

Efficient synthesis of (2*R*,3*R*)- and (2*S*,3*S*)-2,3-diaminobutane-1,4-diol and their dibenzyl ethers [†]

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Abstract: (2*R*,3*R*)-2,3-Diaminobutane-1,4-diol **6** and its dibenzyl ether **7** were efficiently synthesized starting from L-tartaric acid **1a**. The crucial step, debenzylation of intermediate dibenzylazido **4**, was accomplished in good yield by boron trichloride–dimethyl sulfide complex. The enantiomeric series was similarly obtained starting from D-tartaric acid. © 1997 Elsevier Science Ltd

Introduction

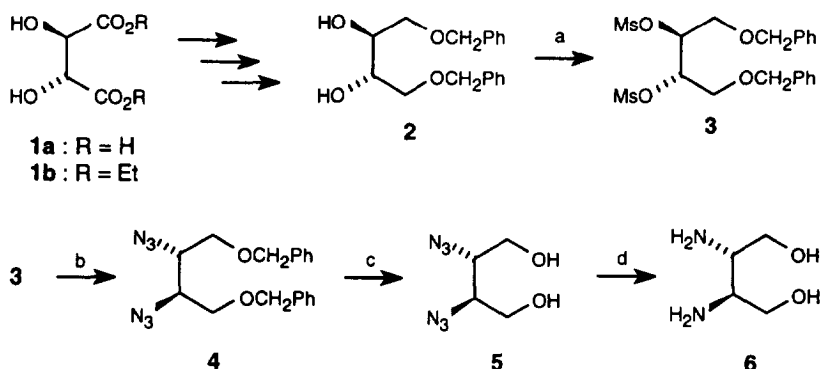
In many reactions optically active vicinal diamines constitute interesting chiral auxiliaries. Enantiomerically pure 1,2-diphenylethylenediamine or 1,2-diaminocyclohexane, for instance, afford asymmetric induction for Diels–Alder and aldol reactions,¹ for allylation² and propargylation³ processes, for the alkyl additions to carbonyl compounds,⁴ and more recently, for epoxidation⁵ reactions. We were interested in the synthesis of (2*R*,3*R*)-2,3-diaminobutane-1,4-diol **6** or its enantiomer as building blocks for the preparation of ligands, suitable for the development of asymmetric catalysts. Although the stereoisomers of 1,4-diaminobutane-2,3-diol are well documented,⁶ this is not the case for 2,3-diaminobutane-1,4-diol isomers. Hanessian *et al.* reported on the synthesis of (2*S*,3*S*)-2,3-diaminobutane-1,4-diol starting from D-mannitol with the sacrifice of two asymmetric carbons. This compound was used for the preparation of analogs of *cis*-platin antitumor agents.⁷ In this paper, we report about an efficient synthesis of both (2*R*,3*R*)-**6** and (2*S*,3*S*)-2,3-diaminobutane-1,4-diol, starting from L- and D-tartaric acid.

Results and discussion

Starting from (+)-diethyl tartrate **1b**, diol **2** was prepared according to lit.⁸ in a four step synthesis, then transformed by standard methods (mesylation and reaction with sodium azide in DMF or DMSO) into diazide **4**.^{9,10} Debenzylation of **4** was a critical step. The benzyl groups were conveniently removed^{11,23,24} by boron trichloride–dimethyl sulfide complex in dichloromethane¹² (in 81% yield, using 2.5 equiv. of BCl₃·Me₂S) to afford highly crystalline **5**. Transformation of **2** to **5** was performed on up to 9 mmol scale in a 72% overall yield, without purification of intermediate **3**. Catalytic hydrogenation of the azido groups using Adams' catalyst under an atmospheric pressure of H₂ afforded bis-aminoalcohol **6**. Adams' catalyst was found to be clearly superior to other catalysts (Pd/C and Pearlman's catalyst).¹³

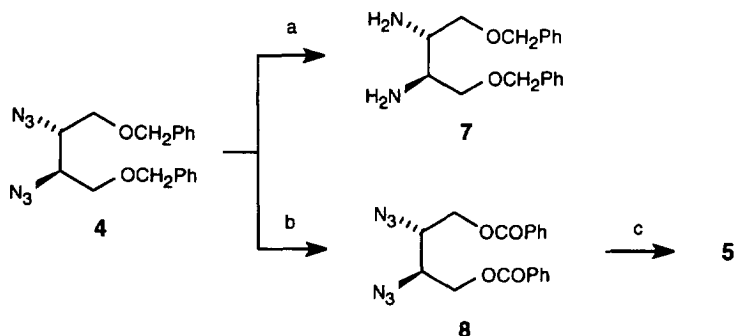
[†] Dedicated to Professor Waldemar Adam on the occasion of his 60th birthday.

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a MsCl, Et₃N, CH₂Cl₂, 0°C, 1 h, 99%. b NaN₃, DMSO, 80°C, 24 h, 95%. c BCl₃·Me₂S, CH₂Cl₂, r.t., 2-3 h, 81%. d H₂, PtO₂, MeOH/H₂O 3:2, r.t., 24 h, 98%.

