JOC Article

RCM Approaches toward the Diastereoselective Synthesis of Vicinal *trans*-Diaminocyclitols from L-Serine

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Starting from L-serine, the asymmetric synthesis of four diaminocyclitol derivatives as sugar-based glycosidase inhibitors has been achieved using ring-closing metathesis (RCM) as a key step. Introduction of vicinal *trans*-diamino functionality onto the acyclic precursors was accomplished by highly diastereoselective addition of Grignard reagent to imine, and the elaboration of polyhydroxylic groups was effected via diastereoselective olefin epoxidation or dihydroxylation. The absolute configurations of final products were confirmed by 2D NMR studies.

Introduction

Recently, interest has continued to mount in new applications of natural and unnatural glycosidase inhibitors in basic research and biomedical investigations.[1] Many D-glucose- and D-galactose-derived glycosylamines,[2] polyhydroxylated piperidines,[3] and various derivatives of inositol[4] and streptamine[5] have been synthesized and have shown inhibitory activities more potent than those of their corresponding parent compounds or nonbasic analogues. Because many of these agents represent early intermediates in the inositol-phosphate cycle, they have been used as probes for investigating the inositol phosphate cycle as well as potential competitive or selective glycosidase inhibitors. Furthermore, many of these compounds have potential for use in a wide range of treatments of viral and parasitic protozoa infections, cancer, diabetes, tuberculosis, and lysosomal storage diseases.[6] Several diaminocyclitols have been synthesized and reported to possess strong antibiotic activity.[7] These include streptamine and 2-deoxystreptamine isomers,

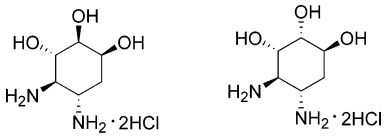

FIGURE 1. Vicinal *trans*-diaminocyclitols **1**−**4**.

which feature a 1,3-arrangement of their two amino groups. Preparations of vicinal *cis*-diamino inositol analogues have also been reported.[5a,8] Many of these reported compounds were synthesized from cyclohexatomic or cyclopentatomic derivatives. In addition, various cyclohexylamine and cyclopentylamine derivatives have appeared in nucleosides studies.[9] Cyclopentylamine derivatives as glycosidase inhibitors have also been examined.[1a,10]

In this paper, we would like to report syntheses of four new carba-sugar derivatives, 6-deoxycyclohexyldiamines (**1** and **2**) and 5-deoxycyclopentyldiamines (**3** and **4**) (Figure 1). Common to all of these are carbon-frame skeletons, vicinal *trans*-diamino functionalities, and polyhydroxyl groups. These carbon-frame skeletons provide

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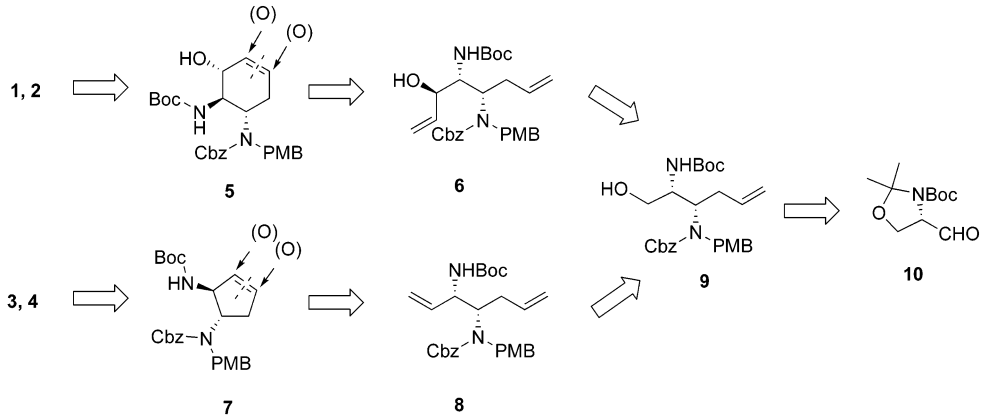


FIGURE 2. Retrosynthetic analysis for the four vicinal *trans*-diaminocyclitols **1**−**4**.

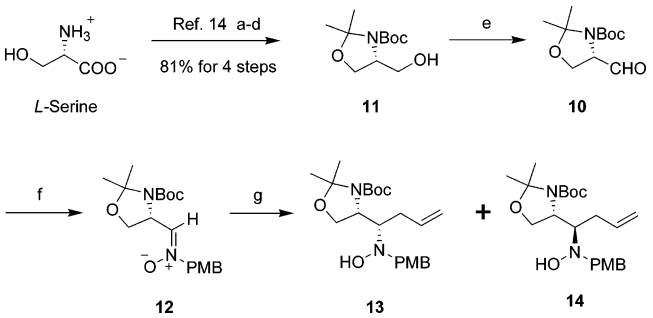
great chemical stability and flexibility. Key to our preparation of vicinal *trans*-diamino functionality at an acyclic stage is diastereoselective addition of allylmagnesium bromide to imine **12** derived from Garner aldehyde. Other features of our synthesis include catalytic ring-closing metathesis (RCM)[11] for construction of the all-carbon rings and substrate-controlled diastereoselective epoxidation or dihydroxylation for the introduction of polyhydroxyl groups with various configurations.

Results and Discussion

The general retrosynthetic analysis of compounds **1**−**4** is outlined in Figure 2. Compounds **1** and **2** can be obtained from a common intermediate **5**, which then can be derived from acyclic diene **6** by an RCM reaction, while olefin **6** is envisaged to be produced by a stereoselective addition of vinylmagmesium bromide to an aldehyde derived from alcohol **9** with anhydrous $ZnCl_2$ as a promotor.[12] Similarly, compounds **3** and **4** can be prepared from a common intermediate **7**, which can be derived from diene **8** by an RCM reaction. Like diene **6**, compound **8** also can be related to alcohol **9**, which in turn can be prepared from L-Garner aldehyde **10**.[13]

The synthesis started from L-serine (Scheme 1). L-Serine was readily converted to alcohol **11** according to known procedure.[14] Swern oxidation of the latter afforded aldehyde **10**, which was used immediately in the next step. Treatment of the freshly prepared Garner aldehyde **10** with *N*-(4-methoxybenzyl)-hydroxylamine and anhydrous $MgSO_4$ in dry CH_2Cl_2 at room temperature gave nitrone **12** (74% yield from alcohol **11**). Nitrone **12** was then treated with allylmagnesium bromide (3.0 equiv) in the presence of anhydrous $ZnBr_2$ (1.0 equiv) at −70 °C with anhydrous tetrahydrofuran and anhydrous ether (1:1, v/v) as the cosolvent.[13,15] As expected, the desired *syn*-adduct **13** was obtained as the predominant product in 87% yield along with the *anti*-isomer **14** in 9% yield.

SCHEME 1[a]



[a] Reagents and conditions: (a) HCl, MeOH, reflux, 100%; (b) Boc_2O, Et_3N, THF, 88%; (c) 2,2-DMOP, $BF_3{\cdot}Et_2O$, acetone, 94%; (d) LAH, anhydrous THF, −10 °C, 98%; (e) DMSO, $(COCl)_2$, Et_3N, CH_2Cl_2; (f) *N*-(4-methoxybenzyl)-hydroxylamine, anhydrous $MgSO_4$, CH_2Cl_2, 74% (for 2 steps); (g) anhydrous $ZnBr_2$, allylmagnesium bromide in Et_2O, anhydrous THF/Et_2O 1:1 (v/v), −70 °C, 4 h; **13** (87%), **14** (9%).

TABLE 1. Results of Addition of Allylmagnesium Bromide to Nitrone 12[a]

entry	Lewis acid	solvent	*syn*-**13** (%)	*anti*-**14** (%)	**13**:**14**
1	none	THF	66	30	2.2:1
2	$ZnBr_2$	THF	78	19	4.1:1
3	$ZnBr_2$	Et_2O	59	9	6.6:1
4	$ZnBr_2$	THF/Et_2O 1:1	87	9	9.7:1

[a] All reactions were carried out at −70 °C.

