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Synthesis of New Aminocyclitols by Selective Epoxidation of *N*-Benzyl-*N*-methyl-2-cyclohepten-1-amine and *tert*-Butyl 4-[benzyl(methyl)amino]-2,3,4,7-tetrahydro-1*H*-azepine-1-carboxylate

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Abstract—Synthesis of *N*-benzyl-*N*-methyl-2-cyclohepten-1-amine and *tert*-butyl 4-[benzyl(methyl)amino]-2,3,4,7-tetrahydro-1*H*-azepine-1-carboxylate from cyclic allyl acetates was performed. The features of stereoselective epoxidation of these substrates were investigated. The subsequent epoxide opening with water led to the formation of new pseudosaccharides, (1*RS*,2*RS*,3*RS*)-3-[benzyl(methyl)amino]-1,2-cycloheptanediol, (1*RS*,2*RS*,3*SR*)-3-[benzyl(methyl)amino]-1,2-cycloheptanediol, and (3*RS*,4*RS*,5*RS*)-3-[benzyl(methyl)amino]-4,5-azepanediol.

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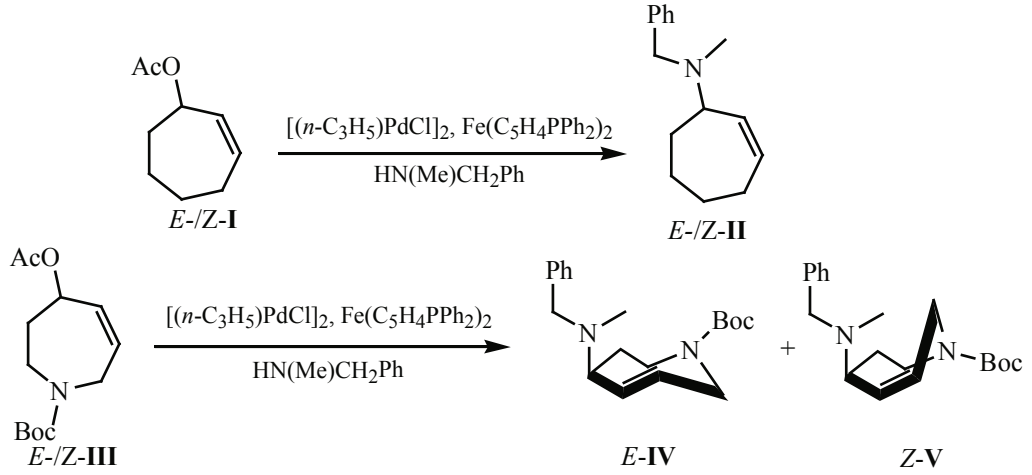
Aminocyclitols are indispensable part of many natural and synthetic biologically active substances of aminoglycoside type, antibiotics among them. Nowadays a considerable attention is attracted to the synthesis of mimetics of this fragment. This is due to the significant role played by the presence of a carbocyclic aminoalcohol and the stereochemistry in governing the biological activity of such compounds [1]. In the case of synthetic antibiotics underlain by pseudosaccharides a possibility arises to prepare compounds with preliminary determined stereochemistry [2, 3].

The main starting material for the synthesis of aminoglycoside mimetics are cycloalkenes containing in most cases a priori one or several stereocenters. These

Scheme 1.

