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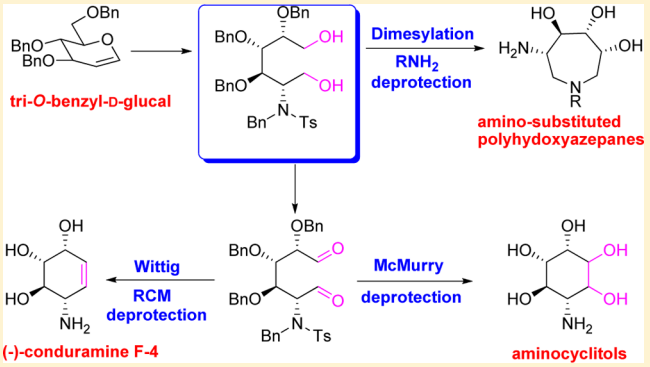
A Chiron Approach to Diversity-Oriented Synthesis of Aminocyclitols, (−)-Conduramine F-4 and Polyhydroxyaminoazepanes from a Common Precursor

Vimal Kant Harit and Namakkal G. Ramesh*

Department of Chemistry, Indian Institute of Technology Delhi, Hauz Khas, New Delhi 110016, India

Supporting Information

ABSTRACT: The total syntheses of aminocyclitols, (−)-conduramine F-4, and polyhydroxyaminoazepanes have been achieved from a common precursor derived from tri-*O*-benzyl-D-glucal through a 'diversity-oriented' approach. Tri-*O*-benzyl-D-glucal was converted into a protected 1,6-diol through a sequence of steps that include transformation to a 2-tosylamidoglucose derivative, selective deprotection of primary C-6 benzyloxy group, $LiAlH_4$-mediated one-step reduction of acetate groups, and reductive ring opening of the resulting hemiacetal as the key steps. The 1,6-diol served as a common precursor in our diversity oriented approach toward the target molecules. Mesylation of the diol followed by double nucleophilic substitution reaction with primary amines led to the synthesis of amino-substituted polyhydroxyazepanes. On the other hand, dialdehyde obtained from the oxidation of 1,6-diol was found to be a convenient starting material for the synthesis of aminocyclitols and (−)-conduramine F-4. McMurry coupling of the dialdehyde was successfully employed, for the first time, to construct the carbocyclic framework of aminoyclitols, while bis-Wittig olefination of the dialdehyde followed by Grubb's(II)-catalyzed RCM delivered (−)-conduramine F-4. The stereochemistry of newly created chiral centers in aminocyclitols was established through single crystal X-ray crystallography and detailed NOE studies.



INTRODUCTION

Aminocyclitols **1**, also regarded as amino-carbasugars, are an important class of compounds that have received wide attention in recent years due to their varied medicinal applications.[1] They are found as structural motifs in a variety of aminoglycoside antibiotics such as hygromycin A **2**,[2] minosaminomycin **3**,[3] etc. (Figure 1) and also serve as valuable synthons for the synthesis of natural Amaryllidaceae alkaloids.[4] Aminocyclitol phytoceramides have the capacity to modulate the response arising from invariant natural killer T-cell (INKT) activation.[5] *N*-Alkylamino-*myo*-inositol derivatives are identified as chemical chaperones for Gaucher's disease.[6] Aminocyclitol derivatives are also found to be inhibitors of glycosidases[7] and cell growth.[8] Several strategies,[9−11] including chemo-enzymatic approach,[12] SmI_2-mediated pinacol-type coupling,[13] and intramolecular NHC-catalyzed benzoin-type condensation,[14] are available for the construction of aminocyclitol frameworks. Interestingly, McMurry coupling of a suitably substituted acyclic dialdehyde, wherein carbocyclization accompanied by installation of two of the hydroxyl groups of aminocyclitols, has never been investigated.

Conduramines, synthetic amino-analogues of naturally occurring conduritols, are known for their selective glycosidase inhibitory activities, and as a result, they have become attractive targets for synthetic organic chemists.[1a,15] One of them is (+)-conduramine F-4 **4** whose *N*-alkyl derivatives are, very recently, identified as potential chemical chaperones for G_{M1} gangliosidosis, a rare disease caused by the mutation of lysosomal β-galactosidase.[16,17] Only two strategies for the synthesis of conduramine F-4 are reported either through a chemoenzymatic approach[18] or starting from (+)-*proto*-quercitol.[16] Noticeably, a carbohydrate-based approach to either (+)- or (−)-conduramine F-4 is still at large.

Iminocyclitols, referred to as iminosugars, have found wide applications as drugs and chaperones for various cell-mediated disorders and lysosomal storage diseases.[19] While extensive research has been carried out on the chemistry and biology of five- and six- membered iminocyclitols and the molecular basis for their binding with glycosidases,[19,20] such studies on azepanes (seven-membered iminocyclitols) are in an infant stage, though they have also been found to be inhibitors of glycosidases. Unlike their conformationally rigid five- and six-membered counterparts, polyhydroxyazepanes, such as **6**, due to their flexibility can adopt different conformations, and hence they can be better accommodated within the active site of glycoside hydrolases, resulting in enhanced inhibition.[21] Studies further reveal that replacement of one or more of the hydroxyl

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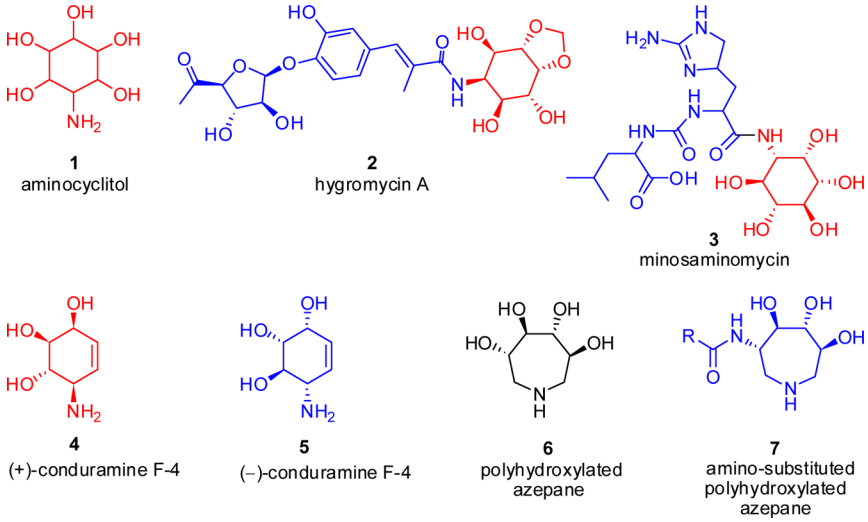
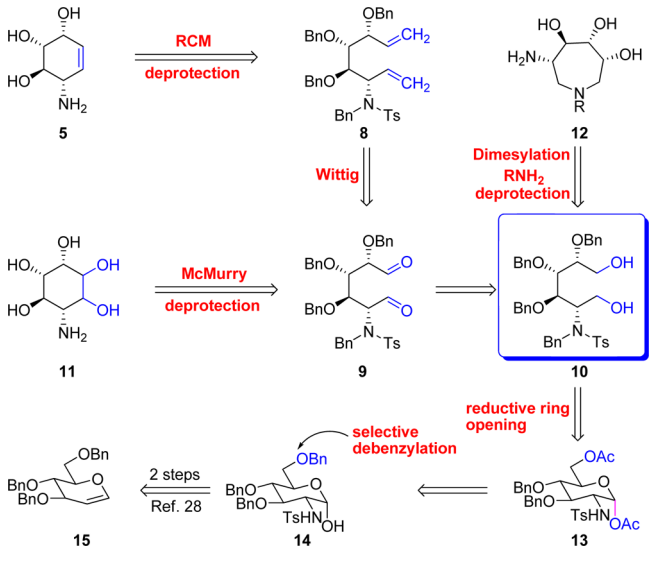


Figure 1. Structures of aminocyclitol antibiotics, conduramine F-4, and polyhydroxyazepanes.

groups of polyhydroxyazepanes with an amino group further increases their inhibitory activities.[22,23] Compound **7** is strong inhibitor of *N*-acetylglucosaminidases.[23] Molecular basis for inhibition with glycoside hydrolases reveals that amino-azepane **7** binds 140 times more tightly than the product *O*-GlcNAC itself.[21b] The amino-azepane core in the fungal metabolite (−)-balanol is crucial for its inhibition against protein kinase.[24,25] These significant findings have prompted a spurt in developing novel methodologies for the synthesis of amino-azepanes.[26]

Synthesis of skeletally and stereochemically diverse biologically active small molecules and their building blocks, from a common precursor, referred to as 'diversity-oriented synthesis' (DOS)[27] has proven to be a successful paradigm in organic synthesis in the last decade. As a part of our research on the use of readily available glycals for the synthesis of natural products and their analogues,[28] we conceived and successfully accomplished a DOS strategy towards the synthesis of aminocyclitols, (−)-conduramine F4, and aminoazepanes from a common precursor derived from tri-*O*-benzyl-D-glucal which we present here.

Scheme 1. Retrosynthesis of Aminocyclitols, (−)-Conduramine F-4, and Polyhydroxyaminoazepanes



RESULTS AND DISCUSSION

Our retrosynthesis of target molecules is given in Scheme 1. As depicted, (−)-conduramine F-4, aminocyclitols, and amino-azepanes could be obtained from a common diol **10**. Oxidation of the diol to the dialdehyde **9** and subsequent bis-Wittig olefination followed by RCM would deliver (−)-conduramine F-4 **5**. On the other hand, construction of the cyclohexane ring of aminocyclitols **11** could be achieved through McMurry coupling of the dialdehyde **9**. Dimesylation of the diol **10** and nucleophilic substitution with amines would result in the formation of amino-azepanes **12**. 1,6-Diol **10**, in turn, could be obtained by the reductive ring opening of bis-acetate **13**, generated through chemoselective deprotection of C-6 primary benzyloxy group of hemiacetal **14**. Tri-*O*-benzyl-D-glucal **15** could be transformed into hemiacetal **14** in two steps using a modified procedure developed in our lab.

Synthesis of the Common Precursor 10. Our synthesis of glucose derived 1,6-diol **10** commenced with the conversion of tri-*O*-benzyl-D-glucal **15** to 2-deoxy-2-sulfonamido-D-glucose **14** in two steps following a modified procedure of Danishefsky[29] reported by us earlier.[28] Next, selective debenzylation of the primary benzyloxy group of **14**, under acetolysis condition, was attempted. The debenzylative acetylation reaction proceeded smoothly with $ZnCl_2$ in acetic anhydride-acetic acid in a ratio of 5:1. During this process, the anomeric hydroxyl group also was acetylated to give the 1,6-*O*-diacetate **13**. Exposure of the diacetate to an excess of $LiAlH_4$ in THF led to the reduction of the acetate groups accompanied by concomitant reductive ring opening of the resulting hemiacetal to afford the triol **16**. Attempts to selectively oxidize the primary hydroxyl groups of **16** to the corresponding dialdehyde were in vain. One-pot silylation of all the hydroxyl groups of **16** followed by quinolinium fluorochromate (QFC)-mediated deprotective oxidation of primary hydroxyl groups to get **19**, following the procedure of Chandrasekar,[30] was unsuccessful with our substrate. Efforts to realize this protocol in a stepwise manner through the synthesis of the tris-silyl ether **18** followed by its exposure to QFC also did not give the desired result. Hence it was decided to follow protection−deprotection strategy to obtain the 1,6-diol **10**. In this direction, the primary

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Scheme 2. Synthesis of Common Precursor 10

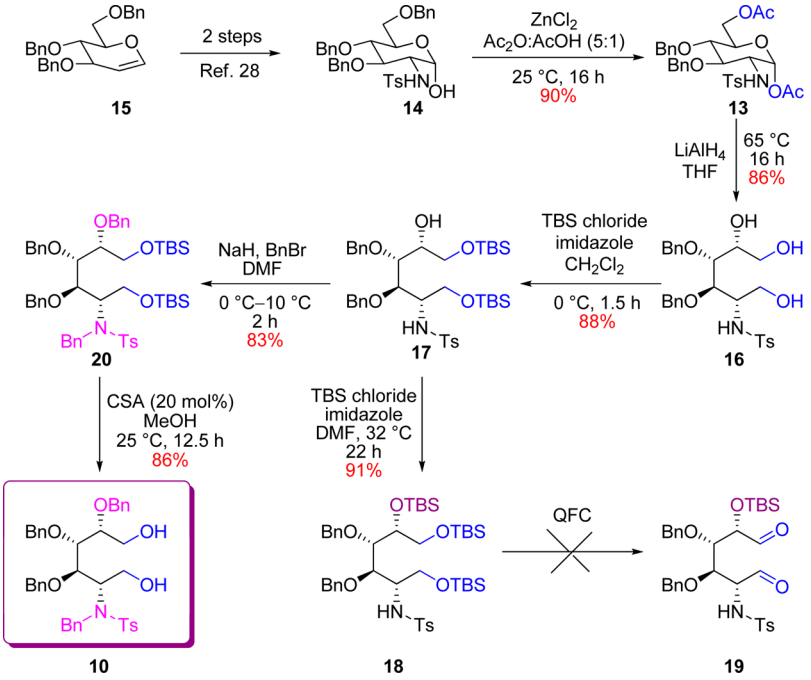
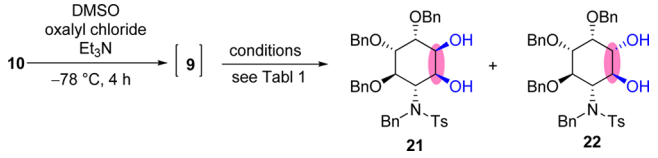


Table 1. Reaction Optimization Conditions for McMurry Coupling



entry	reagents (equiv)/solvents	time (h)	temp. (°C)	yield (%)[a]	ratio (**21**: **22**)[b]
1	Zn–Cu (40); $TiCl_4$ (20); THF	23	80	0	–
2	Zn (4); $TiCl_4$ (2); pyridine (20 μL); THF	4.5	78	56	0.5:1
3	Zn (50); $TiCl_4$ (25); CuCl (5); DME	40	86	31	0.72:1
4	Zn (20); $TiCl_4$ (10); CuCl (0.2); THF	4	80	63	0.7:1
5	LAH (5); $TiCl_4$ (10); Et_3N(6); DME	1.4	95	10	1:0.6
6	Mg (10); $TiCl_4$ (5); $HgCl_2$ (0.2); THF	10	80	0	–

[a]Isolated yields after column chromatography for two steps from **10**. [b]Ratio based on isolated yields.

hydroxyl groups of triol **16** were converted as their TBS ethers (**17**) and the resulting secondary hydroxyl and amino groups were benzylated to get compound **20**. Desilyation of **20** was smoothly accomplished using a catalytic amount of camphor sulfonic acid to get the 1,6-diol **10** (Scheme 2).

