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Ring Opening Reactions of 1,2-Didehydroprolines. Part II. Synthesis of 5-Amino-2,4-dihydroxypentanoic Acids, their 2-Piperidones and Pentanolides [1]

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Summary. NMR spectroscopic investigations on 1,2-didehydroproline in alkaline deuterium oxide revealed incorporation of deuterium at position C-3, presumably due to the presence of acyclic 5-amino-2-oxopentanoate in solution. Reduction of this equilibrium mixture with hydride reagents generally yields prolines together with the 2-hydroxy acids. It could be shown that the ratio of the two products depends strongly on the *pH*. This allowed the optimization of reaction conditions for the preparation of the target compounds (2*R*,4*R*)- and (2*S*,4*R*)-5-amino-2,4-dihydroxypentanoic acid. In order to separate these isomers and unambiguously assign their respective structures, the (3*R*,5*R*)- and (3*S*,5*R*)-3,5-dibenzoyloxy-2-piperidones were synthesized as the key intermediates by lactamization and benzoylation. Lactames were also directly transformed to the corresponding lactones.

Keywords. 1,2-Didehydroprolines; Deuteroprolines; Carbonyl reduction; 2-Piperidones; Amino acids.

Introduction

In aqueous solution 1,2-didehydroproline (**2a**) is in a structural equilibrium with the acyclic 5-amino-2-oxopentanoic acid (**4a**). Fairly stable, **4a** can be obtained on a preparative scale [2]. The hydroxy derivative **2b**, however, undergoes rapid elimination of water, leading to pyrrole-2-carboxylic acid. As salts **1a**, **1b**, both **3a**, and **3b** show diminished tendency to decompose [2, 3].

NMR spectroscopic investigation of **1a** in alkaline solution in deuterium oxide ($pH^* \sim 13$) revealed incorporation of deuterium into position C-3, presumably due to the presence of minor amounts of the 2-oxocarboxylate **3a** or of its enolate. These small amounts could not be detected by NMR, but the explanation is

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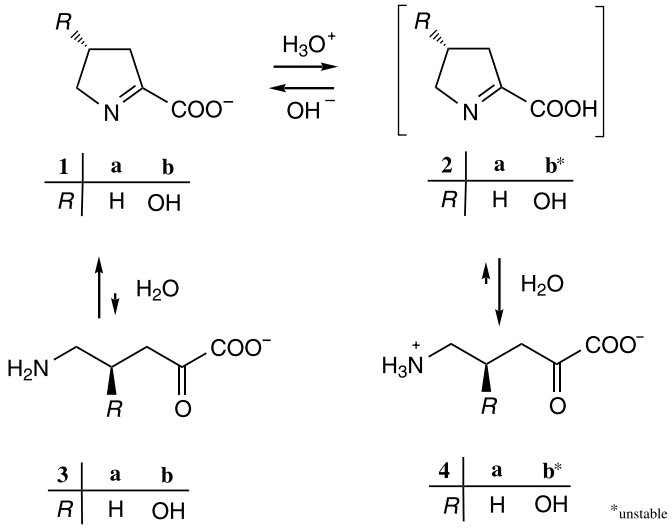
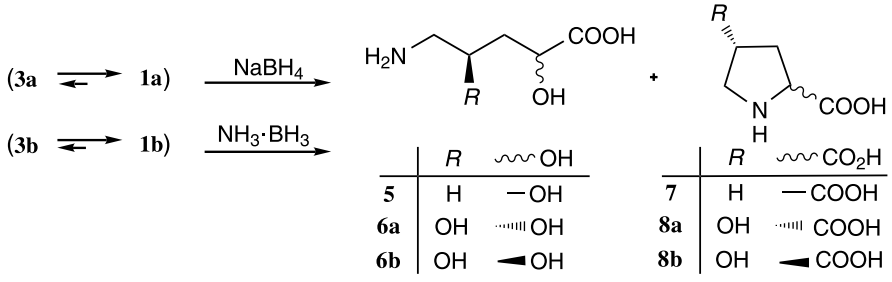


Scheme 1



Scheme 2

supported by the result that reduction of **2a** and **2b** generally yields the 2-hydroxyacids **5**, **6a**, and **6b** apart from the expected prolines **7**, **8a**, and **8b**.