These two diastereomers could be easily separated by silica gel column chromatography. The absolute configuration of **13** was ultimately confirmed by NMR studies on compound **20** (^{1}H NMR, NOESY) at a later stage. Direct assignments of ^{1}H NMR chemical shifts of both the NOH of *syn*-isomer **13** (6.99 ppm) and *anti*-isomer **14** (5.36 ppm) matched referenced patterns.[13] As shown in Table 1, $ZnBr_2$ and the THF/ether cosolvent system were critical for good diastereoselectivity to be obtained.

Reductive cleavage of the N−O bond of the major adduct **13** was achieved using zinc−copper(II) in acetic acid/water to give the corresponding secondary amine **15** in high yield (Scheme 2). Amine **15** was then treated with

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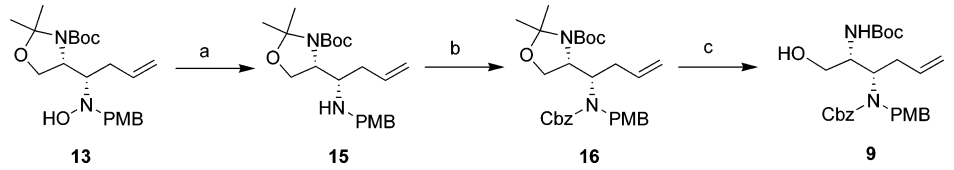
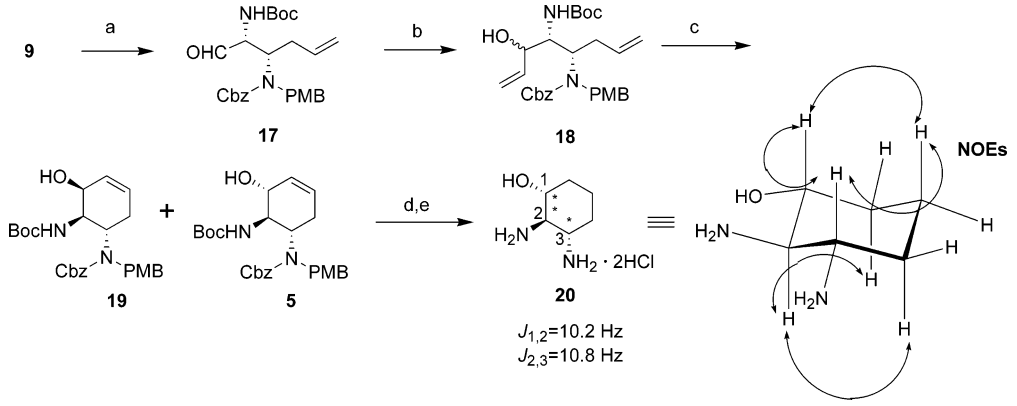
SCHEME 2[a]



[a] Reagents and conditions: (a) Zn−Cu(OAc)$_2$, AcOH/H_2O, 70 °C; (b) CbzCl, EtOAc/saturated aqueous $NaHCO_3$; (c) *p*-TsOH·H_2O (cat.), MeOH, reflux (85% overall).

SCHEME 3[a]



[a] Reagents and conditions: (a) DMSO, $(COCl)_2$, Et_3N, CH_2Cl_2; (b) anhydrous $ZnCl_2$, vinylmagnesium bromide, anhydrous THF, −70 to −30 °C (79% yield for 2 steps); (c) Grubbs catalyst (8 mol %), CH_2Cl_2; **5** (83%), **19** (7%); (d) H_2, 20% $Pd(OH)_2$/C (cat.), MeOH; (e) 3 N HCl, MeOH, rt (83% for 2 steps).

benzyl chloroformate (CbzCl) in ethyl acetate and saturated aqueous $NaHCO_3$ (1:1, v/v) at room temperature to afford compound **16** quantitatively. Selective acetonide hydrolysis in methanol in the presence of *p*-TsOH hydrate yielded the primary alcohol **9**, which was a common key intermediate for the synthesis of all four final products.

As shown in Scheme 3, treatment of aldehyde **17**, freshly prepared by Swern oxidation of alcohol **9**, with vinylmagnesium bromide (3.0 equiv) and anhydrous $ZnCl_2$ (1.5 equiv) in tetrahydrofuran at −30 °C gave a mixture of epimeric dienes **18** (79% yield in 2 steps). In the presence of bis(tricyclohexylphosphine)benzylidene ruthenium(IV) dichloride (Grubbs catalyst), RCM reaction of the diastereomeric mixture **18** in anhydrous CH_2Cl_2 under N_2 afforded the separable cyclohexene derivative **5** and its diastereoisomer **19** in 90% yield (ratio of **5**:**19** = 92:8). The relative configuration (and by consequence the absolute) of major product **5** was confirmed by NMR analysis of **20**, which was obtained by hydrogenation of **5** and subsequent treatment with hydrochloric acid. The results of NOESY studies of **20** are shown in Scheme 3.

After confirming the stereochemistry of key intermediate **5**, our attentions were directed to the elaboration of hydroxyls in the cyclohexene ring (Scheme 4). Treatment of cyclohexene **5** with a catalytic amount of OsO_4 and 4-methylmorpholine *N*-oxide (NMO) as a co-oxidant gave predominantly the *trans*-adduct **21** (93%). The diastereoisomeric ratio of dihydroxylation products is 89.6:10.4 as determined by HPLC analysis. Full deprotection of **21** with 12 N HCl in refluxed methanol afforded final product **1** in 92% yield. The relative configuration was confirmed by NOESY studies. Compound **5** was treated with 3-chloroperoxybenzoic acid (*m*-CPBA) to give epoxide **22** in 72% yield. Subsequent regioselective opening of the epoxide by water was realized under acidic condition on treatment with 0.2 N H_2SO_4/dioxane (1:1, v/v)[16] to afford the triol **23** in 82% yield as a single product as determined by HPLC and ^1H NMR measurements. Finally, protective groups of **23** were removed with 12 N HCl in refluxed methanol to afford final product **2**, whose relative configuration (and by consequence the absolute) was also confirmed by NOESY experiment.

As shown in Figure 2, for the syntheses of cyclopentane derivatives **3** and **4**, diene **8** was the initially proposed precursor for RCM reaction. In practice, Wittig reaction of aldehyde **17** with Ph_3PCH_3Br under various conditions could not afford the desired product **8**. The reaction mixture was very complicated and the starting material decomposed under the strong basic conditions. However, treatment of aldehyde **17** with (carbethoxymethylene)-triphenylphosphorane (Ph_3P═CHCOOEt) in tetrahydrofuran furnished (2*E*)-2,7-diene **24** as a single product in high yield (93% for 2 steps, Scheme 5). RCM reaction of diolefin **24** under the above-mentioned conditions afforded cyclopentene **7** in excellent yield.

Cyclopentene **7** was then treated with NMO and a catalytic amount of OsO_4 to give a diastereomeric mixture of diols in 94% yield with product **25** predominating in a 95:5 ratio as determined by HPLC. Deprotection of **25** with 12 N HCl in MeOH afforded **3** in 95% yield. Alternatively, epoxidation of **7** with *m*-CPBA in the presence of $NaHCO_3$ afforded the single *syn*-epoxide **26**