Synthesis of Aminocyclitols Using McMurry Coupling. It was envisaged that dialdehyde **9**, obtained by the oxidation of diol **10**, would be a suitable substrate for investigating McMurry coupling[31] that would lead either to protected aminocyclitols or conduramine F-4. Toward this direction, diol **10** was first oxidized to dialdehyde **9** under Swern condition using DMSO and oxalyl chloride. Though the oxidation proceeded smoothly, the product was found to decompose during purification by column chromatography over silica gel. Hence, the crude product was taken to the next step after ascertaining its formation by ^{1}H NMR spectroscopy. McMurry coupling of dialdehyde **9** was initially attempted with Zn-Cu in the presence of $TiCl_4$. However, the outcome was not promising with no useful products being formed in the reaction (entry 1, Table 1). The change of metal from zinc to magnesium was equally discouraging (entry 6). Use of $LiAlH_4$ as a reducing agent did show some positive results with new compounds being formed, but the yields were very low (entry 5). After several attempts, zinc along with $TiCl_4$ and a catalytic amount of CuCl in THF at 80 °C were found to be the most appropriate condition, affording a mixture of two compounds that could be readily separated by column chromatography (entry 4, Table 1). Careful analysis of their spectral data (IR, NMR and HRMS) indicated that both of them were aminocyclitols formed in a ratio of 0.7:1 with a total yield of 63% (two steps from **10**). Interestingly, the reaction did not proceed further to give the corresponding cyclohexene derivative even after a prolonged reaction time. The stereochemistry of the newly created chiral centers of more polar major compound **22**, a solid, was identified through single crystal X-ray crystallography (see Supporting Information). Subsequent confirmation also came from the nonoptical activity of the product **27**, being *meso*, obtained after complete deprotection of **22** (Scheme 4). The stereochemistry of the less polar minor diastereomer **21**, a viscous liquid, however, could not be arrived at from its ^{1}H NMR spectrum due to overlapping of signals of various protons. Hence the free

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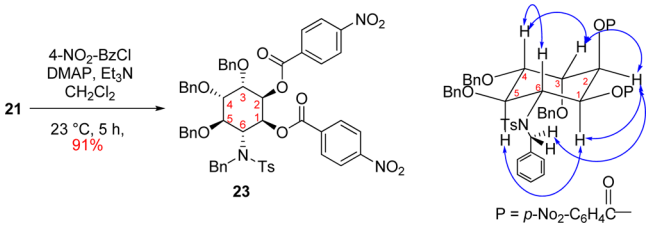
hydroxyl groups of compound **21** were converted to their *p*-nitrobenzoyl derivatives **23** (Scheme 3). The *cis* stereochemical

Scheme 3. Synthesis of Compound 23 and Its NOE Correlation



relationship between H-1 and H-2 in **23** was initially deduced based on the coupling constant values. In its ^{1}H NMR spectrum, H-6 resonated at δ 5.47 as a dd with J = 11.1 and 10.8 Hz due to its coupling with H-5 and H-1. The two large coupling constants of H-6 with H-5 and H-1 confirmed its diaxial relationship with both of them. With H-1 being in axial position, the weak coupling constant observed between H-1 and H-2 and *vice versa* (~3.3 Hz) suggested that they are in a *cis* stereochemical relationship to each other. Subsequently, through detailed 2D NMR studies and NOE correlations, the relative (*cis*) and absolute stereochemistries of the newly formed chiral centers were unambiguously confirmed (Scheme 3).

A rationale for selective formation of only two stereoisomeric diols **21** and **22**, out of four possible, during McMurry coupling may be explained as follows. Intramolecular pinacol coupling reaction under McMurry condition has been known to proceed through coupling of radicals on a titanium particle/surface, and the product stereochemistry is mainly controlled by steric interactions in the newly formed ring.[31c] In the diradical intermediates **I** and **II** as well as in their respective cyclized titano-pinacolates **V** and **VI**, the bulky −NBnTS group poses a severe steric hindrance to the adjacent axial −O[Ti] and hence are unfavorable. Absence of such an hindrance in titano-pinacolates **VII** and **VIII** makes them favorable, with a greater preference, among them, for *trans*-di-O[Ti] intermediate (**VIII**) over the *cis*-di-O[Ti] intermediate (**VII**), leading to the formation of diol **22** (major) and **21** (minor), respectively (Figure 2).

In order to complete the synthesis, compounds **21** and **22** were deprotected in a two-step process. First N-detosylation was performed using Na-Hg in DMF to get the amines **24** and **25**, respectively. Subsequent catalytic hydrogenation in the presence of 10% Pd/C under acidic medium deprotected both *O*- and *N*-benzyl groups to give the aminocyclitols **26** and **27**. As *N*-acetyl derivatives of aminocyclitols have been shown to be better inhibitors of *N*-acetylhexosaminidases, chemoselective N-acetylation of **26** and **27** has also been carried out to get compounds **28** and **29** (Scheme 4).[32]

Total Synthesis of (−)-Conduramine F-4. Synthesis of (−)-conduramine F-4 was envisioned through the RCM of diene **8** that could be readily obtained by bis-Wittig olefination of **9**. Thus, exposure of crude **9** to methyltriphenylphosphonium bromide in the presence of BuLi as a base proceeded to give the diene **8** in 60% yield (for two steps from **10**). Initial RCM of diene **8** with Grubbs'-I catalyst was not successful. However, Grubbs'-II catalyst proved effective, albeit slow, and the protected (−)-conduramine F-4 **30** was isolated in 70% yield, in 72 h, along with 20% recovery of unreacted starting material. N-Detosylation of compound **30** was then carried out with Na-Hg to get the amino derivative **31**. When single step cleavage of both *N*- and *O*-benzyl groups of **31** was attempted under Birch condition, the reaction was not clean, resulting in the formation of a complex mixture. In contrast, its *N*-acetyl derivative **32**, underwent a smooth deprotection when exposed to Na/liq. NH_3 to afford (−)-conduramine F-4 **5**. Advantageously, the intermediate **31** also allowed us to obtain *N*-benzyl-(−)-conduramine F-4 **34** through chemoselective O-debenzylation in the presence of *N*-benzyl group,[33] by exposing **31** to BCl_3. *N*-benzyl-(−)-conduramine F-4 was isolated as its hydrochloride salt **33**, which when neutralized with saturated NH_4OH liberated the free amine **34** (Scheme 5).

Synthesis of Polyhydroxyaminoazepanes. Toward the synthesis of amino-substituted polyhydroxyazepanes, diol **10** was first converted to the dimesyl derivative **35**. Upon heating with benzylamine at 100 °C, dimesylate **35** underwent a facile double nucleophilic substitution to deliver the azepane **36**. The reaction was also successful with butylamine and hydroxyethyl amine and the corresponding azepanes **37** and **38**. Protected azepanes **36**−**38** were taken through a two-step deprotection sequence to get the final amino-substituted polyhydroxyazepanes **42**−**44** in high yields. It has been reported that polyhroxyazepanes with an acetamido group at the 2-position were found to be strong inhibitors of *N*-acetylhexosaminidases.[23] Hence, it was of our interest to acetylate the C2-amino group of compounds **42**−**44**. The acetamido derivatives **45**−**47** were obtained in good yields. However, in the case of compound **42**, the reaction afforded diacetate **45** irrespective

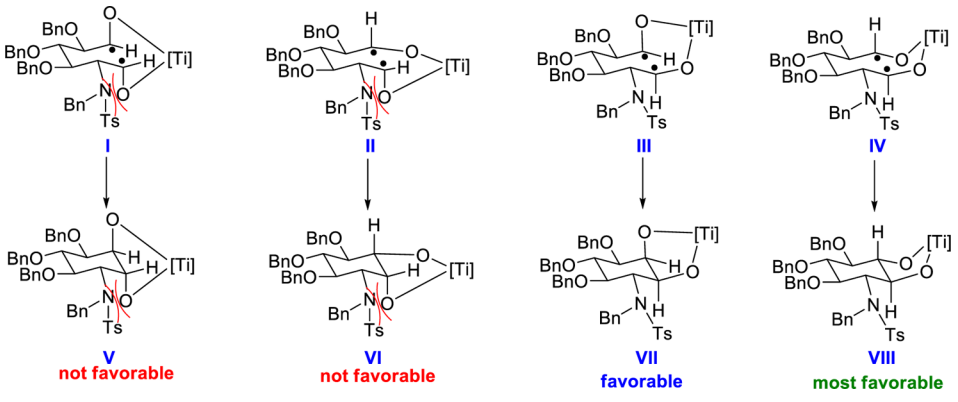


Figure 2. Probable mechanistic explanation for selectivity in McMurry coupling of compound **9**.

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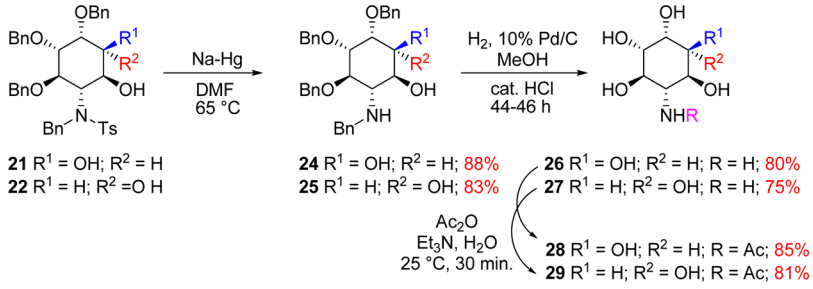
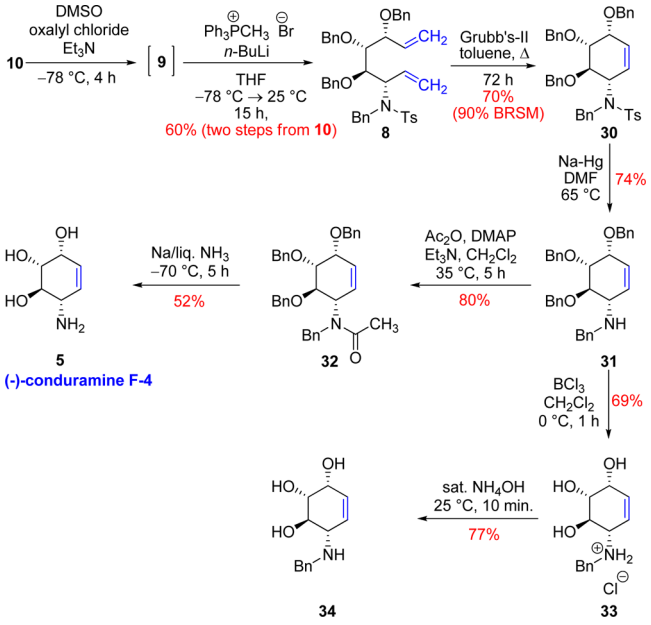
Scheme 4. Synthesis of Aminocyclitols



Scheme 5. Total Synthesis of (−)-Conduramine F-4 and Its *N*-Benzyl Derivative



of the amount of acetic anhydride used in the reaction, and efforts to selectively acetylate the primary amino group at C-2 position did not succeed (Scheme 6).

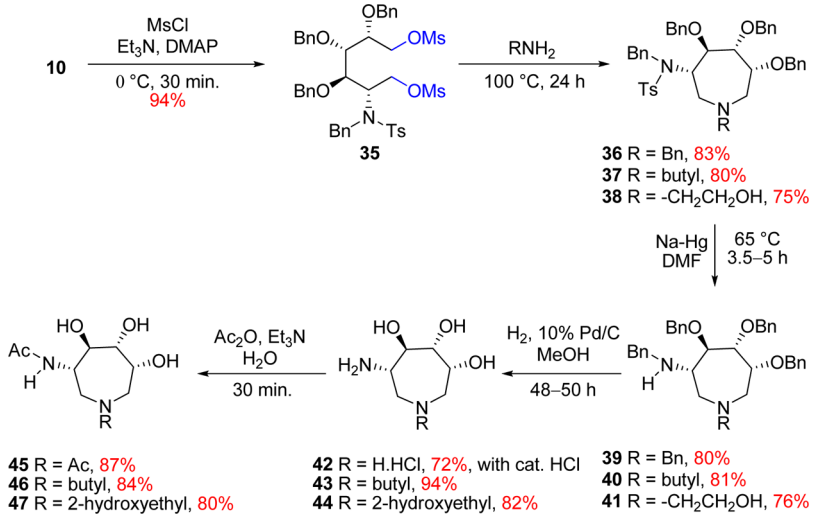
CONCLUSION

In summary, we have employed a 'reagent-based diversity'[33] on a tri-*O*-benzyl-D-glucal derived 'common precursor' for successful synthesis of three structurally different molecules of biological and medicinal relevance. Moreover, our protocol involving an early stage installation of the amino group is distinctly different from most of the existing strategies that rely on its introduction toward the completion of the synthesis. For the first time, application of McMurry coupling for the construction of the six-membered ring of aminocyclitols has been demonstrated. Total synthesis of (−)-conduramine F-4 reported here represents the first carbohydrate-based approach. Extension of the present methodology for the synthesis of amino-azepanes to other amines would provide access to a library of N-substituted derivatives for structure−activity relationship studies. The strategy presented in the manuscript is flexible and can be adopted for use with other sugars to obtain different stereoisomers of these biologically important compounds.

EXPERIMENTAL SECTION

General Experimental Methods. All experiments were performed in an oven-dried apparatus and in dry solvents unless otherwise mentioned. Commercial grade solvents were distilled and dried as per standard procedures and were stored over 4 Å molecular sieves wherever applicable. IR spectra were recorded as a KBr pellet or neat (ATR) and expressed in cm^{-1}. High-resolution mass spectra were recorded on a Q-TOF instrument using electrospray ionization (ESI) as the source. ^1H NMR (300 and 400 MHz) and ^{13}C NMR (75 and 100 MHz) spectra were recorded using $CDCl_3$, CD_3OD, C_6D_6, or

Scheme 6. Synthesis of Amino-Substituted Polyhydroxyazepanes



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D_2O as a solvent. Chemical shifts have been reported in ppm downfield to tetramethylsilane, and coupling constants are expressed in Hertz (Hz). Optical rotations were measured at indicated temperatures and solvents. Commercial TLC plates were used, and the spots were visualized by exposure to the required developing agent/reagent. Column chromatography was performed over silica gel (230−400 mesh).