Results and Discussion

We became interested in the reduction processes when it turned out that the ratio of the products could be controlled by fixing the *pH* of the reaction medium. When the reductions were carried out with sodium tetrahydroborate or with $NH_3 \cdot BH_3$ at *pH* ~13, the acylic 2-hydroxy acids **5**, **6a**, and **6b** formed in amounts up to 65%. At *pH* values resulting from the hydrolysis of the tetrahydroborate or stabilized at ~ 8 by addition of ammonium chloride, formation of prolines **7**, **8a**, and **8b** took place exclusively, with only ~ 5% of **5**, **6a**, and **6b**.

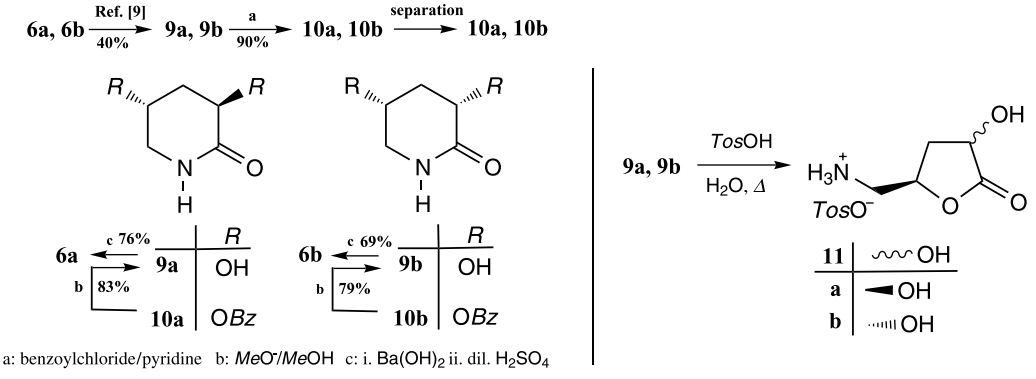
As an explanation for this dichotomy we would like to suggest that the primary amino group in **3a** or **3b** (with strongly alkaline medium, in contrast to the protonated species **4a** and **4b** at lower *pH*) attaches as a nucleophile to the reducing agent, which then by intramolecular hydrogen transfer reduces the 2-oxo moiety. This accelerating entropic effect recompenses the kinetic disadvantage due to the

unfavorable equilibrium of **3a**, **3b** *versus* **1a**, **1b**. Whereas the assistance of hydroxy and oxo groups in directing the hydride transfer towards certain functionalities is well established [4], there are no references yet on the supporting role of amines for reduction processes carried out in protic polar solvents.

Controlling the ratio of products by adjusting the *pH* allows the synthesis of 5-amino-2-hydroxycarboxylates and of prolines in moderate and good yields. A result of our deuteration experiments is the synthesis of the deuterated 2-hydroxyamino acid [3,3-$^2H_2$]-**5** and of 3,3-dideuteroproline ([3,3-$^2H_2$]-**7**). The latter compound is produced in 84% yield, thereby extending the list of published deuterated prolines [5].

The main intention of the investigation was the synthesis and characterization of yet unreported isomeric amino acids (2*R*,4*R*)- and (2*S*,4*R*)-5-amino-2,4-dihydroxypentanoic acid (**6a**, **6b**) and their lactames **9a**, **9b**. *Traube* and *Fischer* have described [6] the synthesis of an δ-amino-α,γ-dioxyvaleric acid and the conversion to the lactame and lactone but neglected to comment on the stereochemistry of their products. Six-membered nitrogen containing heterocycles with hydroxyl groups frequently occur in natural products and are part of several biologically active compounds [7].

Starting material for the sodium salt **1b** was the readily available methyl (*R*)-4-hydroxy-1-pyrroline-2-carboxylate [8], which was saponified and brought to $pH \sim 13$ with aqueous sodium hydroxide. Reduction with $NH_3 \cdot BH_3$ gave a mixture of 56–60% **6a**:**6b** (1:1) and 40–44% of the isomeric 4-hydroxyprolines (**8a**, **8b**), which were removed by ion exchange chromatography. The mixture of **6a** and **6b** obtained in about 50% yield could not be resolved and was therefore converted to the dihydroxylactames **9a**, **9b** by the hexamethyldisilazan method described by *Pellegata et al.* [9] in 40% yield. The mixture **9a**, **9b** also resisted separation, but the corresponding dibenzoates **10a**, **10b** could be separated quantitatively resulting in pure **10a** and **10b**. Diols **9a** and **9b** were recovered by transesterification according to *Zemplen* [10]. Since the free amino acids **6a** and **6b** are known [6] to rapidly lactonize in the presence of excessive mineral acid, ring opening of **9a** and **9b** was carried out with aqueous barium hydroxide followed by the addition of sulfuric acid, avoiding any ion exchange procedure.



