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Total Synthesis of (+)-Lycoricidine, Conduramine B-1, ent-C-1, C-4, D-1, ent-F-1, ent-F-4, and Formal Synthesis of (#)-Laminitol — a C2-Symmetric Chiral Pool-Based Flexible Strategy

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Total Synthesis of (+)-Lycoricidine, Conduramine B-1, *ent*-C-1, C-4, D-1, *ent*-F-1, *ent*-F-4, and Formal Synthesis of (–)-Laminitol — a C_2-Symmetric Chiral Pool-Based Flexible Strategy

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KEYWORDS: Lycoricidine, Conduramine, Laminitol, Chiral Pool, Tartaric acid.

ABSTRACT: Facile and diversity oriented synthetic strategy towards aminocyclitol natural products from inexpensive C_2-symmetric L-tartaric acid was developed. Pivotal epoxide was used as a common intermediate to accomplish eight diverse target molecules in six to eleven steps. Various allyl amine type conduramines were synthesized in a diastereoselective manner. Heck arylation was explored to construct phenanthridone ring in a concise synthesis of (+)-lycoricidine. In addition, a highly efficient formal synthesis of (–)-laminitol was developed.

INTRODUCTION

The *Amaryllidaceae* alkaloids family,[1] such as lycoricidine (**1** Figure 1) and narciclasine (**2**) gained attention for their biological properties ranging from antitumor to antiviral, antibacterial, antifungal, antimalarial and analgesic activities.[2] However, the precise mechanisms of their action have not been fully elucidated. First isolated from the bulbs of *Lycoris radiate,*[3] lycoricidine has multiple chiral centers stimulating interest in the synthesis of this natural product difficult to obtain in multi-gram scale from natural sources. Since the first total synthesis by Ohta in 1976,[4] around 20 papers have been published disclosing the synthetic approaches to lycoricidine **1**.[5] Among the recent examples, an expedite 6-step synthesis of lycoricidine reported by Sarlah provided a final product in 26 % yield.[5g] At the same time, other aminocyclohexenetriols (e.g., conduramines, a family of diastereomerically diverse allyl amine small molecule analogs of conduritol) have continued to attract synthetic interest due to their stereoisomeric architectures and unique biological activities (Figure 1).[6] Several synthetic approaches toward construction of the requisite stereoisomeric skeleton for the synthesis of conduramines A-1,[7] B-1,[6b,8] D-1,[7c,9] E-1,[7a,f,10] C-1,[7a,b,9,11] C-4,[7c,12] F-1,[6c,7b,c,f,10,13] and F-4[14] have been reported. Conduramines also serve as chiral pools for the synthesis of various natural products, such as (+)-valienamine,[7a] (+)-lycoricidine and (+)-narciclasine[15] that possess potent glucosidase inhibitory[6] and a broad spectrum of anticancer activities respectively. Although many creative approaches toward the lycoricidine and

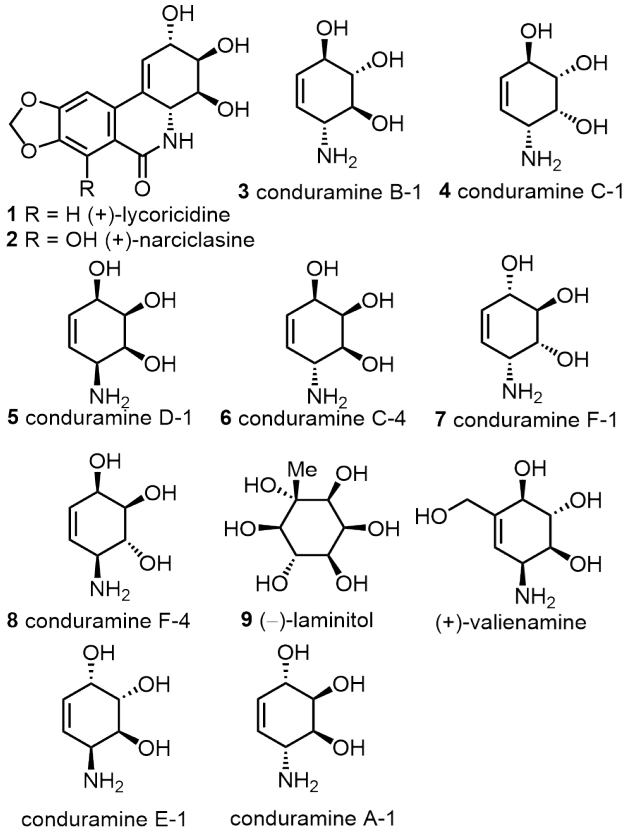
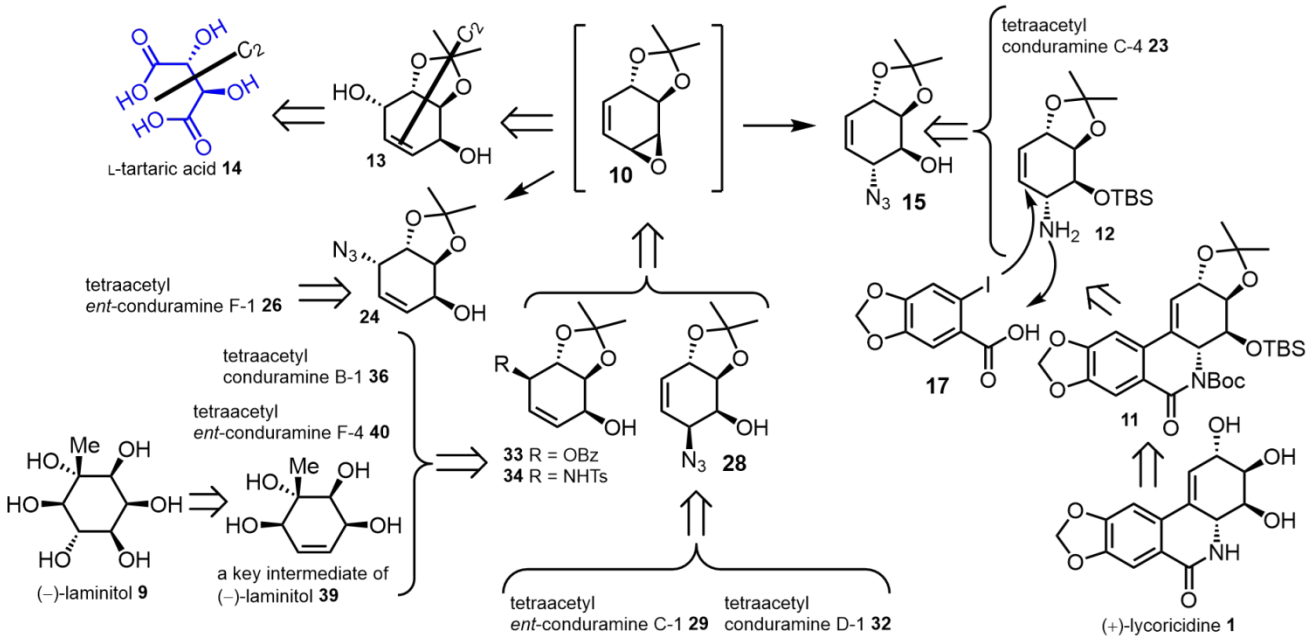


Figure 1. Structure of some conduramines and aminocyclitol-type natural products.