*1,6-Di-O-acetyl-3,4-di-O-benzyl-2-deoxy-2-(p-toluenesulfonamido)-α-D-gluco Pyranose (**13**).* Compound **14**[28] (19.2 g, 31.8 mmol) was dissolved in a 5:1 mixture of acetic anhydride (175 mL) and acetic acid (35 mL). Anhydrous zinc chloride (21.67 g, 159 mmol) was added to the reaction mixture portion wise over a period of 10 min. The reaction mixture was then stirred at room temperature under nitrogen atmosphere. After completion of the reaction (16 h, TLC), ethyl acetate (500 mL) was added to the reaction mixture, and it was washed with water (6 × 200 mL), followed by saturated aqueous sodium bicarbonate solution (4 × 100 mL). Solvent was removed under vacuum, and the resulting crude reaction mixture was purified by column chromatography over silica gel using ethyl acetate as an eluent to get the diacetate **13** as a pale yellow viscous liquid. Crystallization of the product in a mixture of ethyl acetate in hexane (1:4) afforded compound **13** (17.1 g, 90%) as white crystals. Mp 102−105 °C; TLC: R_f 0.5 (hexane/ethyl acetate, 3:2); $[\alpha]_D^{31}$ +38.5 (*c* 0.53, $CHCl_3$); IR (KBr) ν_{max} 3246, 3064, 3033, 2984, 2920, 2878, 1771, 1714, 1598, 1495, 1446, 1373, 1337, 1267, 1210, 1162, 1134, 1084, 1051, 932, 899, 849, 813, 739, 696, 667, 613 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.7 Hz, 2H), 7.30−7.16 (m, 12H), 5.81 (d, *J* = 3.9 Hz, 1H), 5.57 (t, *J* = 9.3 Hz, 1H exchangeable with D_2O), 4.83 (d, *J* = 9.9 Hz, 1H), 4.77 (d, *J* = 10.8 Hz, 1H), 4.69 (d, *J* = 10.8 Hz, 1H), 4.49 (d, *J* = 10.8 Hz, 1H), 4.26−4.14 (m, 2H), 3.82−3.77 (m, 1H), 3.72 (m, 1H), 3.60−3.57 (m, 2H), 2.36 (s, 3H), 2.05 (s, 3H), 2.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6 (s), 168.9 (s), 143.9 (s), 137.7 (s), 137.37 (s), 137.34 (s), 129.9 (d), 128.5 (d), 128.3 (d), 128.0 (d), 127.9 (d), 127.8 (d), 126.8 (d), 90.7 (d), 79.9 (d), 77.1 (d), 75.7 (t), 75.1 (t), 70.8 (d), 62.3 (t), 56.1 (d), 21.5 (q), 20.8 (2*q*); HRMS (ESI): $[M + Na]^+$ calcd for $C_{31}H_{35}NNaO_9S$: 620.1925; found: 620.1909.

*3,4-Di-O-benzyl-2-deoxy-2-(p-toluenesulfonamido)-D-glucitol (**16**).* Diacetate **13** (5 g, 8.37 mmol) was dissolved in dry THF (50 mL) under nitrogen atmosphere. Reaction mixture was immersed in an ice bath (0 °C), and $LiAlH_4$ (1.11 g, 29.18 mmol) was added to the reaction mixture, in portions, over a period of 20 min. The reaction mixture was subsequently refluxed at 65 °C for 16 h after which it was cooled to 0 °C (bath temperature), and 10% HCl solution was added dropwise until the effervescence subsided. Water (100 mL) was then added and extracted with ethyl acetate (3 × 100 mL). Solvent was evaporated under vacuum to get the crude product as a white solid. Purification of the product by column chromatography over silica gel using a mixture of hexane and ethyl acetate (2:3) afforded triol **16** (3.7 g, 86%) as a white solid. Mp 108−111 °C; TLC: R_f 0.3 (hexane/ethyl acetate, 1:4); $[\alpha]_D^{19}$ +5.05 (*c* 0.97, CH_2Cl_2); IR (KBr) ν_{max} 3562, 3490, 3265, 3063, 3032, 2936, 2879, 1598, 1496, 1453, 1319, 1124, 1044, 931, 875, 814, 734, 696, 679, 651 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.1 Hz, 2H), 7.27−7.16 (m, 12H), 5.24 (bm, 1H exchangeable with D_2O), 4.67 (d, *J* = 11.4 Hz, 1H), 4.59 (d, *J* = 11.4 Hz, 1H), 4.50 (d, *J* = 11.4 Hz, 1H), 4.43 (d, *J* = 11.4 Hz, 1H), 3.75 (bs, 1H), 3.61−3.58 (m, 3H), 3.55−3.51 (m, 2H), 3.43 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.23 (dd, *J* = 11.1, 6.3 Hz, 1H), 2.32 (s, 3H), 2.16 (bm, 3H exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.7 (s), 138.1 (s), 137.9 (s), 129.2 (d), 128.0 (d), 127.8 (d), 127.5 (d), 127.9 (d), 127.2 (d), 126.6 (d), 78.5 (d), 77.9 (d), 74.4 (t), 73.6 (t), 71.9 (d), 63.0 (t), 61.4 (t), 55.7 (d), 21.1 (q); HRMS (ESI): $[M + H]^+$ calcd for $C_{27}H_{34}NO_7S$: 516.2050; found: 516.2050.

*3,4-Di-O-benzyl-1,6-di-O-(tert-butyldimethylsilyl)-2-deoxy-2-(p-toluenesulfon amido)-D-glucitol (**17**).* A solution of triol **16** (8.1 g, 15.71 mmol) in dry CH_2Cl_2 (80 mL) was cooled to 0 °C. Imidazole (2.35 g, 34.56 mmol) and TBSCl (5.21 g, 34.56 mmol) were added successively at 0 °C, and the reaction mixture was stirred at the same temperature. After completion (1.5 h, TLC), reaction was stopped, and solvent was evaporated under vacuum. Ethyl acetate (300 mL) was added to the resulting residue, the organic layer was washed with water (3 × 200 mL), and solvent was evaporated under vacuum to get the crude product as a white mass. Purification of the product by column chromatography over silica gel using a mixture of hexane and ethyl acetate (9:1) afforded the bis-silylated derivative **17** (10.3 g, 88%) as a white solid. Mp 109−111 °C; TLC: R_f 0.55 (hexane/ethyl acetate, 4:1); $[\alpha]_D^{31}$ +16.8 (*c* 0.77, CH_2Cl_2); IR (KBr) ν_{max} 3484, 3166, 3031, 2953, 2927, 2881, 2855, 1598, 1460, 1403, 1358, 1336, 1256, 1164, 1096, 1066, 1049, 933, 836, 814, 773, 732, 675, 701, 666 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.8 Hz, 2H), 7.25−7.16 (m, 12H), 4.98 (d, *J* = 8.4 Hz, 1H), 4.71 (d, *J* = 10.8 Hz, 1H), 4.58 (d, *J* = 11.4 Hz, 1H), 4.46 (m, 2H), 3.91 (dd, *J* = 6.6, 2.1 Hz, 1H), 3.61−3.50 (m, 5H), 3.40−3.30 (m, 2H), 2.32 (s, 3H), 1.56 (bs, 1H exchangeable with D_2O), 0.84 (s, 9H), 0.74 (s, 9H), −0.001 (s, 3H), −0.004 (s, 3H), −0.12 (s, 3H), −0.13 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.2 (s), 138.4 (s), 138.26 (s), 138.24 (s), 129.6 (d), 128.45 (d), 128.41 (d), 128.0 (d), 127.9 (d), 127.8 (d), 127.6 (d), 127.1 (d), 78.4 (d), 77.5 (d), 75.3 (t), 74.3 (t), 72.5 (d), 63.7 (t), 62.1 (t), 55.6 (d), 26.0 (q), 25.9 (q), 21.5 (q), 18.3 (s), 18.1 (s), −5.23 (q), −5.27 (q), −5.42 (q), −5.49 (q); HRMS (ESI): $[M + Na]^+$ calcd for $C_{39}H_{61}NNaO_7SSi_2$: 766.3602; found: 766.3592.

*3,4-Di-O-benzyl-1,5,6-tri-O-(tert-butyldimethylsilyl)-2-deoxy-2-(p-toluenesulf onamido)-D-glucitol (**18**).* To a solution of disilyl compound **17** (0.2 g, 0.27 mmol) in dry DMF (1.5 mL) were added imidazole (0.183 g, 2.69 mmol) and TBSCl (0.121 g, 0.80 mmol) at room temperature (32 °C). After completion (22 h, TLC), ethyl acetate (50 mL) was added to the reaction mixture and washed with water (7 × 20 mL). Solvent was evaporated under vacuum to get the crude product as a pale yellow liquid. Purification of the product by column chromatography over silica gel using a mixture of hexane and ethyl acetate (9.5:0.5) afforded the tris-silylated derivative **18** (0.21 g, 91%) as a viscous transparent liquid. TLC: R_f 0.35 (hexane/ethyl acetate, 9:1); $[\alpha]_D^{30}$ +8.4 (*c* 1.2, $CHCl_3$); IR (KBr) ν_{max} 3284, 3032, 2931, 2857, 1465, 1411, 1335, 1254, 1160, 1089, 841, 777, 662 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.4 Hz, 2H), 7.35−7.23 (m, 12H), 4.94 (d, *J* = 9.6 Hz, 1H exchangeable with D_2O), 4.89 (d, *J* = 11.2 Hz, 1H), 4.75 (d, *J* = 11.2 Hz, 1H), 4.66 (d, *J* = 11.2 Hz, 1H), 4.47 (d, *J* = 11.2 Hz, 1H), 4.11−4.09 (m, 1H), 4.04 (d, *J* = 8.0 Hz, 1H), 3.81 (dd, *J* = 7.6, 2.0 Hz, 1H), 3.75−3.66 (m, 2H), 3.55−3.49 (m, 1H), 3.38 (t, *J* = 9.6 Hz, 1H), 3.24 (dd, *J* = 9.6, 4.8 Hz, 1H), 2.42 (s, 3H), 0.96 (s, 9H), 0.95 (s, 9H), 0.83 (s, 9H), 0.19 (s, 3H), 0.18 (s, 3H), 0.12 (s, 3H), 0.11 (s, 3H), −0.061 (s, 3H), −0.066 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.1 (s), 139.27 (s), 139.21 (s), 138.6 (s), 129.6 (2*d*), 128.3 (2*d*), 128.1 (2*d*), 127.83 (2*d*), 127.80 (2*d*), 127.5 (d), 127.3 (d), 126.9 (2*d*), 82.3 (d), 75.6 (d), 75.06 (t), 75.03 (d), 74.7 (t), 64.5 (t), 62.1 (t), 56.6 (d), 26.2 (3*q*), 26.0 (3*q*), 25.9 (3*q*), 21.4 (q), 18.5 (s), 18.2 (s), 18.1 (s), −4.2 (q), −4.5 (q), −5.1 (q), −5.2 (q), −5.53 (q), −5.55 (q); HRMS (ESI): $[M + Na]^+$ calcd for $C_{45}H_{75}NNaO_7SSi_3$: 880.4465; found: 880.4464.

*3,4,5-Tri-O-benzyl-1,6-di-O-(tert-butyldimethylsilyl)-2-deoxy-2-(N-benzyl-N-p-toluenesulfonyl)amino-D-glucitol (**20**).* A solution of compound **17** (10.2 g, 13.71 mmol) in dry DMF (100 mL) was cooled to 0 °C. Sodium hydride (1.64 g in 60% paraffin oil, 41.12 mmol) was added over a period of 30 min while stirring at 0 °C, followed by benzyl bromide (3.58 mL, 30.16 mmol). The reaction mixture was then stirred at 10 °C for 2 h, cooled to 0 °C, and quenched by dropwise addition of saturated ammonium chloride solution until the effervesence stopped. An additional 300 mL water was added to the reaction mixture, and it was extracted with ethyl acetate (3 × 100 mL). The combined organic layer was concentrated under vacuum to get crude product as a white solid. Purification by column chromatography over silica gel using a mixture of hexane and ethyl acetate (9:0.5) as an eluent afforded the benzylated derivative **20** (10.5 g, 83%) as a colorless viscous liquid. TLC: R_f 0.4 (hexane/ethyl acetate, 9:1); $[\alpha]_D^{19}$ +33.1 (*c* 0.48, CH_2Cl_2); IR (neat) ν_{max} 3029, 2953, 2931, 2886, 2857, 1599, 1495, 1457, 1343, 1254, 1161, 1093, 1044, 1004, 842, 777, 698, 675 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.1 Hz, 2H), 7.40−7.07 (m, 22H), 4.80 (d, *J* = 11.7 Hz, 1H), 4.69−4.62 (m, 2H), 4.57−4.50 (m, 2H), 4.40 (d, *J* = 10.5 Hz, 1H), 4.33 (d, *J* = 15.9 Hz, 1H), 4.15−4.07 (m, 2H), 4.00 (t, *J* = 5.4 Hz, 1H), 3.96−3.83 (m, 4H),

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J. Org. Chem. 2016, 81, 11574−11586

3.79−3.74 (m, 1H), 3.30 (bm, 1H), 2.35 (s, 3H), 0.91 (s, 9H), 0.77 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H), −0.11 (s, 3H), −0.13 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.1 (s), 139.4 (s), 139.2 (s), 138.9 (s), 138.5 (s), 137.9 (s), 129.5 (d), 129.1 (d), 128.2 (d), 128.0 (d), 127.7 (d), 127.4 (d), 127.3 (d), 127.2 (d), 127.1 (d), 81.4 (d), 79.9 (d), 78.5 (d), 75.0 (t), 74.1 (t), 72.8 (t), 63.4 (t), 61.5 (d), 60.7 (t), 50.0 (t), 26.1 (q), 25.9 (q), 21.5 (q), 18.4 (s), 18.1 (s), −5.10 (q), −5.12 (q), −5.4 (2xq); HRMS (ESI): $[M + Na]^+$ calcd for $C_{53}H_{73}NNaO_7SSi_2$: 946.4538; found: 946.4534.