Further elaboration of **6**, for example to optically active ligands, was hampered by its poor solubility in most organic solvents. It was therefore desirable to prepare derivatives with suitable O-protection. Although the dibenzoate of **6** could not be obtained,¹⁴ the dibenzyl ether derivative **7** was easily and quantitatively prepared by catalytic hydrogenation of **4** under more convenient conditions than previously reported⁹ (LiAlH₄, 66%).



a H₂, Pd/C, MeOH, ca. 20°C, 24 h, quant. b RuCl₃·x H₂O, NaIO₄, CCl₄/CH₃CN/H₂O 2:2:3, 15°C, 2 d, 92%. c K₂CO₃, MeOH, ca. 20°C, 24 h, 84%.

Starting from the *2R,3R*-enantiomer of diol **2**,¹⁶ generated from D-tartaric acid, (*2S,3S*)-2,3-diaminobutane-1,4-diol and its dibenzyl ether were equally prepared. As expected, all intermediates have the same physical properties as their enantiomers **6** and **7**, derived from L-tartaric acid, except a nearly opposite optical rotation.

The specific rotation $[\alpha]_D$ of (*2R,3R*)-2,3-diazidobutane-1,4-diol **5** [-15.7 ($c=6$, MeOH)] differed considerably from the value reported by Hanessian *et al.* for (*2S,3S*)-**5** [$+41.4$ ($c=0.5$, MeOH)] prepared from D-mannitol.⁷ However, there was no evidence that (*2R,3R*)-**5** was partially racemized, since rebenzylation (NaH, PhCH₂Br) afforded a dibenzyl ether **4** with a nearly identical $[\alpha]_D$ value [-44.3 , ($c=5.8$, CHCl₃)] as before debenzylation [-47.6 , ($c=6$, CHCl₃)]. Furthermore, compound **5** with a nearly identical $[\alpha]_D$ of -16.6 ($c=0.97$, MeOH) was also obtained from **4** *via* catalytic RuO₄ oxidation¹⁵ to dibenzoate **8**, which was deprotected by base-catalyzed methanolysis. Further proof of the enantiomeric purity of **5** was obtained by preparing its (*2S,3S*)-enantiomer (formally the same compound as reported by Hanessian). Diesterification of **5** and its (*2S,3S*)-enantiomer by (*S*)- α -methoxyphenylacetic acid using Steglich method¹⁷ afforded distinct diastereoisomeric diesters **10** and **11**.

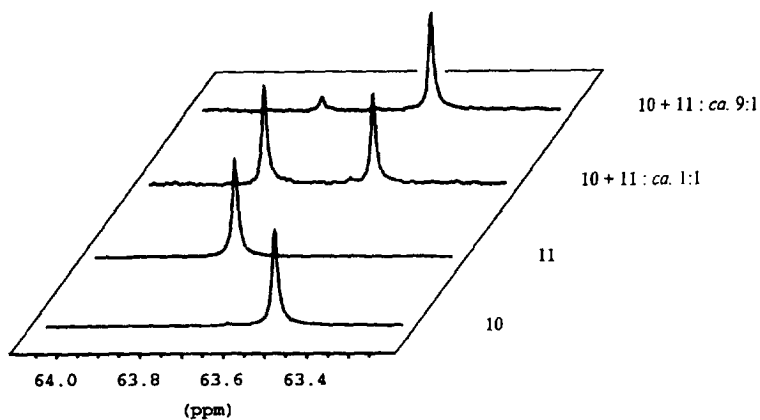
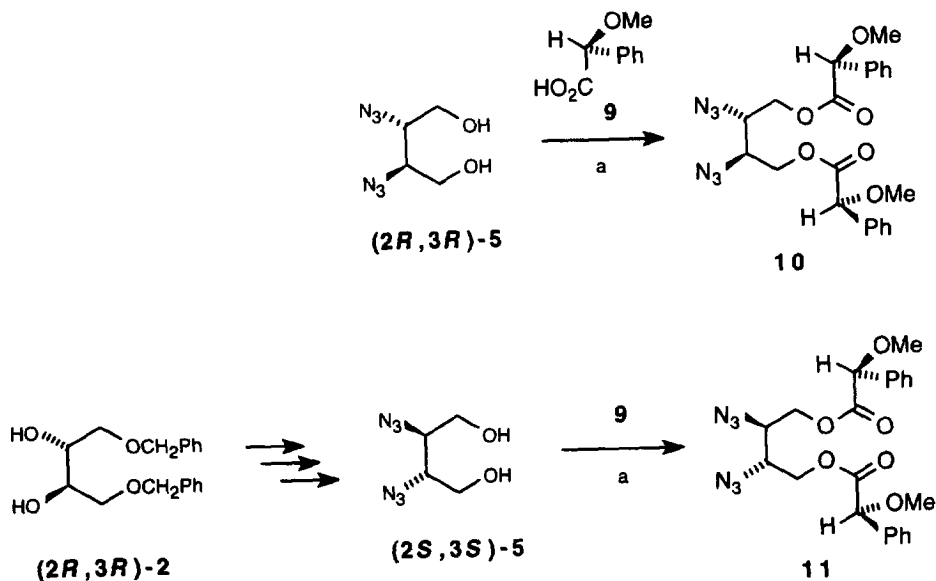


Figure 1. Zoomed ^1H decoupled ^{13}C NMR spectra (63.22 to 64.07 ppm) of **10**, **11**, and two mixtures.



a DCC, DMAP cat., THF, 20°C, 2.5 h, 86% for **10** and 93% for **11**.