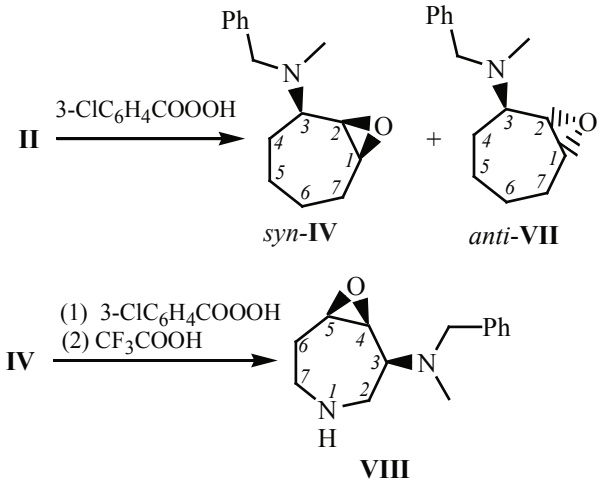


cycloalkanes can be prepared from the corresponding allyl alcohols and their derivatives. Palladium catalysis is the most efficient in reactions of allyl alcohols and their derivatives with various nucleophiles [4]. We showed that using as catalyst *n*-allylpalladium(II) chloride dimer and the ligand 1,1'-bis(diphenylphosphanyl)ferrocene made it possible to perform the nucleophilic substitution of the acetate group in 2-cycloheptenyl acetate (**I**) for *N*-benzyl-*N*-methylamine affording compound **II** in a relatively high yield. In the reaction of *tert*-butyl-4-(acetoxy)-2,3,4,7-tetrahydro-1*H*-azepine-1-carboxylate (**III**) with *N*-benzyl-*N*-methylamine formed two isomers **IV** and **V** in a ratio 3 : 1, which were successfully separated by chromatography (Scheme 1).

In the ^{1}H NMR spectrum of compound **II** a characteristic singlet signal is observed at 2.24 ppm belonging to the methyl group protons, and also an *AB* system of nonequivalent protons of the methylene group of the benzyl substituent in the region 3.53–3.68 ppm with a geminal coupling constant of ^2J 13.4 Hz.

To prove the structure of **IV** and **V** isomers we analyzed the spectra COSY ^{1}H-^{1}H. It was presumed that the reaction would afford a mixture of two regioisomers: *tert*-butyl-4-[benzyl(methyl)amino]-2,3,4,7-tetrahydro-1*H*-azepine-1-carboxylate and *tert*-butyl-6-[benzyl(methyl)-amino]-2,3,6,7-tetrahydro-1*H*-azepine-1-carboxylate. However the COSY spectra of the reaction products did not contain the correlation peaks corresponding to the coupling of the double bond protons with the protons bound to C^3 indicating the formation of two stereomers **IV** and **V**. Their spatial arrangement was analyzed applying NOESY spectra. The NOESY spectrum of isomer **IV** lacks the correlation peak H^5/H^6, consequently, these atoms are located in the *trans*-position, and the presence of the corresponding correlation peak in the spectrum of compound **V** indicates the *cis*-arrangement of the hydrogen atoms at the double bond.

Scheme 2.

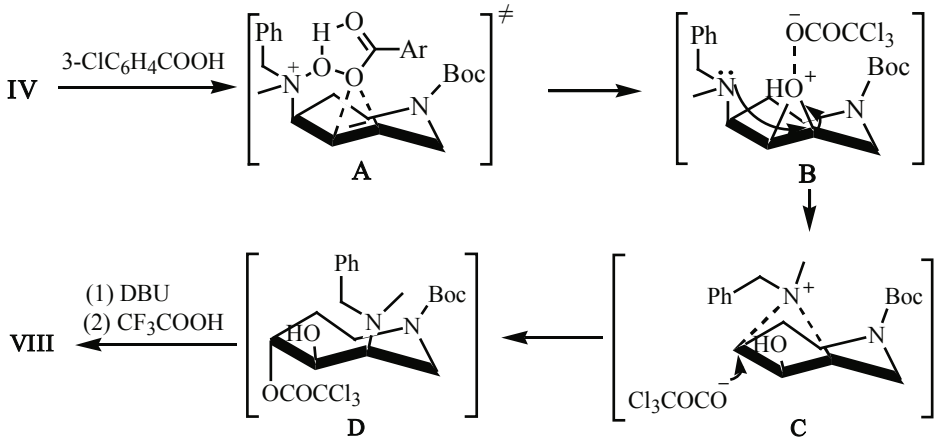


In the next stage we carried out the epoxidation of the obtained allylamines by treating with 3-chloro-perbenzoic acid under acid conditions [5]. Before analyzing the stereochemistry of epoxides obtained by the oxidation of heterocyclic allylamines **IV** and **V** we first removed the Boc-protection in order to obtain narrower signals in the ^{1}H NMR spectra (Scheme 2).