*3,4,5-Tri-O-benzyl-2-deoxy-2-(N-benzyl-N-p-toluenesulfonyl)-amino-D-glucitol (**10**).* Compound **20** (10 g, 10.82 mmol) was placed in a 100 mL round-bottomed flask and dissolved with dry MeOH (100 mL). Camphor-10-sulfonic acid (0.502 g, 20 mol %) was added to it. After 12.5 h (TLC), the reaction was stopped, and the solvent was evaporated under vacuum. The crude reaction mixture was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (7:3) as an eluent to get **10** (6.5 g, 86%) as a colorless viscous liquid. TLC: R_f 0.4 (hexane/ethyl acetate, 1:1); $[\alpha]_D^{25}$ +17.1 (*c* 1.5, CH_2Cl_2);IR (neat) ν_{max} 3431, 3062, 3029, 2924, 2875, 1598, 1495, 1454, 1335, 1210, 1158, 1091, 858, 815, 734, 697 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.1 Hz, 2H), 7.39−7.14 (m, 22H), 4.68 (d, *J* = 11.4 Hz, 1H), 4.58−4.50 (m, 4H), 4.44−4.35 (m, 3H), 4.17−4.158 (m, 1H), 3.93−3.87 (m, 3H), 3.81−3.76 (m, 2H), 3.61 (dd, *J* = 11.7, 5.4 Hz, 1H), 3.38 (dd, *J* = 11.7, 6.3 Hz, 1H), 2.38 (s, 3H), 2.05 (bm, 2H exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.3 (s), 138.2 (s), 138.0 (s), 137.5 (s), 129.5 (d), 128.9 (d), 128.4 (d), 128.39 (d), 128.30 (d), 128.2 (d), 128.0 (d), 127.8 (d), 127.79 (d), 127.71 (d), 127.5 (d), 127.3 (d), 79.7 (d), 78.5 (d), 77.6 (d), 74.4 (t), 74.1 (t), 71.9 (t), 61.5 (d), 60.9 (t), 60.7 (t), 50.0 (t), 21.4 (q); HRMS (ESI): $[M + Na]^+$ calcd for $C_{41}H_{45}NNaO_7S$:718.2809; found: 718.2806.

*3,4,5-Tri-O-benzyl-2-deoxy-2-(N-benzyl-N-p-toluenesulfonyl)-amino-D-gluco-hexodialdehyde (**9**).* A solution of oxalyl chloride (1.24 mL, 14.37 mmol) in dry dichloromethane (40 mL) was cooled to −78 °C. Dry DMSO (1.02 mL, 14.37 mmol) was added to it dropwise over a period of 10 min under nitrogen atmosphere. The reaction mixture was allowed to stir for 20 min at this temperature, and then diol **10** (1 g, 1.44 mmol) dissolved in 10 mL of dry dichloromethane was added slowly over a period of 15 min. The reaction mixture was then stirred at −78 °C for 3 h. Triethylamine (4.01 mL, 28.74 mmol) was added over a period of 15 min. The reaction vessel was removed from the cooling bath and stirred at 25 °C (bath temperature) for 30 min, after which ethyl acetate (200 mL) was added to it. The organic layer was washed with water (7 × 60 mL) and concentrated under vacuum. The crude dialdehyde **9** was obtained as a pale yellow viscous liquid (0.99 g, 99.6%). As the dialdehyde was quite unstable, it was taken for subsequent reaction, without purification, after ascertaining its formation through ^{1}H NMR spectrum.

*(1R,2S,3R,4S,5S,6S)-1,2,3-Tri-O-benzyl-6-(N-benzyl-N-p-toluesulfonyamino)-4,5-dihydroxycyclohexane (**21**) and (1R,2S,3R,4R,5S,6S)-1,2,3-Tri-O-benzyl-6-(N-benzyl-N-p-toluensulfonyl)amino-4,5-dihydroxycyclohexane (**22**).* In a 100 mL round-bottomed flask, $TiCl_4$ (1.57 mL, 14.31 mmol) was placed in dry THF (20 mL) and cooled to 0 °C. Zinc powder (1.87 g, 28.62 mmol) was added to it portion wise, during which the color of the reaction mixture changed from yellow to violet. Cuprous chloride (0.028 g, 0.29 mmol) was then added to it and refluxed at 80 °C for 1 h. Crude dialdehyde **9** (0.99 g, 1.43 mmol) dissolved in dry THF (10 mL) was added dropwise over a period of 30 min, and refluxing was continued for 4 h. The reaction mixture was cooled to 0 °C and quenched with saturated sodium bicarbonate solution. The resulting mass was filtered through a Celite bed. The residue was washed with ethyl acetate (3 × 10 mL), water (100 mL) was added to the filtrate, and the organic layer was separated. The aqueous layer was further extracted with ethyl acetate (3 × 20 mL). The combined organic layer was concentrated under vacuum. Purification of the product was done by column chromatography over silica gel using a mixture of hexane and ethyl acetate (3:1) as an eluent to get the cyclic diols **21** (0.25 g, 25%) as a colorless viscous liquid and **22** (0.38 g, 38%) as a white solid.

*Data for Compound **21**.* TLC: R_f 0.55 (hexane/ethyl acetate, 1:1); $[\alpha]_D^{25}$ −9.25 (*c* 0.92, $CHCl_3$); IR (KBr) ν_{max} 3481, 3061, 3029, 2920, 1598, 1494, 1452, 1321, 1207, 1150, 1092, 927, 868, 812, 732, 696 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.5 Hz, 2H), 7.34−6.93 (m, 22H), 4.74−4.69 (m, 2H), 4.62−4.39 (m, 5H), 4.17−4.10 (m, 1H), 4.03−3.87 (m, 4H), 3.67 (d, *J* = 15.9 Hz, 1H), 3.17 (d, *J* = 10.5 H, 1H), 3.09 (bs, 1H D_2O exchangeable), 2.52 (bs, 1H D_2O exchangeable), 2.27 (s, 3H);^{1}H NMR (300 MHz, MeOD) δ 7.73 (d, *J* = 7.5 Hz, 2H), 7.33−7.04 (m, 22H), 4.65−4.47 (m, 5H), 4.40−4.30 (m, 3H), 4.05 (d, *J* = 15.6 Hz, 1H), 3.93−3.88 (m, 3H), 3.72 (t, *J* = 9.6 Hz, 1H), 3.58 (d, *J* = 10.2 Hz, 1H), 2.30 (s, 3H);^{13}C NMR (75 MHz, $CDCl_3$) δ 142.9 (s), 138.4 (s), 138.2 (s), 137.2 (s), 129.1 (d), 128.6 (d), 128.3 (d), 128.2 (d), 128.0 (d), 127.9 (d), 127.88 (d), 127.82 (d), 127.6 (d), 127.5 (d), 127.4 (d), 127.2 (d), 82.4 (d), 75.3 (d), 73.4 (t), 73.0 (t), 72.5 (t), 69.0 (d), 67.6 (d), 61.0 (d), 47.5 (t), 21.5 (q); ^{13}C NMR (75 MHz, MeOD) δ 144.1 (s), 140.1 (s), 139.9 (s), 139.6 (s), 139.4 (s), 138.6 (s), 130.3 (d), 130.1 (d), 129.3 (d), 129.2 (d), 129.09 (d), 129.06 (d), 129.02 (d), 128.8 (d), 128.63 (d), 128.61 (d), 128.2 (d), 83.5 (d), 77.2 (d), 76.1 (d), 74.4 (t), 74.1 (t), 73.4 (t), 70.8 (d), 67.9 (d), 61.9 (d), 48.3 (t), 21.5 (q); HRMS (ESI): $[M + Na]^+$ calcd for $C_{41}H_{43}NNaO_7S$: 716.2652; found: 716.2652.

*Data for Compound **22**.* Mp 102−105 °C; TLC: R_f 0.35 (hexane/ethyl acetate, 1:1); $[\alpha]_D^{25}$ −3.6 (*c* 0.573, $CHCl_3$); IR (KBr) ν_{max} 3577, 3383, 3061, 3030, 2922, 2886, 1598, 1495, 1452, 1403, 1359, 1330, 1259, 1210, 1157, 1114, 1081, 1053, 926, 887, 812, 744, 698, 659 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.1 Hz, 2H), 7.38−7.03 (m, 22H), 4.83 (d, *J* = 11.4 Hz, 1H), 4.69−4.53 (m, 4H), 4.48−4.41 (m, 2H), 3.98−3.92 (m, 3H), 3.73 (d, *J* = 15.6 Hz, 1H), 3.54−3.47 (m, 1H), 3.37−3.33 (m, 1H), 3.28−3.22 (m, 1H), 2.40 (d, *J* = 3.6 Hz, 1H, D_2O exchangeable), 2.30 (s, 3H), 2.25 (d, *J* = 5.7 Hz 1H, D_2O exchangeable);^{1}H NMR (300 MHz, MeOD) δ 7.76 (d, *J* = 8.1 Hz, 2H), 7.35−7.22 (m, 17H), 7.14−7.10 (m, 3H), 6.97 (t, *J* = 7.5 Hz, 2H), 4.79−4.71 (m, 2H), 4.63 (d, *J* = 11.4 Hz, 1H), 4.56−4.51 (m, 2H), 4.26−4.10 (m, 3H), 4.06−3.99 (m, 2H), 3.77−3.66 (m, 2H), 3.55 (dd, *J* = 9.9, 1.2 Hz, 1H), 3.45 (dd, *J* = 9.0, 1.2 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.9 (s), 138.8 (s), 138.3 (s), 137.8 (s), 137.7 (s), 137.0 (s), 129.1 (d), 128.8 (d), 128.5 (d), 128.4 (d), 128.29 (d), 128.24 (d), 128.1 (d), 127.9 (d), 127.8 (d), 127.6 (d), 127.5 (d), 127.4 (d), 83.6 (d), 76.4 (d), 74.6 (t), 73.9 (d), 73.7 (d), 73.5 (t), 72.5 (t), 69.3 (d), 62.6 (d), 47.3 (t), 21.5 (q); ^{13}C NMR (75 MHz, MeOD) δ 144.1 (s), 140.5 (s), 140.1 (s), 139.63 (s), 139.60 (s), 138.4 (s), 130.5 (d), 130.0 (d), 129.5 (d), 129.35 (d), 129.31 (d), 129.1 (d), 129.0 (d), 128.99 (d), 128.97 (d), 128.6 (d), 128.4 (d), 128.2 (d), 84.7 (d), 78.8 (d), 76.5 (d), 75.8 (t), 74.8 (d), 74.6 (t), 73.3 (t), 69.4 (d), 64.0 (d), 48.1 (t), 21.4 (q); HRMS (ESI): $[M + Na]^+$ calcd for $C_{41}H_{43}NNaO_7S$: 716.2652; found: 716.2651.

*(1S,2R,3S,4S,5R,6R)-1,2-Bis-(4-nitro)benzoyloxy-3,4,5-tri-O-benzyl-6-(N-benzyl-N-p-toluensulfonyl)aminocyclohexane (**23**).* Diol **21** (0.04 g, 0.057 mmol) dissolved in dry dichloromethane (0.6 mL) was placed in a 100 mL round bottomed flask. 4-Nitrobenzoyl chloride (0.0267 g, 0.144 mmol), triethyl amine (0.0261 mL, 0.173 mmol), and DMAP (0.0014 g, 0.0115 mmol) were added to it sequentially, and it was stirred at 23 °C for 5 h. Dichloromethane (30 mL) was added to the reaction mixture, washed with water (3 × 10 mL), and the solvent was concentrated under vacuum. Purification of the product was done through column chromatography over silica gel using a mixture of hexane and ethyl acetate (9:0.5) as an eluent to get bis-4-nitrobenzoyl derivative **23** (0.052 g, 91%) as a pale yellow low melting solid. TLC: R_f 0.34 (hexane/ethyl acetate, 9:1); $[\alpha]_D^{27}$ −43.57 (*c* 0.28, $CHCl_3$); IR (KBr) ν_{max} 3060, 3030, 2923, 1735, 1604, 1528, 1496, 1454, 1344, 1277, 1209, 1157, 1097, 1013, 928, 870, 843, 814, 782, 747, 720, 699, 661, 601 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6) δ 8.36 (d, *J* = 8.4 Hz, 2H), 7.94 (d, *J* = 7.8 Hz, 2H), 7.84 (d, *J* = 8.4 Hz, 2H), 7.70 (d, *J* = 8.4 Hz, 3H), 7.61 (d, *J* = 8.4 Hz, 3H), 7.41−7.34 (m, 5H), 7.27 (t, *J* = 7.2 Hz, 3H), 7.12−7.05 (m, 6H), 6.99−6.94 (m, 3H), 6.61 (d, *J* = 7.8 Hz, 2H), 6.26 (t, *J* = 3.3 Hz, 1H), 5.47 (dd, *J* = 11.1, 10.8 Hz, 1H), 5.04 (d, *J* = 10.2 Hz, 1H), 4.93 (d, *J* = 11.4 Hz, 1H), 4.64−4.39 (m, 8H), 4.15 (d, *J* = 7.5 Hz, 1H), 3.90 (t, *J* = 3.0 Hz, 1H), 3.47 (d, *J* = 15.6 Hz, 1H), 1.85 (s, 3H); ^{13}C NMR (75 MHz, C_6D_6) δ 164.1 (s), 163.9 (s), 151.0 (s), 150.9 (s), 142.8 (s), 138.6 (s), 138.5 (s), 137.9 (s), 137.8 (s),

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J. Org. Chem. 2016, 81, 11574−11586

136.8 (s), 134.9 (s), 134.2 (s), 131.3 (d), 130.7 (d), 129.3 (d), 129.2 (d), 129.1 (d), 128.8 (d), 128.7 (d), 128.6 (d), 128.5 (d), 127.8 (d), 123.8 (d), 123.7 (d), 82.6 (d), 74.2 (t), 73.7 (d), 73.18 (t), 73.18 (d), 72.5 (t), 69.9 (d), 69.1 (d), 58.5 (d), 47.5 (t), 21.1 (q); HRMS (ESI): $[M + Na]^+$ calcd for $C_{55}H_{49}N_3NaO_{13}S$: 1014.2878; found: 1014.2863.

General Procedure for N-Detosylation Reaction. N-Tosylated derivative (1 equiv) was dissolved in a solvent mixture of DMF and methanol. Disodium hydrogen phosphate dihydrate (5 equiv) was added to the reaction mixture followed by 3% Na-Hg (20 equiv). The reaction mixture then stirred at 65 °C, and after completion (TLC), ethyl acetate was added to it, washed with water, and solvent was concentrated under vacuum. Purification of the product was done by column chromatography over silica gel to get the N-detosylated derivatives.