Although **10** and **11** could not be readily differentiated from their ^1H NMR spectra, the ^{13}C NMR chemical shifts of all carbons except that of the carbonyl were found to be different. To confirm that ^{13}C NMR could be used to distinguish **10** and **11**, a spectrum of a mixture of these two compounds in nearly equal amounts was recorded. Clear splitting of carbon resonances resulted, demonstrating the effectiveness of this method.^{18,25}

High field ^{13}C NMR spectra of **10** and **11** alone showed only one set of signals. The other diastereoisomer was not detected, thus proving the enantiomeric purity of **5** and its $(2S,3S)$ -enantiomer as prepared in this work. To confirm that the detection limit of high field ^{13}C NMR is well below 10%, a spectrum of a 9:1 mixture of **10** and **11** was also recorded. The minor amount of **11** was easily detected by a second set of distinct peaks. For instance, zoomed spectra of the methylene carbon α to the oxygen atom, for which the chemical shift difference is the biggest, are shown below for **10** and **11** alone as well as for their 1:1 and 9:1 mixtures (Figure 1).

Conclusion

In summary, L-tartaric acid proved to be a suitable starting material for the synthesis of enantiomerically pure (2*R*,3*R*)-2,3-diaminobutane-1,4-diol **6** and its dibenzyl ether **7**. It is advantageous that, in contrast to starting from mannitol, the tartaric route allows also the synthesis of the (2*S*,3*S*)-enantiomers.

Further work will focus on the application of (2*R*,3*R*)-2,3-diaminobutane-1,4-diol **6** and its dibenzyl ether **7** for the synthesis of C₂-symmetric optically active ligands and catalysts.

Experimental section

(2*S*,3*S*)-1,4-Bis(benzyloxy)butane-2,3-diol dimethanesulfonate **3**

Methanesulfonyl chloride (1.86 mL, 24 mmol, 1.2 equiv.) was slowly added to a cooled solution at 0°C of diol **2** (3.02 g, 10 mmol) and triethylamine (4.18 mL, 30 mmol, 1.5 equiv.) in anhydrous dichloromethane (50 mL). After stirring for 1 hour at 0°C, the reaction mixture was allowed to warm up *ca.* 20°C. Water was added and the resulting mixture was extracted three times with ethyl acetate. Combined organic phases were successively washed with brine and water, dried (MgSO₄) and concentrated. Chromatography on silica gel using ethyl acetate/petroleum ether 1:4 as eluent afforded purified dimesylate **3** as a white solid (4.54 g, 99%, R_f=0.34 with ethyl acetate/petroleum ether 2:3, m.p. 73°C); IR (Nujol, NaCl): ν 3027, 1455, 1364 (S=O), 1332, 1173 (S=O), 1121, 1103, 913, 900, 815, 753, 734, 702, 676 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.39–7.27 (m, 10H, Ph), 5.02–4.97 (m, 2H, CH-OMs),¹⁹ 4.57 (d, 2H, *J*=11.6 Hz, CH₂Ph), 4.47 (d, 2H, *J*=11.6 Hz, CH₂Ph), 3.80–3.72 (m, 4H, OCH₂),¹⁹ 3.04 (s, 6H, OMs); ¹³C NMR (100 MHz, CDCl₃): δ 136.90 (2C ipso), 128.58 (pseudo dd, *J*=160.3, 7.4 Hz, 4C meta), 128.17 (broad dt, *J*=161.0, 7.2 Hz, 2C para), 128.05 (dm, *J*=158 Hz, 4C ortho), 78.73 (dp, *J*=150.5, 2.1 Hz, 2 CH-OMs), 73.67 (ttt, *J*=142.5, 4.5, 2.7 Hz, 2 CH₂Ph), 68.64 (ttt, *J*=144.0, 4.2, 1.5 Hz, 2 CH₂O), 38.78 (q, *J*=139.6 Hz, 2 SO₂OCH₃); [α]_D²¹ = -11.45, [α]₄₃₆²¹ = -22.1, [α]₃₆₅²¹ = -32.7 (c=10, CHCl₃); Anal. Calcd for C₂₀H₂₆O₈S₂: C, 52.39; H, 5.71; Found: C, 52.54; H, 5.82.

From the 2*R*,3*R* -enantiomer of diol **2** (derived from unnatural tartaric acid), the 2*R*,3*R* -enantiomer of **3** was also prepared in the same manner and gave [α]_D²³ = +10.9, [α]₄₃₆²³ = +21.0, [α]₃₆₅²³ = +31.3 (c=7.5, CHCl₃).