a: benzoylchloride/pyridine b: *MeO*⁻/*Me*OH c: i. $Ba(OH)_2$ ii. dil. H_2SO_4

Scheme 3

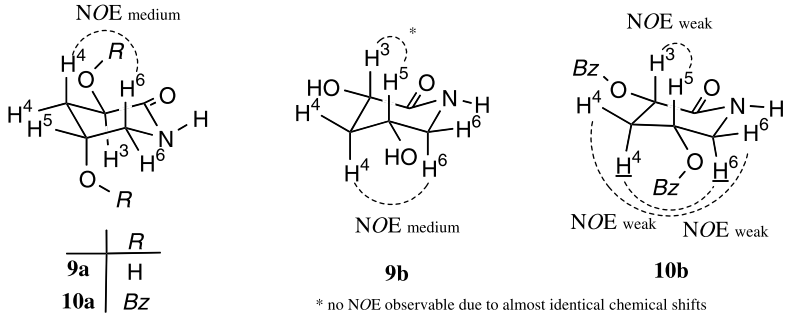


Fig. 1. N*O*Es of **9a**, **9b**, **10a**, and **10b**

Using the aforementioned high lactonization tendency to advantage we finally could show that the diastereomeric lactones **11a** and **11b** are readily obtained as nicely crystallizing 4-methylbenzenesulfonates in a single step hydrolyzing-recyclizing procedure starting with the dihydroxylactames **9a** and **9b**.

The configurations of **6a** (2*R*,4*R*) and **6b** (2*S*,4*R*) were established by NMR spectroscopy interpreting the vicinal ^{1}H,^{1}H-coupling constants of the dibenzoates **10a** and **10b** as well as by interpreting their 2D-N*O*ESY spectra. The experimental data indicate an unequivocal chair conformation for **10a** and agree with the predicted N*O*Es and the expected long range W-couplings between H^4 and H^6 and H^5 and NH, which were found to be 2.0 and 0.8 Hz. The unprotected **9a** shows essentially the same conformation. In the case of the *cis*-configured compounds **9b** differs significantly from **10b**. The NMR data of **9b** indicate a chair geometry with both hydroxy groups in equatorial position. Reduced diaxial couplings (between $\underline{H}^4$ and H^5, and H^5 and $\underline{H}^6$) point to a slightly distorted chair conformation in the dibenzoyl lactame **10b**. This is also borne out by small long range W-couplings (of 0.5 and 0.9 Hz) as well as by weak N*O*Es between the two proton pairs H^4 and H^6 and $\underline{H}^4$ and $\underline{H}^6$.

Experimental

Melting points (uncorrected) were determined on a *Kofler* heating table. Optical rotations were measured on a Polarimeter 241 (Perkin-Elmer). NMR spectra were recorded on a Bruker Avance DRX 400 WB NMR spectrometer in D_2O solutions at a temperature of 298 K (if not otherwise indicated). For ^{1}H NMR spectra (resonance frequency 400.13 MHz) the HOD signal was used as internal reference ($\delta = 4.90$). ^{13}C NMR spectra were recorded at a frequency of 100.62 MHz with sodium 3-trimethylsilyl-1-propansulfonate as external reference (if not otherwise indicated). Coupling constants for strongly coupled spin systems were derived from simulations with the Xsim/NUMRIT software package (version 971120) [10] on a Silicon Graphics O2 workstation. Acidities in D_2O solutions are reported as pH^* – values. They are the result of measurements with test paper and are not to be confused with *pD*s. Column dimensions used for ion exchange and column chromatography were 20×1.4 cm (A), 35×3.5 cm (B), and 27×2 cm (C). The separation of benzoates **10a** and **10b** was performed by cyclic chromatography on a Chromatotron, model 8924 (Co. Harrison Research, Palo Alto, USA); thickness of the silica layer 4 mm. Elemental analyses of **6a**, **6b**, **9a**, **9b**, **10a**, **10b**, **11a**, and **11b** agreed favourably with the calculated values.

