

Synthetic Approach to *N*-Alkylated 2,5-Diamino-2,5-dideoxy-1,4;3,6-dianhydroalditols by Reductive Alkylation

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N,N'-Dialkylated 2,5-diamino-2,5-dideoxy-1,4;3,6-dianhydroalditols, representing interesting basic catalysts for polyaddition reactions, are synthesized by different reductive alkylation procedures in satisfactory yields. *D-Gluco*- and *L-ido*-*N,N'*-dialkyl-2,5-diamino-2,5-dideoxy-1,4;3,6-dianhydroalditols **7–8**, **10–15** are accessible by reaction of the corresponding diamines with carbonyl compounds and reduction of the intermediately formed imine. For the synthesis of *D-manno*-*N,N'*-dialkylated diamines, an alternative route via 1,4;3,6-dianhydro-*D*-threo-2,5-hexodiulose (**18**) is established, thus avoiding the six-step synthesis towards 1,4;3,6-dianhydro-*D*-mannitol (**2**). Reductive alkylation of diketone **18** yields stereospecifically only the alkylated diamine **21** with *D-manno*-configuration. In case of the monoketones only 1,4;3,6-dianhydro-*L*-sorbitol (**16**) can be transformed stereospecifically to *N*-2-pentyl-5-amino-5-deoxy-1,4;3,6-dianhydro-*D*-sorbitol (**19**), whereas 1,4;3,6-dianhydro-*D*-fructose (**17**) yields a mixture of *D-manno*- and *D-gluco*-monoamines **20a** and **20b** by reductive alkylation with 2-pentylamine and sodium borohydride.

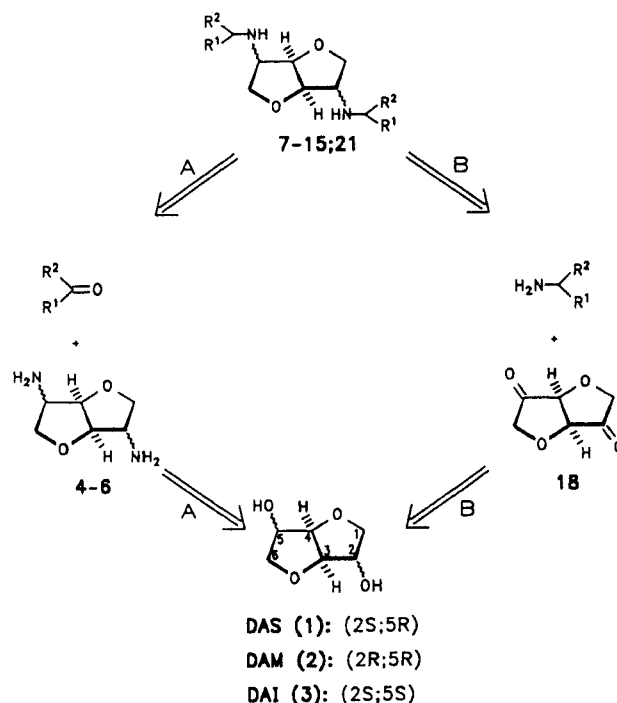
There is a facile access to the three stereoisomeric 1,4;3,6-dianhydroalditols, 1,4;3,6-dianhydro-*D*-sorbitol (DAS, **1**), 1,4;3,6-dianhydro-*D*-mannitol (DAM, **2**) and 1,4;3,6-dianhydro-*L*-iditol (DAI, **3**), which represent interesting precursors for the preparation of biopolymers. The two remaining hydroxy groups can be easily functionalized and the resulting heterocyclic compounds contain four chiral centers with a fixed stereochemistry. Within the last two decades they have become industrially more important (e.g. production of DAS: 1000t/a),¹ and some recent papers dealt with the polymerization of anhydro- and dianhydroalditols to polyesters,² polycarbonates,³ and polyethers.^{4–6} The corresponding 2,5-diamino-1,4;3,6-dianhydroalditols **4–6**, accessible by a three-step synthesis from dianhydroalditols, could be polymerized to give polyamides^{7–9} and polyurethanes.^{3,10}

N,N'-dialkylated secondary amines represent valuable basic catalysts for polyaddition reactions of isocyanates to polyurethanes and polyureas.^{11,12} In addition to their function as catalyst they can also be incorporated into the polymer chain by reaction with isocyanate. It was of interest to prepare a new generation of such catalysts based on dianhydroalditols.

For the synthesis of *N,N'*-dialkylated-2,5-diamino-2,5-dideoxy-1,4;3,6-dianhydroalditols **7–15**, **21** reductive alkylation as one of the best explored methods for synthesis of secondary and tertiary amines was chosen. The variety of described methods can be divided into two groups: i) catalytic hydrogenations of the intermediately formed imine^{13,14} and ii) reduction of the imines employing complex hydrides. The second method is optimized by use of selective reducing agents such as sodium cyanoborohydride¹⁵ or sodium triacetoxyborohydride¹⁶ and in situ reduction of the formed imine without concomitant reaction of the starting carbonyl compound.