Scheme 1 Retrosynthesis of Conduramine B-1, *ent*-C-1, C-4, D-1, e*nt*-*F*-1 and e*nt*-F-4, Key Intermediate of (–)-Laminitol, and (+)-Lycoricidine.



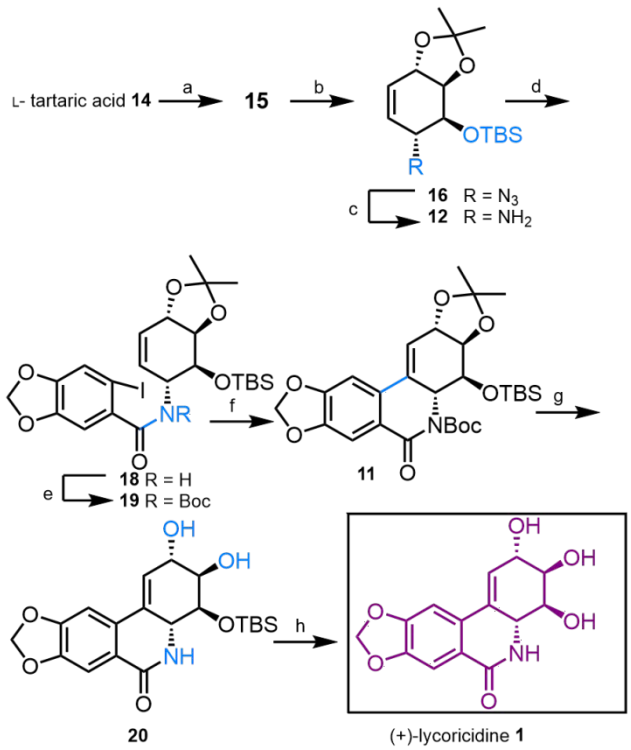
conduramine scaffolds have been developed, the majority of strategies gave the product in low yields. Thus, from a practical viewpoint, the high-yielding protocols for the chemical synthesis of lycoricidine and conduramines are highly desired. Not only the total synthesis of these natural products has gained attention, but their precursors also became valuable targets. Thus, we envisioned stereochemical diversity synthesis of conduramines and lycoricidine. Importantly, an efficient synthesis of libraries based on these natural products would facilitate basic SAR studies to identify the core pharmacophore and furnish potent and selective analogs, which are difficult to obtain through the direct modification of natural products.

Recently, we reported an efficient synthetic strategy for various natural products including (–)-hygromycin A,[16] conduramines A-1[7a] and E-1,[7a,h] and (+)-valienamine,[7a] a key intermediate of (+)-pancratistatin, from the common chiral substrates. Herein, we present a *C*2-symmetric chiral pool-based approach. This expeditious and diastereoselective protocol delivers synthetically challenging (+)-lycoricidine (**1**), and stereomerically diverse conduramines (**3-8**) through an allylic epoxide **10**, which is prepared from inexpensive L-(+)-tartaric acid. In a complementary note, we also report a formal synthesis of (–)-laminitol **9**.[17] (Figure 1).

RESULTS AND DISCUSSION

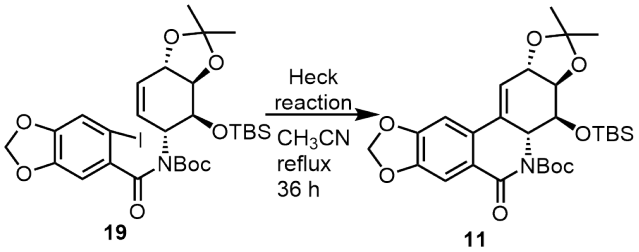
We designed a concise convergent strategy to access (+)-lycoricidine and various conduramines from the same readily available intermediate. Scheme 1 outlines our overall retrosynthesis. In lycoricidine synthesis, we planned to explore Heck arylation and amidation for the construction of the required phenanthiridine **11** from allyl amine **12**, which could be derived from L-(+)-tartaric acid **14** through allylic epoxide **10**. The compound **10** could be obtained from diol **13** through activation of one hydroxyl group as an electrophile and intramolecular displacement by another hydroxyl nucleophile. Finally, conduramines **3-8** were ex-

Scheme 2 Total Synthesis of (+)-Lycoricidine 1.



Reagents and conditions: (a) ref. 7a, **16**, 39% (4 steps from **14**) (b) NaH, TBSCl, THF, r.t., 6 h, 82%. (c) LAH, ether, 0 °C, 1 h, 93% (d) **17**, DCC, DMAP, THF, r.t. 12 h, 90%. (e) Boc_2O, DMAP, CH_3CN, 90 °C, 3 h, 89%. (f) $Pd(OAc)_2$, PPh_3, Tl(OAc), CH_3CN, 90 °C, 36 h, 78%. (g) $Mg(ClO_4)_2$, CH_3CN, 90 °C, 5 h, 67%. (h) TBAF, THF, r.t., 3 h, 79%. Abbreviations: TBAF = tetra-*n*-butylammonium fluoride.

Table 1 Optimization of the phenanthiridine 11



Entry	$Pd(OAc)_2$ (mol%)	Base	PPh_3 (equiv.)	Yield (%)[a]
1	3	Et_3N	0.12	40[b]
2	20	Tl(OAc)	1	78
3	20	Cs_2CO_3	1	55
4	20	K_2CO_3	1	60[c]

[a] Isolated Yield. [b] Dehalogened product was observed. [C] Side product **12** was observed.