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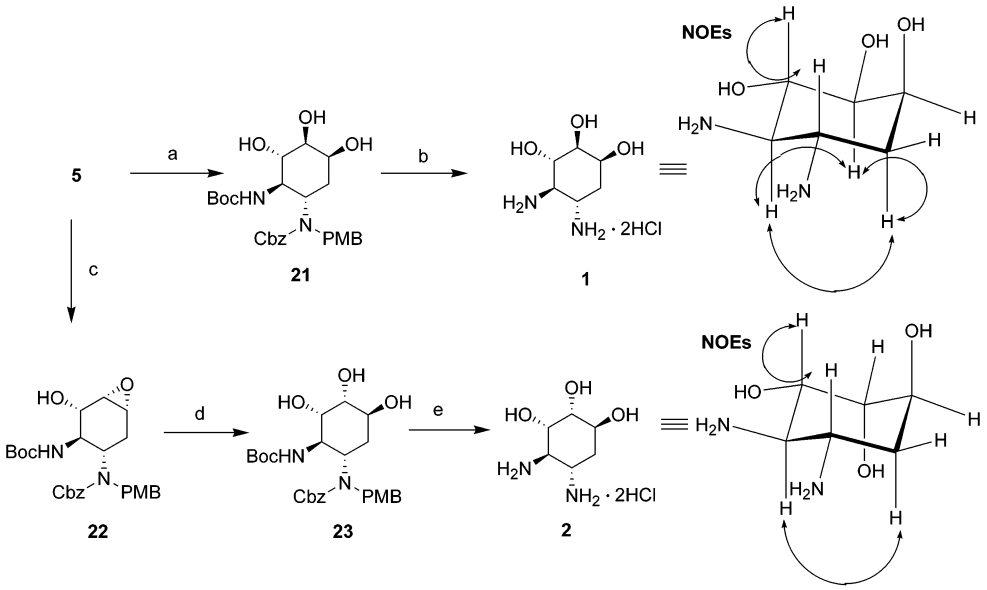
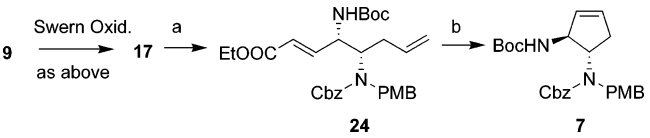
SCHEME 4[a]



[a] Reagents and conditions: (a) OsO_4;(cat.), NMO, acetone/H_2O, rt, 9:1 (v/v), 93%; (b) 12 N HCl, reflux, 92%; (c) *m*-CPBA, Na_2HPO_4, CH_2Cl_2, 15 °C, 72%; (d) 0.2 N H_2SO_4, dioxane, 10 °C, 82%; (e) 12 N HCl, reflux, 87%.

SCHEME 5[a]



[a] Reagents and conditions: (a) $Ph_3P{=}CHCOOEt$, THF, 93% from alcohol **9**; (b) Grubbs catalyst (5 mol %), CH_2Cl_2, 99%.

in 78% yield; its *anti*-diastereomer was not observed.[17] However, the regioselectivity was very poor (as measured by HPLC and ^1H NMR) when the epoxide **26** was treated with 0.2 N H_2SO_4/dioxane (1:1, v/v) to give a diastereomeric mixture of *anti*-diols **27**. This unexpected result led us to explore the possibilities of regio- and stereoselective epoxide opening by an intramolecular nucleophilic approach. Treatment of **26** with catalytic amount of D-camphor-10-sulfonic acid[18] in dichloromethane smoothly gave **28** (86% yield) as a single product. The structure and relative configuration of **28** were confirmed by NOESY studies. Refluxing **28** in 12 N HCl and then recrystallization from MeOH afforded **4** in 94% yield (Scheme 6).

Summary

In conclusion, four carbocyclic sugar-like derivatives of 6-deoxycyclohexyl diamine or 5-deoxycyclopentyl diamine with vicinal *trans*-diamino functionalities and polyhydroxy groups have been synthesized diastereoselectively through a common intermediate **9**. The vicinal *trans*-diamino moieties were introduced by a highly diastereoselective addition reaction. The cycloalkene rings were efficiently constructed by RCM reactions from diene precursors, and polyhydroxylic groups were elaborated either by substrate-controlled diastereoselective epoxidation/epoxide opening or direct dihydroxylation. Stereochemistries of these final products were well-controlled and confirmed by NMR studies. Utilization of these vicinal diamino polyhydroxycycloalkane derivatives in biological studies is under way in our laboratory, and these results will be reported in due course.

Experimental Section

(*Z*)-*N*-[(4*R*)-3-(*tert*-Butoxycarbonyl)-2,2-dimethyl-1,3-oxazolidin-4-ylidene]- 4-methoxybenzylamine *N*-Oxide (12). To a solution of oxalyl chloride (3.9 mL, 4.5 mmol, 1.5 equiv) in dry CH_2Cl_2 (150 mL) was added slowly DMSO (6.5 mL, 90 mmol, 3.0 equiv) in dry CH_2Cl_2 (25 mL) at −78 °C under N_2. After 30 min, alcohol **11** (7.0 g, 30 mmol) in dry CH_2Cl_2 (100 mL) was added dropwise at −78 °C. The mixture was stirred for additional 2 h at −78 °C, and then Et_3N (30 mL) was added at −78 °C. After 20 min, the mixture was warmed to room temperature, and saturated aqueous NH_4Cl (100 mL) was added. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were washed with saturated aqueous NH_4Cl (3 × 100 mL) and brine (3 × 100 mL), dried ($MgSO_4$), and concentrated in vacuo to give Garner aldehyde **10**, which was used directly without further purification.

To a solution of the above freshly prepared aldehyde **10** in dry CH_2Cl_2 (100 mL) was added sequentially anhydrous $MgSO_4$ (7.2 g, 60 mmol, 2.0 equiv) and *N*-hydroxy(4-methoxybenzyl) methanamine[19] (4.6 g, 30 mmol, 1.0 equiv). The resulting mixture was stirred at room temperature overnight. The solid in the mixture was filtered, and the filtrate was concentrated in vacuo to yield the crude product, which was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 1:2) to give nitrone **12** (8.1 g, 74% for 2 steps) as a white solid, mp 55−56 °C. $[\alpha]^{23}_D$ −56.5 (*c* 1.15, $CHCl_3$). IR (KBr): 3078, 3011, 2975, 2936, 1702, 1614, 1516, 1382, 1255, 1176, 1089, 853 cm^{-1}. ^1H NMR (300 MHz, 55 °C, $CDCl_3$): δ 1.39 (s, 9H), 1.46−1.55 (m, 6H), 3.80 (s, 3H), 4.01−4.04 (m, 1H), 4.17 (dd, J = 6.9, 9.6 Hz, 1H), 4.80 (s, 2H), 4.92-

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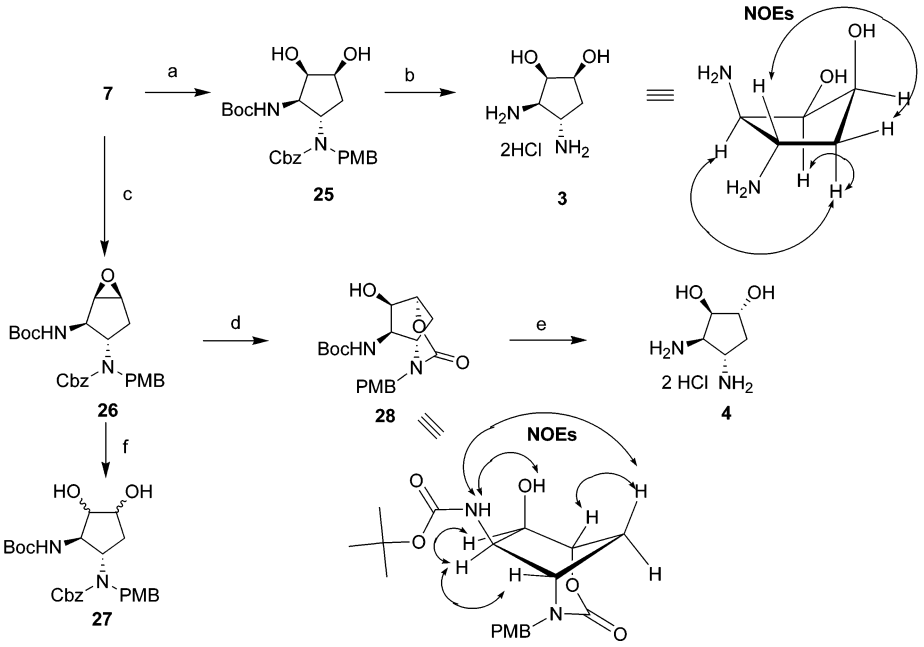
SCHEME 6[a]



[a] Reagents and conditions: (a) OsO_4 (cat.), NMO, acetone/H_2O, rt, 9:1 (v/v), 94%; (b) 12 N HCl, reflux, 95%; (c) *m*-CPBA, $NaHCO_3$, CH_2Cl_2, 15 °C, 78%; (d) cat. D-CSA, CH_2Cl_2, 86%; (e) 12 N HCl, reflux, 94%; (f) 0.2 N H_2SO_4, dioxane, 10 °C, 75%.