The epoxidation of compound **II** in the presence of toluenesulfonic acid resulted in the formation of a mixture of *syn*-epoxide **VI** and *anti*-epoxide **VII** in the ratio 2 : 1, whereas the oxidation in the presence of trichloroacetic acid [6] afforded only *anti*-epoxide **VII** in a lower yield, and in trifluoroacetic acid the reaction did not occur. These facts confirm the assumption on the significant influence of the nature of the acid used for the protonation of the nitrogen atom in the allylamine prior to adding the oxidant into the reaction mixture. The epoxidation process of cyclohept-2-enol is known to possess low cis-diastereoselectivity [7] caused by the high conformational flexibility of the cycloheptene. The high *trans*-diastereoselectivity of epoxidation of compound **II** in the presence of trichloroacetic acid shows, that in the transition state the seven-membered ring is in the *chair* conformation, and the olefin epoxidation proceeds from the sterically more accessible side. The formation of *syn*-epoxide **VI** at the use of toluenesulfonic acid demonstrates that the nature of the acid protonating the nitrogen not only influences the stability of the transition state, but also governs the diastereoselectivity of the oxidation process. The presence of the correleation peaks in the NOESY spectrum at 3.29/2.92 and 3.09/2.92 ppm indicates the coupling of H^{2e}/H^{3a} and H^{1e}/H^{3a} respectively, consequently, compound **VI** is a β-oriented epoxide. The absence of the cross-peak H^{3a}/H^{1a} and the presence of the cross-peak H^{2a}/H^{1a} (3.15/2.48 ppm) in the NOESY spectrum of compound **VII** show that it is an α-oriented epoxide. The vicinal constant for *syn*-epoxide **VI** $^3J_{\mathrm{H}2e_{\mathrm{H}}3a}$ amounts to 5.2 Hz, for *anti*-epoxide **VII**, $^3J_{\mathrm{H}2a_{\mathrm{H}}3a}$ 7.2 Hz confirming the axial location of the hydrogen atoms at C^2 and C^3 in the α-oriented epoxide **VII**.

The analysis of the epoxidation products of compounds **IV** and **V** showed that the mechanism of this reaction is significantly influenced by the presence of a

Scheme 3.



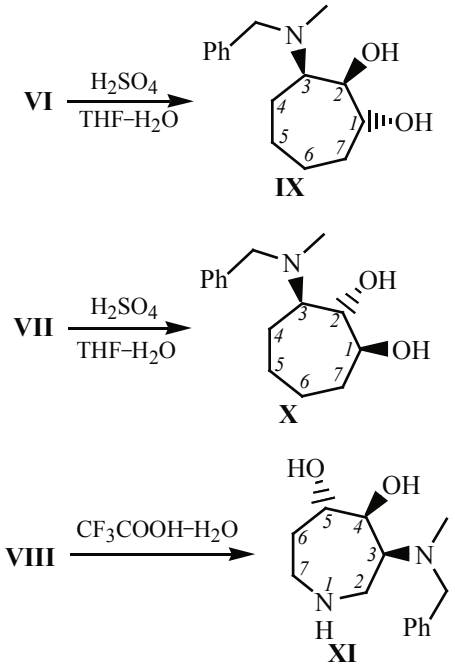
heteroatom in the seven-membered ring. The epoxidation of isomer **IV** where the hydrogen atoms at the double bond are present in the trans-position in trichloroacetic acid with subsequent Boc-deprotection leads to the formation of regioisomer **VIII**. Thus an intramolecular rearrangement occurs in the course of the oxidation. The structure of obtained epoxide **VIII** was proved by registering 2D NMR spectra with homonuclear correlation COSY and NOESY. In the COSY spectrum cross-peaks were observed corresponding to the spin-spin coupling of the protons H^6/H^5, H^4/H^3, and H^3/H^2, confirming the formation of regioisomer **VIII**. The analysis of the obtained correlations in the NOESY spectrum shows that in epoxide **VIII** molecule the NOE-effect is observed between the protons H^4/H^3 and H^4/H^5, indicating their close spatial proximity (β-oriented epoxide).