*Incorporation of Deuterium into **2a** and its Reduction Products*

Solutions (~ 0.2 M) of sodium 1-pyrroline-2-carboxylate (Na-**1a**) [3] in D_2O adjusted to $pH^* \sim 13$ with aqueous NaOD (40%) were investigated by ^1H and ^{13}C NMR spectroscopy after equilibrating for 12 d. Integration of the residual hydrogen at C-3 showed about 10 atomic %, practically exclusively due to the monodeutero compound. The ^{13}C NMR data of the C-3 dideuterated products are followed by the data of the monodeuterated materials in brackets.

Sodium 3,3-Dideutero-1-pyrroline-2-carboxylate (Na-3,3-$^2H_2$-**1a**)

^{13}C NMR (dioxane = 67.19 ppm): $\delta = 22.22$ [22.32] (C-4), 35.73 (quint, $J(^{13}C, ^2H) = 20$ Hz) [36.02, t, $J = 20$ Hz] (C-3), 60.81 (C-5), 142.47 (C=N), 176.23 (CO) ppm.

Reduction at $pH^* \sim 13$

5-Amino-3,3-dideutero-2-hydroxypentanoic acid (3,3-$^2H_2$-**5**)

An equilibrated solution of Na-**1a** in D_2O/NaOD was reduced (ice bath) with the sixfold molar amount of $NaBH_4$. After 12 h the reaction mixture was adjusted to *pH* 2 with 6 *M* HCl and desalted as usual (Dowex 50 W, eluent 1 *M* NH_3). After evaporation of the eluates *in vacuo*, the oily residue formed crystals upon addition of hot methanol yielding 50–65% product. Minor amounts of by-product 3,3-$^2H_2$-**7** were obtained upon concentrating the mother liquors of the crystallization *in vacuo* to dryness and passing the residue through a column of Dowex 50 W (dimension A/4 mmol scale) with 5 dm^3 of H_2O. 3,3-$^2H_2$-**7** contained 13% D at C-2; ^{13}C NMR (dioxane = 67.19 ppm): $\delta = 22.93$ [23.02] (C-4), 30.48 (quint, $J(^{13}C, ^2H) = 19.8$ Hz) [30.89, t, $J = 19$ Hz] (C-3), 39.68 (C-5), 71.73 [71.78] (C-2), 182.98 (CO) ppm; ^{13}C NMR spectrum of the undeuterated material: Ref. [12].

Reduction at $pH^* \sim 8$

3,3-Dideuteroproline (3,3-$^2H_2$-**7**)

The strongly basic solution of Na-3,3-$^2H_2$-**1a** was brought to $pH \sim 7$–8 with 6 *M* HCl and buffered by addition of NH_4Cl (2.4 molar amount) before the reducing agent was added. Reduction and isolation of the product by washing the Dowex 50 W with H_2O were carried out as described for $pH^* \sim 13$ (see above). Yield of 3,3-$^2H_2$-**7** 84%; D content at C-2 7%; ^{13}C NMR (dioxane = 67.19 ppm): $\delta = 23.95$ [24.05] (C-4), 28.77 (quint, $J(^{13}C, ^2H) = 20.9$ Hz) [29.08, t, $J = 20.6$ Hz] (C-3), 46.47 (C-5), 61.49 [61.55] (C-2), 175.02 (CO) ppm.

*(3R,5R)- and (3S,5R)-3,5-Dibenzoyloxy-2-piperidone **10a** and **10b***

Crude methyl (*R*)-4-hydroxy-1-pyrroline-2-carboxylate (prepared on a 40 mmol scale according to Ref. [8]) was dissolved under Ar in 70 cm^3 of 1 *M* NaOH in an ice bath. $NH_3 \cdot BH_3$ (1.0 g, 32 mmol) was added to the stirred solution, and stirring was continued for 72 h at room temperature. The reaction mixture was adjusted to *pH* 2 by addition of 6 *M* HCl and was desalted as usual (Dowex 50 W, column B). Evaporation of the eluates *in vacuo* afforded about 6 g of an oil that partly crystallized. NMR analysis indicated that the mixture consisted of **6a** + **6b** (56–60%, 1:1) and of the hydroxyprolines **8a** + **8b** (40–44%, 1:4). To remove **8a**, **8b** the oil was passed through a Dowex 50 W column (dimension C) by rinsing with 15 dm^3 of H_2O. Elution with 1 *M* NH_3 and evaporation of the fractions left behind the crude **6a**, **6b** (3.2 g, 54%) as a foam. Cyclization to the lactames **9a** and **9b** was achieved by the hexamethyldisilazane method described in Ref. [9]. Yield 1.12 g (40%); colourless needles.

