2.83 (1H, m, H-34b); 2.65-2.75 (1H, m, H-12a); 2.51 (1H, s, H-9); 2.49-2.61 (1H, m, H-12b); 2.17-2.32 (4H, m, H-22; H-1); 1.96-2.12 (1H, m, H-15b); 1.89 (3H, s, $COCH_3$); 1.85-2.02 (2H, m, H-23); 1.82-1.94 (1H, m, H-4); 1.75-1.85 (1H, m, H-7b); 1.73-1.89 (2H, m, H-2); 1.68 (1H, t, *J* = 11.5 Hz; H-5); 1.55 (3H, s, H-26); 1.54-1.65 (2H, m, H-35); 1.47 (3H, s, H-27); 1.42-1.53 (1H, m, H-6a); 1.21-1.31 (1H, m, H-15a); 1.18-1.31 (2H, m, H-36); 1.06-1.18 (1H, m, H-7a); 1.05 (3H, s, H-18); 1.04 (3H, s, H-30); 0.98 (3H, d, *J* = 6.5 Hz; H-28); 0.92 (3H, s, H-19); 0.87-0.97 (1H, m, H-6b); 0.82 (3H, t, *J* = 7.4 Hz; H-37).
^{13}C NMR ($CDCl_3$, δ): 209.70 (C-11); 170.00 (C-21); 169.92 (<u>C</u>OCH_3); 145.35 (C-17); 132.83 (C-25); 131.22 (C-20); 122.51 (CH-24); 74.06 (C-16); 59.58 (C-3); 58.43 (C-9); 51.38 (COO<u>C</u>H_3); 48.57 (C-14); 47.31 (C-34); 47.24 (C-13); 44.64 (C-12); 40.86 (C-8); 40.01 (C-5); 38.06 (C-15); 36.88 (C-10); 32.57 (C-4); 31.91 (C-7); 28.75 (CH_2-22); 28.71 (C-1); 27.77 (CH_2-23); 27.39 (C-35); 25.58 (CH_3-26); 23.53 (C-2); 22.09 (C-30); 21.89 (C-19); 20.76 (CO<u>C</u>H_3); 20.35 (C-6); 19.96 (C-36); 17.60 (CH_3-27);16.78 (C-18); 14.85 (C-28); 13.45 (C-37).
MALDI TOF/TOF: m/z $[M+H]^+$ calculated for $C_{36}H_{57}NO_5$: 583.84; found 584.43;
Anal. Calcd for $C_{36}H_{57}NO_5$: C, 74.06; H, 9.84; N, 2.40; O, 13.70. Found C, 73.92; H, 9.79; N, 2.43.

General procedure for the titanium–mediated reductive amination of diketones 1 or **2.**
A mixture of the diketone (**1** or **2**) (0.5 mmol), titanium (IV) isopropoxide (55 mg, 0.17 mmol) and ethylenediamine (180 mg, 3.0 mmol) in absolute methanol (5 mL) was stirred under argon at room temperature for 2-3 hours. Sodium borohydride (38 mg, 1.0 mmol) was then added at -78ºC and the resulting mixture was stirred for an additional 2 hours raising the temperature to 20°C. The reaction was then quenched by adding water (5 mL). Stirring was maintained at room temperature for 20 minutes. After the filtration, washing with methanol, the organic layer was separated and concentrated in vacuo to afford the expected crude amine which was purified by column chromatography on silica gel.

(2Z)-2-{(3b,4a,5a,8a,9b,11a,13a,14b,16b)-16-(Acetyloxy)-3-[(2-aminoethyl) amino]-11-hydroxy-4,8,10,14-tetramethylgonan-17-ylidene}-6-methylhept-5-enoic acid (6).
Purification by column chromatography (silica gel; chloroform / methanol, 2:1).
Yield: 78%, yellow crystals, m.p. 298-300°C, $[\alpha]_D^{20}$ +45.4° (*c* 0.75, $CHCl_3$).
^{1}H NMR (MeOD, δ): 5.81 (1H, d, *J* = 7.5 Hz; H-16); 5.17 (1H, d, *J* = 6.5 Hz; H-24); 4.20-4.39 (1H, m,

H-11); 2.96-3.06 (1H, m, H-13); 2.89-2.99 (2H, m, H-34); 2.66-3.08 (2H, m, H-33); 2.47-2.57 (1H, m, H-22a); 2.29-2.38 (1H, m, H-22b); 2.27-2.35 (1H, m, H-12a); 2.14-2.29 (1H, m, H-3); 2.09-2.20 (2H, m, H-23); 2.05-2.15 (1H, m, H-15b); 2.00-2.13 (1H, m, H-1a); 1.98 (3H, s, $COCH_3$); 1.86-1.99 (1H, m, H-2a); 1.80-1.92 (1H, m, H-1b); 1.78-1.90 (1H, m, H-12b); 1.73-1.85 (1H, m, H-7b); 1.72-1.83 (1H, m, H-6a); 1.68 (3H, s, H-26); 1.63-1.74 (1H, m, H-5); 1.63 (3H, s, H-27); 1.56-1.65 (1H, m, H-9); 1.49-1.64 (1H, m, H-2b); 1.40-1.50 (1H, m, H-4); 1.34 (3H, s, H-30); 1.19-1.26 (1H, m, H-15a); 1.11-1.19 (1H, m, H-6b); 1.08-1.21 (1H, m, H-7a); 1.02 (3H, s, H-19); 1.00 (3H, d, *J* = 6.8 Hz; H-28); 0.97 (3H, s, H-18).