Taking into consideration the above reasoning we suggested the epoxidation mechanism for this type compounds (Scheme 3). In the initial stage substrate **IV** reacts with 3-chloroperbenzoic acid in the presence of trichloroacetic acid leading to the formation of transition state **A** [5]. Further the protonation of oxygen occurs (intermediate **B**). Therewith the nucleophile attacks not the carbon atoms of the oxirane ring , but the carbon atom linked to the nitrogen (transition state **C**) giving intermediate **D**.

At the use of toluenesulfonic acid no corresponding epoxide is formed. This is due to the occurrence in this case parallel to the epoxidation the Boc-deprotection of substrates **IV** and **V** resulting in the decomposition of the initial compounds. Isomer **V** having the *boat* conformation under these epoxidation conditions is oxidized nonselectively providing as a result a complex mixture of regio- and stereoisomers whose chromatographic separation seems impossible. The formation of isomer mixture is confirmed by the presence of two singlets at 2.30 and 2.36 ppm corresponding to the protons of the methyl groups of isomers.

Further we carried out the oxirane ring opening in epoxides **VI–VIII** by treating with water in the presence of acid (Scheme 4).

Scheme 4.



Ar = 3-ClC_6H_4.

The direction of the opening of the epoxide ring in compounds **VI–VIII** is consistent with the mechanism of the acid hydrolysis of epoxides [5]. The optimum condition for carbocyclic epoxides **VI** and **VII** is the application of sulfuric acid in the system THF–water. In the event of epoxide **VIII** trifluoroacetic acid should be used as solvent, and the rate of the epoxide ring opening is significantly lower than for the carbocyclic substrates. Therefore longer time of maintenance of the reaction mixture till the complete conversion of epoxide is required resulting in lower yield of the target compound X due to the formation of intractable side products.

Therefore we have confirmed that the epoxidation involving *N*-benzyl-*N*-methyl-2-cyclohepten-1-amine proceeds with a low diastereoselectivity, but we have succeeded to separate the obtained diastereomers by chromatography. This provides a possibility to obtain finally aminocyclitols of diverse spatial arrangement. The presence of a nitrogen atom in the ring of *tert*-butyl-4-[benzyl(methyl)amino]-2,3,4,7-tetrahydro-1*H*-azepine-1-carboxylate is an additional factor affecting the epoxidation mechanism and its regio- and stereoslectivity. Along with the conformational flexibility and lability of the seven-membered carbocycles governing the stereoselectivity of the epoxidation process, the possibility of intermolecular rearrangements should also be taken into consideration. The results obtained make it possible to perform a targeted synthesis of diastereomers of aminocyclitols for preparing new mimetics of aminoglycosides.

EXPERIMENTAL

^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were registered on a spectrometer Varian Mercury Plus 400. GC-MS spectra were recorded on an instrument Thermo Fisher Scientific Surveyor MSQ [chemical ionization at the atmospheric pressure (APCI)]. High resolution mass spectra were taken on an instrument Bruker Daltonics MicroTOF II [electrospray ionization (ESI)]. The reaction progress was monitored and the homogeneity of compounds obtained was tested by TLC on Sorbfil plates, development with iodine vapor and 1% solution in acetone of 2,2-dihydroxyindane-1,3-dione. The column chromatography was carried out on silica gel Merck 40-60.