The benzoylation of **9a**, **9b** was carried out in 30 cm^3 of ice cold $CHCl_3$ with the four times molar amount of benzoyl chloride and pyridine, and catalysis with 4-(dimethylamino)pyridine (5 mol%). After 10 h at room temp. the solvent was removed *in vacuo*. The residue was taken up in 80 cm^3 of ethyl acetate, and the solution was extracted subsequently with H_2O, 1 *M* HCl, and finally with satd. aqueous $NaHCO_3$. The organic layer was dried (Na_2SO_4) and the solvent evaporated *in vacuo*. Thin layer analysis (silica, $CHCl_3$:*Me*OH = 95:5) of the crude oil (3.8 g) indicated **10a** ($R_f = 0.46$), **10b** ($R_f = 0.30$), and components at the start and the front. Chromatography of the oil on a Chromatotron ($CHCl_3$:*Me*OH = 99:1) afforded **10a** and **10b** (1.3 g each, 90%).

(3R,5R)-3,5-Dibenzoyloxy-2-piperidone (**10a**, $C_{19}H_{17}NO_5$)

Colourless needles, mp 147–149°C ($CHCl_3$:ether = 1:9); $[\alpha]_D^{20} = 172.5°\ cm^2\ g^{-1}$ ($c = 1.53$, $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta = 2.44$ (ddd, $J = 2.9$, 11.4, 13.7 Hz, C–C*H*H–C), 2.70 (dddd, $J = 2.0$, 4.5, 6.4, 13.7 Hz, C–CH*H*–C), 3.62 (dddd, $J = 2.0$, 2.9, 2.9, 13.6 Hz, N–C*H*H), 3.80 (ddd, $J = 1.4$, 3.8, 13.6 Hz, N–CH*H*), 5.60 (ddddd, $J = 0.8$, 2.9, 2.9, 3.8, 4.5 Hz, O–CH), 5.79 (dd, $J = 6.4$, 11.4 Hz, O–CH), 6.15 (bs, NH), 7.35–7.48 (m, $4H_{Ar}$), 7.51–7.63 (m, $2H_{Ar}$), 7.99–8.11 (m, $4H_{Ar}$) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 31.58$ (CH_2), 46.20 (N–CH_2), 66.34 (O–CH), 66.39 (O–CH), 128.38, 128.58, 129.77, 129.97, 133.34, 133.60 (Ar), 129.30, 129.49 (Ar_{qu}), 165.62, 165.70, 168.40 (CO) ppm.

(3S,5R)-3,5-Dibenzoyloxy-2-piperidone (**10b**, $C_{19}H_{17}NO_5$)

Colourless fluffy needles, mp 114–116°C ($CHCl_3$:ether = 1:9); $[\alpha]_D^{20} = 59.2°\ cm^2\ g^{-1}$ ($c = 1.03$, $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta = 2.46$ (dddd, $J = 0.9$, 6.7, 8.0, 14.2 Hz, C–C*H*H–C), 2.74 (dddd, $J = 0.5$, 4.9, 7.1, 14.2 Hz, C–CH*H*–C), 3.63 (dddd, $J = 0.9$, 3.8, 4.9, 13.1 Hz, N–C*H*H), 3.71 (dddd, $J = 0.5$, 2.4, 4.0, 13.1 Hz, N–CH*H*), 5.46 (ddddd, $J = 0.5$, 4.0, 4.9, 4,9, 6.7 Hz, O–CH), 5.62 (dd, $J = 7.1$, 8.0 Hz, O–CH), 6.21 (bs, NH), 7.30–7.44 (m, $4H_{Ar}$), 7.47–7.59 (m, $2H_{Ar}$), 7.97–8.04 (m, $4H_{Ar}$) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 32.59$ (CH_2), 45.49 (N–CH_2), 65.48 (O–CH), 66.29 (O–CH), 128.27, 128.45, 129.77, 129.94, 133.24, 133.43 (Ar), 129.34, 129.41 (Ar_{qu}), 165.54, 165.61, 168.40 (CO) ppm.