In the present case there are two possible synthetic routes towards the *N,N'*-dialkylated-2,5-diamino-2,5-dideoxy-

1,4;3,6-dianhydroalditols. The diamines can be reacted with aldehydes and ketones and the imines formed reduced towards the alkylated amines (Scheme 1, retrosynthetic route A). The other approach starts with oxidation of the alditols to ketones followed by reductive alkylation with primary amines to furnish the desired products (Scheme 1, retrosynthetic route B). The stereochemistry at the alkyl side-chain in compounds **7–9** and **19–21** could be of interest, however, this was not further investigated because the point was beyond the purpose of this study.

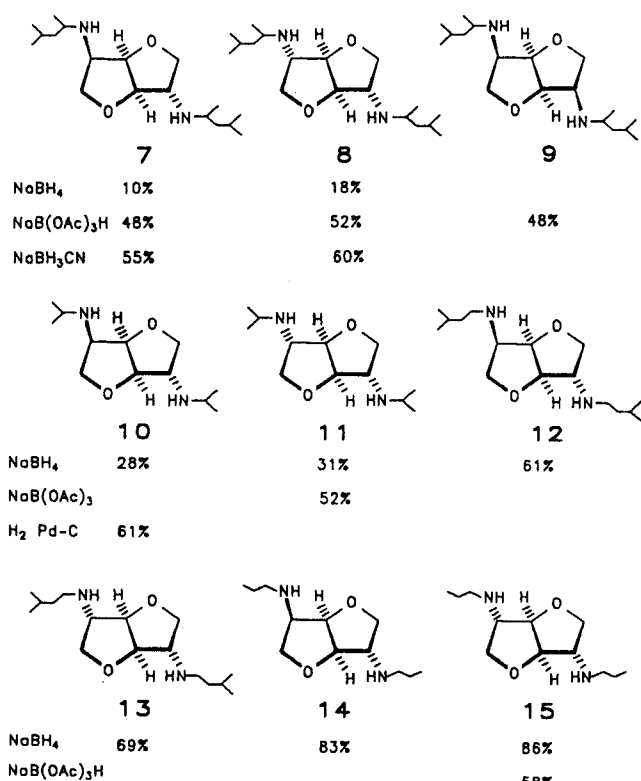


Scheme 1

The *D-gluco* **4** and *L-ido* **6** 2,5-diamines can be synthesized in an overall yield of 26 to 58 % starting with commercially available DAS (**1**) and DAM (**2**) by known procedures.³ The *D-manno* isomer was obtained from DAI (**3**) which in turn can be prepared from DAM (**2**) by Mitsunobu reaction, benzylation and cleavage of blocking groups in 71 % yield. Thus, for the synthesis of 2,5-diamino-2,5-dideoxy-1,4;3,6-dianhydro-*D*-mannitol (**5**) starting with DAM (**2**) the overall yield is diminished to 11 %.⁷

The diamines are reacted with four equivalents of carbonyl compounds in boiling anhydrous methanol with powdered molecular sieves (3Å) for 6 h. Addition of an excess of sodium borohydride and stirring for additional 4 h at ambient temperature yield the desired dialkylated diamines **7–15**, which can be purified by column flash chromatography. The results, summarized in Scheme 2, demonstrate the gradually decreasing reactivity of car-

bonyl compounds in going from the highly reactive propionaldehyde to the sterically most hindered and low reactive 4-methyl-2-pentanone.



Scheme 2

Reaction with sodium cyanoborohydride in anhydrous methanol at pH 6 and stirring for 72 h at ambient temperature or with in situ generated sodium triacetoxyborohydride in anhydrous methanol and stirring for 18 h in a nitrogen atmosphere at ambient temperature leads to the formation of compounds **7–9**, **11**, and **15** in about 50–60 % yield. For reaction with sterically hindered ketones the second method seems to be preferable but in the case of propionaldehyde the sodium borohydride method still gives better yields.