(br, 1H), 6.66 (bs, 1H), 6.90 (d, J = 8.1 Hz, 2H), 7.30 (d, J = 8.4 Hz, 2H) ppm. ESIMS (*m*/*z*, %): 365.2 (M + H^+, 100%). Anal. Calcd for $C_{19}H_{28}N_2O_5$: C 62.62, H 7.74, N 7.69. Found: C 62.52, H 7.90, N 7.53.

Hydroxylamines 13 and 14. To a stirred solution of nitrone **12** (8.0 g, 22 mmol) in anhydrous THF and anhydrous Et_2O (400 mL, 1:1) at room temperature under N_2 was added anhydrous $ZnBr_2$ (4.95 g, 22 mmol). After being stirred at room temperature for 30 min, the reaction mixture was cooled to −70 °C and treated with allylmagnesium bromide (1.0 M in Et_2O, 66 mL, 66 mmol, 3.0 equiv) dropwise. The resulting suspension was stirred at −70 °C for an additional 4 h until it was quenched with 1 N NaOH (200 mL) at −70 °C and warmed to room temperature. The layers were separated, and the aqueous layer was extracted with Et_2O (3 × 100 mL). The combined organic layers were washed with saturated aqueous NH_4Cl (3 × 100 mL) and brine (3 × 100 mL), dried (Na_2SO_4), and concentrated in vacuo to give the crude mixture of hydroxylamines **13** and **14**, which were separated and purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 40:1 to 20:1) to afford *syn*-isomer **13** (7.85 g, 87%) and *trans*-isomer **14** (0.82 g, 9%) as colorless oils. Data for **13**: $[\alpha]^{19}_D$ −22.10 (*c* 1.28, $CHCl_3$). IR (neat): 3357, 3075, 2979, 2937, 1670, 1514, 1410, 1249, 1174, 1107 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.43 (s, 3H), 1.50 (s, 3H), 1.52 (s, 9H), 2.04−2.13 (m, 1H), 2.70−2.76 (m, 1H), 2.81−2.91 (m, 1H), 3.73 (d, J = 13.8 Hz, 1H), 3.78 (s, 3H), 3.86−3.93 (m, 2H), 4.01−4.06 (m, 1H), 4.05 (d, J = 13.8 Hz, 1H), 5.02−5.13 (m, 2H), 5.93−6.02 (m, 1H), 6.80 (d, J = 8.7 Hz, 2H), 6.99 (s, 1H, ex. D_2O), 7.25 (d, J = 8.7 Hz, 2H) ppm. ESIMS (*m*/*z*, %): 407.1 (M + H^+, 100%), 429.1 (M + Na^+, 15%). Anal. Calcd for $C_{22}H_{34}N_2O_5$: C 65.00, H 8.43, N 6.89. Found: C 64.96, H 8.63, N 7.01. Data for **14**: $[\alpha]^{19}_D$ −20.25 (*c* 1.18, $CHCl_3$). IR (neat): 3472, 3076, 2978, 2936, 1699, 1614, 1514, 1394, 1250, 1175, 1085 cm^{-1}. ^1H NMR (300 MHz, 55 °C, $CDCl_3$): δ 1.24 (bs, 3H), 1.48 (s, 9H), 1.68 (bs, 3H), 2.27−2.30 (m, 1H), 2.68−2.75 (m, 1H), 3.13−3.28 (m, 1H), 3.71−3.78 (m, 1H), 3.77 (s, 3H), 3.80−3.83 (m, 1H), 3.92−4.09 (m, 1H), 4.07 (d, J = 9.0 Hz, 1H), 4.24 (d, J = 9.0 Hz, 1H), 5.01−5.13 (m, 2H), 5.36 (s, 1H, ex. D_2O), 5.75−5.83 (m, 1H), 6.82 (d, J = 8.7 Hz, 2H), 7.22 (d, J = 8.7 Hz, 2H) ppm. ESIMS (*m*/*z*, %): 407.1 (M + H^+, 100%), 429.1 (M + Na^+, 10%). Anal. Calcd for $C_{22}H_{34}N_2O_5$: C 65.00, H 8.43, N 6.89. Found: C 65.28, H 8.30, N 6.97.

Secondary Amine 15. To a solution of copper(II) acetate (385 mg, 2.1 mmol, 0.1 equiv) in acetic acid (25 mL) was added Zn dust (6.83 g, 105 mmol, 5.0 equiv). The mixture was stirred at 25 °C for 15 min under N_2. A solution of the hydroxylamine **13** (8.5 g, 21 mmol) in acetic acid (25 mL) and water (12 mL) was then added and the reaction was heated at 70 °C for 2 h. The disodium salt of EDTA (23.4 g, 63 mmol, 3.0 equiv) was added at room temperature, and the pH was adjusted to 10 by addition of 4 N NaOH. The solution was extracted with ethyl acetate (3 × 250 mL). The combined organic layers were washed with saturated aqueous EDTA (3 × 250 mL), saturated aqueous NH_4Cl (3 × 250 mL), and brine (3 × 250 mL), dried (Na_2SO_4), and concentrated in vacuo to yield crude product **15** as a colorless oil, which could be used directly without further purification. An analytical sample of **15** was obtained by column chromatography on silica gel (petroleum ether/ethyl acetate = 5:1). $[\alpha]^{20}_D$ −14.4 (*c* 1.03, $CHCl_3$). IR (neat): 3346, 3075, 2978, 2937, 1699, 1613, 1513, 1390, 1366, 1246, 1176 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.47 (s, 9H), 1.51 (bs, 6H), 1.93−2.05 (m, 1H), 2.41−2.43 (m, 1H), 3.01−3.08 (m, 1H), 3.69−3.77 (m, 2H), 3.79 (s, 3H), 3.91 (m, 1H), 4.03−4.13 (m, 2H), 5.06−5.13 (m, 2H), 5.68−5.75 (m, 1H), 6.84 (d, J = 8.0 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H) ppm. ESIMS (*m*/*z*, %): 391.1 (M + H^+, 100%). Anal. Calcd for $C_{22}H_{34}N_2O_4$: C 67.66, H 8.78, N 7.17. Found: C 67.46, H 8.49, N 6.99.

Alcohol 9. To a solution of crude **15** (21 mmol) in ethyl acetate (100 mL) was added saturated aqueous $NaHCO_3$ (100 mL) in one portion. Benzyl chloroformate (3.0 mL, 21 mmol, 1.0 equiv) was added dropwise at 0 °C, and the reaction mixture was stirred at room temperature overnight. The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 100 mL). The combined organic layers were washed with saturated aqueous NH_4Cl (3 × 100 mL) and brine (3 × 100 mL), dried (Na_2SO_4), and concentrated in vacuo to give the crude product **16** as a colorless oil, which was used directly for the next step without further purification.

To a solution of crude **16** (21 mmol) in MeOH (750 mL) was added a catalytic amount of *p*-TsOH hydrate (200 mg, 0.05 equiv) at room temperature. The reaction mixture was heated

to reflux for 1 h. The solvent was evaporated, and the residue was diluted with ethyl acetate (500 mL), washed with saturated aqueous $NaHCO_3$ (3 × 100 mL) and brine (3 × 100 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give alcohol **9** (8.64 g, 85% from **13**) as a colorless oil. $[\alpha]^{20}_D$ −5.9 (*c* 0.97, $CHCl_3$). IR (neat): 3413, 3069, 2978, 2935, 1687, 1613, 1514, 1249, 1175 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.41 (s, 9H), 2.34−2.50 (m, 2H), 3.45−3.55 (m, 2H), 3.79 (s, 3H), 3.77−3.84 (m, 1H), 4.23 (d, J = 15.9 Hz, 1H), 4.34−4.36 (m, 1H), 4.56 (d, J = 15.9 Hz, 1H), 4.91−5.03 (m, 2H), 5.16−5.26 (m, 2H), 5.47−5.57 (m, 1H), 6.81 (d, J = 8.7 Hz, 2H), 7.12 (d, J = 8.1 Hz, 2H), 7.31−7.40 (m, 5H) ppm. ESIMS (*m*/*z*, %): 485.1 (M^+ + H, 15%), 507.1 (M + Na^+, 100%). Anal. Calcd for $C_{27}H_{36}N_2O_6$: C 66.92, H 7.49, N 5.78. Found: C 67.16, H 7.56, N 5.64.