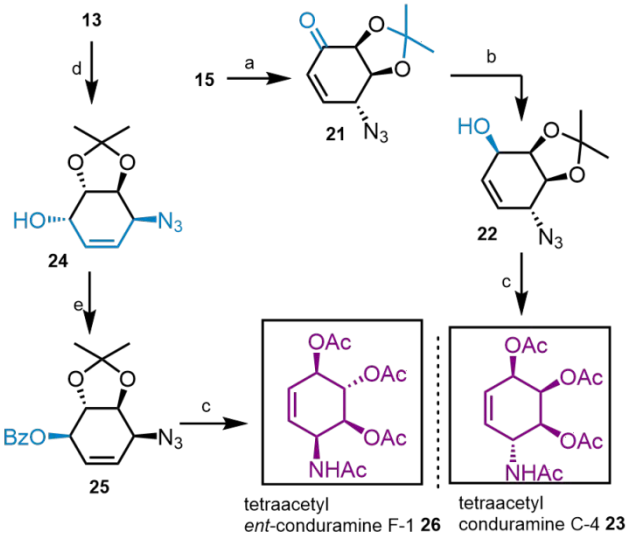
pected to arise via S_N2 and S_N2' reactions at allylic epoxide **10** with nitrogen, halogen and oxygen nucleophiles.

Synthesis of (+)-lycoricidine **1** commenced with preparation of cyclic diol **13** from the commercially available and inexpensive L-tartaric acid **14** (Scheme 2) by following the procedures reported by our group[7a,h,16,18] and others.[19] Cyclic diol **13** was subjected to a base-promoted monotriflation of the hydroxyl group, followed by intramolecular displacement by another hydroxyl nucleophile to furnish pivotal epoxide **10**. A nucleophilic ring opening of the allylic epoxide **10** at the allylic carbon with an azide ion gave 1,2-type azido alcohol **15** with the inversion of configuration. Previously, we demonstrated an efficient strategy to access both 1,2- and 1,4-type azido alcohols.[7a] In order to obtain a suitable substrate for Heck arylation, secondary alcohol **15** was protected with TBS and subsequently the azido group was reduced by LAH to give allyl amine **12** in 93% yield. Amidation of **12** with 6-iodopiperonylic acid **17**[20] in the presence of DCC and DMAP afforded the desired amide **18** in excellent yield.

The next objective was the formation of the final phenanthiridine ring via an intramolecular Heck reaction. First, we tested Heck arylation on secondary amide **18** that only gave a dehalogenated compound along with starting material. According to the literature reports,[5b,21] tertiary amides are more suitable for the intramolecular Heck arylation. Therefore, we prepared tertiary amide (**19**) by treating **18** with Boc_2O and DMAP at 90 °C. After screening the reaction conditions for Heck cyclization, we identified $Pd(OAc)_2$ in CH_3CN to give product in acceptable yields.

We also examined the effect of bases, including TEA, Tl(OAc), Cs_2CO_3 and K_2CO_3 (Table 1). Similar to Ogawa's[5e] results, the optimized Heck conditions with $Pd(OAc)_2/PPh_3$ using thallium(I) salt as a base furnished tetracyclic phenanthirdine ring (**11**) with the highest yield (78%). Final deprotection consisted of removal of *tert*-butyloxycarbonyl and acetonide by the treatment of **11** with catalytic $Mg(ClO_4)_2$[22] in acetonitrile, and TBS removal with TBAF in THF at room temperature to afford (+)-lycoricidine **1**. Physical properties of (+)-lycoricidine **1** were found to be in accordance with the literature reports.[5] The developed C_2-symmetric chiral pool-based strategy, which entailed only 11 steps from the very cheap L-tartaric acid **14**, provided (+)-lycoricidine in 10% overall yield.

Scheme 3. Synthesis of Conduramine C-4 and *ent*-Conduramine F-1.

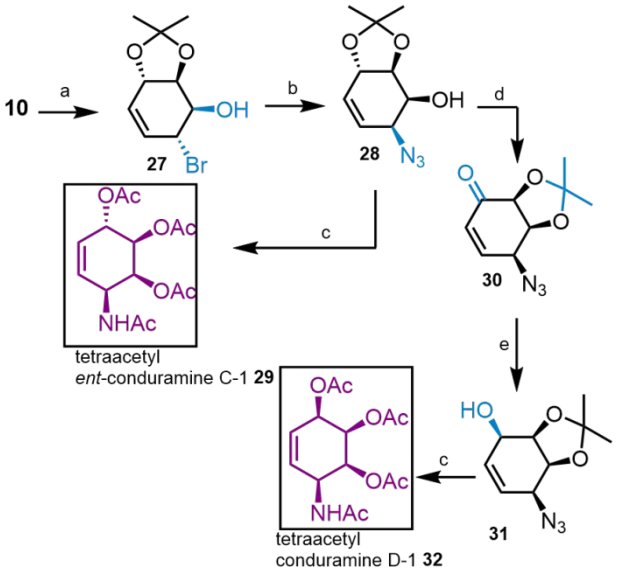


Reagents and conditions: (a) 5 mol% TFA, CH_2Cl_2, 10 °C, 4 h; then DMP, 30 min., 77%. (b) DIBAL-H, CH_2Cl_2, –78 °C, 30 min., *S*-isomer 8%, *R*-isomer 68% (*S*:*R* = 1:8.5). (c) LAH, ether, 0 °C, 1 h; then 80% AcOH, 110 or 50 °C, 22 h; then Ac_2O, pyridine, r.t., 16 h, **23**: 58%, **26**: 89%. (d) ref. 7a, 70%. (e) PPh_3, DEAD, BzOH, THF, 2 h, 87%. Abbreviations: DEAD = diethyl azodicarboxylate. DMP = Dess-Martin periodinane. TFA = trifluoroacetic acid. DIBAL-H = diisobutylaluminum hydride. LAH = lithium aluminium hydride.

Following the steps from Scheme 2, the synthesis of 1,2-*anti*-type azido alcohol **15** was achieved in four steps from L-tartaric acid **1**.[7a,16] The subsequent conversion of the *trans*-acetonide to a more stable *cis*-acetonide was performed by treating the azido alcohol **15** with TFA (0.02 equiv.) (Scheme 3). Oxidation of the allylic alcohol with Dess-Martin periodinane gave enone **21** in high yield. Although reduction of α,β-unsaturated ketones have been reported, conditions for the reduction of enone **21** had to be optimized with regard to selectivity and yield. Several reagents, such as $NaBH_4/CeCl_3{\cdot}7H_2O$, $LiBH_4/CeCl_3{\cdot}7H_2O$, $NaBH_4$, $Zn(BH_4)_2$, $LiAlH(OtBu)_3$, $LiAlH(OtBu)_3/LiI$, and L-selectride, were found to be ineffective to reduce enone **21**. Fortunately, we found that treatment of enone **21** with DIBAL-H at –78 °C furnished **22** in good yield with good selectivity (68%, α:β = 1: 8.5).