*(1R,2S,3R,4S,5S,6S)-1,2,3-Tris-benzyloxy-6-(N-benzylamino)-4,5-dihydroxycyclohexane (**24**).* Compound **21** (0.8 g, 1.15 mmol) was subjected to N-detosylation reaction as per the general procedure described above in DMF (15 mL) and methanol (5 mL), in the presence of $Na_2HPO_4{\cdot}2H_2O$ (1.03 g, 5.76 mmol) and 3% Na-Hg (17.67 g, 23.06 mmol) for 3.5 h. Product was purified by column chromatography using a mixture of hexane and ethyl acetate (2:3) to get **24** (0.55 g, 88%) as a colorless viscous liquid. TLC: R_f 0.39 (hexane/ethyl acetate, 1:4); $[\alpha]_D^{18}$ −8.57 (*c* 0.21, $CHCl_3$); IR (KBr) ν_{max} 3410, 3063, 3029, 2905, 2869, 1495, 1453, 1367, 1215, 1097, 1061, 750,697 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.34−7.20 (m, 20H), 5.06 (d, J = 11.1 Hz, 1H), 4.80−4.63 (m, 5H), 4.16 (t, J = 3.3 Hz, 1H), 3.99−3.88 (m, 4H), 3.79 (dd, J = 10.2, 2.7 Hz, 1H), 3.71 (d, J = 12.6 Hz, 1H), 2.88 (t, J = 9.3 Hz, 1H), 2.01 (bm, 3H D_2O exchangeable); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.1 (s), 138.7 (s), 138.5 (s), 138.4 (s), 128.5 (d), 128.44 (d), 128.41 (d), 128.29 (d), 128.25 (d), 128.06 (d), 128.03 (d), 127.76 (d), 127.72 (d), 127.6 (d), 127.1 (d), 81.7 (d), 78.4 (d), 75.8 (d), 74.9 (t), 73.3 (t), 72.6 (t), 68.9 (d), 68.8 (d), 59.7 (d), 50.0 (t); HRMS (ESI): $[M + H]^+$ calcd for $C_{34}H_{38}NO_5$: 540.2744; found: 540.2744.

*(1R,2S,3R,4R,5S,6S)-1,2,3-Tris-benzyloxy-6-(benzylamino)-4,5-dihydroycyclohexane (**25**).* Compound **22** (0.75 g, 1.08 mmol) was subjected to N-detosylation reaction as per the general procedure described above in DMF (15 mL) and methanol (5 mL), in the presence of $Na_2HPO_4{\cdot}2H_2O$ (0.962 g, 5.4 mmol) and 3% Na-Hg (16.57 g, 21.62 mmol) for 4 h. Product was purified by column chromatography using a mixture of hexane and ethyl acetate (1:1) to get **25** (0.483 g, 83%) as a white solid. Mp 68−71 °C; TLC: R_f 0.46 (hexane/ethyl acetate, 1:4); $[\alpha]_D^{34}$ −2.51 (*c* 2.31, $CHCl_3$); IR (KBr) ν_{max} 3390, 3061, 3029, 2915, 1600, 1492, 1455, 1360, 1212, 1143, 1058, 733, 697, 603 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.36−7.27 (m, 17H), 7.24−7.22 (m, 3H),5.05 (dd, J = 11.1, 5.1 Hz 2H), 4.77−4.66 (m, 4H), 4.08 (t, J = 2.4 Hz, 1H), 4.02−3.92 (m, 2H), 3.80 (d, J = 12.9 Hz, 1 H), 3.71 (t, J = 9.9 Hz, 1H), 3.53 (dd, J = 9.6, 2.4 Hz, 1H), 3.41 (dd, J = 9.3, 2.7 Hz, 1H), 2.50 (t, J = 10.2 Hz, 1H), 1.68 (bm, 3H D_2O exchangeable); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.3 (s), 138.8 (s), 138.6 (s), 138.1 (s), 128.59 (d), 128.54 (d), 128.4 (d), 128.3 (d), 128.1 (d), 127.8 (d), 127.7 (d), 127.1 (d), 83.1 (d), 79.2 (d), 77.2 (d), 75.3 (t), 74.9 (t), 73.6 (d), 72.7 (t), 71.6 (d), 62.2 (d), 51.3 (t); HRMS (ESI): $[M + H]^+$ calcd for $C_{34}H_{38}NO_5$: 540.2744; found: 540.2739.

*(1R,2S,3S,4S,5S,6S)-6-Amino-1,2,3,4,5-pentahydroxycyclohexane (**26**).* Compound **24** (0.15 g, 0.278 mmol) was dissolved in ethanol (3 mL). 10% Palladium on charcoal (0.03 g, 20% w/w) was added, followed by slow addition of HCl (0.1 mL). Hydrogen gas was bubbled slowly into the reaction mixture continuously while stirring at room temperature for 44 h. The reaction mixture was filtered through bed of Celite pad, and the filtrate was concentrated under vacuum. After neutralization by the addition of aqueous ammonium hydroxide solution (∼1 mL), the resulting solution was directly loaded on to a silica gel column and purified using a mixture of acetonitrile and aqueous ammonium hydroxide solution (3:1) to get **26** (0.04 g, 80%) as colorless viscous liquid. TLC: R_f 0.24 (CH_3CN/NH_4OH, 3:2); $[\alpha]_D^{28}$ −40.22 (*c* 0.44, H_2O); IR (neat) ν_{max} 3491, 3083, 2925, 1529, 1409, 1099, 1073 cm^{-1}. ^1H NMR (300 MHz, D_2O) δ 3.84 (bm, 2H), 3.67 (dd, J = 10.5, 1.8 Hz, 1H), 3.56 (dd, J = 9.9, 2.1 Hz, 1H), 3.46 (t, J = 9.9 Hz, 1H), 2.94 (t, J = 10.5 Hz, 1H); ^1H NMR (300 MHz, MeOD) δ 3.99 (bm, 2H), 3.86 (d, J = 10.5 Hz, 1H), 3.75−3.66 (m, 2H), 3.12 (t, J = 10.2 Hz, 1H); ^{13}C NMR (75 MHz, D_2O) δ 71.49 (d), 71.40 (d), 70.5 (d), 70.1 (d), 68.2 (d), 54.4 (d); HRMS (ESI): $[M + H]^+$ calcd for $C_6H_{14}NO_5$: 180.0866; found: 180.0867.

*(1R,2S,3S,4R,5S,6S)-6-Amino-1,2,3,4,5-pentahydroxycyclohexane (**27**).* Compound **25** (0.2 g, 0.37 mmol) was dissolved in ethanol (4 mL). 10% Palladium on charcoal (0.04 g, 20% w/w) was added followed by slow addition of HCl (0.1 mL). Hydrogen gas was bubbled slowly into the reaction mixture continuously while stirring at room temperature for 46 h. The reaction mixture was filtered through a bed of Celite pad and the filtrate was concentrated under vacuum. After neutralization by the addition of aqueous ammonium hydroxide solution (1 mL), the resulting solution was directly loaded on to a silica gel column and purified using a mixture of acetonitrile and aqueous ammonium hydroxide solution (10:2) to get **27** (0.05 g, 75%) as a colorless viscous liquid. TLC: R_f 0.22 (CH_3CN/NH_4OH, 3:2); $[\alpha]_D^{30}$ +0.00 (*c* 0.57, H_2O); IR (neat) ν_{max} 3072, 2925, 1530, 1095, 1062 cm^{-1}. ^1H NMR (300 MHz, D_2O) δ 3.98 (t, 2.7 Hz, 1H), 3.64 (m, 2H) 3.47 (m, 2H), 2.80 (t, J = 10.5 Hz, 1H); ^{13}C NMR (75 MHz, D_2O) δ 71.8 (d), 71.7 (d), 69.4 (d), 56.3 (d); HRMS (ESI): $[M + H]^+$ calcd for $C_6H_{14}NO_5$: 180.0866; found: 180.0865.

*(1R,2S,3R,4S,5S,6S)-6-(N-Acetyl)amino-1,2,3,4,5-pentahydroxycyclohexane (**28**).* Polyhydroxyaminocyclitol **26** (0.03 g, 0.167 mmol) was dissolved in water (0.2 mL). Triethyl amine (0.0188 g, 0.184 mmol) in MeOH (0.1 mL) was added dropwise followed by acetic anhydride (0.01845 g, 0.184 mmol) dissolved in MeOH (0.1 mL). Reaction mixture was stirred at room temperature for 30 min, after which it was directly loaded on to a silica gel column, and the product was eluted with a mixture of acetonitrile and aqueous ammonium hydroxide solution (3:1) to get **28** (0.031 g, 85%) as a colorless viscous liquid. TLC: R_f 0.26 (CH_3CN/NH_4OH, 3:2); $[\alpha]_D^{20}$ −49.05 (*c* 0.316, MeOH); IR (neat) ν_{max} 3268, 1629, 1568, 1441, 1378, 1322, 1071, 1015, 666 cm^{-1}. ^1H NMR (300 MHz, MeOD) δ 4.06−3.99 (m, 1H), 3.95−3.93 (m, 2H), 3.77−3.73 (m, 2H), 3.61−3.54 (m, 1H), 2.02 (s, 3H); ^{13}C NMR (75 MHz, MeOD) δ 174.7 (s); 73.5 (d); 73.3 (d); 72.9 (d); 72.7 (d); 71.2 (d), 55.4 (d), 22.9 (q);[10d,32] HRMS (ESI): $[M + Na]^+$ calcd for $C_8H_{15}NNaO_6$: 244.0791; found: 244.0783.

*(1R,2S,3S,4R,5S,6S)-6-(N-Acetyl)amino-1,2,3,4,5-pentahydroxycyclohexane (**29**).* Polyhydroxyaminocyclitol **27** (0.015 g, 0.083 mmol) was dissolved in water (0.15 mL). Triethyl amine (0.0094 g, 0.092 mmol) dissolved in MeOH (0.1 mL) was added dropwise, followed by acetic anhydride (0.00923 g, 0.092 mmol) dissolved in MeOH (0.1 mL). Reaction mixture was then stirred at room temperature for 30 min after which it was directly loaded on to a silica gel column, and the product was eluted with a mixture of acetonitrile and aqueous ammonium hydroxide solution (3:2) to get **29** (0.015 g, 81%) as a colorless viscous liquid. TLC: R_f 0.30 (CH_3CN/NH_4OH, 3:2); $[\alpha]_D^{20}$ +0.00 (*c* 0.212, H_2O); IR (neat) ν_{max} 3272, 1629, 1570, 1442, 1378, 1323, 1073, 1016, 666, 605 cm^{-1}. ^1H NMR (300 MHz, D_2O) δ 3.92 (bs, 1H), 3.54−3.38 (m, 5H), 1.88 (s, 3H); ^{13}C NMR (75 MHz, D_2O) δ 176.0 (s); 73.2 (d); 73.1 (d); 71.9 (d); 56.9 (d); 23.4 (q);[10d,32] HRMS (ESI): $[M + Na]^+$calcd for $C_8H_{15}NNaO_6$: 244.0791; found: 244.0787.

*(3R,4R,5R,6S)-6-(N-Benzyl-N-p-toluenesulfonyl)amino-3,4,5-tris-benzyloxy-1,7-octa-diene (**8**).* To a solution of methyltriphenylphosphonium bromide (2.05 g, 5.74 mmol) in dry THF (20 mL), *n*-butyllithium (3.41 mL of 1.6 M solution in hexane, 5.46 mmol) was added dropwise over a period of 15 min under nitrogen atmosphere at 0 °C. The reaction mixture was brought to 25 °C and stirred for 30 min. The resulting light yellow clear solution was cooled to −78 °C. Crude dialdehyde **9** (0.945 g, 1.37 mmol) in dry THF (10 mL) was added slowly over a period of 30 min at −78 °C. After the addition, the reaction mixture was allowed to warm to 25 °C on its own (approximately 4 h) and stirred for additional 11 h. Water (100 mL) was added and extracted with ethyl acetate (3 × 40 mL). The combined organic layer was concentrated under vacuum to get the crude diene as a viscous yellow liquid. Purification was done by column chromatography over silica gel using a mixture of hexane and ethyl acetate (9:1) as an eluent to get diene **8** (0.56 g, 60% from

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compound **10**) as a colorless viscous liquid. TLC: R_f 0.6 (hexane/ethyl acetate, 4:1); $[\alpha]_D^{20}$ +4.8 (*c* 0.58, CH_2Cl_2); IR (KBr) ν_{max} 3062, 3029, 2978, 2919, 2865, 1598, 1495, 1453, 1336, 1304, 1153, 1087, 1068, 1026, 928, 812, 732, 695, 668 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.1 Hz, 2H), 7.32−7.13 (m, 22H), 6.0−5.78 (m, 2H), 5.42−5.35 (m, 2H), 5.01 (d, *J* = 10.5 Hz, 1H), 4.79 (d, *J* = 17.1 Hz, 1H), 4.60−4.39 (m, 7H), 4.29 (d, *J* = 11.7 Hz, 1H), 4.21 (d, *J* = 11.1 Hz, 1H), 4.14 (t, *J* = 7.2 Hz, 1H), 4.06 (bm, 1H), 3.64−3.62 (m, 1H), 2.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.0 (s), 139.0 (s), 138.9 (s), 138.6 (s), 138.0 (s), 137.5 (s), 136.1 (d), 134.1 (d), 129.3 (d), 129.2 (d), 128.4 (d), 128.2 (d), 128.1 (d), 127.96 (d), 127.95 (d), 127.8 (d), 127.6 (d), 127.5 (d), 127.36 (d), 127.31 (d), 120.0 (t), 119.8 (t), 81.1 (2*d*), 80.9 (d), 74.6 (t), 73.9 (t), 70.2 (t), 62.5 (d), 51.3 (t), 21.5 (q); HRMS (ESI): $[M + Na]^+$ calcd for $C_{43}H_{45}NNaO_5S$: 710.2911; found: 710.2915.