^{13}C NMR (MeOD, δ): 178.33 (C-21); 171.91 ($\underline{C}OCH_3$); 138.16 (C-17); 136.94 (C-20); 130.96 (C-25); 124.07 (CH-24); 74.53 (C-16); 67.16 (C-11); 62.56 (C-3); 49.08 (C-9); 48.58 (C-14); 44.87 (C-33); 43.35 (C-5); 42.34 (C-13); 39.22 (C-34); 39.18 (C-8); 37.01 (C-4); 34.02 (C-15); 36.20 (C-10); 36.19 (C-12); 34.02 (C-1); 32.05 (C-7); 29.60 (CH_2-22); 27.78 (CH_2-23); 27.09 (C-2); 24.61 (CH_3-26); 23.09 (C-19); 22.71 (C-30); 21.52 (C-6); 19.85 ($CO\underline{C}H_3$); 16.67 (CH_3-27); 16.59 (C-18); 14.87 (C-28).

MALDI TOF/TOF: m/z $[M]^+$ calculated for $C_{33}H_{54}N_2O_5$: 558.79; found 557.52;

Anal. Calcd for $C_{33}H_{54}N_2O_5$: C, 70.93; H, 9.74; N, 5.01; O, 14.32. Found C, 70.89; H, 9.77; N, 5.05.

Methyl(2Z)-2-{(3b,4a,5a,8a,9b,11a,13a,14b,16b)-16-(acetyloxy)-3-[(2-amino-ethyl)amino]-11-hydroxy-4,8,10,14-tetramethylgonan-17-ylidene}-6-methylhept-5-enoate (7).

Purification by column chromatography (silica gel; chloroform / methanol, 10:1).

Yield: 85%, yellow crystals, m.p. 200-202°C, $[\alpha]_D^{20}$ +10.6° (*c* 1.13, $CHCl_3$).

^{1}H NMR (CDCl3, δ): 5.81 (1H, d, *J* = 8.5 Hz; H-16); 5.05 (1H, t, *J* = 6.8 Hz; H-24); 4.27-4.31 (1H, m, H-11); 3.61 (3H, s, $COOCH_3$); 2.99 (1H, d, *J* = 11.6 Hz; H-13); 2.71-2.80 (1H, m, H-34a); 2.67-2.85 (2H, m, H-35); 2.50-2.58 (1H, m, H-34b); 2.35-2.55 (2H, m, H-22); 2.21-2.30 (1H, m, H-12a); 2.08-2.22 (1H, m, H-15b); 2.01-2.21 (1H, m, H-2a); 1.98-2.08 (1H, m, H-3); 1.95 (3H, s, $COCH_3$); 1.93-2.16 (2H, m, H-23); 1.77-1.89 (1H, m, H-12b); 1.77-1.83 (1H, m, H-7b); 1.70-1.95 (2H, m, H-1); 1.64-1.73 (1H, m, H-6a); 1.64 (3H, s, H-26); 1.56 (3H, s, H-27); 1.51-1.61 (1H, m, H-5); 1.49-1.52 (1H, m, H-9); 1.32-1.42 (1H, m, H-4); 1.21-1.30 (1H, m, H-2b); 1.29 (3H, s, H-30); 1.18-1.28 (1H, m, H-15a); 1.05-1.14 (1H, m, H-7a); 1.03-1.14 (1H, m, H-6b); 0.95 (3H, s, H-19); 0.90 (3H, d, *J* = 6.2 Hz; H-28); 0.87 (3H, s, H-18).

^{13}C NMR (CDCl3, δ): 170.85 (C-21); 170.62 ($\underline{C}OCH_3$); 148.24 (C-17); 132.59 (C-25); 130.34 (C-20); 122.95 (CH-24); 74.41 (C-16); 67.92 (C-11); 62.70 (C-3); 51.39 ($COO\underline{C}H_3$); 49.05 (C-9); 48.61 (C-14); 48.36 (C-34); 43.89 (C-13); 43.70 (C-5); 41.09 (C-35); 39.30 (C-8); 38.96 (C-15); 37.08 (C-4); 36.61 (C-10); 35.79 (C-12); 34.57 (C-1); 32.59 (C-7); 29.00 (C-2); 28.82 (CH_2-22); 28.23 (CH_2-23); 25.64 (CH_3-26); 23.88 (C-19); 23.69 (C-30); 21.41 (C-6); 20.89 ($CO\underline{C}H_3$); 17.66 (CH_3-27); 17.61 (C-18); 14.85 (C-28).

MALDI TOF/TOF: m/z $[M+H]^+$ calculated for $C_{34}H_{56}N_2O_5$: 572.82; found 573.46;

Anal. Calcd for $C_{34}H_{56}N_2O_5$: C, 71.29; H, 9.85; N, 4.89; O, 13.97. Found C, 71.25; H, 9.84; N, 4.87.

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