The remaining steps to the final product consisted of azide reduction, acetonide deprotection, and acylation of hydroxyl and amino groups. To improve overall yield, we aimed to accomplish the transformations in one pot. Thus, treatment of **22** with $LiAlH_4$ subsequent acetonide deprotection and preacylation in one pot provided the desired tetraacetyl conduramine C-4 **23** (Scheme 3).

Scheme 4. Synthesis of Conduramine C-1 and Conduramine D-1.



Reagents and conditions: (a) ref. 7h, 16, 87%. (b) NaN_3, NH_4Cl, DMF, r.t., 12h, 91%. (c) LAH, ether, 0 °C, 1 h; then 80% AcOH, 50 or 110 °C, 22 h; then Ac_2O, pyridine, r.t., 16 h, **29**: 68% or **32**: 62%. (d) 4 mol% TFA, CH_2Cl_2, 10 °C, 2 h; then DMP, 30 min., 66%. (e) $NaBH_4$, $CeCl_3{\cdot}7H_2O$, MeOH, –78 °C, 1 h, 91%.

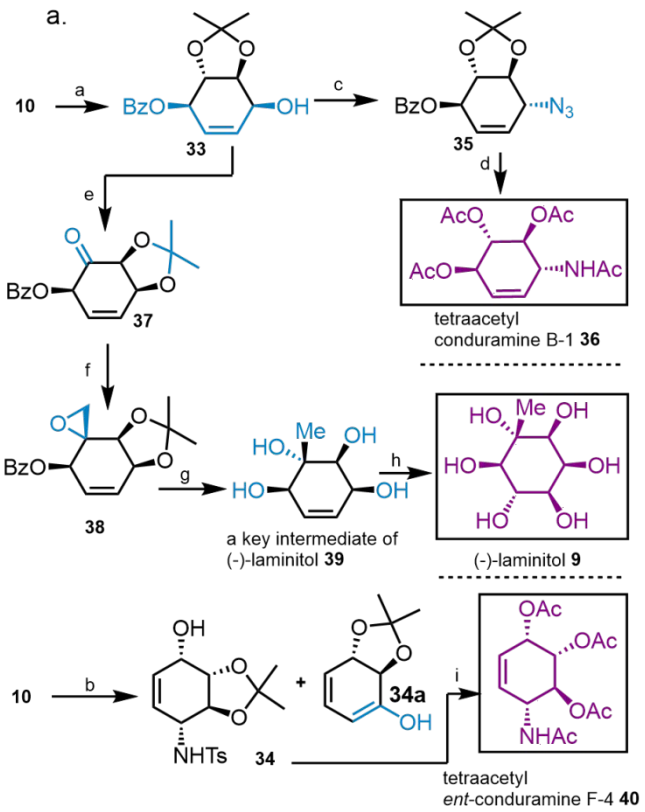
The 1,4-*anti*-type azido alcohol **24** was synthesized from cyclic diol **13** through [3,3] sigmatropic rearrangement.[7a] In order to attain the desired configuration, the allylic hydroxyl group of **24** was subjected to Mitsunobu inversion.[23] Thus, treatment of **24** with DEAD, BzOH, and PPh_3 in THF for 2 hours provided 1,4-*syn*-type azido alcohol derivative **25** in 89% yield. Reduction of **25** with $LiAlH_4$, followed by the one-pot acetonide deprotection and peracylation afforded the tetraacetyl *ent*-conduramine F-1 **26** (Scheme 3).

In order to obtain 1,2-*cis*-type azido alcohol **28,** we decided to perform a double S_N2 on the allylic epoxide **10**. The bromo-hydrin **27** was prepared from allylic epoxide **10** in a regioselective manner.[7h,16] The bromohydrin **27** was subjected to nucleophilic substitution with azide to give azido alcohol **28**. Treatment of **28** with $LiAlH_4$, followed by the one-pot acetonide deprotection and peracylation afforded the tetraacetyl *ent*-conduramine C-1 **29** (Scheme 4).

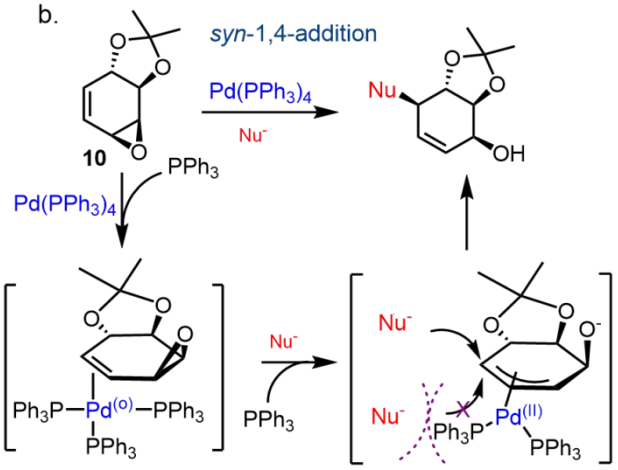
Toward product **32**, the TFA-catalyzed rearrangement of **28** gave thermally stable *cis*-fused acetonide, which led to enone **30** after oxidation with Dess-Martin periodinane. Unlike the conversion of **21** to **22**, the Luche reduction of enone **30** yielded 1,4-*cis*-type azido alcohol **31**.[24] Luche reduction from the convex face of the ketone gave only a single isomer with good yield. Further treatment of **31** conduramine D-1 **32**.

in the presence of 2 mol% $Pd(PPh_3)_4$, the 1,4-*syn* allylic alcohol **33** was obtained (Scheme 5a). Similarly, the palladium-catalyzed nucleophilic opening of allyl epoxide **10** with $TsNH_2$/$TsNHNa$[25] in CH_3CN at 40 °C gave 1,4-*syn*-amide **34** along with small amount of diene **34a**. The high stereoselectivity of 1,4-*syn*-addition could be explained by the

Schemes 5a and 5b Synthesis of Conduramine B-1, *ent*-Conduramine F-4, Formal Synthesis of Laminitol and plausible mechanism for soft nucleophile induction.