*(3R,4R,5R,6S)-6-(N-Benzyl-N-p-toluenesulfonyl)amino-3,4,5-tris-benzyloxy-cyclohex-1-ene (**30**).* Diene **8** (0.7 g, 1.02 mmol) was dissolved in dry toluene (10 mL). Nitrogen gas was purged into the reaction mixture for 20 min. Grubb's II catalyst (0.0202 g, 2.33 mol %) was added and refluxed (115 °C bath temperature). After 24 h, another 0.0202 g, 2.33 mol % of the catalyst was added, and refluxing was continued. After another 24 h a third portion 0.0202 g, 2.33 mol % of the catalyst was added, and refluxing was continued for another 24 h. Even after 72 h of refluxing, the reaction did not go to completion (TLC), and it was stopped. The reaction mixture was cooled to room temperature, and the solvent was concentrated under vacuum. The resulting residue was directly loaded on to a silica gel column and eluted with a mixture of hexane and ethyl acetate (9:1) to get the protected conduramine F-4 **30** (0.47 g, 70%) as a pale yellow viscous liquid along with unreacted diene **8** (0.14 g, 20%). TLC: R_f 0.41 (hexane/ethyl acetate, 4:1); $[\alpha]_D^{30}$ −15.38 (*c* 0.39, CH_2Cl_2); IR (KBr) ν_{max} 3062, 3029, 2922, 2866, 1598, 1494, 1453, 1339, 1154, 1090, 1057, 1027, 911, 883, 814, 781, 729, 695, 660 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.8 Hz, 2H), 7.32−7.04 (m, 22H), 5.77−5.72 (m, 1H), 5.13 (d, *J* = 9.9 Hz, 1H), 4.67−4.51 (m, 7H), 4.04 (d, *J* = 15.6 Hz, 1H), 3.97−3.88 (m, 3H), 3.40 (dd, *J* = 9.6, 3.0 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.2 (s), 139.0 (s), 138.8 (s), 138.4 (s), 138.0 (2*s*), 131.0 (d), 129.7 (d), 129.0 (d), 128.6 (d), 128.4 (d), 128.1 (d),127.9 (d), 127.88 (d), 127.85 (d), 127.7 (d), 127.6 (d), 127.56 (d), 127.54 (d), 127.2 (d), 81.4 (d), 76.1 (d), 74.1 (t), 72.7 (t), 72.0 (t), 71.4 (d), 62.3 (d), 48.6 (t), 21.6 (q); HRMS (ESI): $[M + Na]^+$ calcd for $C_{41}H_{41}NNaO_5S$: 682.2598; found: 682.2598.

*(3R,4R,5R,6S)-6-(N-Benzyl)amino-3,4,5-tris-benzyloxy-cyclohex-1-ene (**31**).* Compound **30** (0.55 g, 0.833 mmol) was subjected to N-detosylation reaction as per the general procedure described earlier in DMF (8 mL) and methanol (2 mL), in the presence of $Na_2HPO_4 \cdot 2H_2O$ (0.742 g, 4.17 mmol) and 3% Na-Hg (12.78 g, 16.67 mmol) for 3.5 h. Product was purified by column chromatography using a mixture of hexane and ethyl acetate (4:1) to get **31** (0.31 g, 74%) as pale yellow viscous liquid. TLC: R_f 0.46 (hexane/ethyl acetate, 3:2); $[\alpha]_D^{28}$ +9.1 (*c* 0.37, $CHCl_3$), $[\alpha]_D^{25}$ −6.7 (*c* 0.296, CH_2Cl_2); IR (KBr) ν_{max} 3060, 3028, 2918, 2858, 1603, 1494, 1452, 1364, 1092, 1072, 1026, 731, 695 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.41−7.20 (m, 20H), 5.89−5.79 (m, 2H), 4.94 (d, *J* = 11.7 Hz, 1H), 4.78−4.68 (m, 5H), 4.15 (t, *J* = 3.6 Hz, 1H), 4.08((dd, *J* = 8.7, 6.6 Hz, 1H), 3.77−3.67 (m, 3H), 3.32 (d, *J* = 6.3 Hz, 1H), 2.11 (bs, 1 H exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.6 (s), 138.98 (s), 138.93 (s), 138.7 (s), 131.8 (d), 128.5 (d), 128.47 (d), 128.44 (d), 128.1 (d), 127.9 (d), 127.7 (d), 127.69 (d), 127.66 (d), 126.9 (d), 125.8 (d), 79.8 (d), 77.5 (d), 74.3 (t), 72.7 (t), 72.1 (d), 71.7 (t), 59.6 (d), 50.2 (t); HRMS (ESI): $[M + H]^+$ calcd for $C_{34}H_{36}NO_3$: 506.2690; found: 506.2675.

*(3R,4R,5R,6S)-6-(N-Acetyl-N-benzyl)amino-3,4,5-trihydroxy-cyclohex-1-ene (**32**).* Compound **31** (0.55 g, 1.09 mmol) was dissolved in dry dichloromethane (5 mL). Acetic anhydride (0.154 mL, 1.63 mmol) was added to it, followed by triethyl amine (0.303 mL, 2.18 mmol) and DMAP (0.0266 g, 0.217 mmol). The reaction mixture was stirred at 35 °C for 5 h. Dichloromethane (30 mL) was added and washed with water (3 × 10 mL). The organic layer was concentrated under vacuum. Purification of the product by column chromatography over silica gel using a mixture of hexane and ethyl acetate (4:2) as an eluent to delivered the *N*-acetyl derivative **32** (0.48 g, 80%) as a colorless viscous liquid. TLC: R_f 0.38 (hexane/ethyl acetate, 7:3); $[\alpha]_D^{29}$ +54.62 (*c* 1.34, $CHCl_3$); IR (KBr) ν_{max} 3061, 3029, 2923, 2865, 1642, 1494, 1450, 1409, 1362, 1097, 1066, 1026, 732, 696 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) (mixture of rotamers) δ 7.41−7.08 (m, 20H), 5.95−5.85 (m, 1H), 5.57−5.54 (m, 1H), 4.99−4.34 (m, 8H), 4.21−4.04 (m, 3H), 3.78−3.58 (m, 1H), 2.32 and 1.95 (s, 3H) [methyl signals of acetyl group due to rotamers]; ^{13}C NMR (75 MHz, $CDCl_3$) (as a mixture of rotamers) δ 172.2 (s), 172.0 (s), 139.4 (s), 139.1 (s), 138.7 (s), 138.4 (s), 138.3 (s), 131.2 (d), 129.4 (d), 128.7 (d), 128.4 (d), 128.3 (d), 128.1 (d), 127.9 (d), 127.8 (d), 127.7 (d), 127.4 (d), 127.0 (d), 126.9 (d), 125.7 (d), 81.6 (d), 79.1 (d), 76.7 (d), 75.9 (d), 75.0 (t), 73.3 (t), 72.6 (t), 72.5 (t), 72.1 (t), 71.8 (d), 71.6 (t), 71.2 (d), 62.8 (d), 56.5 (d), 49.0 (t), 45.8 (t), 22.5 (q), 22.3 (q); HRMS (ESI): $[M + Na]^+$ calcd for $C_{36}H_{37}NNaO_4$: 570.2614; found: 570.2609.

*(3R,4R,5R,6S)-6-Amino-3,4,5-trihydroxy-cyclohex-1-ene (−)-(Conduramine F-4) (**5**).* In a 100 mL three-necked round bottomed flask, cooled to −70 °C, ammonia gas was condensed (about 20 mL). Finely divided sodium pieces were added to it until the color of the solution turned dark blue, and compound **32** (0.25 g, 0.456 mmol) was added. When the blue color of the solution disappeared, a few more fine pieces of sodium were added, and the blue color resurfaced. This procedure was repeated until the blue color of the solution persisted (without fading) for 5 h, which required a total 0.315 g (13.69 mmol) of sodium. The reaction mixture was then quenched at −70 °C by slow addition of benzene (5 mL), followed by a dropwise addition of water (5 mL) at which time the blue color of the reaction mixture completely disappeared. Water (4 mL) was then added to the reaction mixture at −70 °C, and it was allowed to warm to room temperature and stirred at same temperature until the excess ammonia was evaporated. The benzene layer was then separated, and the aqueous layer was directly loaded onto the silica gel column and eluted with a mixture of acetonitrile and ammonium hydroxide (7:3) to get (−)-conduramine F-4 **5** (0.034 g, 52%) as a colorless viscous liquid. TLC: R_f 0.37 (CH_3CN/NH_4OH, 4:1); $[\alpha]_D^{26}$ −50.0 (*c* 0.198, H_2O); IR (neat) ν_{max} 3239, 2931, 1626, 1525, 1396, 1280, 1061, 911, 863, 797, 607 cm^{-1}. ^1H NMR (300 MHz, MeOD) δ 6.07 (dd, *J* = 9.9, 4.5 Hz, 1H), 5.82 (d, *J* = 9.9 Hz, 1H), 4.31 (t, *J* = 3.9 Hz, 1H), 3.87 (t, *J* = 8.7 Hz, 1H), 3.72−3.64 (m, 2H); ^1H NMR (300 MHz, D_2O) δ 6.02−5.98 (m, 1H), 5.72 (d, *J* = 9.9 Hz, 1H), 4.27 (t, *J* = 3.9 Hz, 1H), 3.78−3.60 (m, 3H);[18a] ^{13}C NMR (75 MHz, MeOD) δ 132.4 (d), 125.9 (d), 72.1 (d), 69.8 (d), 67.2 (d), 55.0 (d); HRMS (ESI): $[M + H]^+$ calcd for $C_6H_{12}NO_3$: 146.0812; found: 146.0811.

*(3R,4R,5R,6S)-6-(N-Benzyl)amino-3,4,5-trihydroxy-cyclohex-1-ene Hydrochloride (**33**).* Compound **31** (0.27 g, 0.534 mmol) was dissolved in dry dichloromethane (2 mL) at 0 °C. Boron trichloride (3.2 mL of 1 M solution in CH_2Cl_2, 3.2 mmol) was added dropwise and stirred at 0 °C for 1 h, after which it was quenched by the addition of MeOH (3 mL). The solvent was concentrated under vacuum. The resulting residue was directly loaded on to a silica gel column, and the product was purified by eluting using a mixture of dichloromethane and methanol (9:1) to get product **33** (0.1 g, 69%) as a pale yellow viscous liquid. The ^1H NMR spectral data of the compound were found to be in agreement with that of the literature values reported for its hydrochloride enantiomer. TLC: R_f 0.15 (CH_2Cl_2/methanol, 9:1); $[\alpha]_D^{19}$ +12.87 (*c* 0.202, MeOH); IR (neat) ν_{max} 3416, 3279, 3095, 2927, 2786, 1629, 1574, 1454, 1374, 1243, 1216, 1099, 1075, 991, 750, 700, 604 cm^{-1}. ^1H NMR (300 MHz, MeOD) δ 7.58−7.55 (m, 2H), 7.51−7.47 (m, 3H), 6.19−6.14 (m, 1H), 5.93 (dd, *J* = 10.2, 1.8 Hz, 1H), 4.37 (s, 2H), 4.29 (t, *J* = 4.2 Hz, 1H), 4.11 (t, *J* = 8.7 Hz, 1H), 3.74 (d, *J* = 7.5 Hz, 1H), 3.63 (dd, *J* = 9.0, 4.2 Hz, 1H);[17b] ^{13}C NMR (75 MHz, MeOD) δ 135.0 (d), 132.5 (s), 131.1 (d), 130.6 (d), 130.3 (d), 123.3 (d), 72.5 (d), 68.2 (d), 67.1 (d), 60.8 (d), 49.7 (t); HRMS (ESI): $[M + H]^+$ calcd for $C_{13}H_{18}NO_3$: 236.1281; found: 236.1286.

*(3R,4R,5R,6S)-6-(N-Benzyl)amino-3,4,5-trihydroxy-cyclohex-1-ene (**34**).* Compound **33** (0.03 g, 0.11 mmol) was placed in a 25 mL round-bottomed flask, and it was neutralized by the addition of saturated ammonium hydroxide solution (~1 mL) at room temper-

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J. Org. Chem. 2016, 81, 11574−11586

ature in 10 min. The resulting aqueous solution was loaded on to a silica gel column and purified using a mixture of dichloromethane and methanol (9:1) to get the free amine **34** (0.02 g, 77%) as a pale yellow viscous liquid. TLC: R_f 0.15 (CH_2Cl_2/methanol, 9:1); $[\alpha]_D^{31}$ +14 (*c* 0.55, MeOH); IR (neat) ν_{max} 3292, 3029, 2921, 2852, 1735, 1584, 1495, 1452, 1405, 1070, 745, 697 cm^{-1}. ^1H NMR (300 MHz, D_2O) δ 7.27−7.17 (m, 5H), 5.80 (ddd, *J* = 9.6, 4.5, 1.8 Hz, 1H), 5.69(dd, *J* = 10.2, 1.2 Hz, 1H), 4.09 (t, *J* = 4.5 Hz, 1H), 3.88 (d, *J* = 13.2 Hz, 1H), 3.74 (d, *J* = 13.2 Hz, 1H), 3.63 (t, *J* = 9.6 Hz, 1H), 3.39 (dd, *J* = 10.2, 4.2 Hz, 1H), 3.23 (d, *J* = 8.4 Hz, 1H); ^1H NMR (300 MHz, MeOD) δ 7.46−7.31 (m, 5H), 5.98 (ddd, *J* = 10.2, 4.5, 2.1 Hz, 1H), 5.88 (dd, *J* = 9.9, 1.8 Hz, 1H), 4.23 (t, *J* = 4.2 Hz, 1H), 4.09 (d, *J* = 12.9 Hz, 1H), 3.98 (d, *J* = 12.9 Hz, 1H), 3.89 (dd, *J* = 9.6, 8.1 Hz, 1H), 3.55 (dd, *J* = 9.6, 4.2 Hz, 1H), 3.33−3.31 (m, 1H); ^{13}C NMR (75 MHz, D_2O) δ 135.93 (s), 129.15 (2*d*), 129.05 (2*d*), 128.36 (d), 127.45 (d), 71.41 (d), 68.59 (d), 66.26 (d), 59.59 (d), 48.91 (t); ^{13}C NMR (75 MHz, MeOD) δ 137.7 (s), 131.1 (d), 130.1 (d), 129.7 (d), 129.0 (d), 128.2 (d), 73.1 (d), 69.8 (d), 67.6 (d), 61.2 (d), 50.5 (t); HRMS (ESI): $[M + H]^+$ calcd for $C_{13}H_{18}NO_3$: 236.1281, found 236.1276.