Diolefin 18. A routine Swern oxidation of alcohol **9** (5.8 g, 12 mmol) gave the corresponding crude aldehyde **17**, which was used directly for the next step without further purification.

To a solution of anhydrous $ZnCl_2$ (2.46 g, 18 mmol, 1.5 equiv) in anhydrous THF (300 mL) was added vinylmagnesium bromide (1.0 M in THF, 36 mL, 36 mmol, 3.0 equiv) at −70 °C under N_2. After the mixture was stirred at this temperature for 30 min, a solution of freshly prepared aldehyde **17** in anhydrous THF (60 mL) was added dropwise. The whole mixture was stirred at −70 °C for 2 h and warmed to −30 °C for additional 4 h, before it was quenched with 1 N NaOH (120 mL) at −30 °C. The resulting mixture was warmed to room temperature, and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 100 mL). The combined organic layers were washed with saturated aqueous NH_4Cl (3 × 100 mL) and brine (3 × 100 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 6:1) to give a diastereomeric mixture **18** (4.8 g, 79% for 2 steps) as a colorless oil. IR (neat): 3421, 3074, 2961, 2930, 1691, 1613, 1514, 1249, 1176 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): d 1.39 (s, 9H), 2.33−2.42 (m, 2H), 2.26−2.30 (br, 1H, ex. D_2O), 3.79 (s, 3H), 3.81−3.86 (m, 1H), 4.25−4.44 (m, 3H), 4.85−4.94 (m, 2H), 5.13−5.32 (m, 5H), 5.44 (br, 1H), 5.81−5.85 (m, 1H), 6.81−6.88 (m, 2H), 7.13−7.15 (m, 2H), 7.27−7.32 (m, 5H) ppm. ESIMS (*m*/*z*, %): 511.3 (M + H^+, 100%), 533.2 (M + Na^+, 40%). Anal. Calcd for $C_{29}H_{38}N_2O_6$: C 68.21, H 7.50, N 5.49. Found: C 68.19, H 7.66, N 5.61.

(1*R*,2*R*,6*S*)-{6-[Benzyloxycarbonyl-(4-methoxybenzyl)-amino]-2-hydroxy-cyclohex-3-enyl}-carbamic Acid *tert*-Butyl Ester (5) and (1*R*,2*S*,6*S*)-{6-[Benzyloxycarbonyl-(4-methoxybenzyl) -amino]-2-hydroxy-cyclohex-3-enyl}-carbamic Acid *tert*-Butyl Ester (19). To a solution of alcohol **18** (4.8 g, 9.4 mmol) in anhydrous CH_2Cl_2 (500 mL) was added bis(tricyclohexylphosphine)benzylidene ruthenium(IV) dichloride (Grubbs catalyst) (618 mg, 0.75 mmol, 0.08 equiv) under N_2. The reaction mixture was stirred at room temperature overnight. After all starting material disappeared, water (50 mL) was added and stirred vigorously at room temperature for 1 h. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with brine (3 × 100 mL), dried (Na_2SO_4), and concentrated in vacuo. The crude mixture was separated and purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 8:1 to 4:1) to afford **5** (3.20 g, 83%) and **19** (0.31 g, 7%) as pale brown waxes, and repeated (twice to trice) silica gel column chromatography was performed in order to obtain off-white waxes for analysis. Data for **5**: $[\alpha]^{18}_D$ −48.0 (*c* 1.49, $CHCl_3$). IR (KBr): 3348, 3066, 2959, 1696, 1614, 1514, 1309, 1248, 1174 cm^{-1}. ^1H NMR (300 MHz, 55 °C, $CDCl_3$): δ 1.43 (s, 9H), 2.03−2.10 (m, 1H), 2.30−2.39 (m, 1H), 3.24 (br, 1H, ex. D_2O), 3.78 (s, 3H), 3.74−3.83 (m, 1H), 4.20 (d, J = 16.5 Hz, 1H), 4.12−4.23 (m, 2H), 4.60 (d, J = 16.5 Hz, 1H), 5.15 (d, J = 12.3 Hz, 1H), 5.23 (d, J = 12.3 Hz, 1H), 5.54−5.62 (m, 2H), 6.81 (d, J = 8.4 Hz, 2H), 7.13 (d, J = 8.1 Hz, 2H), 7.24−7.38 (br, 5H) ppm. ESIMS (*m*/*z*, %): 383.1 (M + H^+ − Boc, 100%), 483.1 (M + H^+, 98%), 505.1 (M + Na^+, 25%). Anal. Calcd for $C_{27}H_{34}N_2O_6$: C 67.20, H 7.10, N 5.81. Found: C 67.08, H 7.18, N 5.59. Data for **19**: $[\alpha]^{19}_D$ −19.1 (*c* 1.43, $CHCl_3$). IR (KBr) 3439, 3065, 3033, 2976, 2933, 1701, 1613, 1514, 1247, 1171 cm^{-1}. ^1H NMR (300 MHz, 55 °C, $CDCl_3$): δ 1.42 (s, 9H), 1.69 (br, 1H, ex. D_2O), 2.11−2.17 (m, 1H), 2.19−2.29 (m, 1H), 3.77 (s, 3H), 3.97−4.05 (m, 1H), 4.17 (d, J = 15.9 Hz, 1H), 4.24−4.34 (m, 2H), 4.70 (d, J = 15.0 Hz, 1H), 5.14 (d, J = 12.0 Hz, 1H), 5.23 (d, J = 12.0 Hz, 1H), 5.72−5.75 (m, 2H), 6.80 (d, J = 8.4 Hz, 2H), 7.13 (d, J = 8.4 Hz, 2H), 7.28 (br, 5H) ppm. ESIMS (*m*/*z*, %): 383.2 (M + H^+ − Boc, 40%), 483.3 (M + H^+, 100%), 505.1 (M + Na^+, 20%). Anal. Calcd for $C_{27}H_{34}N_2O_6$: C 67.20, H 7.10, N 5.81. Found: C 67.28, H 7.12, N 5.79.

(1*R*,2*R*,3*S*)-2,3-Diaminocyclohexanol Hydrochloride (20). A mixture of compound **5** (482 mg, 1 mmol) and 20% palladium hydroxide on activated charcoal (48 mg, 10% w/w) in MeOH (10 mL) was stirred under H_2 atmosphere (1 atm) at 35 °C for 24 h. The solid was filtered off, and the filtrate was evaporated. The residue was treated with 3 N HCl in MeOH (20 mL) at 0 °C and then stirred at room temperature overnight. MeOH was removed in vacuo. The residue was recrystallized from EtOH to afford **20** (168 mg, 83%) as an off-white solid. $[\alpha]^{20}_D$ −7.3 (*c* 1.78, H_2O). IR (KBr): 3336, 2869, 2618, 1510, 1071, 1014 cm^{-1}. ^1H NMR (500 MHz, D_2O): δ 1.21−1.32 (m, 2H, H_{5a}, H_{6a}), 1.37−1.50 (m, 1H, H_{4a}), 1.70−1.75 (m, 1H, H_{5e}), 1.93−1.95 (m, 1H, H_{6e}), 1.99−2.04 (m, 1H, H_{4e}), 3.06 (dd, 1H, $J_{1,2}$ = 10.2 Hz, $J_{2,3}$ = 10.8 Hz, H_2), 3.35 (td, 1H, $J_{2,3}$ = $J_{3,4a}$ = 10.8 Hz, $J_{3,4e}$ = 4.2 Hz, H_3), 3.54 (td, 1H, $J_{1,2}$ = $J_{1,6a}$ = 10.2 Hz, $J_{1,6e}$ = 4.5 Hz, H_1) ppm. ^{13}C NMR (125 MHz, D_2O): δ 21.98, 31.19, 34.17, 53.08, 60.13, 71.60 ppm. ESIMS (*m*/*z*, %): 131.2 (M + H^+, 100%). HR-MALDI-MS calcd for $C_6H_{15}N_2O$ (M + H^+) 131.1179, found 131.1185.