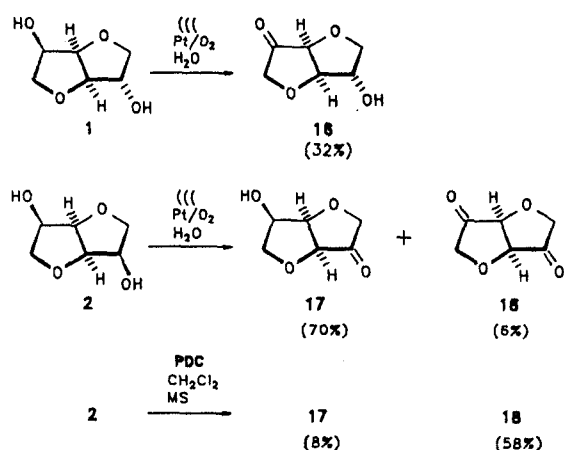
Compared to these results catalytic hydrogenation with palladium-on-carbon and hydrogen under pressure (30 bar) represents a good alternative to reductive alkylation with complex hydrides. Thus reaction of **4** with acetone in anhydrous methanol and catalytic hydrogenation for 6 h yields 61 % of compound **10** compared to 28 % yield obtained by the sodium borohydride method. The results clearly demonstrate that the stereochemistry of the diamines are much less important for the yields than the steric hindrance at the carbonyl compounds.

Further, the alternative route via oxidized 1,4;3,6-dianhydroalditols and reductive alkylation was investigated with 2-pentylamine using the sodium borohydride method. Heyns et al.¹⁷ developed the catalytic oxidation of dianhydroalditols by platinum(0) Adams catalyst in an oxygen atmosphere and showed that only *endo*-hydroxy groups can be oxidized to ketones by this method. Here the catalytic oxidation was performed with prerduced platinum(IV) oxide catalyst but instead of stirring ultrasonication was used.^{18,19} In the case of DAS (**1**) only the oxidation of the *endo*-hydroxy group occurred and

Table 1. ^1H NMR (250 MHz) CDCl_3 , δ

Assign- ment	Product								
	7	8	9	10	11	12	13	14	15
H-1 a	3.94 (dd)	3.90 (ddd)	4.02 (ddd)	3.93 (dd)	3.91 (dd)	3.98 (dd)	3.94 (dd)	3.97 (dd)	3.93 (dd)
H-1 b	3.60 (dd)	3.54 (ddd)	3.22 (ddd)	3.59 (dd)	3.55 (dd)	3.68 (dd)	3.65 (dd)	3.67 (dd)	3.63 (dd)
H-2	3.30 (m)	3.29 (dd)	3.40 (ddd)	3.29 (dd)	3.31 (dd)	3.25 (m)	3.27 (dd)	3.26 (m)	3.25 (dd)
H-3	4.37 (d, br)	4.35 (dd)	4.44 (dd)	4.38 (dd)	4.37 (s)	4.42 (dd)	4.46 (m)	4.41 (dd)	4.46 (dd, br)
H-4	4.42 (dd)	= H-3	= H-3	4.44 (dd)	= H-3	4.53 (dd)	= H-3	4.50 (dd)	= H-3
H-5	3.33 (m)	= H-2	= H-2	3.32 (ddd)	= H-2	3.25 (m)	= H-2	3.26 (m)	= H-2
H-6 a	3.85 (dd)	3.84 (ddd)	= H-1 a	3.89 (dd)	= H-1 a	3.84 (dd)	= H-1 a	3.83 (dd)	= H-1 a
H-6 b	3.94 (dd)	3.48 (ddd)	= H-1 b	3.22 (dd)	= H-1 b	3.25 (m)	= H-1 b	3.26 (m)	= H-1 b
NH	3.60 (dd)	1.30 (2H, br)	2.00 (2H, br)	1.70 (2H, br)	1.30 (2H, br)	1.85 (2H, br)	1.80 (2H, br)	2.10 (2H, br)	2.20 (2H, br)
H-1'	1.01/0.98 (6H, d/d)	0.98 (6H, d)		1.04/1.00 (12H, d/d)	1.04/1.00 (12H, d/d)	2.63 (4H, m)	2.73 (4H, m)	2.60 (4H, m)	2.61 (4H, m)
H-2'	2.70 (2H, m)	2.70 (2H, m)	1.02 (6H, d)	2.85 (2H, m)	2.85 (2H, m)	1.36 (4H, m)	1.37 (4H, m)	1.50 (4H, m)	1.50 (4H, m)
H-3'	1.24/1.09 (4H, m/m)	1.22/1.10 (4H, m/m)	2.75 (2H, m)	= H-1' (2H, m)	= H-1' (2H, m)	1.60 (2H, m)	1.62 (2H, m)	0.90 (6H, t)	0.91 (6H, t)
H-4'	1.60 (2H, m)	1.60 (2H, m)	1.31/1.18 (4H, m)			0.85 (12H, d)	0.89 (12H, d)		
H-5'	0.84 (6H, d)	0.84 (6H, d)	1.64 (2H, m)			= H-4' (12H, d)	= H-4' (12H, d)		
H-6'	0.81 (6H, d)	0.82 (6H, d)	0.87 (6H, d)						