*3,4,5-Tri-O-benzyl-2-deoxy-2-(N-benzyl-N-p-toluenesulfonyl)-amino-1,6-Di-O-(methanesulfonyl)-D-glucitol (**35**).* To diol **10** (1 g, 1.44 mmol) dissolved in dry dichloromethane (20 mL), triethylamine (1.02 mL, 4.31 mmol), DMAP (35.13 mg, 20 mol %), and mesyl chloride (278 μL, 3.59 mmol) were added at 0 °C. After 30 min, the reaction mixture was directly concentrated under vacuum. The crude residue was then subjected to column chromatography over silica gel and eluted using a mixture of hexane and ethyl acetate (3:2) to obtain **35** (1.15 g, 94%) as a colorless viscous liquid. TLC: R_f 0.3 (hexane/ethyl acetate, 3:2); $[\alpha]_D^{30}$ +25 (*c* 1.27, $CHCl_3$); IR (neat) ν_{max} 3062, 3030, 2934, 2872, 1598, 1496, 1454, 1357, 1176, 960, 817, 738, 698, 657 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.8 Hz, 2H), 7.27−7.10 (m, 22H), 4.64−4.21 (m, 10H), 4.14−4.09 (m, 2H), 3.29 (bm, 2H), 3.76 (bm, 2H), 2.79 (s, 3H), 2.52 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.9 (s), 137.89 (s), 137.82 (s), 137.5 (s), 137.2 (s), 136.9 (s), 129.8 (d), 129.1 (d), 128.7 (d), 128.56 (d), 128.53 (d), 128.4 (d), 128.1 (d), 127.96 (d), 127.91 (d), 127.8 (d), 127.7 (d), 78.3 (2*d*), 78.0 (d), 74.8 (t), 74.1 (t), 73.0 (t), 69.0 (t), 65.8 (t), 58.7 (d), 50.0 (t), 37.4 (q), 36.9 (q), 21.6 (q); HRMS (ESI): $[M + Na]^+$ calcd for $C_{43}H_{49}NNaO_{11}S_3$: 874.2360; found: 874.2371.

*(3R,4R,5R,6S)-3,4,5-Tris-benzyloxy-6-(N-benzyl-N-p-toluene-sulfonyl)amino-1-N-benzylazepane (**36**).* Compound **35** (1.2 g, 1.41 mmol) was dissolved in benzylamine (8 mL) and stirred at 100 °C for 24 h. It was then cooled to room temperature, diluted with ethyl acetate (150 mL), and washed with water (4 × 50 mL) and 10% HCl (3 × 50 mL). The organic layer was was concentrated under vacuum, and the product was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (3:2) to get **36** (0.9 g, 83%) as a viscous colorless liquid. TLC: R_f 0.4 (hexane/ethyl acetate, 4:1); $[\alpha]_D^{30}$ −21.78 (*c* 0.56, $CHCl_3$); IR (KBr) ν_{max} 3062, 3029, 2922, 2854, 1599, 1494, 1453, 1338, 1206, 1156, 1091, 1027, 929, 814, 737, 698, 664, 601 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.8 Hz, 2H), 7.44−7.7.19 (m, 27H), 4.73 (d, *J* = 12.0 Hz, 1H), 4.63−4.48 (m, 4H), 4.44−4.20 (m, 4H), 3.97 (bm, 2H), 3.89 (bm, 1H), 3.60 (d, *J* = 13.5 Hz, 1H), 3.53 (d, *J* = 13.5 Hz, 1H), 3.21 (t, *J* = 10.5 Hz, 1H), 2.92 (t, *J* = 10.8 Hz, 1H), 2.80 (d, *J* = 10.2 Hz, 1H), 2.54 (d, *J* = 12.6 Hz, 1H), 2.40 (s, 3H); ^1H NMR (300 MHz, MeOD) δ 7.64 (d, *J* = 8.1 Hz, 2H), 7.31−7.13 (m, 27H), 4.57 (d, *J* = 11.7 Hz, 1H), 4.48 (d, *J* = 11.7 Hz, 1H), 4.41−4.25 (m, 4H), 4.19 (d, *J* = 11.4 Hz, 1H), 4.0−3.97 (m, 2H), 3.85 (bm, 2H), 3.71 (dd, *J* = 9.0, 3.3 Hz, 1H), 3.43 (d, *J* = 13.5 Hz, 2H), 2.95 (dd, *J* = 13.2, 10.2 Hz, 1H), 2.76 (dd, *J* = 12.0, 9.6 Hz 1H), 2.62 (dd, *J* = 12.0, 2.7 Hz, 1H), 2.39 (d, *J* = 13.2 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.8 (s), 138.8 (s), 138.4 (s), 138.2 (s), 137.9 (s), 129.4 (d), 128.6 (d), 128.4 (d), 128.3 (d), 128.25 (d), 128.21 (d), 127.7 (d), 127.5 (d), 127.47 (d), 127.40 (d), 127.0 (d), 79.6 (d), 79.2 (d), 76.9 (d), 72.7 (t), 72.0 (t), 71.4 (t), 64.1 (d), 61.5 (t), 55.5 (t), 52.7 (t), 49.6 (t), 21.4 (q); ^{13}C NMR (75 MHz, MeOD) δ 144.8 (s), 139.76 (s), 139.71 (s), 139.6 (s), 139.5 (s), 139.4 (s), 130.7 (d), 130.0 (d), 129.6 (d), 129.3 (d), 129.2 (d), 129.0 (d), 128.8 (d), 128.7 (d), 128.6 (d), 128.5 (d), 128.2 (d), 80.6 (d), 80.1 (d), 77.5 (d), 73.8 (t), 72.9 (t), 72.4 (t), 65.1 (d), 62.3 (t), 56.6 (t), 53.8 (t), 50.7 (t), 21.4 (q); HRMS (ESI): $[M + H]^+$ calcd for $C_{48}H_{51}N_2O_5S$: 767.3513; found: 767.3536.

*(3R,4R,5R,6S)-3,4,5-Tris-benzyloxy-6-(N-benzyl-N-p-toluene-sulfonyl)amino-1-N-butylazepane (**37**).* Compound **35** (0.8 g, 0.94 mmol) was dissolved in butylamine (8 mL), and the reaction mixture was stirred at 100 °C for 24 h. It was then cooled to room temperature, diluted with ethyl acetate (150 mL), and washed with water (4 × 50 mL) and 10% HCl (3 × 50 mL). The organic layer was concentrated under vacuum, and the product was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (7:1) to get **37** (0.55 g, 80%) as a viscous colorless liquid. TLC: R_f 0.5 (hexane/ethyl acetate, 4:1); $[\alpha]_D^{31}$ −16.32 (*c* 0.24, $CHCl_3$); IR (KBr) ν_{max} 3062, 3030, 2954, 2929, 2865, 1599, 1494, 1453, 1336, 1156, 1089, 1068, 1027, 908, 811, 729, 697, 661 cm^{-1}. ^1H NMR (300 MHz, MeOD) δ 7.73 (d, *J* = 8.1 Hz, 2H), 7.30−7.16 (m, 20H), 7.01−7.07 (m, 2H), 4.61 (d, *J* = 11.7 Hz, 1H), 4.52−4.41 (m, 4H), 4.34 (d, *J* = 15.9 Hz, 1H), 4.17−4.13 (d, *J* = 11.7 Hz, 1H), 3.93−3.85 (m, 3H), 3.81−3.80 (m, 1H), 3.69 (dd, *J* = 9.0, 3.3 Hz 1H), 2.96−2.81 (m, 2H), 2.68 (dd, *J* = 12.3, 2.7 Hz 1H), 2.36−2.33 (m, 4H), 2.24 (bm, 2H), 1.30−1.22 (m, 4H), 0.89 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, MeOD) δ 144.7 (s), 139.7 (s), 139.6 (s), 130.8 (d), 129.6 (d), 129.4 (d), 129.3 (d), 129.2 (d), 129.1 (d), 128.9 (d), 128.7 (d), 128.69 (d), 128.63 (d), 128.56 (d), 128.50 (d), 80.6 (d), 79.8 (d), 77.1 (d), 73.9 (t), 72.8 (t), 72.5 (t), 64.4 (d), 57.2 (t), 56.3 (t), 54.4 (t), 50.6 (t), 30.1 (t), 21.54 (t), 21.51 (q), 14.3 (q); HRMS (ESI): $[M + H]^+$ calcd for $C_{45}H_{53}N_2O_5S$: 733.3670; found: 733.3657.

*(3R,4R,5R,6S)-3,4,5-Tris-benzyloxy-6-(N-benzyl-N-p-toluene-sulfonyl)amino-1-N-(2-hydroxyethyl)azepane (**38**).* Compound **35** (0.3 g, 0.35 mmol) was dissolved in ethanolamine (4 mL), and the reaction mixture was stirred at 80 °C for 24 h. It was then cooled to room temperature, diluted with ethyl acetate (150 mL), and washed with water (4 × 50 mL) and 10% HCl (3 × 50 mL). The organic layer was concentrated under vacuum, and product was purified by column chromatography over silica gel using a mixture of hexane and ethyl acetate (3:2) to get **38** (0.19 g, 75%) as a viscous colorless liquid. TLC: R_f 0.27 (hexane/ethyl acetate, 3:2); $[\alpha]_D^{31}$ −17.21 (*c* 0.6, $CHCl_3$); IR (KBr) ν_{max} 3543, 3086, 3062, 3029, 2925, 2868, 1598, 1494, 1453, 1334, 1207, 1154, 1089, 1065, 1026, 927, 884, 812, 738, 696, 663 cm^{-1}. ^1H NMR (300 MHz, MeOD) δ 7.71 (d, *J* = 8.1 Hz, 2H), 7.29−7.15 (m, 20H), 7.07−7.04 (m, 2H), 4.60 (d, *J* = 11.7 Hz, 1H), 4.51−4.29 (m, 5H), 4.14 (d, *J* = 11.4 Hz, 1H), 3.96−3.87 (m, 3H), 3.80−3.79 (m, 1H), 3.71 (dd, *J* = 9.0, 3.3 Hz, 1H), 3.45 (t, *J* = 5.7 Hz, 2H); 3.04−2.90 (m, 2H), 2.76 (dd, *J* = 12.3, 2.7 Hz, 1H), 2.54−2.40 (m, 3H), 2.34 (s, 3H); ^{13}C NMR (75 MHz, MeOD) δ 144.7 (s), 139.7 (s), 139.6 (2*s*), 139.54 (s), 139.51 (s), 130.7 (d), 129.5 (d), 129.4 (d), 129.3 (d), 129.2 (d), 129.1 (d), 128.8 (d), 128.6 (d), 128.58 (d), 128.51 (d), 80.6 (d), 79.9 (d), 77.3 (d), 73.9 (t), 72.8 (t), 72.5 (t), 64.5 (d), 60.3 (t), 58.9 (t), 56.8 (t), 54.7 (t), 50.3 (t), 21.5 (q); HRMS (ESI): $[M + H]^+$ calcd for $C_{43}H_{49}N_2O_6S$: 721.3306; found: 721.3306.

*(3R,4R,5R,6S)-3,4,5-Tris-benzyloxy-6-(N-benzyl)amino-1-N-benzy-lazepane (**39**).* Compound **36** (1.0 g, 1.3 mmol) was subjected to N-detosylation reaction as per the general procedure described earlier in DMF (10 mL) and methanol (5 mL), in the presence of $Na_2HPO_4 \cdot 2H_2O$ (1.16 g, 6.52 mmol) and 3% Na-Hg (19.98 g, 26.08 mmol) for 3.5 h (via TLC). The product was purified by column chromatography using a mixture of hexane and ethyl acetate (3:2) to get **39** (0.64 g, 80%) as a colorless viscous liquid. TLC: R_f 0.4 (hexane/ethyl acetate, 3:2); $[\alpha]_D^{30}$ +4.03 (*c* 0.52, $CHCl_3$); IR (KBr) ν_{max} 3327, 3061, 3027, 2864, 1603, 1494, 1452, 1353, 1207, 1089, 1067, 1026, 908, 731, 694 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.30−7.21 (m, 23H), 7.12 (d, *J* = 6.6 Hz, 2H), 4.72−4.64 (m, 2H), 4.61−4.53 (m, 3H), 4.43 (d, *J* = 11.7 Hz, 1H), 3.94−3.89 (m, 2H), 3.76−3.72 (m, 2H), 3.62−3.43 (m, 3H), 3.02 (dd, *J* = 12.0, 7.8 Hz, 1H), 2.84−2.75 (m, 2H), 2.70−2.63 (m, 2 H), 1.86 (bm, 1H exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.6 (s), 139.4 (s), 138.9 (s), 138.6 (s), 138.5 (s), 129.0 (d), 128.4 (d), 128.3 (d), 128.0 (d), 127.9 (d), 127.7 (d), 127.6 (d), 127.5 (d), 127.1 (d), 126.7 (d), 83.2 (d), 82.5 (d), 77.5 (d), 73.0 (t), 72.6 (t), 71.6 (t), 63.1 (t), 61.2 (d), 55.3 (t), 52.9 (t), 51.1 (t); HRMS (ESI): $[M + H]^+$ calcd for $C_{41}H_{45}N_2O_3$: 613.3424; found: 613.3394.

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*(3R,4R,5R,6S)-3,4,5-Tris-benzyloxy-6-(N-benzyl)amino-1-N-butylazepane (**40**).* Compound **37** (0.5 g, 0.68 mmol) was subjected to N-detosylation reaction as per the general procedure described earlier in DMF (10 mL) and methanol (3 mL), in the presence of $Na_2HPO_4 \cdot 2H_2O$ (0.60 g, 3.41 mmol) and 3% Na-Hg (10.46 g, 13.64 mmol) for 5 h. The product was purified by column chromatography using a mixture of hexane and ethyl acetate (7:3) to get **40** (0.32 g, 81%) as colorless viscous liquid. TLC: R_f 0.34 (hexane/ethyl acetate, 7:3); $[\alpha]_D^{31}$ +6.19 (*c* 0.59, $CHCl_3$); IR (KBr) ν_{max} 3330, 3061, 3028, 2952, 2927, 2860, 1494, 1453, 1360, 1205, 1088, 1067, 1027, 907, 731, 695 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.33−7.20 (m, 20H), 4.74−4.56 (m, 5H), 4.41 (d, *J* = 11.7 Hz, 1H), 3.93−3.65 (m, 5H), 3.00 (dd, *J* = 12.0 Hz, 1H), 2.83−2.64 (m, 4H), 2.50 (t, *J* = 7.2 Hz, 2H), 1.90 (bm, 1H exchangeable with D_2O), 1.43 (quintet, *J* = 7.2 Hz, 2H), 1.35−1.25 (m, 2H), 0.88 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.6 (s), 138.9 (s), 138.7 (s), 138.5 (s), 128.5 (d), 128.39 (d), 128.35 (d), 128.1 (d), 128.0 (d), 127.7 (d), 127.6 (d), 127.53 (d), 127.50 (d), 126.8 (d), 82.9 (d), 82.1 (d), 77.5 (d), 72.9 (t), 72.5 (t), 71.7 (t), 61.4 (d), 58.5 (t), 55.1 (t), 53.4 (t), 51.5 (t), 29.7 (t), 20.6 (t), 14.1 (q); HRMS (ESI): $[M + H]^+$ calcd for $C_{38}H_{47}N_2O_3$: 579.3581; found: 579.3576.