*(3R,5R)- and (3S,5R)-3,5-Dihydroxy-2-piperidones **9a** and **9b***

Under Ar three small drops of a 1 *M* solution of $NaOCH_3$ in CH_3OH were added to solutions of 1.5 mmol of **10a** or **10b** in 50 cm^3 of dry CH_3OH. After 48–60 h the starting materials and the intermediate mono benzoates could not longer be detected by thin layer chromatography (silica 60, $CHCl_3$:*Me*OH = 9:1). Acetic acid (1 drop) was added, the solvent was evaporated *in vacuo*, and the residue was filtered through a short column of silica (eluent: $CHCl_3$:*Me*OH = 7:3) and crystallized from CH_3OH–ether.

(3R,5R)-3,5-Dihydroxy-2-piperidone (**9a**, $C_5H_9NO_3$)

Yield 83%; colourless needles, mp 131–133°C; $[\alpha]_D^{20} = 61.8°\ cm^2\ g^{-1}$ ($c = 1.2$, *Me*OH); ^{1}H NMR: $\delta = 2.13$ (ddd, $J = 2.9$, 10.8, 13.6 Hz, C–C*H*H–C), 2.49 (dddd, $J = 1.8$, 5.1, 6.3, 13.6 Hz, C–CH*H*–C), 3.41 (ddd, $J = 1.8$, 3.4, 13.5 Hz, N–C*H*H), 3.70 (dd, $J = 3.8$, 13.5 Hz, N–CH*H*), 4.48 (dddd, $J = 2.9$, 3.4, 3.8, 5.1 Hz, O–CH), 4.53 (dd, $J = 6.3$, 10.8 Hz, O–CH) ppm; ^{13}C NMR: $\delta = 35.91$ (CH_2), 48.39 (N–CH_2), 63.63 (O–CH), 64.69 (O–CH), 175.18 (CO) ppm.

(3S,5R)-3,5-Dihydroxy-2-piperidone (**9b**, $C_5H_9NO_3$)

Yield 79%; colourless crystals, mp 138°C; $[\alpha]_D^{20} = 17.3°\ cm^2\ g^{-1}$ ($c = 1.1$, *Me*OH); ^{1}H NMR: $\delta = 1.94$ (ddd, $J = 8.8$, 10.5, 12.7 Hz, C–C*H*H–C), 2.68 (dddd, $J = 1.3$, 4.8, 6.8, 12.7 Hz, C–CH*H*–C), 3.34

(dd, $J = 7.0$, 12.6 Hz, N–C*H*H), 3.59 (ddd, $J = 1.3$, 4.7, 12.6 Hz, N–CH*H*), 4.369 (dddd, $J = 4.7$, 4.8, 7.0, 8.8 Hz, O–CH), 4.372 (dd, $J = 6.8$, 10.5 Hz, O–CH) ppm; ^{13}C NMR: $\delta = 37.72$ (CH_2), 47.64 (N–CH_2), 63.31 (O–CH), 65.75 (O–CH), 175.53 (CO) ppm.

*(2R,4R)- and (2S,4R)-5-Amino-2,4-dihydroxypentanoic Acids **6a** and **6b***

Under Ar a solution of 1 mmol of **9a** or **9b** in 5 cm^3 of half saturated aqueous $Ba(OH)_2$ was heated to 100°C (1.5 h). The mixture was brought to room temperature and was carefully adjusted to *pH* 6 with 1 *M* H_2SO_4. Then $BaSO_4$ was removed by filtration. The filtrate and washings were concentrated *in vacuo* and the viscous residue was covered with little CH_3OH. On chilling in the refrigerator crystallization initiated.

(2R,4R)-5-Amino-2,4-dihydroxypentanoic acid (**6a**, $C_5H_{11}NO_4$)

Yield 76%; colourless crystals, mp > 185°C (dec); $[\alpha]_D^{20} = 19.0° \text{ cm}^2 \text{ g}^{-1}$ ($c = 1.03$, H_2O); ^{1}H NMR: $\delta = 1.67$, 1.86 (AB-part of an ABMX-spin system, $J = 2.0$, 3.1, 9.4, 9.6, 14.1 Hz, m, CH_2), 2.90, 3.10 (AB-part of an ABM-spin system, $J = 3.0$, 9.5, 13.2 Hz, CH_2–N), 4.00 (M-part, $J = 3.0$, 3.1, 9.4, 9.5 Hz, CH–O), 4.12 (X-part, $J = 2.0$, 9.6 Hz, CH–CO) ppm; ^{13}C NMR: $\delta = 39.20$ (CH_2), 45.1 (CH_2–N), 65.30 (CH–O), 69.20 (CH–CO), 181.54 (CO) ppm.