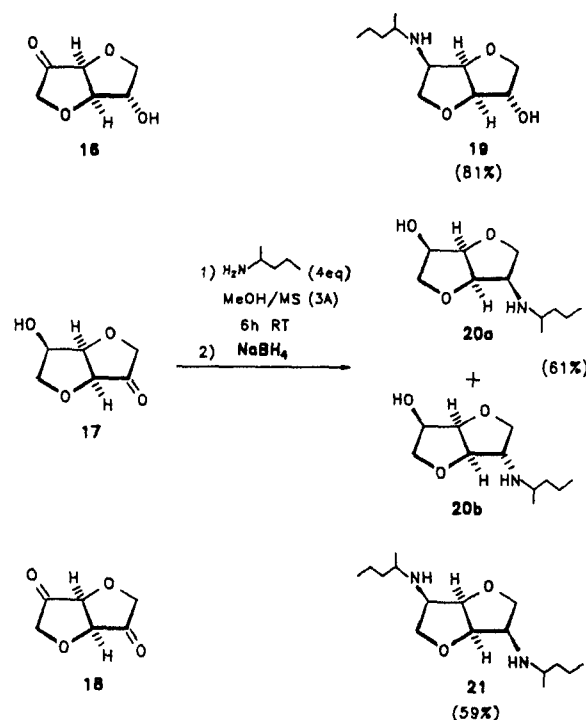
thus the monoketone **16** was obtained in comparable yield (32 %) (Ref. 17: 39 %). In contrast to the results of Heyns et al., oxidation of DAM (**2**) furnished the monoketone **17** as the major product (70 %) and in addition only 6 % of the diketone **18**. Therefore, a chemical oxidation of DAM (**2**) with pyridinium dichromate and powdered molecular sieves (3Å) as a promotor^{20,21} was employed and this gave predominantly the diketone **18** (59 %) and only 8 % of the monoketone **17** (Scheme 3). The ¹³C NMR spectra of these ketones in deuterium oxide show hydrated carbonyl signals (e.g. for **17** C-2-hydrated: 102.2 ppm) whereas in acetonitrile-*d*₃ the free carbonyl group is observed (for **17** C-2: 213.3 ppm).



Scheme 3

Reaction of **18** with eight equivalents of 2-pentylamine in boiling anhydrous methanol and powdered molecular sieves and reduction with an excess of sodium borohydride gave in 59 % only the *D*-manno-dialkylated diamine **21**. The *D*-manno-configuration can be assigned by comparison of ¹H NMR chemical shifts and coupling constants. The monoketone **16** in a corresponding reaction led to the *D*-gluco-mono-*N*-alkylated product **19** in 81 % yield.

1,4;3,6-Dianhydro-*D*-fructose (**17**) gave an inseparable mixture of *D*-manno- **20a** and *D*-gluco- **20b** -mono- *N*-alkylated compounds in 61 % overall yield (Scheme 4). It should be pointed out that sodium borohydride is assumed to attack the imine formed in general from the *exo*-position to furnish only *endo*-amino groups. On the other hand the *endo*-hydroxy group in **17** allows obviously an *endo*-attack presumably by coordination of BH₄⁻ with the *endo*-oxygen and this leads to a mixture of *endo*- and *exo*-amino groups in **20a** and **20b** (Scheme 5).

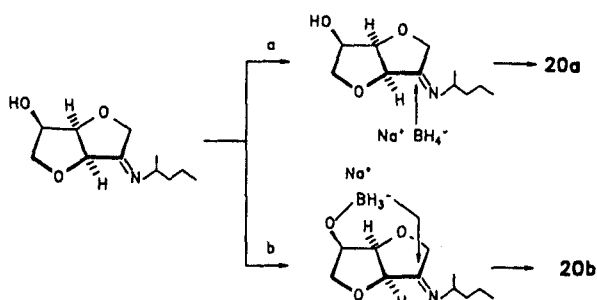


Scheme 4

Table 2. Coupling Constants (Hz) for the ¹H NMR (250 MHz) spectra of Compounds 7–15

² J/ ³ J	Product								
	7	8 ^a	9 ^a	10	11	12	13	14	15
J _{1a,1b}	9.2	9.2	8.0	9.2	9.6	9.2	9.2	9.2	9.2
J _{1a,2}	5.6	5.2	8.0	5.6	5.2	5.6	5.2	5.6	4.8
J _{1b,2}	4.0	3.2	10.0	4.0	3.2	3.2	3.6	3.6	3.2
J _{2,3}	1.6	0.0	4.0	1.2	0.0	0.8	0.0	0.8	0.0
J _{3,4}	4.0	0.0	0.0	4.0	0.0	4.0	0.0	4.0	0.0
J _{4,5}	4.0	0.0	4.0	4.0	0.0	4.0	0.0	4.0	0.0
J _{5,6a}	5.2	5.2	8.0	5.2	5.2	4.8	5.2	5.2	4.8
J _{5,6b}		3.2	10.0	7.6	3.2	—	3.6	—	3.2
J _{6a,6b}	9.6	9.2	8.0	9.2	9.6	9.2	9.2	9.2	9.2
J _{1',2'}	6.0	6.0	6.0	6.0	6.0	—	—	—	—
J _{2',3'}	—	—	—	6.0	6.0	—	—	7.6	8.0
J _{3',4'}	—	—	—	—	—	6.4	6.0	—	—
J _{3',5'}	0.0	0.0	0.0	—	—	6.4	6.0	—	—
J _{4',5'}	6.0	6.4	5.6	—	—	—	—	—	—
J _{4',6'}	6.0	6.4	5.6	—	—	—	—	—	—