***N*-Benzyl-*N*-methyl-2-cyclohepten-1-amine (II).** To a solution of 18 mg (0.005 mmol) of *n*-allyl-palladium(II) chloride dimer and 70 mg (0.125 mmol) of 1,1'-bis-(diphenylphosphanyl)ferrocene in 50 mL of toluene was added at stirring 5.0 mmol of cyclic allyl acetate. The mixture was stirred for 10 min, and then 1.82 g (15.0 mmol) of *N*-benzyl-*N*-methylamine was added. The reaction mixture was stirred at room temperature for 4 h, then it was diluted with 50 mL of 5% water solution of sodium hydroxide, the organic layer was separated, the solvent was removed in a vacuum. The residue was chromatographed on silica gel (eluent hexane–ethyl acetate, 3 : 1). Yield 0.94 g (87%). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.20–2.08 br.m (8H, $4CH_2$), 2.24 s (3H, NCH_3), 3.38 d (1H, CH, ^2J 7.5 Hz), 3.57 d, 3.64 d (2H, $C\underline{H}_2Ph$, ^2J 15.0, ^2J 13.4 Hz), 5.75–5.95 m (2H, CH=CH), 7.12–7.42 m (5H, Ph). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 26.96 (C^5), 28.70 (C^6), 28.74 (C^7), 29.14 (C^4), 37.95 (NCH_3), 57.89 (CH_2Ph), 64.11 (C^3), 126.75, 128.27, 128.78 (C_{arom}), 131.02 (C^2), 135.40 (C^1), 140.30 (C_{arom}). Found, *m/z:* 216.27 $[M]^+$ (APCI), 216.1745 $[M + H]^+$ (ESI). $C_{15}H_{21}N$. Calculated *M* 216.1747.

Compounds **IV, V** were obtained similarly.

***tert*-Butyl-4-[benzyl(methyl)amino]-(*E*)-2,3,4,7-tetrahydro-1*H*-azepine-1-carboxylate (IV).** Yield 0.85 g (54%). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.44 s (9H, Boc), 1.76–2.12 m (2H, 3-CH_2), 2.22 s (3H, NCH_3), 3.39–3.85 m (6H, $3CH_2N$), 3.87–4.20 br.m (1H, CH), 5.72–5.92 m (2H, CH=CH), 7.18–7.40 m (5H, Ph). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 27.30 (C^6), 27.48 (C^2), 27.63 [$C(\underline{C}H_3)_3$], 36.99 (NCH_3), 45.58 (C^7), 56.88 ($\underline{C}H_2Ph$), 62.13 (C^5), 78.08 [$\underline{C}(CH_3)_3$], 126.06, 127.46, 127.69 (C_{arom}), 128.05 (C^3), 132.05 (C^4), 139.32 (C_{arom}), 153.80 (C=O). Found, *m/z:* 317.24 $[M]^+$ (APCI), 317.2229 $[M + H]^+$ (ESI). $C_{19}H_{28}N_2O_2$. Calculated *M* 317.2224.

***tert*-Butyl-4-[benzyl(methyl)amino]-(*Z*)-2,3,4,7-tetrahydro-1*H*-azepine-1-carboxylate (V).** Yield 0.29 g (18%). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.41–1.51 m (2H, 3-CH_2), 1.46 s (9H, Boc), 2.29 s (3H, NCH_3), 2.89–3.21 br.m (1H, CH), 3.42–4.78 br.m (6H, $3CH_2N$), 5.74–5.87 m (2H, CH=CH), 7.17–7.37 m (5H, Ph). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 27.29 (C^6), 27.61 [$C(\underline{C}H_3)_3$], 36.87 (NCH_3), 44.12 (C^2), 44.24 (C^7), 56.92 ($\underline{C}H_2Ph$), 60.38 (C^5), 78.02 [$\underline{C}(CH_3)_3$], 126.05, 127.46 (C_{arom}), 127.71 (C^3), 127.77 (C_{arom}), 133.74 (C^4), 139.31 (C_{arom}), 153.86 (C=O). Found, *m/z:* 317.24 $[M]^+$ (APCI), 317.2233 $[M + H]^+$ (ESI). $C_{19}H_{28}N_2O_2$. Calculated *M* 317.2224.

1,2-Epoxy-3-(*N*-benzyl-*N*-methylamino)cycloheptanes VI, VII. To a solution of 0.94 g (4.4 mmol) of

compound **II** in 50 mL of dichloromethane was added at stirring 2.50 g (15.4 mmol) of trichloroacetic acid. The mixture was stirred for 30 min, then 0.91 g (5.3 mmol) of *m*-chloroperbenzoic acid was added by portions. The reaction mixture was stirred at room temperature for 3 h. The excess of *m*-chloroperbenzoic acid was neutralized with 1 mL of saturated water solution of sodium sulfite and the saturated water solution of sodium hydrogen carbonate was used to adjust the medium to pH 8.0. The organic layer was separated and to the solution was added at stirring 0.67 g (4.4 mmol) of 1,8-diazabicyclo[5.4.0]undec-7-ene. The reaction mixture was stirred at room temperature for 1 h, diluted with water, the organic layer was separated and dried with sodium sulfate. The solvent was removed at a reduced pressure, the residue was subjected to chromatography on silica gel (eluent hexane–ethyl acetate, 2 : 1).