(2S,4R)-5-Amino-2,4-dihydroxypentanoic acid (**6b**, $C_5H_{11}NO_4$)

Yield 69%; colourless leaflets, mp > 175°C (dec); $[\alpha]_D^{20} = -28.6° \text{ cm}^2 \text{ g}^{-1}$ ($c = 1.02$, H_2O); ^{1}H NMR: $\delta = 1.85$, 1.90 (AB-part of an ABMX-spin system, $J = 5.0$, 6.1, 6.9, 7.3, 14.5 Hz, CH_2), 2.93, 3.17 (AB-part of an ABM-spin system, $J = 3.3$, 9.2, 13.1 Hz, CH_2–N), 4.00 (M-part, $J = 3.3$, 6.1, 6.9, 9.2 Hz, CH–O), 4.07 (X-part, $J = 5.0$, 7.3 Hz, CH–CO) ppm; ^{13}C NMR: $\delta = 39.12$ (CH_2), 44.63 (CH_2–N), 65.81 (CH–O), 69.82 (CH–CO), 180.97 (CO) ppm.

*(2R,4R)- and (2S,4R)-5-Amino-2-hydroxy-4-pentanolide, 4-Methylbenzenesulfonates **11a** and **11b***

A solution of 79 mg (0.6 mmol) of **9a** or **9b**, resp., and 130 mg (0.68 mmol) of 4-methylbenzenesulfonic acid hydrate in 0.2 cm^3 of H_2O was heated to 100°C (3 h). The water was evaporated *in vacuo*. The residual oil crystallized on covering with acetonitrile. Crystals were obtained in nearly quantitative yields after washing with acetonitril.

(2R,4R)-5-Amino-2-hydroxy-4-pentanolide, 4-Methylbenzenesulfonates
(**11a**, $C_{12}H_{17}NO_6S$)

Colourless needles, mp > 160°C (dec); $[\alpha]_D^{20} = -34.6° \text{ cm}^2 \text{ g}^{-1}$ ($c = 1.2$, H_2O); ^{1}H NMR (310 K): $\delta = 2.23$ (ddd, $J = 10.4$, 10.8, 12.7 Hz, CH–C*H*H–CH), 2.62 (s, CH_3), 3.09 (ddd, $J = 5.6$, 8.6, 12.7 Hz, CH–CH*H*–CH), 3.52 (dd, $J = 9.0$, 14.1 Hz, C*H*H–N), 3.70 (dd, $J = 2.6$, 14.1 Hz, CH*H*–N), 5.03 (dd, $J = 8.6$, 10.8 Hz, CO–CH), 5.06 (dddd, $J = 2.6$, 5.6, 9.0, 10.4 Hz, CH–O), 7.57–7.99 (m, $4H_{Ar}$) ppm; ^{13}C NMR: $\delta = 21.22$ (Me), 34.33 (CH_2), 43.39 (CH_2–N), 68.24 (CH–CO), 74.41 (CH–O), 126.11, 130.20 (Ar), 140.17, 143.25 (Ar_{qu}) ppm.

(2S,4R)-5-Amino-2-hydroxy-4-pentanolide, 4-Methylbenzenesulfonates
(**11b**, $C_{12}H_{17}NO_6S$)

Colourless leaflets, mp > 175°C (dec); $[\alpha]_D^{20} = -46.5° \text{ cm}^2 \text{ g}^{-1}$ ($c = 1$, H_2O); ^{1}H-NMR: $\delta = 2.52$ (s, CH_3), 2.56, 2.59 (AB-part of an ABMX-spin system, $J = 3.8$, 7.6, 8.6, 8.6, 13.6 Hz, CH–CH_2–CH),

3.36. 3.50 (AB-part of an ABX-spin system, $J = 2.9$, 10.8, 14.0 Hz, CH_2–N), 4.82 (M-part, $J = 7.6$, 8.6, CH–CO), 5.12 (X-part, $J = 2.9$, 3.8, 8.6, 10.8 Hz, CH–O), 7.47–7.85 (m, $4H_{Ar}$) ppm; ^{13}C NMR: $\delta = 21.21$ (Me), 33.28 (CH_2), 43.55 (CH_2–N), 67.06 (CH–CO), 75.81 (CH–O), 126.09, 129.62 (Ar), 140.15, 143.24 (Ar_{qu}) ppm.

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