^a ⁴J: J_{1a,4} = J_{3,6a}: 1.6 (**8**); 5.2 (**9**); J_{1b,4} = J_{3,6b}: 4.4 (**8**); 4.4 Hz (**9**).



Scheme 5

In summary alkylated 2,5-diamino-2,5-dideoxy-1,4,3,6-dianhydroalditols can be synthesized by reductive alkylation of the corresponding diamines with carbonyl compounds either by reduction with sodium borohydride or for sterically hindered ketones with selective reducing agents such as sodium cyanoborohydride, sodium triacetoxyborohydride or catalytic hydrogenation under pressure in yields of 50 to 85 %. For syntheses of *D*-manno-dialkylated diamines the reductive alkylation of 1,4,3,6-dianhydro-*D*-threo-2,5-hexodiulose (**18**) with amines would be preferred to the reaction of 2,5-diamino-2,5-dideoxy-1,4,3,6-dianhydro-*D*-mannitol. From commercially available dianhydroalditols an overall yield of 35 % in a two-step synthesis is obtained by the oxidation route whereas the seven-step reaction starting from DAM (**2**) gives **21** in 5 % overall yield.

NMR: Bruker CA-250 ^1H : 250 MHz. TLC: aluminium foils, silica gel GF₂₅₄ (Merck); detection: spraying with ethanolic H_2SO_4 (20 %) and heating. Column chromatography: silica gel (40–60 μm , Merck) using the flash-technique. Melting points: (not corrected) Reichert heating microscope. Optical rotation: Perkin-Elmer 243 in 1 dm cuvettes at 20 °C and 598 nm. Catalytic hydrogenation: Berghof (HR 100) high pressure autoclave. Catalytic oxidation: immersion ultrasonic horn Bandlin (Sonoplus HD 60).

For the determination of combustion analytical C,H data, optical rotations and melting points the alkylated diamines were transformed into their hydrochlorides by treating with 1 N methanolic HCl and filtration of the precipitated products. For all new compounds satisfactory microanalyses obtained: C \pm 0.41, H \pm 0.16, Cl \pm 0.44, N \pm 0.27.

For compounds 7–9 and 19–21 the diastereomeric ratio due to the *N*-alkyl side-chain was not investigated.

Reductive Alkylation; General Procedure:

Diamines (2 mmol) were reacted with carbonyl compounds (8 mmol) in anhydrous MeOH (10 mL). For 1,4,3,6-dianhydroketones (2 mmol) 2-pentylamine (8 mmol) was used.

Method A: The solution was refluxed for 6 h (for 1,4,3,6-dianhydroketones stirred at r. t.) with activated powdered molecular sieves (3Å, 1 g). After cooling to r. t., NaBH_4 (excess) was added and stirring was continued for 4 h. For removal of the unreacted NaBH_4 the solution was treated with conc. HCl (pH 1). Extraction with CHCl_3 at pH 10 (adjusted by addition of solid NaHCO_3 and Na_2CO_3), drying (Na_2SO_4) and evaporation yielded a light yellow syrup, which was purified by column chromatography using toluene, CHCl_3 , MeOH 6 : 3 : 1 as eluent.

Method B: The above solution was treated with 1 N methanolic HCl until pH 6 was reached and NaBH_3CN (2.5 mmol) was added. After stirring for 72 h at r. t., the reaction mixture was worked up as described for Method A.

Method C: AcOH (13.5 mmol) were added to the above solution and after 2 h stirring was allowed to form $\text{NaB}(\text{OAc})_3\text{H}$. After 24 h, additional NaBH_4 (2 mmol) was added and stirring was con-

tinued for another 18 h. After dilution with H_2O (20 mL), workup was performed as described for Method A.

Method D: The above solution was allowed to react under a N_2 atmosphere for 4 h in an autoclave. Then Pd-C (10 %, 200 mg) was added and kept for 6 h under 30 bar H_2 pressure. The catalyst was filtered and the solvent was evaporated. The obtained syrup was purified by column chromatography.

N,N-Bis(4-methyl-2-pentyl)-2,5-diamino-2,5-dideoxy-1,4,3,6-dianhydro-*D*-sorbitol (**7**):

Method A: 2,5-Diamino-2,5-dideoxy-1,4,3,6-dianhydro-*D*-sorbitol (**4**, 281 mg, 1.95 mmol) was reacted with methyl isobutyl ketone (1 mL, 0.79 g, 7.8 mmol); yield: 61 mg (10 %).