(2*R*,3*R*)-1,4-Bis(benzyloxy)-2,3-diazidobutane **4**

A mixture of dimesylate **3** (1.36 g, 3 mmol) and sodium azide (682 mg, 10.5 mmol, 1.75 equiv.) in DMSO (9 mL) was stirred at 80°C for 1 d, cooled to rt, and the white suspension was diluted with water/brine 1:1 (18 mL). The water layer was extracted three times with ethyl acetate and the combined organic extracts were dried over MgSO₄. Concentration *in vacuo* and chromatography of the remaining brown liquid on silica gel using ether/petroleum ether 1:9 as eluent afforded purified diazide **4** as a colorless liquid (1.00 g, 95%, R_f=0.23 with ether/petroleum ether 1:4); IR (neat, NaCl): ν 3089, 3065, 3032, 2904, 2866, 2106 (N₃), 1497, 1454, 1271, 1113, 1027, 738, 698 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.39–7.28 (m, 10H, Ph), 4.55 (s, 4H, CH₂Ph), 3.77–3.71 (m, 2H, CH-N₃),¹⁹ 3.70–3.62 (m, 4H, OCH₂);¹⁹ ¹³C NMR (100 MHz, CDCl₃): δ 137.33 (2C ipso), 128.50 (d pseudo d, *J*=160.0, 7.0 Hz, 4C meta), 127.95 (dtt, *J*=160.6, 7.0, 1.2 Hz, 2C para), 127.75 (dm, *J*=158.2 Hz, 4C ortho), 73.52 (tm, *J*=142.1 Hz, 2 CH₂Ph), 69.57 (ddtd, *J*=143.6, 143.3, 4.2, 3.0 Hz, 2 OCH₂), 60.92 (dm, *J*=143.8 Hz, 2 CH-N₃); [α]_D²¹ = -47.6, [α]₄₃₆²¹ = -93, [α]₃₆₅²¹ = -136 (c=6, CHCl₃); Anal. Calcd for C₁₈H₂₀N₆O₂: C, 61.35, H, 5.72, N, 23.85; Found: C, 60.98; H, 5.72, N, 23.82.

Diazide **4** (20 mmol reaction scale) could be obtained directly from diol **2** without purification of the intermediate dimesylate **3** in an overall yield of 91%.

From the 2*R*,3*R* -enantiomer of **3**, the 2*S*,3*S* -enantiomer of **4** was also prepared in the same manner and gave [α]_D²⁴ = +47.0, [α]₄₃₆²⁴ = +92 (c=5, CHCl₃).

(2R,3R)-2,3-Diazidobutane-1,4-diol 5*Using boron trichloride–dimethyl sulfide complex*

To a cooled (-40°C , nitrogen) solution of dibenzyl ether **4** (1.06 g, 3 mmol) in dry dichloromethane (24 mL), a 2 M solution of boron trichloride–dimethyl sulfide complex in dichloromethane (7.5 mL, 15 mmol, 2.5 equiv.) was slowly added *via* syringe. After warming to *ca.* 20°C , the mixture was stirred until precipitation of diazidodiol **5** indicated the end of the reaction (2 to 3 hours). The reaction mixture was quenched with a saturated sodium hydrogen carbonate solution (215 mL) and the aqueous layer was extracted three times with ethyl acetate. After drying over MgSO_4 the combined organic layers were concentrated to afford a pale brown solid of crude diazidodiol **5**. Purification by a short chromatography on silica gel using ethyl acetate/petroleum ether 2:3 as eluent afforded **5** as white crystals²⁰ (1.25 g, 81%, $R_f=0.11$ with ethyl acetate/petroleum ether 1:1, m.p. $79\text{--}80^{\circ}\text{C}$); IR (Nujol, NaCl): ν 3275 (broad), 2155, 2124, 2089, 1732, 1711, 1466, 1459, 1378, 1349, 1334, 1272, 1074, 1059, 984, 721 cm^{-1} ; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 4.39 (t, 2H, $J=5.4$ Hz, OH), 3.90–3.75 (m, 4H, CH_2OH),¹⁹ 3.73–3.66 (m, 2H, CH-N_3);¹⁹ $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 64.11 (broad d, $J=144.8$ Hz, CHN_3), 62.83 (td, $J=143, 3.5$ Hz, CH_2OH); $[\alpha]_{\text{D}}^{22}=-15.7$, $[\alpha]_{436}^{22}=-27.0$ ($c=6$, MeOH); MS (70 eV, EI) m/z (%): 28 (97) $[\text{N}_2]^+$, 31 (100) $[\text{CH}_2=\text{OH}]^+$; MS (CI, CH_4) m/z (%): 60 (100), 145 (12.3) $[\text{M}+\text{H}-\text{N}_2]^+$, 173 (67.2) $[\text{M}+\text{H}]^+$.

In the same manner, debenylation of the 2*S*,3*S*-enantiomer of **4** afforded the 2*S*,3*S*-enantiomer of **5** with $[\alpha]_{\text{D}}^{22}=+16.0$, $[\alpha]_{436}^{22}=+26.9$ ($c=5$, MeOH).