(1*R*,2*S*,3*S*,4*S*,6*S*)-{6-[Benzyloxycarbonyl-(4-methoxybenzyl)-amino]-2,3,4-trihydroxy-cyclohexyl}-carbamic Acid *tert*-Butyl Ester (21). To a solution of **5** (241 mg, 0.5 mmol) in a mixture of acetone and water (10 mL, 9:1, v/v) was added 4-methyl morpholine *N*-oxide (150 mg, 1.1 mmol, 2.2 equiv) and a catalytic amount of OsO_4 (2 drops of 2.5% OsO_4 solution in ^{t}BuOH) at room temperature. After being stirred at room temperature overnight, the reaction mixture was quenched with a few drops of saturated aqueous $NaHSO_3$. The solvent was evaporated. The residue was diluted with ethyl acetate (20 mL) and washed with brine (3 × 10 mL), dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 1:5) to give triol **21** (239 mg, 93%) as a white wax. $[\alpha]^{20}_D$ −20.4 (*c* 0.64, $CHCl_3$). IR (KBr): 3406, 2932, 1691, 1614, 1514, 1248, 1174 cm^{-1}. ^1H NMR (300 MHz, 55 °C, $CDCl_3$): δ 1.41 (s, 9H), 1.70 (bs, 1H), 1.83−1.88 (m, 1H), 3.38−3.41(m, 1H), 3.61−3.65 (m, 1H), 3.77 (s, 3H), 3.98−3.99 (m, 1H), 4.17 (d, J = 15.6 Hz, 1H), 4.30 (br, 2H), 4.60 (d, J = 15.6 Hz, 1H), 5.11 (d, J = 11.7 Hz, 1H), 5.19 (d, J = 12.0 Hz, 1H), 6.79 (d, J = 8.1 Hz, 2H), 7.10 (br, 2H), 7.28 (br, 5H) ppm. ESIMS (*m*/*z*, %): 517.3 (M + H^+, 100%). Anal. Calcd for $C_{27}H_{36}N_2O_8$: C 62.78, H 7.02, N 5.42. Found: C 62.48, H 7.30, N 5.13.

(1*S*,2*S*,3*S*,4*R*,5*S*)-4,5-Diaminocyclohexane-1,2,3-triol hydrochloride (1). A mixture of triol **21** (130 mg, 0.25 mmol) and 12 N HCl (10 mL) was refluxed for 2 days under N_2. The solvent was removed in vacuo to give the crude product, which was recrystallized from MeOH to afford **1** (55 mg, 93%) as an off-white solid. $[\alpha]^{20}_D$ +15.9 (*c* 0.66, H_2O). IR (KBr): 3366, 2908, 1601, 1506, 1037 cm^{-1}. ^1H NMR (400 MHz, D_2O): δ 1.75 (ddd, 1H, $J_{1,6a}$ = 2.4 Hz, $J_{5,6a}$ = 12.3 Hz, $J_{6a,6e}$ = 14.4 Hz, H_{6a}), 2,17 (ddd, 1H, $J_{1,6e}$ = 3.9 Hz, $J_{5,6e}$ = 4.5 Hz, $J_{6a,6e}$ = 14.4 Hz, H_{6e}), 3.12 (dd, 1H, $J_{3,4}$ = 9.9 Hz, $J_{4,5}$ = 10.5 Hz, H_4), 3.46 (dd, 1H, $J_{1,2}$ = 3.0 Hz, $J_{2,3}$ = 9.6 Hz, H_2), 3.64 (ddd, 1H, $J_{4,5}$ = 10.5 Hz, $J_{5,6e}$ = 4.5 Hz, $J_{5,6a}$ = 12.3 Hz, H_5), 3.71 (dd, 1H, $J_{2,3}$ = 9.6 Hz, $J_{3,4}$ = 9.9 Hz, H_3), 4.02−4.05 (m, 1H, H_1) ppm. ^{13}C NMR (100 MHz, D_2O): δ 35.30, 49.32, 58.30, 69.37, 71.56, 75.63 ppm.

ESIMS (*m*/*z*, %): 163.1 (M + H$^+$, 100%). HR-MALDI-MS calcd for $C_6H_{15}N_2O_3$ (M + H$^+$) 163.1077, found 163.1079.

(1*S*,2*S*,3*R*,4*S*,6*R*)-{4-[Benzyloxycarbonyl-(4-methoxybenzyl)-amino]-2-hydroxy-7-oxa-bicyclo[4.1.0]hept-3-yl}-carbamic Acid *tert*-Butyl Ester (22). To a stirred suspension of **5** (482 mg, 1.0 mmol) and Na_2HPO_4 (284 mg, 2.0 mmol, 2.0equiv) in CH_2Cl_2 (10 mL) was added *m*-CPBA (336 mg, 70%, 1.5 mmol, 1.5 equiv) in one portion at 0 °C. The resulting suspension was stirred at 15 °C for 24 h before saturated aqueous Na_2SO_3 (10 mL) was added to quench the reaction. The resulting two-phase mixture was stirred vigorously for 15 min. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with saturated aqueous Na_2SO_3 (3 × 10 mL), saturated aqueous $NaHCO_3$ (3 × 10 mL), and brine (3 × 10 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give epoxide **22** (359 mg, 72%) as a white wax. $[\alpha]^{19}_D$ −34.17 (*c* 0.66, $CHCl_3$). IR (KBr): 3362, 2976, 2931, 1699, 1613, 1514, 1248, 1173 cm^{-1}. ^{1}H NMR (300 MHz, 55 °C, $CDCl_3$): δ 1.42 (s, 9H), 1.92−2.01 (m, 1H), 2.03−2.08 (m, 1H), 2.84 (br, 1H, ex. D_2O), 3.13−3.16 (m, 1H), 3.32−3.34 (m, 1H), 3.79 (s, 3H), 3.82−3.89 (m, 2H), 4.03−4.21 (m, 2H), 4.52 (d, J = 13.1 Hz, 1H), 5.12 (d, J = 12.3 Hz, 1H), 5.21 (d, J = 12.3 Hz, 1H), 6.82 (d, J = 8.7 Hz, 2H), 7.12 (d, J = 8.7 Hz,2H), 7.30 (br, 5H) ppm. ESIMS (*m*/*z*, %): 499.3 (M + H$^+$, 90%), 521.2 (M + Na$^+$, 100%). Anal. Calcd for $C_{27}H_{34}N_2O_7$: C 65.04, H 6.87, N 5.62. Found: C 65.26, H 7.16, N 5.32.