Method B: Compound **4** (280 mg, 1.94 mmol) was reacted with 4-methyl-2-pentanone (1 mL, 0.79 g, 7.8 mmol); yield: 334 mg (55 %).

Method C: Compound **4** (263 mg, 1.83 mmol) was reacted with 4-methyl-2-pentanone (1 mL, 0.79 g, 7.8 mmol); yield: 274 mg (48 %).

7-Dihydrochloride: $[\alpha]_{\text{D}}^{20} = +85.4^\circ$ ($c = 0.98$, H_2O); mp < 300 °C.

N,N-Bis(4-methyl-2-pentyl)-2,5-diamino-2,5-dideoxy-1,4,3,6-dianhydro-*L*-iditol (**8**):

Method A: 2,5-Diamino-2,5-dideoxy-1,4,3,6-dianhydro-*L*-iditol (**6**, 291 mg, 2.02 mmol) was reacted with methyl isobutyl ketone (1 mL, 0.79 g, 7.8 mmol); yield: 113 mg (18 %).

Method B: Compound **6** (280 mg, 1.94 mmol) was reacted with 4-methyl-2-pentanone (1 mL, 0.79 g, 7.8 mmol); yield: 363 mg (60 %).

Method C: Compound **6** (264 mg, 1.87 mmol) was reacted with 4-methyl-2-pentanone (1 mL, 0.79 g, 7.8 mmol); yield: 297 mg (52 %).

8-Dihydrochloride: $[\alpha]_{\text{D}}^{20} = +32.2^\circ$ ($c = 0.78$, H_2O); mp 182 °C.

N,N-Bis(4-methyl-2-pentyl)-2,5-diamino-2,5-dideoxy-1,4,3,6-dianhydro-*D*-mannitol (**9**):

Method C: 2,5-Diamino-2,5-dideoxy-1,4,3,6-dianhydro-*D*-mannitol (**5**; 288 mg, 2.0 mmol) was reacted with 4-methyl-2-pentanone (1 mL; 0.79 g, 7.8 mmol); yield: 298 mg (48 %).

9-Dihydrochloride: $[\alpha]_{\text{D}}^{20} = +53.8^\circ$ ($c = 0.92$, H_2O); mp 231 °C.

N,N-Diisopropyl-2,5-diamino-2,5-dideoxy-1,4,3,6-dianhydro-*D*-sorbitol (**10**):

Method A: 2,5-Diamino-2,5-dideoxy-1,4,3,6-dianhydro-*D*-sorbitol (**4**; 273 mg, 1.90 mmol) was reacted with acetone (0.65 mL, 0.5 g, 8.4 mmol); yield: 121 mg (28 %).

Method D: Compound **4** (268 mg, 1.86 mmol) was reacted with acetone (0.65 mL, 0.5 g, 8.4 mmol); yield: 254 mg (60 %).

10-Dihydrochloride: $[\alpha]_{\text{D}}^{20} = +81.2^\circ$ ($c = 1.01$, H_2O); mp 240 °C (dec.)

N,N-Diisopropyl-2,5-diamino-2,5-dideoxy-1,4,3,6-dianhydro-*L*-iditol (**11**):

Method A: 2,5-Diamino-2,5-dideoxy-1,4,3,6-dianhydro-*L*-iditol (**6**; 284 mg, 1.904 mmol) was reacted with methyl isobutyl ketone (0.65 mL, 0.5 g, 8.4 mmol); yield: 139 mg (31 %).

Method C: **6** (316 mg, 2.19 mmol) was reacted with 4-methyl-2-pentanone (0.65 mL, 0.5 g, 8.4 mmol); yield: 260 mg (52 %).

11-Dihydrochloride: $[\alpha]_{\text{D}}^{20} = +32.8^\circ$ ($c = 0.98$, H_2O); mp 230 °C.

N,N-Bis(3-methylbutyl)-2,5-diamino-2,5-dideoxy-1,4,3,6-dianhydro-*D*-sorbitol (**12**):

Method A: 2,5-Diamino-2,5-dideoxy-1,4,3,6-dianhydro-*D*-sorbitol (**4**; 273 mg, 1.90 mmol) was reacted with 3-methylbutyraldehyde (1 mL, 0.8 g, 9.18 mmol); yield: 293 mg (61 %).

12-Dihydrochloride: $[\alpha]_{\text{D}}^{20} = +86.0^\circ$ ($c = 1.01$, H_2O), mp 240 °C.