Reagents and conditions: (a) $Pd(PPh_3)_4$, BzOH, THF, 0 °C, 30 min., 95%. (b) $TsNH_2$, TsNHNa, $Pd(PPh_3)_4$, THF, 0 °C to r.t., 30 h, **34**: 69%, **34a**: 8% (ca. 8.5:1 dr). (c) MsCl, Et_3N, DMF, 0 °C, 20 min.; then NaN_3, 2 h, 88%. (d) LAH, ether, 0 °C, 1 h; then 80% AcOH, 50 °C, 22 h; then Ac_2O, pyridine, r.t., 16 h, 67%. (e) 6 mol% TFA, CH_2Cl_2, 50 °C, 30 h; then DMP, r.t., 15 h, 71%. (f) CH_2N_2, MeOH, r.t., 20 min., 70%. (g) LAH, ether, 0 °C, 1 h; then 80% AcOH, 110 °C, 22 h, 91%. (h) ref 17a, 26% (2 steps). (i) Na, NH_3, –78 °C, 45 min.; then 80% AcOH, 50 °C, 18 h; then Ac_2O, pyridine, cat. DMAP, r.t., 18 h, 82%.



steric bulk of the palladium(II) complex, which shields the α face of the palladium π-allyl system from the attack by soft nucleophile (Scheme 5b).[26]

The remaining steps towards tetraacetyl conduramine B-1, tetraacetyl *ent*-conduramine F-4 and laminitol **9** are presented in Scheme 5a. The allylic alcohol unit in **33** was converted to allylic azide through mesylation, followed by nucleophilic displacement with sodium azide to give allylic azide **35**. Reduction of **35** with $LiAlH_4$, followed by the one-pot acetonide deprotection and peracylation afforded the tetraacetyl conduramine B-1 **36** (Scheme 5).

As in the prior cases, the *trans*-acetonide **33** was converted to *cis*-acetonide, which was then subjected to oxidation affording **37**. Diazomethane-mediated transformation of ketone **37** into *exo*-epoxide **38** was accomplished in high yield.[27] In order to obtain the tetraol **39**, which is a key intermediate *en route* to (–)-laminitol **9**,[17a] the *exo*-epoxide **38** was subjected to $LiAlH_4$-promoted reduction and HOAc-promoted deprotection steps. Starting from L-tartaric acid, the formal synthesis of (–)-laminitol was accomplished in 10 steps with 8.7% overall yield (Scheme 5a). Starting from the pivotal epoxide **10**, the tosylamide **34** was prepared in a regioselective manner via the double S_N2 on the allylic epoxide. After careful optimization of the reaction conditions, the treatment of the tosylamide **34** with Na/NH_3, followed by acetonide hydrolysis and peracetylation resulted in the efficient formation of tetraacetyl *ent*-conduramine F-4 **40** in 82% yield (Scheme 5a).

CONCLUSION

In summary, we developed several synthetic routes for the synthesis of various aminocyclitol-type natural products starting from the pivotal allylic epoxide. Our protocols provided an easy access to 1,2-*syn*-, 1,2-*anti*-, 1,4-*syn*-, and 1,4-*anti*-amino precursors in high yields. The *C*2-symmetric chiral pool approach through 1,2-*anti*-amino intermediate was shown to be highly valuable for the total synthesis of (+)-lycoricidine, which was obtained in 11 steps in 10% overall yield. In addition, we accomplished an expeditious synthesis toward conduramines, including B-1, *ent*–C-1, C-4, D-1, *ent*–F-1, *ent*–F-4, from single intermediate, allyl epoxide **10**. The palladium(II)-mediated allylic substitution reaction of soft nucleophile with palladium π-allyl system provided 1,4-*syn*-alcohol intermediate, which was used to accomplish the formal synthesis of (–)-lamintol. The versatile protocol presented above should streamline generation of aminocyclitol-containing natural products and derivatives for the investigation of their biological activities.

EXPERIMENTAL SECTION

All reactions were carried out under an inert atmosphere of N_2 unless mentioned otherwise, and standard syringe–septa techniques were followed. Solvents were purchased from commercial solvent and used without further purification. The progress of all the reactions were monitored by TLC, using TLC glass plates precoated with silica gel 60 F254 (Merck). The TLC was detected by UV light (254 nm), or phosphomolybdic acid. Column chromatography was performed on Merck silica gel 60 (230-400 mesh). ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded with a Varian VXR-400 MHz spectrometer at 25 °C and chemical shifts were measured in δ (ppm) with residual solvent peaks as internal standards ($CDCl_3$, δ 7.24 ppm and CD_3OD, δ 3.30 ppm, in ^1H NMR and $CDCl_3$, δ 77 ppm, CD_3OD, δ 49 ppm, in $^{13}C\{^1H\}$ NMR). Coupling constants (*J*), measured in Hz. Data are represented as follows:chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad). High-resolution mass spectra were determined on a Jeol JMS-HX 110 spectrometer. Optical rotations were obtained on an Optical Activity AA-100 polarimeter.

(((3a*R*,4*S*,5*R*,7a*S*)-5-azido-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[*d*][1,3]dioxol-4-yl)oxy)(*tert*-butyl)dimethylsilane (16). To a suspension of NaH (60%, 132 mg, 3.30 mmol, 4.2 equiv.) in anhydrous THF (5 mL) was added azido alcohol **15**[7a] (167 mg, 0.79 mmol, 1.0 equiv.) dissolved in anhydrous THF (5 mL) at room temperature under nitrogen atmosphere and allowed to stir for 10 min., followed by TBSCl (*tert*-butylchlorodimethylsilane) (241 mg, 1.58 mmol, 2.0 equiv.) in anhydrous THF (5 mL) was added dropwise and stirred for 6 h at room temperature until TLC indicated disappearance of starting material (EtOAc : hexane = 1 : 3, R_f startng metarial : alcohol = 0.4 : 0.9). Upon completion, it was carefully quenched with water at 0 °C and diluted with EtOAc (15 mL) and washed with water (10 mL) and then brine. The aqueous layer was extracted with EtOAc (2×10 mL) and the combined organic phases were dried over $MgSO_4$, concentrated in *vacuo*. The resulting residue was purified by silica gel column chromatography using EtOAc : hexane (1 : 10) as eluents to give silyl ether **16** as white soild (213 mg, 82%). R_f = 0.90 (silica gel, EtOAc : hexane = 1 : 3); $[\alpha]_D^{25}$ = -121° (c 2.1, CH_2Cl_2); IR (film) ν_{max} 2932, 2097, 1698, 1649, 1383, 836 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.33 (dd, *J*=10.4, 0.8 Hz, 1H), 5.58 (ddd, *J*=10.4, 3.2, 0.8 Hz, 1H), 4.49-4.46 (m, 1H), 4.24 (br, 1H), 3.87-3.86 (m, 1H), 3.50 (dd, *J*=8.4, 2.0 Hz, 1H), 1.44 (s, 3H), 1.41 (s, 3H), 0.87 (s, 9H), 0.09 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 131.0, 123.0, 111.4, 78.6, 71.2, 70.3, 64.6, 26.9, 26.5, 25.7, 18.1, -4.6, -5.1; HRMS (FAB, magnetic sector) m/z: $[M+H]^+$ calcd for $C_{15}H_{28}N_3O_3Si$ 326.1900; found 326.1901.