(1*R*,2*S*,3*R*,4*S*,6*S*)-{6-[Benzyloxycarbonyl-(4-methoxybenzyl)-amino]-2,3,4-tri hydroxyl-cyclohexyl}-carbamic Acid *tert*-Butyl Ester (23). To a mixture of 0.2 N H_2SO_4 and dioxane (20 mL, 1:1, v/v) was added epoxide **22** (396 mg, 0.79 mmol) at 0 °C. The reaction mixture was stirred at 10 °C for 8 h and then treated with saturated aqueous $NaHCO_3$ (20 mL). The mixture was extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with brine (3 × 10 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 1:5) to give triol **23** (334 mg, 82%) as a white wax. $[\alpha]^{20}_D$ −37.0 (*c* 1.09, $CHCl_3$). IR (KBr): 3404, 2976, 2932, 1691, 1614, 1514, 1248, 1174 cm^{-1}. ^{1}H NMR (300 MHz, 55 °C, $CDCl_3$): δ 1.34 (s, 9H), 1.52−1.56 (m, 1H), 1.97−2.10 (m, 1H), 3.70 (s, 3H), 3.81 (bs, 2H), 3.97−3.98 (m, 1H), 4.17 (d, J = 15.6 Hz, 1H), 4.28 (br, 2H), 4.49 (d, J = 15.6 Hz, 1H), 5.07 (d, J = 12.3 Hz, 1H), 5.13 (d, J = 12.3 Hz, 1H), 6.71 (d, J = 8.7 Hz, 2H), 7.05 (d, J = 8.7 Hz, 2H), 7.18−7.22 (m, 5H) ppm. ESIMS (*m*/*z*, %): 417.3 (M + H$^+$ − Boc, 40%), 517.3 (M + H$^+$, 100%). Anal. Calcd for $C_{27}H_{36}N_2O_8$: C 62.78, H 7.02, N 5.42. Found: C 63.02, H 7.26, N 5.14.

(1*S*,2*R*,3*S*,4*R*,5*S*)-4,5-Diaminocyclohexane-1,2,3-triol Hydrochloride (2). Triol **23** (260 mg, 0.5 mmol) was converted into compound **2** (103 mg, 87%) according to a similar procedure for compound **1**, as an off-white solid. $[\alpha]^{20}_D$ −18.0 (*c* 0.91, H_2O). IR (KBr): 3360, 2926, 1602, 1505, 1039 cm^{-1}. ^{1}H NMR (500 MHz, D_2O): δ 1.82−1.98 (m, 2H, H_{6a}, H_{6e}), 3.32 (dd, 1H, $J_{3,4}$ = 10.3 Hz, $J_{4,5}$ = 10.6 Hz, H_4), 3.53 (td, 1H, $J_{4,5}$ = $J_{5,6a}$ = 11.1 Hz, $J_{5,6e}$ = 4.9 Hz, H_5), 3.76−3.82 (m, 2H, H_2, H_3), 3.89−3.91 (m, 1H, H_1) ppm. ^{13}C NMR (125 MHz, D_2O): δ 32.61, 49.49, 55.49, 69,68, 69.87, 72.89 ppm. ESIMS (*m*/*z*, %): 163.1 (M + H$^+$, 100%). HR-MALDI-MS calcd for $C_6H_{15}N_2O_3$ (M + H$^+$) 163.1077, found 163.1078.

(4*S*,5*S*,2*E*)-Ethyl {5-[Benzyloxycarbonyl-(4-methoxybenzyl)amino]-(4-*t*-butoxycarbonyl amino)octa-2,7-dienate (24). To a solution of freshly prepared aldehyde **17** (3.5 g, 7.2 mmol) in THF (250 mL) was added in one portion (carbethoxymethylene)triphenylphosphorane (Ph_3P=CHCOOEt) (5.0 g, 14.4 mmol, 2.0 equiv) at 0 °C. The reaction mixture was stirred at room temperature overnight. The solvent was removed in vacuo, and the crude product was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 6:1) to afford (2*E*)-2,7-diene **24** (3.72 g, 93%) as a colorless oil. $[\alpha]_D^{19}$ −22.3 IR (neat): 3350, 3066, 1987, 2906, 1727, 1687, 1612, 1513, 1249, 1222 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.28 (m, 3H), 1.41 (s, 9H), 2.31−2.39 (m, 1H), 2.41−2.51 (m, 1H), 3.65−3.76 (m, 1H), 3.80 (s, 3H), 4.12−4.19 (m, 2H), 4.26 (d, J = 16.8 Hz, 1H), 4.39 (d, J = 16.2 Hz, 1H), 4.43−4.44 (m, 1H), 4.92−5.04 (m, 2H), 5.14−5.28 (m, 2H), 5.46−5.61 (m, 1H), 5.76−5.95 (m, 1H), 6.62−6.72 (m, 1H), 6.80 (d, J = 8.4 Hz, 2H), 7.10 (d, J = 8.7 Hz, 2H), 7.24−7.39 (m, 5H) ppm. ^{1}H NMR (300 MHz, $CDCl_3$, 327 K): δ 1.28 (t, J = 7.2 Hz, 3H), 1.42 (s, 9H), 2.42 (br, 2H), 3.73−3.75 (m, 1H), 3.80 (s, 3H), 4.19 (q, J = 7.2 Hz, 2H), 4.35−4.42 (m, 3H), 4.94−4.99 (m, 2H), 5.15−5.24 (m, 2H), 5.49−5.61 (m, 1H), 5.87 (d, J = 15.6 Hz, 1H), 6.69 (dd, J = 6.0, 15.6 Hz, 1H), 6.82 (d, J = 8.1 Hz, 2H), 7.13 (br, 2H), 7.33 (br, 5H) ppm. ESIMS (*m*/*z*, %): 453.2 (M + H$^+$ − Boc, 100%), 553.2 (M + H$^+$, 55%), 575.2 (M + Na$^+$, 50%). Anal. Calcd for $C_{31}H_{40}N_2O_7$: C 67.37, H 7.30, N 5.07. Found: C 67.36, H 7.39, N 4.94.

(1*S*,5*S*)-{5-[Benzyloxycarbonyl-(4-methoxy-benzyl)-amino]-cyclopent-2-enyl}-carbamic Acid *tert*-Butyl Ester (7). To a solution of diolefin **24** (3.5 g, 6.3 mmol) in anhydrous CH_2Cl_2 (630 mL) was added bis(tricyclohexyl phosphine)-benzylidene ruthenium(IV) dichloride (Grubbs catalyst) (260 mg, 0.315 mmol, 0.05 equiv) under N_2. The reaction mixture was stirred at 35 °C for 24 h. After all starting material disappeared, water (50 mL) was added, and the whole mixture was stirred vigorously at room temperature for 1 h. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with brine (3 × 100 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel one time (petroleum ether/ethyl acetate = 5:1) to give compound **7** (2.84 g, 99%) as a pale brown oil, and further twice repeated column chromatography on silica gel gave a colorless oil for analysis. $[\alpha]^{18}_D$ +48.1 (*c* 1.04, $CHCl_3$). IR (neat): 3345, 3064, 3034, 2977, 2935, 1695, 1614, 1514, 1365, 1247, 1173 cm^{-1}. ^{1}H NMR (300 MHz, 55 °C, $CDCl_3$): δ 1.44 (s, 9H), 2.40 (br, 2H), 3.79 (s, 3H), 4.42−4.72 (m, 3H), 4.87 (br, 1H), 5.15 (bs, 2H), 5.64 (br, 1H), 5.74 (br, 1H), 6.82 (d, J = 8.4 Hz, 2H), 7.11 (bs, 2H), 7.19−7.29 (m, 5H) ppm. ESIMS (*m*/*z*, %): 353.2 (M + H$^+$ − Boc, 70%), 453.3 (M + H$^+$, 100%). Anal. Calcd for $C_{26}H_{32}N_2O_5$: C 69.01, H 7.13, N 6.19. Found: C 68.70, H 7.33, N 6.25.

(1*R*,2*R*,3*S*,5*S*)-{5-[Benzyloxycarbonyl-(4-methoxy-benzyl)-amino]-2,3-dihydroxy-cyclopentyl}-carbamic Acid *tert*-Butyl Ester (25). Compound **7** (864 mg, 1.88 mmol) was converted into diol **25** according to a similar procedure as for triol **21**. Purification by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 1:1) afforded **25** (855 mg, 94%) as a white wax. $[\alpha]^{19}_D$ +30.54 (*c* 1.10, $CHCl_3$). IR (KBr): 3421, 3034, 2977, 2934, 1699, 1614, 1514, 1248, 1174 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.43 (s, 9H), 1.74−1.79 (m, 1H), 2.00−2.05 (m, 1H), 2.58 (br, 1H, ex. D_2O), 2.93 (br, 1H, ex. D_2O), 3.79 (s, 3H), 4.06−4.26 (m, 3H), 4.37−4.48 (m, 2H), 4.80−4.82 (m, 1H), 5.14 (bs, 2H), 6.82 (d, J = 8.1 Hz, 2H), 7.08−7.10 (m, 2H), 7.21−7.32 (m, 5H) ppm. ESIMS (*m*/*z*, %): 487.2 (M + H$^+$, 100%). Anal. Calcd for $C_{26}H_{36}N_2O_7$: C 64.18, H 7.04, N 5.76. Found: C 64.26, H 7.25, N 5.67.