Using potassium carbonate in methanol, starting from 8

To a white suspension of dibenzoate **8** (380 mg, 1 mmol) in dry methanol (10 mL) under a nitrogen atmosphere was added potassium carbonate (84 mg, 0.6 mmol, 0.3 equiv.). The suspension was stirred at *ca.* 20°C for 24 h. TLC control of the resulting clear solution showed complete conversion of **8**. After evaporation with a small amount of silica gel and solid transfer on the column a short plug chromatography on silica gel using ethyl acetate/petroleum ether 2:3 afforded purified diazidodiol **5** as white crystals (145 mg, 84%, $[\alpha]_{\text{D}}^{22}=-16.6$, $[\alpha]_{436}^{22}=-29.5$ ($c=0.97$, MeOH)).

(2R,3R)-2,3-Diaminobutane-1,4-diol 6

To a solution of the diazide **5** (100 mg, 0.58 mmol) in methanol-distilled water (3:2, 5 ml) in a 100 mL flask was added 7 mg of PtO_2 (Adam's catalyst). The mixture was hydrogenated at room temperature and atmospheric pressure for 24 h. The catalyst was then removed by filtration over celite and the filtrate was evaporated under vacuum. The residue was coevaporated with ethanol to dryness to afford diaminoalcohol **6** as a colorless syrup (68 mg, 98%); IR (Nujol, NaCl): ν 3353 and 3296 (broad), 2928, 2883, 1593, 1463, 1381, 1044 cm^{-1} ; $^1\text{H NMR}$ (400 MHz, CD_3OD): δ 4.59 (broad s, OH and NH_2), 3.61 (pseudo dd, 2H, $J=11.0, 5.0$ Hz, CH_2OH),¹⁹ 3.52 (pseudo dd, 2H, $J=11.0, 6.0$ Hz, CH_2OH),¹⁹ 2.88–2.79 (m, 2H, CH-NH_2);¹⁹ $^{13}\text{C NMR}$ (100 MHz, CD_3OD): δ 65.01 (tm, $J=139$ Hz, CH_2OH), 55.10 (dm, $J=136$ Hz, CH-NH_2); $[\alpha]_{\text{D}}^{25}=+4.8$, $[\alpha]_{436}^{25}=+9.3$ ($c=1.24$, MeOH);²¹ MS (70 eV, EI) m/z 60 (base peak) $[\text{M}/2\text{ e.g. H}_2\text{N-CH-CH}_2\text{OH}]^+$.

In the same manner, hydrogenation of the 2*S*,3*S*-enantiomer of **5** afforded the 2*S*,3*S*-enantiomer of **6** with $[\alpha]_{\text{D}}^{24}=-3.8$, $[\alpha]_{436}^{24}=-7.3$, $[\alpha]_{365}^{24}=-11.6$ ($c=1.46$, MeOH).

(2R,3R)-1,4-Bis(benzyloxy)-2,3-diaminobutane 7

To a solution of dibenzyl ether **4** (930 mg, 2.65 mmol) in methanol (30 mL) was added 10% Pd/C (180 mg). The mixture was hydrogenated at *ca.* 20°C and atmospheric pressure for 24 h. The catalyst was then removed by filtration over celite and the filtrate was evaporated under vacuum to dryness to afford diamine **7** as a colorless syrup which crystallized after prolonged storage in a freezer yielding white crystals melting at $46\text{--}47^{\circ}\text{C}$ (790 mg, quant.); IR (neat, NaCl): ν 3373 (broad), 3030, 2902, 2859, 1454, 1097, 1077, 738, 699 cm^{-1} ; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.37–7.26 (m, 10H, Ph), 4.50 (s, 4H, CH_2Ph), 3.50 (pseudo dd, 2H, $J=9.2, 4.4$ Hz, CH_2O),¹⁹ 3.42 (pseudo dd, 2H, $J=9.2, 6.5$ Hz,

CH_2O),¹⁹ 3.03–2.98 (m, 2H, CH-NH_2),¹⁹ 1.71 (s, 4H, CH-NH_2); ¹³C NMR (100 MHz, CDCl_3): δ 138.19 (2C ipso), 128.43 (d pseudo d, $J=159.8$, 6.7 Hz, 4C meta), 127.70 (4C ortho and 2C para), 73.53 (tt, $J=140.4$, 3.3 Hz, 2 CH_2Ph), 73.30 (tm, $J=141.4$ Hz, 2 CH_2O), 52.64 (d sextet, $J=135.0$, 2.7 Hz, 2 CH-NH_2); $[\alpha]_{\text{D}}^{21.5}=+10.35$, $[\alpha]_{436}^{21.5}=+20.55$, $[\alpha]_{365}^{21.5}=+31.45$ ($c=4$, CHCl_3); HRMS (FAB, *m*-nitrobenzyl alcohol matrix) $\text{C}_{18}\text{H}_{25}\text{N}_2\text{O}_2$: $[\text{M}+\text{H}]^+$ (base peak) calcd 301.1916, found 301.1915.