(1*RS*,2*SR*,3*RS*)-1,2-**Epoxy**-3-(***N*-benzyl-*N*-methylamino)cycloheptane (VI).** Yield 0.15 g (15%). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.70–0.82 m (1H, CH_2), 1.26–1.60 m (4H, $2CH_2$), 1.62–1.70 m (1H, CH_2), 1.71–1.79 m (2H, CH_2), 2.32 s (3H, NCH_3), 2.92 d.d (1H, 1-CH, ^3J 11.5, ^3J 2.3 Hz), 3.08 t (1H, 3-CH, ^3J 5.2 Hz), 3.29 d (1H, 2-CH, ^3J 4.7 Hz), 3.58 d, 3.78 d (2H, C$\underline{H}_2$Ph, ^2J 13.5 Hz), 7.14–7.46 m (5H, Ph). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 23.31 (C^4), 24.09 (C^6), 27.30 (C^5), 28.27 (C^7), 38.17 (NCH_3), 53.00 (C^1), 58.14 ($\underline{C}H_2$Ph), 59.90 (C^2), 63.68 (C^3), 126.70, 128.09, 128.55 and 135.73 (C_{arom}). Found, *m/z:* 232.20 $[M]^+$ (APCI), 232.1699 $[M+H]^+$ (ESI). $C_{15}H_{21}NO$. Calculated *M* 232.1696.

(1*RS*,2*SR*,3*SR*)-1,2-Epoxy-3-(*N*-benzyl-*N*-methylamino)cycloheptane (VII). Yield 0.34 g (33%). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.19–1.27 m (1H, CH_2), 1.30–1.41 m (2H, CH_2), 1.54–1.75 m (2H, CH_2), 1.85–1.98 m (2H, CH_2), 2.23–2.27 m (1H, CH_2), 2.29 s (3H, NCH_3), 2.51 d.d (1H, 3-CH, ^3J 10.4, ^3J 7.2 Hz), 2.98–3.06 m (1H, 1-CH), 3.14 d.d (1H, 2-CH, ^3J 7.0, ^3J 5.0 Hz), 3.66 d, 3.73 d (2H, C$\underline{H}_2$Ph, ^2J 13.4 Hz), 7.12–7.46 m (5H, Ph). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 24.11 (C^6), 29.17 (C^5), 29.75 (C^7), 30.87 (C^4), 38.30 (NCH_3), 53.09 (C^1), 55.87 (C^2), 58.70 ($\underline{C}H_2$Ph), 65.88 (C^3), 126.80, 128.01, 128.78, 135.85 (C_{arom}). Found, *m/z:* 232.20 $[M]^+$ (APCI), 232.1694 $[M+H]^+$ (ESI). $C_{15}H_{21}NO$. Calculated *M* 232.1696.