(1*S*,2*R*,3*R*,4*S*)-3,4-Diaminocyclopentane-1,2-diol Hydrochloride (3). Diol **25** (243 mg, 0.5 mmol) was converted into compound **3** (97 mg, 95%) according to a similar procedure as for compound **1**, as an off-white solid. $[\alpha]^{20}_D$ +20.9 (*c* 1.20, H_2O). IR (KBr): 3370, 2995, 1589, 1489, 1046, 816 cm^{-1}. ^{1}H NMR (300 MHz, D_2O): d 1.86 (dt, 1H, $J_{5\alpha,5\beta}$ = 14.4 Hz, $J_{1,5\alpha}$ = $J_{4,5\alpha}$ = 6.5 Hz, $H_{5\alpha}$), 2.25 (ddd, 1H, $J_{1,5\beta}$ = 4.8 Hz, $J_{4,5\beta}$ = 9.6 Hz, $J_{5\alpha,5b}$ = 14.4 Hz, $H_{5\beta}$), 3.70 (dd, 1H, $J_{2,3}$ = 5.8 Hz, $J_{3,4}$ = 10.5 Hz, H_3), 3.91 (dt, 1H, $J_{4,5\beta}$ = 9.6 Hz, $J_{3,4}$ = $J_{4,5\alpha}$ = 6.4 Hz, H_4), 4.22−4.26 (m, 2H, H_1, H_2) ppm. ^{13}C NMR (75 MHz, D_2O): δ 36.53, 54.75, 57.46, 73.62, 73.65 ppm. ESIMS (*m*/*z*, %): 115.2 (M + H$^+$ − H_2O, 55%), 133.2 (M + H$^+$, 100%). HR-MALDI-MS calcd for $C_5H_{13}N_2O_2$ (M + H$^+$) 133.0972, found 133.0971.

(1*R*,2*R*,3*S*,5*S*)-{3-[Benzyloxycarbonyl-(4-methoxy-benzyl)-amino]-6-oxa- bicyclo[3.1.0]hex-2-yl}-carbamic Acid

***tert*-Butyl Ester (26).** To a stirred suspension of **7** (1.36 g, 3.0 mmol) and $NaHCO_3$ (0.51 g, 6.0 mmol, 2.0 equiv) in CH_2Cl_2 (60 mL) was added *m*-CPBA (1.35 g, 70%, 6.0 mmol, 2.0 equiv) in one portion at 0 °C. The resulting suspension was stirred at 15 °C for 24 h before saturated aqueous Na_2SO_3 (50 mL) was added. The resulting two-phase mixture was stirred vigorously for 15 min. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with saturated aqueous Na_2SO_3 (3 × 50 mL), saturated aqueous $NaHCO_3$ (3 × 50 mL), and brine (3 × 50 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to give epoxide **26** (1.09 g, 78%) as a white wax. $[\alpha]^{19}_D$ +31.33 (*c* 1.26, $CHCl_3$). IR (KBr): 3340, 2978, 2936, 1703, 1613, 1515, 1248, 1173 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.44 (s, 9H), 1.96−2.14 (m, 2H), 3.43 (bs, 1H), 3.55 (bs, 1H), 3.79 (s, 3H), 4.29 (d, J = 16.2 Hz, 1H), 4.40−4.78 (m, 3H), 5.14−5.23 (m, 2H), 6.82 (d, J = 8.4 Hz, 2H), 7.07−7.12 (m, 2H), 7.22−7.42 (m, 5H) ppm. ESIMS (*m*/*z*, %): 469.3 ($M + H^+$, 100%), 491.2 ($M + Na^+$, 10%). Anal. Calcd for $C_{26}H_{32}N_2O_6$: C 66.65, H 6.88, N 5.98. Found: C 66.62, H 6.99, N 5.88.

(1*R*,5*S*,6*R*,7*R*)-[7-Hydroxy-4-(4-methoxy-benzyl)-3-oxo-2-oxa-4-aza-bicyclo [3.2.1]oct-6-yl]-carbamic Acid *tert*-Butyl Ester (28). To a solution of epoxide **26** (580 mg, 1.23 mmol) in CH_2Cl_2 (60 mL) was added D-camphor-10-sulfonic acid (143 mg, 0.62 mmol, 0.5 equiv) at 0 °C. The reaction mixture was stirred at room temperature for 24 h before it was quenched with saturated aqueous $NaHCO_3$ (20 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with brine (3 × 20 mL), dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 1:1) to give compound **28** (403 mg, 86%) as a white wax. $[\alpha]^{19}_D$ −27.99 (*c* 1.09, $CHCl_3$). IR (KBr): 3437, 2930, 1681, 1614, 1514, 1461, 1248, 1174 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.45 (s, 9H), 1.73−1.77 (m, 1H), 1.88 (bs, 1H, ex. D_2O), 1.96−2.01 (m, 1H), 3.55 (bs, 1H), 3.80 (s, 3H), 4.06 (d, J = 14.7 Hz, 1H), 4.13 (dd, J = 5.1, 6.9 Hz, 1H), 4.53−4.57 (m, 2H), 5.02 (d, J = 14.7 Hz, 1H), 5.48 (d, J = 4.5 Hz, 1H, ex. D_2O), 6.86 (d, J = 8.7 Hz, 2H), 7.29 (d, J = 8.4 Hz, 2H) ppm. ESIMS (*m*/*z*, %): 379.2 ($M + H^+$, 100%). Anal. Calcd for $C_{19}H_{26}N_2O_6$: C 60.30, H 6.93, N 7.40. Found: C 60.27, H 7.00, N 7.21.

(1*R*,2*R*,3*R*,4*S*)-3,4-Diaminocyclopentane-1,2-diol Hydrochloride (4). Compound **28** (118 mg, 0.31 mmol) was converted into compound **4** (60 mg, 94%) according to a similar procedure as for compound **1**, as an off-white solid. $[\alpha]^{20}_D$ +16.6 (*c* 2.68, H_2O). IR (KBr): 3370, 3003, 1599, 1489, 1047, 816 cm^{-1}. ^1H NMR (300 MHz, D_2O): δ 1.61 (ddd, 1H, $J_{4,5\beta}$ = 4.5 Hz, $J_{1,5\beta}$ = 4.2 Hz, $J_{5\alpha,5\beta}$ = 14.6 Hz, $H_{5\beta}$), 2.52 (ddd, 1H, $J_{1,5\beta}$ = 5.5 Hz, $J_{4,5\alpha}$ = 9.0 Hz, $J_{5\alpha,5\beta}$ = 14.6 Hz, $H_{5\alpha}$), 3.72 (ddd, 1H, $J_{3,4}$ = 6.0 Hz, $J_{4,5\beta}$ = 5.0 Hz, $J_{4,5\alpha}$ = 9.0 Hz, H_4), 3.81 (dd, 1H, $J_{2,3}$ = 6.0 Hz, $J_{3,4}$ = 6.0 Hz, H_3), 4.00−4.04(m, 1H, H_1), 4.08−4.10(m, 1H, H_2) ppm. ^{13}C NMR (75 MHz, D_2O): δ 37.19, 5437, 5789, 76.88, 77.01 ppm. ESIMS (*m*/*z*, %): 115.2 ($M + H^+ - H_2O$, 40%), 133.2 ($M + H^+$, 100%). HR-MALDI-MS calcd for $C_5H_{13}N_2O_2$ ($M + H^+$) 133.0972, found 133.0972.

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Supporting Information Available: ^1H and ^{13}C NMR spectra of compounds **1**−**4** and **20** and NOESY spectra of compounds **1**−**3**, **20**, and **28**. This material is available free of charge via the Internet at http://pubs.acs.org.

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