*(3R,4R,5R,6S)-3,4,5-Tris-benzyloxy-6-(N-benzyl)amino-1-N-(2-hydroxyethyl)azepane (**41**).* Compound **38** (0.5 g, 0.69 mmol) was subjected to N-detosylation reaction as per the general procedure described earlier in DMF (7 mL) and methanol (2 mL), in the presence of $Na_2HPO_4 \cdot 2H_2O$ (0.62 g, 3.47 mmol) and 3% Na-Hg (10.63 g, 13.87 mmol) for 5 h. The product was purified by column chromatography using a mixture of hexane and ethyl acetate (9:1) to get **41** (0.3 g, 76%) as a colorless viscous liquid. TLC: R_f 0.34 (chloroform/methanol, 9:1); $[\alpha]_D^{31}$ −18.61 (*c* 0.65, $CHCl_3$); IR (KBr) ν_{max} 3390, 3312, 3085, 3061, 3028, 2858, 1603, 1497, 1453, 1359, 1206, 1064, 1026, 732, 695, 603 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.30−7.21 (m, 20H), 4.73 (d, *J* = 12.0 Hz, 1H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.57−4.52 (m, 3H), 4.46 (d, *J* = 11.7 Hz, 1H), 3.93−3.89 (m, 2H), 3.83−3.80 (m, 1H), 3.77−3.67 (m, 2H), 3.60 (t, *J* = 5.1 Hz, 2H); 3.08−3.02 (dd, *J* = 12.0, 7.8 Hz, 1H), 2.86 (dd, *J* = 13.5, 6.0 Hz, 2H, 1H exchangeable with D_2O), 2.76−2.65 (m, 6H, 1H exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.0 (s), 138.7 (s), 138.4 (s), 138.3 (s), 128.5 (d), 128.45 (d), 128.43 (d), 128.2 (d), 127.9 (d), 127.79 (d), 127.75 (d), 127.68 (d), 127.64 (d), 126.9 (d), 83.1 (d), 80.3 (d), 77.1 (d), 73.5 (t), 72.3 (t), 71.8 (t), 60.1 (t), 59.9 (d), 59.5 (t), 56.5 (t), 53.4 (t), 51.2 (t); HRMS (ESI): $[M + H]^+$ calcd for $C_{36}H_{43}N_2O_4$: 567.3217; found: 567.3217.

*(3R,4R,5R,6S)-6-Amino-3,4,5-trihydroxyazepane hydrochloride (**42**).* To compound **39** (0.35 g, 0.57 mmol) dissolved in ethanol (5 mL), 10% palladium on charcoal (0.105 g, 30% w/w) and HCl (0.23 mL, 2.86 mmol) were added. Hydrogen gas was bubbled into the reaction mixture continuously while stirring at room temperature for 50 h. The reaction mixture was filtered through a Celite bed, and the filtrate was concentrated to get **42** (0.082 g, 72%) as a pale yellow viscous liquid. The product was found to be pure enough as revealed from its NMR spectrum. TLC: R_f 0.11 (acetonitrile/ammonium hydroxide, 7:3); $[\alpha]_D^{31}$ −23.88 (*c* 0.24, H_2O); IR (neat) ν_{max} 3377, 3252, 3003, 2770, 1598, 1566, 1515, 1457, 1353, 1224, 1146, 1102, 1054, 995, 923, 811, 835, 720 cm^{-1}. ^1H NMR (300 MHz, D_2O) δ 4.27−4.29 (m, 1H), 3.82 (t, *J* = 9.0 Hz, 1H), 3.65−3.45 (m, 5H), 3.28 (d, *J* = 14.4 Hz, 1H); ^{13}C NMR (75 MHz, D_2O) δ 75.1 (d), 71.0 (d), 66.5 (d), 48.6 (d), 44.7 (t), 42.6 (t); HRMS (ESI): $[M + H]^+$ calcd for $C_6H_{15}N_2O_3$: 163.1077; found: 163.1085.

*(3R,4R,5R,6S)-6-Amino-3,4,5-trihydroxy-1-N-butylazepane (**43**).* To compound **40** (0.25 g, 0.43 mmol) dissolved in ethanol (5 mL), 10% palladium on charcoal (0.05 g, 20% w/w) was added. Hydrogen gas was bubbled into the reaction mixture continuously while stirring at room temperature for 50 h. The reaction mixture was filtered through Celite bed, and the filtrate was concentrated under vacuum. Product was purified by column chromatography over silica gel using a mixture of acetonitrile and aqueous ammonium hydroxide solution (10:2) to get **43** (0.089 g, 94%) as a colorless viscous liquid. TLC: R_f 0.28 (acetonitrile/ammonium hydroxide, 4:1); $[\alpha]_D^{30}$ −7.14 (*c* 0.35, MeOH); IR (neat) ν_{max} 3402, 3206, 3135, 2962, 2929, 1464, 1095, 1049, 1034, 814, 744, 659 cm^{-1}. ^1H NMR (300 MHz, D_2O) δ 4.08−4.07 (m, 1H), 3.75−3.65 (m, 2H), 3.28 (td, *J* = 7.2, 2.4 Hz, 1H), 3.10−2.94 (m, 3H), 2.86 (dd, *J* = 13.8, 2.4 Hz, 1H), 2.71 (t, *J* = 8.1 Hz, 2H), 1.46 (quintet, *J* = 7.5 Hz, 2H), 1.22 (sextet, *J* = 7.5 Hz, 2H), 0.81 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, D_2O) δ 75.4 (d), 72.5 (d), 69.3 (d), 58.3 (t), 55.7 (t), 52.4 (t), 52.0 (d), 27.1 (t), 19.7 (t), 13.1 (q); HRMS (ESI): $[M + H]^+$ calcd for $C_{10}H_{23}N_2O_3$: 219.1703; found: 219.1697.

*(3R,4R,5R,6S)-6-Amino-3,4,5-trihydroxy-1-N-(2-hydroxyethyl)-azepane (**44**).* To compound **41** (0.3 g, 0.53 mmol) dissolved in ethanol (10 mL), 10% palladium on charcoal (0.06 g, 20% w/w) was added. Hydrogen gas was bubbled slowly into the reaction mixture continuously while stirring at room temperature for 48 h. The reaction mixture was filtered through Celite bed, and the filtrate was concentrated under vacuum. Product was purified by column chromatography over silica gel using a mixture of acetonitrile and aqueous ammonium hydroxide solution (10:2) to get **44** (0.09 g, 82%) as a colorless viscous liquid. TLC: R_f 0.4 (acetonitrile/ammonium hydroxide, 4:1); $[\alpha]_D^{30}$ −5.66 (*c* 0.406, MeOH); IR (neat) ν_{max} 3344, 2888, 1463, 1036, 665 cm^{-1}. ^1H NMR (300 MHz, D_2O) δ 3.97 (bm, 1H), 3.72−3.51 (m, 4H), 3.28 (m, 1H), 2.80−2.74 (m, 2H), 2.69−2.61 (m, 4H); ^{13}C NMR (75 MHz, D_2O) δ 75.5 (t), 75.0 (t), 70.0 (t), 59.3 (d), 58.6 (d), 57.2 (d), 56.3 (d), 53.3 (t); HRMS (ESI): $[M + Na]^+$ calcd for $C_8H_{18}N_2NaO_4$: 229.1158; found: 229.1163.

*(3R,4R,5R,6S)-6-(N-Acetyl)amino-3,4,5-trihydroxy-1-N-acetylazepane (**45**).* Polyhydroxyaminoazepane **42** (0.015 g, 0.075 mmol) was dissolved in water (0.5 mL). Triethyl amine (31.5 μL, 0.227 mmol) in 0.2 mL of MeOH and acetic anhydride (0.017 g, 0.166 mmol) in 0.2 mL of MeOH were added. After 30 min, the reaction mixture was directly loaded on to a silica gel column, and the product was eluted with a mixture of acetonitrile and aqueous ammonium hydroxide solution (6:1) to get **45** (0.0162 g, 87%) as a colorless viscous liquid. TLC: R_f 0.44 (acetonitrile/ammonium hydroxide, 4:1); $[\alpha]_D^{30}$ −19.28 (*c* 0.14, MeOH); IR (neat) ν_{max} 3415, 2924, 1636, 1542, 1430, 1381, 1262, 1096, 1038, 858, 795, 669, 611 cm^{-1}. ^1H NMR (300 MHz, D_2O) (mixture of rotamers) δ 4.25−4.22 (m, 1H), 3.93−3.85 (m, 2H), 3.83−3.78 (m, 1H), 3.73−3.63 (m, 2H), 3.58−3.45 (m, 1H), 3.38−3.31 (m, 1H), 2.15, 2.12 (s, 3H, two signals for rotamers), 1.99, 1.97 (s, 3H, two signals for rotamers); ^{13}C NMR (75 MHz, D_2O) (mixture of rotamers) δ 174.7 (s), 174.5 (s), 173.9 (s), 173.6 (s), 73.9 (d),73.5 (d), 71.4 (2*d*), 69.6 (d), 69.3 (d), 53.4 (d), 52.7 (d), 52.2 (t), 48.4 (t), 48.3 (t), 46.4 (t), 22.1 (q), 22.0 (q), 20.8 (q), 20.3 (q); HRMS (ESI): $[M + Na]^+$ calcd for $C_{10}H_{18}N_2NaO_5$: 269.1107; found: 269.1100.

*(3R,4R,5R,6S)-6-(N-Acetyl)amino-3,4,5-trihydroxy-1-N-butylazepane (**46**).* Polyhydroxyaminoazepane **43** (0.04 g, 0.18 mmol) was dissolved in water (0.5 mL). Triethyl amine (0.0371 g, 0.36 mmol) in 0.2 mL of MeOH and acetic anhydride (0.0281 g, 0.275 mmol) in 0.2 mL of MeOH were added. After 30 min, the reaction mixture was directly loaded on to a silica gel column, and the product was eluted with a mixture of acetonitrile and aqueous ammonium hydroxide solution (6:1) to get **46** (0.04 g, 84%) as a colorless viscous liquid. TLC: R_f 0.4 (acetonitrile/ammonium hydroxide, 4:1); $[\alpha]_D^{28}$ +25 (*c* 0.16, MeOH); IR (neat) ν_{max} 3280, 3084, 2956, 2931, 2871, 1639, 1544, 1455, 1373, 1306, 1073, 1038 cm^{-1}. ^1H NMR (300 MHz, D_2O) δ 4.21 (d, *J* = 5.4 Hz, 1H), 3.92 (t, *J* = 8.1 Hz, 1H), 3.77 (t, *J* = 8.4 Hz, 1H), 3.67 (m, 1H), 3.49−3.37 (m, 2H), 3.27−3.08 (m, 4H), 1.95 (s, 3H), 1.59 (quintet, *J* = 7.2 Hz, 2H), 1.28 (t, *J* = 7.2 Hz, 2H), 0.83 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, D_2O) δ 174.0 (s), 75.1 (d), 72.0 (d), 67.1 (d), 58.3 (t), 54.3 (t), 53.5 (t), 49.2 (d), 25.8 (t), 21.8 (q), 19.2 (t), 12.8 (q); HRMS (ESI): $[M + H]^+$ calcd for $C_{12}H_{25}N_2O_4$: 261.1808; found: 261.1800.

*(3R,4R,5R,6S)-6-(N-Acetyl)amino-3,4,5-trihydroxy-1-N-(2-hydroxyethyl)azepane (**47**).* Polyhydroxyaminoazepane **44** (0.05 g, 0.24 mmol) was dissolved in water (1.0 mL). Triethyl amine (0.049 g, 0.484 mmol) in 0.2 mL of MeOH and acetic anhydride (0.0371 g, 0.36 mmol) in 0.2 mL of MeOH were added. After 30 min, the reaction mixture was directly loaded on to a silica gel column, and the product was eluted with a mixture of acetonitrile and aqueous ammonium hydroxide solution (6:1) to get **47** (0.048 g, 80%) as a colorless

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viscous liquid. TLC: R_f 0.5 (acetonitrile/ammonium hydroxide, 4:1); $[\alpha]_D^{30}$ +14.88 (*c* 0.215, MeOH); IR (neat) ν_{max} 3272, 1632, 1552, 1432, 1374, 1318, 1051 cm^{-1}. ^1H NMR (300 MHz, D_2O) δ 4.21−4.19 (m, 1H), 3.92 (td, *J* = 8.1, 1.8 Hz, 1H), 3.80−3.75 (m, 3H), 3.68 (dd, *J* = 7.8, 1.8 Hz, 1H), 3.43−3.34 (m, 2H), 3.24−3.12 (m, 4H), 1.94 (s, 3H); ^{13}C NMR (75 MHz, D_2O) δ 173.9 (s), 75.2 (d), 72.2 (d), 67.7 (d), 59.5 (t), 56.1 (t), 54.9 (t), 54.4 (t), 49.8 (d), 21.9 (q); HRMS (ESI): $[M + H]^+$ calcd for $C_{10}H_{21}N_2O_5$: 249.1444; found: 249.1451.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01790.

Copies of ^1H and ^{13}C NMR spectra of all new compounds (PDF)

ORTEP and associated X-ray crystallographic data for **22** (CIF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: ramesh@chemistry.iitd.ac.in.

Notes

The authors declare no competing financial interest.

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(32) It may be noted that in an earlier report (ref 10d) on the synthesis of compounds **28** and **29**, whose ^{13}C NMR spectral data were found to be in complete agreement with ours, the authors have wrongly reported the compounds to be ammonium salts of acetic acid and not as *N*-acetyl derivatives. Unambiguous proof that the products are indeed *N*-acetyl derivatives is clearly evident from their HRMS and IR data (see Experimental Section).
(33) *N*-benzyl-(+)-conduramine F-4 hydrochloride (*ent*-**33**) was reported to be a strong inhibitor of β-glucosidase from almonds (IC_{50} = 1.7 μm) (see refs 16 and 17).

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