In the same manner, hydrogenation of the 2*S*,3*S*-enantiomer of **4** afforded the 2*S*,3*S*-enantiomer of **7** with $[\alpha]_{\text{D}}^{24}=-10.65$, $[\alpha]_{436}^{24}=-21.0$, $[\alpha]_{365}^{24}=-32.1$ ($c=3.08$, CHCl_3). It was also obtained as a colorless syrup which crystallized after prolonged storage in a freezer yielding white crystals melting at 46–47°C.

For analytical purposes, diamine **7** was converted into its dibenzamide as follows: Benzoyl chloride (0.35 mL, 3. mmol, 1.5 equiv.) was slowly added to a cooled solution at 0°C of diamine **7** (0.30 g, 1.0 mmol) and triethylamine (0.56 mL, 4 mmol, 2 equiv.) in anhydrous dichloromethane (10 mL). After stirring for 1 hour at 0°C, the reaction mixture was allowed to warm to *ca.* 20°C and stirred for additional 16 h. Water was added and the resulting mixture was extracted three times with ethyl acetate. Combined organic phases were successively washed with brine and water, dried (MgSO_4) and concentrated. Short plug chromatography on silica gel using ethyl acetate/petroleum ether 1:4 as eluent afforded purified dibenzamide as a pale yellow solid (0.5 g, 99%, $R_f=0.45$ with ethyl acetate/petroleum ether 2:3, m.p. 112–114°C). Recrystallization in ethyl acetate/petroleum ether gave a pale yellow powder; IR (Nujol, NaCl): ν 3308 (broad), 1635, 1537, 1532, 1464, 1455, 1109, 694 cm^{-1} ; ¹H NMR (400 MHz, CDCl_3) δ 7.64 (pseudo dd, 4H, $J=8.3$, 1.3 Hz, H ortho), 7.44 (ddt, 2H, $J=8.1$, 6.7, 1.3 Hz, H para), 7.37–7.27 (m, 14H), 4.71–4.61 (m, 2H, CH-NH), 4.51 (d, 2H, $J=11.7$ Hz, CH_2Ph), 4.49 (d, 2H, $J=11.7$ Hz, CH_2Ph), 3.74 (pseudo dd, 2H, $J=9.8$, 3.2 Hz, CH_2O),²² 3.69 (pseudo dd, 2H, $J=9.8$, 4.5 Hz, CH_2O),²² 1.9–1.7 (broad, 2H, NH); ¹³C NMR (100 MHz, CDCl_3) δ 167.61 (2 CO), 137.53 (C ipso of CH_2Ph), 133.99 (C ipso of PhCONH), 131.45 (C para of PhCONH), 128.55 ($\times 2$), 128.49 ($\times 2$), 128.06 ($\times 2$), 128.03 (C para of CH_2Ph), 126.98 ($\times 2$), 73.60 (tm, $J=141$ Hz), 68.99 (tt, $J=143.2$, 4.1 Hz), 51.04 (dm, $J=140.9$ Hz, CH-N); $[\alpha]_{\text{D}}^{21.5}=-70.1$ ($c=6$, CHCl_3); MS (CI, CH_4) m/z (%): 401 (23.8) $[\text{M}+\text{H}-\text{PhCH}_2\text{OH}]^+$, 509 (100) $[\text{M}+\text{H}]^+$, 537 (21.7) $[\text{M}+\text{C}_2\text{H}_5]^+$; Anal. Calcd for $\text{C}_{32}\text{H}_{32}\text{N}_2\text{O}_4$: C, 75.57; H, 6.34; N, 5.51. Found: C, 75.47; H, 6.34; N, 5.47.