(3a*R*,4*S*,5*R*,7a*S*)-4-((*tert*-butyldimethylsilyl)oxy)-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[*d*][1,3] dioxol-5-amine (12). A solution of azido **16** (126 mg, 0.39 mmol, 1 equiv.) in anhydrous ether (5 mL) was dropwisely added to a 0 °C suspension consisting of $LiAlH_4$ (29 mg, 0.77 mmol, 2.0 equiv.) in anhydrous ether (5 mL). After stirring 1 hour at 0 °C, a small amount of water is carefully added to destroy the excess $LiAlH_4$ at 0 °C and diluted with ether (10 mL). The solution was filtered through a pad of Celite, washed with ether (3×5 mL), dried over $MgSO_4$, concentrated in *vacuo*. The resulting residue without purified and gave pure product amine **12** as white soild (108 mg, 93%). R_f = 0.50 (silica gel, EtOAc); $[\alpha]_D^{25}$ = +15.5° (c 1.1, $CHCl_3$); IR (film) ν_{max} 3383, 3330, 1617, 1380, 1230, 1067, 837 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.05 (ddd, *J*=10.1, 1.5, 1.1 Hz, 1H), 5.55-5.51 (m, 1H), 4.49-4.46 (m, 1H), 4.06 (br, 1H), 3.59 (dd, *J*=8.6, 1.8 Hz, 1H), 3.43-3.41 (m, 1H), 1.44 (s, 3H), 1.42 (s, 3H), 0.88 (s, 9H), 0.09 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 130.0, 126.4, 110.9, 78.9, 73.5, 71.8, 57.8, 27.1, 26.6, 25.7, 18.2, -4.6, -4.9; HRMS (FAB, magnetic sector) m/z: $[M+H]^+$ calcd for $C_{15}H_{30}NO_3Si$ 300.1995; found 300.1997.

***N*-((3a*R*,4*S*,5*R*,7a*S*)-4-((*tert*-butyldimethylsilyl)oxy)-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[d][1,3]dioxol-5-yl)-6-iodobenzo[*d*][1,3]dioxole-5-carboxamide (18)**. To a stirred solution of DCC (*N*,*N*′-dicyclohexylcarbodiimide) (344 mg, 1.67 mmol, 2.0 equiv.) in anhydrous THF (10 mL) was added at 0 °C 6-iodopiperonylic acid **17**[20] (239 mg, 1.00 mmol, 1.2 equiv.) and DMAP ((4-dimethylamino)pyridine) (204 mg, 1.67 mmol, 2.0 equiv.) stirred for an additional 30 minutes at 0 °C. The reaction mixture was added a solution of amine **12** (250 mg, 0.83 mmol, 1.0 equiv.) in anhydrous THF (5 mL) at 0 °C and then allowed to stir to room temperature for 12 hours until TLC indicated disappearance of starting material (EtOAc, R_f startng metarial : product = 0.5 : 0.9). Upon completion, it was diluted with EtOAc (20 mL) a was filtered through a pad of Celite, concentrated. The obtained residue was purified by silica gel column chromatography using EtOAc : hexane (1 : 5) as eluents to give carbamate **18** as white soild (413 mg, 90%). R_f = 0.20 (silica gel, EtOAc : hexane = 1 : 5); $[\alpha]_D^{25}$ = -42.0° (c 2.5, $CHCl_3$); IR (film) ν_{max} 3251, 2985, 1639, 1529, 1475, 838 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.19 (s, 1H), 6.89 (s, 1H), 6.27 (ddd, *J*=10.0, 2.4, 1.2 Hz, 1H), 5.98 (s, 2H), 5.67 (d, *J*=8.4 Hz, 1H), 5.55 (dd, *J*=10.0, 4.0 Hz, 1H), 4.61-4.59 (m, 1H), 4.54 (d, *J*= 8.4 Hz, 1H), 4.43 (s, 1H), 3.55 (dd, *J*=8.4, 2.4 Hz, 1H), 1.43 (s, 6H), 0.91 (s, 9H), 0.23 (s, 3H), 0.15 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 167.8, 149.7, 148.4, 135.1, 130.2, 125.2, 119.1, 111.2, 108.9, 102.1, 81.1, 79.6, 71.4, 69.7, 55.4, 27.0, 26.5, 25.8, 18.1, -4.8, -4.9; HRMS (FAB, magnetic sector) m/z: $[M+H]^+$ calcd for $C_{23}H_{33}INO_6Si$ 574.1122; found 574.1119.

***tert*-butyl ((3a*R*,4*S*,5*R*,7a*S*)-4-((*tert*-butyldimethylsilyl) oxy)-2,2-dimethyl-3a,4,5,7a-tetrahydrobenzo[*d*][1,3] dioxol-5-yl)(6-iodobenzo[*d*][1,3]dioxole-5-carbonyl) carbamate (19)**. To a stirred solution of carbamate **18** (100 mg, 0.17 mmol, 1.0 equiv.) in anhydrous CH_3CN (10 mL) was added DMAP ((4-dimethylamino)pyridine) (43 mg, 0.35 mmol, 2.0 equiv.) and $(Boc)_2O$ (di-*tert*-butyldicarbonate) (0.08 mL, 0.34 mmol, 2.0 equiv.) and stirred at 90 °C for 3 h until TLC indicated disappearance of starting material (EtOAc : hexane = 1 : 5, R_f startng metarial : product = 0.2 : 0.5). Upon completion, it was diluted with EtOAc (20 mL) and washed with satd aq. $NaHCO_3$ (8 mL) and then brine. The combined organic layers were dried over $MgSO_4$, filtered and concentrated in *vacuo*. The resulting residue was purified by silica gel column chromatography using EtOAc : hexane (1 : 10) as eluents to give compound **19** as white soild (104 mg, 89%). R_f = 0.50 (silica gel, EtOAc : hexane = 1 : 5); $[\alpha]_D^{25}$ = -23.8° (c 2.1, $CHCl_3$); IR (film) ν_{max} 3420, 2931, 2857, 1737, 1675, 1477, 1234, 1146, 872 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.19 (s, 1H), 6.69 (br, 1H), 6.21 (ddd, *J*=4.4, 3.2, 1.6 Hz, 1H), 5.98 (s, 2H), 5.51 (d, *J*=9.6 Hz, 1H), 5.24 (dd, *J*=4.8, 2.4 Hz, 1H), 4.44 (ddd, *J*=6.4, 4.0, 2.4 Hz, 1H), 4.38 (d, *J*=3.2 Hz, 1H), 4.15 (dd, *J*=8.8, 3.6 Hz, 1H), 1.46 (s, 3H), 1.44 (s, 3H), 1.23 (s, 9H), 0.90 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.2, 151.9, 149.1, 148.2, 137.3, 127.6, 126.7, 118.8, 111.9, 107.9, 102.1, 84.3, 80.7, 79.2, 71.2, 69.8, 63.0, 27.6, 27.4, 26.9, 25.8, 18.2, -4.3, -4.9; HRMS (FAB, magnetic sector) m/z: $[M]^+$ calcd for $C_{28}H_{40}INO_8Si$ 673.1568; found 673.1575.