***N,N*-Bis(3-methylbutyl)-2,5-diamino-2,5-dideoxy-1,4;3,6-dianhydro-L-itol (13):**

Method A: 2,5-Diamino-2,5-dideoxy-1,4;3,6-dianhydro-L-itol (6; 238 mg, 1.65 mmol) was reacted with 3-methylbutyraldehyde (1 mL, 0.8 g, 9.18 mmol); yield: 323 mg (69 %).

13-Dihydrochloride: $[\alpha]_D^{20} = +50.1^\circ$ ($c = 0.97$, H₂O); mp 225 °C (dec.)

***N,N*-Dipropyl-2,5-diamino-2,5-dideoxy-1,4;3,6-dianhydro-D-sorbitol (14):**

Method A: 2,5-Diamino-2,5-dideoxy-1,4;3,6-dianhydro-D-sorbitol (4; 300 mg, 2.08 mmol) was reacted with propionaldehyde (0.7 mL, 0.56 g, 9.6 mmol); yield: 393 mg (83 %).

14-Dihydrochloride: $[\alpha]_D^{20} + 71.8^\circ$ ($c = 0.93$, H₂O); mp 220 °C (dec.)

***N,N*-Dipropyl-2,5-diamino-2,5-dideoxy-1,4;3,6-dianhydro-L-itol (5):**

Method A: 2,5-Diamino-2,5-dideoxy-1,4;3,6-dianhydro-L-itol (6; 209 mg, 1.45 mmol) was reacted with propionaldehyde (0.7 mL, 0.56 g, 9.6 mmol); yield: 284 mg (86 %).

Method C: Compound 6 (308 mg, 2.14 mmol) was reacted with propionaldehyde (0.7 mL, 0.56 g, 9.6 mmol); yield: 282 mg (58 %).

15-Dihydrochloride $[\alpha]_D^{20} + 42.1^\circ$ ($c = 1.03$, H₂O); mp 250 °C (dec.)

1,4;3,6-Dianhydro-L-sorbose (16):

PtO₂ (1 g) was suspended in H₂O (100 mL) and reduced to Pt(0) for 6 h under a H₂ atmosphere and ultrasonification. DAS (1; 1.46 g, 10 mmol) was added and the oxidation was performed for 6 h under an O₂ atmosphere and ultrasonification (60 W, 25 kHz). After filtration of the catalyst, the solution was evaporated and the resulting syrup was purified by column chromatography (toluene/EtOH 3:1); yield: 461 mg (32 %); colorless syrup.

$[\alpha]_D^{20} + 52.8^\circ$ ($c = 0.99$, H₂O) [Lit.¹⁷ $[\alpha]_D^{27} + 64.2^\circ$].

¹H NMR (D₂O): $\delta = 4.01$ (AB, H-1a, H-1b), 4.44 (br s, H-2), 4.41 (d, H-3), 4.71 (d, H-4), 3.84 (d, H-6a), 3.69 (d, H-6b) $J_{AB} = 4.0$, $J_{3,4} = 4.0$, $J_{6a,6b} = 10.0$ Hz.

¹³C NMR (D₂O): $\delta = 70.7$ (C-1), 101.2 (C-2), 81.5 (C-3), 84.3 (C-4), 72.3 (C-5), 71.4 (C-6).

1,4;3,6-Dianhydro-D-fructose (17):

DAM (2; 1.46 g, 10 mmol) was oxidized as described for 16; yield: 1.01 g (70 %); colorless syrup. $[\alpha]_D^{20} + 86.4^\circ$ ($c = 1.03$, H₂O) [Lit.¹⁷ $[\alpha]_D^{27} + 91.9^\circ$].

¹H NMR (D₂O): $\delta = 3.80$ (d, H-1a), 3.64 (d, H-1b), 4.18 (d, H-3), 4.61 (dd, H-4), 4.33 (ddd, H-5), 4.00 (dd, H-6a), 3.54 (dd, H-6b) $J_{1a,1b} = 9.6$, $J_{3,4} = 4.4$, $J_{4,5} = 4.8$, $J_{5,6a} = 7.2$, $J_{5,6b} = 8.8$, $J_{6a,6b} = 9.2$ Hz.

¹³C NMR (D₂O): $\delta = 75.5$ (C-1), 102.2 (C-2), 85.9 (C-3), 83.0 (C-4), 73.1 (C-5), 72.1 (C-6).

¹³C NMR (CD₃CN): $\delta = 73.4$ (C-1), 213.3 (C-2), 82.3 (C-3), 79.2 (C-4), 73.1 (C-5), 72.1 (C-6).

As side product 18 was isolated; yield: 85 mg (6 %).