(2*R*,3*R*)-1,4-Bis(benzoyloxy)-2,3-diazidobutane **8**

To a magnetically stirred biphasic system of carbon tetrachloride (60 mL), acetonitrile (60 mL) and water (90 mL) was added dibenzyl ether **4** (1.06 g, 3 mmol) and sodium metaperiodate (5.4 g, 25.2 mmol, 4.2 equiv.). The resulting mixture was stirred until both phases became clear. Ruthenium trichloride hydrate (25 mg, 0.12 mmol, 0.02 equiv.) was added and the suspension turned rapidly deep brown. The mixture was vigorously stirred for 48 h at 15°C whilst the color gradually faded. The progress of the reaction was monitored by TLC. After cooling to 0°C, ether (120 mL) was added (a deep black color appeared) and vigorous stirring was continued for about 10 min. The organic phase was separated and the aqueous layer extracted with ethyl acetate (3 \times 100 mL). The combined organic layers were washed with brine, dried over MgSO_4 , and concentrated. Chromatography on silica gel using ether/petroleum ether 1:9 afforded purified dibenzoate **8** as colorless crystals (1.05 g, 92%, $R_f=0.11$ with ether/petroleum ether 1:4, m.p. 90–91°C); IR (Nujol, NaCl): ν 3091, 3060, 3034, 2150, 2116, 2083, 1716, 1602, 1583, 1461, 1449, 1389, 1336, 1311, 1276, 1266, 1120, 707 cm^{-1} ; ¹H NMR (400 MHz, CDCl_3) δ 8.06 (pseudo dd, 4H, $J=8.4$, 1.3 Hz, H ortho), 7.60 (ddt, 2H, $J=8.0$, 6.9, 1.3 Hz, H para), 7.46 (pseudo tt, 4H, $J=7.7$, 1.5 Hz, H meta), 4.67 (pseudo dd, 2H, $J=11.7$, 4.3 Hz, CH_2O), 4.57 (pseudo dd, 2H, $J=11.7$, 7.4 Hz, CH_2O),¹⁹ 4.03–3.96 (m, 2H, CH-N_3),¹⁹ ¹³C NMR (100 MHz, CDCl_3): δ 165.96 (2 CO), 133.60 (dddd, $J=161.5$, 7.9, 7.5, 1.2 Hz, 2C para), 129.82 (dm, $J=163.0$ Hz, 4C ortho), 129.04 (2C ipso), 128.61 (dd, $J=162.4$, 7.8 Hz, 4C meta), 64.30 (dddt, $J=151.1$, 149.0, 2.1, 1.5 Hz, 2 CH_2O), 60.36 (dit, $J=143.6$, 2.4, 1.0 Hz, 2 CH-N_3); $[\alpha]_{\text{D}}^{22}=-3.0$, $[\alpha]_{436}^{22}=-1.25$, $[\alpha]_{365}^{22}=+10.5$ ($c=4$, CHCl_3); MS (CI, NH_3) m/z (%): 381 (0.6) $[\text{M}+\text{H}]^+$, 398 (100) $[\text{M}+\text{NH}_4]^+$; Anal. Calcd for $\text{C}_{18}\text{H}_{16}\text{N}_6\text{O}_4$: C, 56.84; H, 4.24; N, 22.09. Found: C, 56.96; H, 4.25; N, 22.53.

Table 1. Chemical shifts and non equal to zero coupling constants of the ABCC'A'B' system observed in ¹H NMR spectra of compounds 2–8, 10, 11

Compound	2	3	4	5	6	7	8	10	11
$\delta_A = \delta_{A'}$ (ppm)	3.586	3.768	3.664	3.856	3.611	3.418	4.670	4.178	4.254
$\delta_B = \delta_{B'}$ (ppm)	3.620	3.753	3.654	3.796	3.524	3.500	4.571	4.123	4.216
$\delta_C = \delta_{C'}$ (ppm)	3.876	4.996	3.739	3.694	2.837	3.009	3.997	3.364	3.414
$J_{AB} = J_{A'B'}$ (Hz)	-9.7	-11.2	-10.0	-11.3	-11.0	-9.2	-11.7	-11.6	-11.6
$J_{AC} = J_{A'C'}$ (Hz)	5.6	3.3	5.5	5.7	5.0	6.5	4.3	4.7	4.6
$J_{BC} = J_{B'C'}$ (Hz)	4.5	6.3	6.5	6.1	6.0	4.4	7.4	6.9	7.3
$J_{CC'}$ (Hz)	3.3	5.0	4.6	5.0	5.0	4.7	4.7	4.7	4.4

All spectra were recorded in CDCl₃ except those of 5 and 6 which were respectively recorded in CD₃COCD₃ and CD₃OD.

Di-(S)- α -methoxyphenylacetate of (2R,3R)-2,3-diazidobutane-1,4-diol 10

To a solution of 5 (43 mg, 0.25 mmol), (S)-(+)- α -methoxyphenylacetic acid (108 mg, 0.65 mmol, 1.3 equiv.) and 4-dimethylaminopyridine (18 mg, 0.15 mmol, 0.3 equiv.) in anhydrous THF (5mL) was added N,N'-dicyclohexylcarbodiimide (165 mg, 0.8 mmol, 1.6 equiv.). After stirring for 2.5 h at *ca.* 20°C, TLC showed a complete conversion of 5 into its corresponding diester. Removal of the formed precipitate by filtration through celite, concentration of the filtrate and short plug chromatography on silica gel using ethyl acetate/petroleum ether 1:4 as eluent afforded purified diester 10 as a colorless liquid (101 mg, 86%, *R*_f=0.12 with ethyl acetate/petroleum ether 1:4); IR (neat, NaCl): ν 3066, 3033, 2994, 2932, 2831, 2110 (N₃), 1757 (C=O), 1494, 1455, 1261, 1171, 1114, 913, 734, 699 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.41 (dm, 4H, *J*=7.8 Hz, H ortho), 7.39–7.30 (m, 6H meta and para), 4.78 (s, 2H, CH-Ph), 4.18 (pseudo dd, 2H, *J*=11.6, 4.9 Hz, CH₂O),¹⁹ 4.12 (pseudo dd, 2H, *J*=11.6, 6.7 Hz, CH₂O),¹⁹ 3.40 (s, 6H, OMe), 3.39–3.34 (m, 2H, CH-N₃);¹⁹ ¹³C NMR (100 MHz, CDCl₃): δ 169.98 (2 CO), 135.64 (2C ipso), 129.13 (dt, *J*=161.0, 7.3 Hz, 2C para), 128.90 (4C meta), 127.21 (4C ortho), 82.22 (d sextet, *J*=146.4, 4.7 Hz, 2 CH-Ph), 63.51 (t pseudo d, *J*=150, 2 Hz, 2 CH₂O), 59.57 (d sextet, *J*=143.4, 2.5 Hz, 2 CHN₃), 57.38 (qd, *J*=142.2, 3.5 Hz, 2 OCH₃); [α]_D²⁴=+66.3, [α]₄₃₆²⁴=+157.7, [α]₃₆₅²⁴=+296.5 (*c*=0.92, CHCl₃); HRMS (FAB, *m*-nitrobenzyl alcohol matrix) C₂₂H₂₅N₆O₆: [M+H]⁺ calcd 469.1836, found 469.1835. (