***tert*-butyl (3a*R*,4*S*,4a*R*,12a*S*)-4-((*tert*-butyldimethylsilyl)oxy)-2,2-dimethyl-6-oxo-4,4a,6,12a-tetrahydrobis([1,3]dioxolo)[4,5-*b*:4',5'-*j*]phenanthridine-5(3a*H*)-carboxylate (11)**. To a stirred solution of PPh_3 (triphenylphosphine) (20 mg, 0.077 mmol, 1.0 equiv.) in anhydrous CH_3CN (2 mL) was added $Pd(OAc)_2$ (palladium(II) acetate) (3.5 mg, 0.016 mmol, 0.20 equiv.) at room temperature and stirred for an additional 30 minutes. The reaction mixture was added a solution of iodobenzene **19** (52 mg, 0.077 mmol, 1.0 equiv.) in anhydrous CH_3CN (1 mL) and Tl(OAc) (thallium acetate) (41 mg, 0.16 mmol, 2.0 equiv.) and stirred at 90 °C for 36 hours until NMR spectrum indicated disappearance of starting material. Upon completion, it was diluted with EtOAc (10 mL) the solution was filtered through a pad of Celite, washed with EtOAc (3×5 mL) and concentrated in *vacuo*. The resulting residue was purified by silica gel column chromatography using EtOAc : hexane (1 : 10) as eluents to give compound **11** as white soild (33 mg, 78%). R_f = 0.50 (silica gel, EtOAc : hexane = 1 : 5); $[\alpha]_D^{25}$ = +132.5° (c 0.4, CH_2Cl_2); IR (film) ν_{max} 2932, 1742, 1675, 1503, 1371, 1250, 1145, 836, 782 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.46 (s, 1H), 6.85 (s, 1H), 6.43 (br, 1H), 6.03 (d, *J*=5.6 Hz, 2H), 4.66 (d, *J*=5.6 Hz, 1H), 4.46 (s, 1H), 4.39 (d, *J*=0.8 Hz, 1H), 3.67 (dd, *J*=5.6, 1.2 Hz, 1H), 1.60 (s, 9H), 1.47 (s, 3H), 1.45 (s, 3H), 0.88 (s, 9H), 0.14 (s, 3H), 0.13 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 164.5, 154.4, 152.2, 148.5, 133.9, 130.0, 126.0, 120.8, 112.0, 107.6, 103.2, 101.9, 84.9, 79.8, 71.6, 67.1, 64.6, 27.7, 26.9, 26.7, 25.7, 17.9, -4.7, -4.9; HRMS (FAB, magnetic sector) m/z: $[M]^+$ calcd for $C_{28}H_{39}NO_8Si$ 545.2445; found 545.2438.

(2*S*,3*R*,4*S*,4a*R*)-4-((*tert*-butyldimethylsilyl)oxy)-2,3-dihydroxy-3,4,4a,5-tetrahydro-[1,3]dioxolo [4,5-*j*]phenanthridin-6(2*H*)-one (20). To a stirred solution of acetonide **11** (102 mg, 0.19 mmol, 1.0 equiv.) in anhydrous CH_3CN (2 mL) was added $Mg(ClO_4)_2$ (magnesium perchlorate) (13 mg, 0.058 mmol, 0.30 equiv.) at room

temperature. The reaction mixture stirred at 90 °C for 5 h until TLC indicated disappearance of starting material (EtOAc : hexane = 2 : 1, R_f startng metarial : product = 0.9 : 0.1). Upon completion, it was diluted with EtOAc (5 mL) the solution was filtered through a pad of Celite, washed with EtOAc (3×3 mL) and concentrated in *vacuo*. The resulting residue was purified by silica gel column chromatography using EtOAc : hexane (1 : 1) as eluents to give diol **20** as white soild (51 mg, 67%). R_f = 0.13 (silica gel, EtOAc : hexane = 2 : 1); $[\alpha]_D^{25}$ = +58.5° (c 0.7, Acetone); IR (film) ν_{max} 3415, 3285, 1669, 1385, 1073, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.45 (br, 1H), 6.75 (br, 1H), 6.02 (dd, *J*=4.4, 1.6 Hz, 2H), 5.97 (br, 1H), 5.73 (br, 1H), 4.39-4.36 (m, 1H), 4.32 (d, *J*=8.4 Hz, 1H), 4.06 (dd, *J*=8.4, 2.4 Hz, 1H), 3.99 (br, 1H), 2.17 (br, 1H), 1.57 (br, 1H), 0.96 (s, 9H), 0.25 (s, 3H), 0.21 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 164.4, 151.2, 148.4, 131.0, 130.4, 121.7, 121.4, 107.4, 102.5, 101.9, 73.5, 72.1, 68.9, 52.8, 25.8, 17.9, -4.0, -4.3; HRMS (FAB, magnetic sector) m/z: $[M+H]^+$ calcd for $C_{20}H_{28}NO_6Si$ 406.1686; found 406.1685.