(3*RS*,4*SR*,5*RS*)-4,5-Epoxy-3-(*N*-benzyl-*N*-methylamino)azepane (VIII). To a solution of 0.85 g (2.7 mmol) of compound **IV** in 50 mL of dichloromethane was added at stirring 1.03 g (5.4 mmol) of toluenesulfonic acid monohydrate. The mixture was stirred for 30 min, then 0.56 g (3.2 mmol) of *m*-chloroperbenzoic acid was added by portions. The reaction mixture was stirred at room temperature for 20 h. The excess of *m*-chloroperbenzoic acid was neutralized with 1 mL of saturated water solution of sodium sulfite and with saturated water solution of sodium hydrogen carbonate the reaction of the medium was adjusted to pH 8.0. The organic layer was separated and at stirring to the solution was added 0.41 g (2.7 mmol) of 1,8-diazabicyclo[5.4.0]undec-7-ene. The stirring was continued for 1 h, the reaction mixture was washed with water (3 × 50 mL), the organic layer was separated and dried with sodium sulfate.. To a solution 1.85 g (16.2 mmol) of trifluoroacetic acid was added, the reaction mixture was stirred at room temperature for 3 h, then it was neutralized with a saturated water solution of potassium carbonate. The water layer was separated and extracted with ethyl acetate (5 × 20 mL), the combined organic solutions were dried with sodium sulfate. The solvent was removed at a reduced pressure. Yield 0.30 g (52%). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.01 d.d.d (1H, 6-CH_2, ^2J 15.9, ^3J 12.4, ^3J 3.9 Hz), 2.32 d.d.d (1H, 6-CH_2, ^2J 15.4, ^3J 6.1, ^3J 4.3 Hz), 2.40 s (3H, NCH_3), 2.50 br.s (1H, NH), 2.63–2.72 m (1H, C$\underline{H}_2$NH), 2.77 d.d (1H, 2-CH, ^3J 12.8, ^3J 10.9 Hz), 2.95 d.t (1H, C$\underline{H}_2$NH, ^2J 13.6, ^3J 3.5 Hz), 3.12 d.d (1H, C$\underline{H}_2$NH, ^2J 12.9, ^3J 3.2 Hz), 3.18 d (1H, 3-CH, ^3J 3.3 Hz), 3.12–3.21 m (1H, 5-CH), 3.40 d (1H, 4-CH, ^3J 4.7 Hz), 3.71 d, 3.84 d (2H, C$\underline{H}_2$Ph, ^2J 13.6 Hz), 7.21–7.40 m (5H, Ph). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 31.22 (C^6), 38.64 (NCH_3), 44.98 (C^7), 45.50 (C^2), 52.40 (C^5), 58.55 ($\underline{C}H_2$Ph), 58.74 (C^4), 64.86 (C^3), 68.86 (C^3), 127.00, 128.40, 128.73, 135.78 (C_{arom}). Found, *m/z:* 233.17 $[M]^+$ (APCI), 233.1643 $[M+H]^+$ (ESI). $C_{14}H_{20}N_2O$. Calculated *M* 233.1648.

3-[Benzyl(methyl)amino]-1,2-cycloheptanediols IX, X. In 20 mL of a mixture THF–water, 2 : 1, was dissolved 0.15 g (0.66 mmol) of epoxide, and at stirring 0.20 g (2.0 mmol) of conc. sulfuric acid was added. The reaction mixture was stirred at 50°C for 2 h. On cooling the reaction mixture was neutralized with the saturated water solution of potassium carbonate and diluted with 20 mL of ethyl acetate. The organic layer was dried with sodium sulfate, the solvent was evaporated in a vacuum, the residue was chromatographed on silica gel (eluent ethyl acetate).

(1*RS*,2*RS*,3*RS*)-3-[Benzyl(methyl)amino]-1,2-cycloheptanediol (IX). Yield 0.12 g (72%). ^{1}H NMR

spectrum (C_6D_6), δ, ppm: 1.97 d.d (1H, CH_2, ^2J 23.7, ^3J 11.5 Hz), 1.23 d.d (1H, CH_2, ^2J 24.5, ^3J 11.3 Hz), 1.29–1.38 m (1H, CH_2), 1.42–1.51 m (1H, CH_2), 1.52–1.75 m (4H, $2CH_2$), 2.05 s (3H, NCH_3), 2.23 s (1H, OH), 2.27 s (1H, OH), 2.93 d.t (1H, 3-CH, ^3J 11.9, ^3J 6.0 Hz), 3.41 d, 3.51 d (2H, C<u>H</u>$_2$Ph, ^2J 13.2 Hz), 3.63–3.70 m (1H, 2-CH), 3.74 t.d (1H, 1-CH, ^3J 9.1, ^3J 2.2 Hz), 7.17–7.37 m (5H, Ph). ^{13}C NMR spectrum (C_6D_6), δ, ppm: 23.78 (C^4), 25.65 (C^5), 27.37 (C^6), 36.46 (C^7), 38,62 (NCH_3), 60.61 (<u>C</u>H_2Ph), 63.27 (C^3), 72.94 (C^1), 75.38 (C^2), 127.98, 128.98, 129.32, 138.84 (C_{arom}). Found, *m/z:* 250.16 $[M]^+$ (APCI), 250.1794 $[M + H]^+$ (ESI). $C_{15}H_{23}NO_2$. Calculated *M* 250.1802.