Di-(S)- α -methoxyphenylacetate of (2S,3S)-2,3-diazidobutane-1,4-diol 11

Diesterification of the 2S,3S-enantiomer of 5 using the foregoing protocol afforded 11 in 93% yield; IR (neat, NaCl): ν 3066, 3033, 2989, 2934, 2831, 2111 (N₃), 1758 (C=O), 1495, 1455, 1249, 1171, 1114, 913, 734, 699 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.41 (dm, 4H, *J*=7.8 Hz, H ortho), 7.39–7.30 (m, 6H meta and para), 4.78 (s, 2H, CH-Ph), 4.25 (pseudo dd, 2H, *J*=11.6, 4.9 Hz, CH₂O),¹⁹ 4.22 (pseudo dd, 2H, *J*=11.6, 7.0 Hz, CH₂O),¹⁹ 3.41 (s, 6H, OMe), 3.44–3.38 (m, 2H, CH-N₃);¹⁹ ¹³C NMR (100 MHz, CDCl₃): δ 169.98 (2 CO), 135.62 (2C ipso), 129.11 (2C para), 128.86 (4C meta), 127.20 (4C ortho), 82.27 (2 CH-Ph), 63.77 (2 CH₂O), 59.70 (2 CHN₃), 57.41 (2 OCH₃);

$[\alpha]_{\text{D}}^{25} = +93.4$, $[\alpha]_{436}^{25} = +204.5$, $[\alpha]_{365}^{25} = +352.4$ ($c = 1.52$, CHCl_3); HRMS (FAB, *m*-nitrobenzyl alcohol matrix) $\text{C}_{22}\text{H}_{25}\text{N}_6\text{O}_6$: $[\text{M}+\text{H}]^+$ calcd 469.1836, found 469.1846.

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11. Although DDQ was already reported to cleave benzyl ethers in the presence of azides,²³ treatment of **4** with an excess of DDQ only resulted in a low yield (*ca.* 20%) of diol **5**. A reagent combination of AlCl_3 and *N,N*-dimethylaniline²⁴ cleanly removed the benzyl groups (in 64% yield when using 4 equiv. of AlCl_3 and 3 equiv. of PhNMe_2 , CH_2Cl_2 , 0 to 20°C followed by 1 h at 20°C) but boron trichloride–dimethyl sulfide complex in dichloromethane¹² proved to be more convenient and efficient.
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13. Hydrogenation of **5** using palladium on carbon or Pearlman's catalyst (10% palladium hydroxide on carbon) led to **6** along with a fair amount (*ca.* 20–30%) of a by-product whose ^{13}C NMR and HRMS indicated that it could be the *N,N'*-dimethyl derivative of **6**. Its formation could be explained by the following side reactions: dehydrogenation of methanol by the catalyst to give formaldehyde, nucleophilic addition of formaldehyde to the primary amino group of **6**, dehydration of the resulting aminoalcohol to yield a putative intermediate methylene imine which would be hydrogenated to give a *N*-methylated amine. Adams' catalyst afforded **6** with only a neglectable amount (*ca.* 5%) of this by-product.
14. Catalytic hydrogenation of diazide **8** only afforded a complex mixture instead of the desired diamine.

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18. This method was already used to check the optical purity of epoxyalcohols obtained by asymmetric Sharpless epoxidation.²⁵ On the other hand, a lanthanide shift experiment was inefficient since no splitting of signals was observed when adding Eu(tfc)₃ to a mixture of **5** and its (2*S*,3*S*)-enantiomer.
19. For ¹H NMR spectra of these compounds, a symmetrical six spins ABCC'A'B' system was observed. Simulation afforded the following NMR parameters
Table 1).
20. In spite of the high N/C ratio of **5**, suggesting a potential explosive hazard, no problem was encountered. However caution is recommended in handling **5**.
21. Specific optical rotation of bis-aminoalcohol **6** could not be measured in water since the aqueous solution of **6** was turbid even after filtration through celite.
22. Whereas in the other tartaric derivatives, an ABCC'A'B' system was observed,¹⁹ the neighboring NH gives further coupling with the two vicinal methine protons leading to a symmetrical eight spin XABCC'A'B'X' system. Irradiation of CH₂O almost collapse the methine protons α to NH to a doublet with a coupling constant $J_{with\ NH}=6.0$ Hz.
23. For example, see N. Ikemoto, S. L. Schreiber, *J. Am. Chem. Soc.* **1992**, *114*, 2524.
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