1,4;3,6-Dianhydro-D-threo-2,5-hexodiulose (18):

To a solution of DAM (2; 1.46 g, 10 mmol) in anhyd. CH₂Cl₂ (50 mL) freshly activated powdered molecular sieves (3 Å, 10 g) and PDC (12 g, 32.01 mmol) were added in small portions. After stirring for 18 h the suspension was evaporated and several times codistilled with toluene. The residue was treated with EtOH, filtered over Celite and evaporated again. The resulting syrup was purified by column chromatography (toluene/EtOH, 3:1); yield: 838 mg (59 %);

$[\alpha]_D^{20} + 108.3^\circ$ ($c = 1.00$, H₂O); mp 114–116 °C [Lit.¹⁷ $[\alpha]_D^{27} + 110.0^\circ$; mp 116 °C].

¹H NMR (D₂O): $\delta = 3.88$ (d, H-1a, H-6a), 3.74 (d, H-1b, H-6b), 4.37 (s, H-3, H-4), $J_{1a,1b} = J_{6a,6b} = 9.6$ Hz.

¹³C NMR (D₂O): $\delta = 75.2$ (C-1, C-6), 102.1 (C-2, C-5), 86.3 (C-3, C-4).

As side product 17 was isolated; yield: 115 mg (8 %).

***N*-(2-Pentyl)-5-amino-5-deoxy-1,4;3,6-dianhydro-D-sorbitol (19):**

Method A: Compound 16 (113 mg, 0.78 mmol) was reacted with 2-pentylamine (0.5 mL, 360 mg, 4.14 mmol); yield: 114 mg (81 %); colorless syrup; $[\alpha]_D^{20} + 53.2^\circ$ ($c = 0.99$, H₂O).

¹H NMR (CDCl₃): $\delta = 3.79$ (AB, H-1a, H-1b), 4.21 (br s, H-2), 4.40 (dd, H-3), 4.59 (dd, H-4), 3.36 (m_c, H-5), 3.94 (dd, H-6a), 3.15 (dd, H-6b), 2.40–2.20 (2 H, br s, NH, OH), 1.04 (3 H, d, H-1'), 2.70 (m_c, H-2'), 1.30 (4 H, m_c, H-3', H-4'), 0.85 (3 H, t, H-5') $J_{AB} = 2.4$, $J_{3,4} = 4.0$, $J_{4,5} = 4.0$, $J_{5,6a} = 7.2$, $J_{5,6b} = 10.0$, $J_{6a,6b} = 8.0$, $J_{1',2'} = 6.0$, $J_{4',5'} = 5.6$ Hz.

***N*-(2-Pentyl)-2-amino-2-deoxy-1,4;3,6-dianhydro-D-mannitol (20a) and -D-sorbitol (20b):**

Method A: Compound 17 (133 mg, 0.92 mmol) was reacted with 2-pentylamine (0.5 mL, 360 mg, 4.14 mmol); yield: 121 mg (61 %); colorless syrup.

¹H NMR (CDCl₃): $\delta = 4.02$ (m_c, H-1b), 3.40 (m_c, H-1b), 3.60 (2 H, m_c, H-2, H-6b), 4.47 (2 H, m_c, H-3, H-4), 4.16 (m_c, H-5), 3.86 (dd, H-6a), 2.38–2.20 (2 H, br s, NH, OH), 1.04 (3 H, d, H-1'), 2.70 (m_c, H-2'), 1.30 (4 H, m_c, H-3', H-4'), 0.84 (3 H, t, H-5') $J_{5,6a} = 5.6$, $J_{6a,6b} = 9.6$, $J_{1',2'} = 6.0$, $J_{4',5'} = 5.6$ Hz.

***N,N*-Bis(2-pentyl)-2,5-diamino-2,5-dideoxy-1,4;3,6-dianhydro-D-mannitol (21):**

Method A: Compound 18 (92 mg/0.65 mmol) was reacted with 2-pentylamine (0.5 mL, 360 mg, 4.14 mmol); yield: 109 mg (59 %); colorless syrup; $[\alpha]_D^{20} + 38.1^\circ$ ($c = 0.93$, H₂O).

¹H NMR (CDCl₃): $\delta = 4.02$ (2 H, ddd, H-1a, H-6a), 3.22 (2 H, ddd, H-1b, H-6b), 3.40 (2 H, ddd, H-2, H-5), 4.43 (2 H, br, dd, H-3, H-4), 2.00–1.80 (2 H, br s, 2 NH); 1.01, 0.97 (2 d, 3 H each, H-1'), 2.66 (2 H, m_c, H-2'), 1.30 (8 H, m_c, H-3', H-4'), 0.84 (6 H, t, H-5') $J_{1a,1b} = J_{6a,6b} = 8.0$, $J_{1a,2} = J_{5,6a} = 8.0$, $J_{1b,2} = J_{5,6b} = 10.0$, $J_{2,3} = J_{4,5} = 4.0$; $J_{1a,4} = J_{3a,6} = 4.4$; $J_{1b,4} = J_{3,6b} = 2.0$, $J_{1',2'} = 6.0$, $J_{4',5'} = 5.6$ Hz.

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