(1*RS*,2*RS*,3*SR*)-3-[Benzyl(methyl)amino]-1,2-cycloheptanediol (X). Yield 0.10 g (64%). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.55–0.64 m (2H, CH_2), 0.66–0.71 m (1H, CH_2), 0.79 d.d (1H, CH_2, ^2J 18.9, ^3J 10.0 Hz), 0.84–0.92 m (2H, CH_2), 0.95–1.10 m (2H, CH_2), 1.39 s (3H, NCH_3), 1.67 t (1H, 3-CH, ^3J 9.4 Hz), 2.54 d.d (1H, 2-CH, ^3J 9.2, ^3J 6.7 Hz), 2.59–2.67 m (1H, 1-CH), 2.73 d, 2.96 d (2H, C<u>H</u>$_2$Ph, ^2J 13.3 Hz), 3.55 d (1H, 1-CHO<u>H</u>, ^3J 3.2 Hz), 3.78 s (1H, 1-CHO<u>H</u>), 6.49–6.65 m (5H, Ph). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 20.85 (C^4), 21.32 (C^5), 24.59 (C^6), 30.50 (C^7), 35.92 (NCH_3), 57.13 (<u>C</u>H_2Ph), 64.70 (C^3), 74.60 (C^1), 76.29 (C^2), 126.58, 127.99, 128.50, 139.19 (C_{arom}). Found, *m/z:* 250.16 $[M]^+$ (APCI), 250.1795 $[M + H]^+$ (ESI). $C_{15}H_{23}NO_2$. Calculated *M* 250.1802.

(3*RS*,4*RS*,5*RS*)-3-[Benzyl(methyl)amino]-4,5-azepanediol (XI). In 20 mL of dichloromethane was dissolved 0.15 g (0.67 mmol) of compound **VIII**, and at stirring 0.76 g (6.7 mmol) of trifluoroacetic acid was added. The reaction mixture was boiled for 8 h, on cooling it was neutralized with the saturated water solution of potassium carbonate. The water layer was separated and extracted with ethyl acetate (5 × 20 mL), the combined organic solutions were dried with sodium sulfate. The solvent was removed at a reduced pressure. Yield 0.07 g (41%). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.53 d (1H, 6-CH_2, ^2J 14.4 Hz), 1.83 d.d (1H, 6-CH_2, ^2J 14.4, ^3J 11.0 Hz), 2.18 c (3H, NCH_3), 2.52–2.61 m (1H, 7-CH_2), 2.63–2.73 m (1H, 7-CH_2), 2.82 d.d (1H, 2-CH_2, ^2J 12.3, ^3J 6.4 Hz), 2.90–3.00 m (1H, 2-CH_2), 3.24 br.s (1H, NH), 3.24 d.d (1H, 3-CH, ^3J 9.8, ^3J 6.5 Hz), 3.57 d, 3.71 d (2H, C<u>H</u>$_2$Ph, ^2J 13.9 Hz), 3.78 d (1H, 5-CH, ^3J 5.1 Hz), 4.52 br.s (2H, 2OH), 7.09–7.41 m (5H, Ph). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 35.45 (C^6), 38.26 (NCH_3), 41.10 (C^7), 44.93 (C^2), 57.42 (<u>C</u>H_2Ph), 58.73 (C^3), 69.27 (C^5), 73.06 (C^4), 127.58 (C_{arom}). Found, *m/z:* 251.16 $[M]^+$ (APCI), 251.1754 $[M + H]^+$ (ESI). $C_{14}H_{22}N_2O_2$. Calculated *M* 251.1754.

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