(2*S*,3*R*,4*S*,4a*R*)-2,3,4-trihydroxy-3,4,4a,5-tetrahydro-[1,3]dioxolo[4,5-*j*]phenanthridin-6(2*H*)-one (+)-lycoricidine (1). To a stirred solution of silyl ether **20** (51 mg, 0.13 mmol, 1.0 equiv.) in anhydrous THF (2 mL) was added TBAF (tetrabutylammonium fluoride) (1 M in THF, 0.14 mL, 0.14 mmol, 1.1 equiv.) at room temperature for an additional 3 hours until TLC indicated disappearance of starting material (MeOH : $CHCl_3$ = 1 : 8, R_f startng metarial : product = 0.8 : 0.3). Upon completion, the solvent was removed under reduced pressure and the residue was purified by normal phase silica gel column with eluted by MeOH : $CHCl_3$ = 1 : 4 to give a white solid, wash with acetone at 0 °C, collect the solid, remove acetone in *vacuo* and obtain (+)-lycoricidine **1** as a white solid (29 mg, 79%). Spectroscopic data was identical to that reported previously.[5b,c] R_f = 0.30° (silica gel, MeOH : $CHCl_3$ = 1 : 8); $[\alpha]_D^{20}$ = +181° (c 0.21, pyridine) [lit.[5b] $[\alpha]_D^{24}$ = +204° (c 0.21, pyridine), lit.[5a] $[\alpha]_D^{20}$ = +180° (c 0.45, pyridine), lit.[5e] $[\alpha]_D^{20}$ = +182° (c 0.21, pyridine), lit.[5f] $[\alpha]_D^{22}$ = +187° (c 0.50, pyridine)]; IR (film) ν_{max} 3371, 3347, 2917, 1644, 1471, 1122, 873 cm^{-1}; ^1H NMR (400 MHz, CD_3OD): δ 7.31 (s, 1H), 7.07 (s, 1H), 6.09-6.07 (m, 1H), 5.98 (d, *J*=0.8 Hz, 1H, AB**q**), 5.96 (d, J=0.8 Hz, 1H, AB**q**), 4.31-4.28 (m, 1H), 4.17-4.15 (m, 1H), 3.85-3.82 (m, 2H); $^{13}C\{^1H\}$ NMR (150 MHz, CD_3OD): δ 166.6, 153.5, 150.1, 133.4, 132.7, 123.3, 122.8, 107.7, 104.4, 103.6, 74.4, 70.9, 70.8, 53.9; HRMS (EI, magnetic sector) m/z: $[M]^+$ calcd for $C_{14}H_{13}NO_6$ 291.0743; found 291.0740.

(3a*S*,7*R*,7a*S*)-7-azido-2,2-dimethyl-7,7a-dihydrobenzo[*d*][1,3]dioxol-4(3a*H*)-one (21). To a stirred solution of 1,2-azido alcohol **15**[5a] (157 mg, 0.75 mmol, 1.0 equiv.) in anhydrous CH_2Cl_2 (5.0 mL) was added trifluoroacetic acid (0.5 M in CH_2Cl_2, 75 µL, 0.038 mmol, 0.050 equiv.) at 0 °C and stirred for an additional 4 hours at 0 °C until TLC indicated disappearance of starting material (EtOAc : hexane = 1 : 3, R_f startng metarial : allylic alcohol = 0.5 : 0.4). Upon completion, the reaction mixture was added Dess-Martin periodinane (477 mg, 1.13 mmol, 1.5 equiv.) at 0 °C and stirred for an additional 30 minutes at 0 °C until TLC indicated disappearance of starting material (EtOAc : hexane = 1 : 3, R_f allylic alcohol : product = 0.5 : 0.6). Upon completion, the solution was filtered through a pad of Celite, concentrated. The obtained residue was purified by silica gel column chromatography using EtOAc : hexane (1 : 5) as eluents to give α,β-unsaturated ketone **21** as colorless oil (120 mg, 77%). R_f = 0.59 (silica gel, EtOAc : hexane = 1 : 3); $[\alpha]_D^{25}$ = -190° (*c* 3.1, $CHCl_3$); IR (film) ν_{max} 2110, 1693, 1380, 1223, 1160, 1078, 855 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.76 (ddd, *J*=10.0, 4.0, 1.2 Hz, 1H), 6.24 (ddd, *J*=10.0, 1.2, 0.4 Hz, 1H), 4.53 (ddd, *J*=5.6, 4.0, 1.2 Hz, 1H), 4.41 (d, *J*=5.6 Hz, 1H), 4.37-4.34 (m, 1H), 1.41 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 193.0, 142.6, 130.2, 110.7, 77.5, 74.2, 57.4, 27.3, 25.8; HRMS (EI, magnetic sector) m/z: $[M]^+$ calcd for $C_9H_{11}N_3O_3$ 209.0801; found 209.0802.

(3a*R*,4*R*,7*R*,7a*S*)-7-azido-3a,4,7,7a-tetrahydro-2,2-dimethylbenzo[*d*][1,3]dioxol-4-ol (22b). To a stirred solution of ketone **21** (35 mg, 0.17 mmol, 1.0 equiv.) in anhydrous CH_2Cl_2 (1.0 mL) was cooled to -78 °C and then was slowly added DIBAL-H (diisobutylalummium hydride) (1 M in hexane, 0.25 mL, 0.25 mmol, 1.5 equiv.) and stirred for an additional 30 minutes at –78 °C until TLC indicated disappearance of starting material (EtOAc : hexane = 1 : 3, R_f startng metarial : product : diastereomer = 0.6 : 0.3 : 0.45). Upon completion, it was quenched with satd aq. NH_4Cl, diluted with EtOAc (10 mL) and washed with satd aq. NH_4Cl (3 mL) and then brine. The combined organic layers were dried over $MgSO_4$, filtered and concentrated in *vacuo*. The resulting residue was purified by silica gel column chromatography using EtOAc : hexane (1 : 4) as eluents to give alcohol (product **22b** as colorless oil 24 mg, 68% and diastereomer **22a** as colorless oil 2.8 mg, 8%). R_f = 0.27 (silica gel, EtOAc : hexane = 1 : 3); $[\alpha]_D^{25}$ = -213° (*c* 0.3, $CHCl_3$); IR (film) ν_{max} 3262, 2099, 1649, 1212, 1090, 894 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.14 (dddd, *J*=10.0, 3.6, 0.8, 0.8 Hz, 1H), 5.92 (dddd, *J*=10.0, 4.8, 1.6 , 0.8 Hz, 1H), 4.47 (ddd, *J*=7.2, 4.8, 0.8 Hz, 1H), 4.36-4.32 (m, 1H), 4.31-4.25 (m, 2H), 2.57 (d, *J*=6.8 Hz, 1H), 1.42 (s, 3H), 1.35 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 135.3, 126.5, 109.9, 77.2, 75.3, 64.7, 58.1, 26.2, 24.5; HRMS (EI, magnetic sector) m/z: $[M]^+$ calcd for $C_9H_{13}N_3O_3$ 211.0957; found 211.0952.

(3a*R*,4*S*,7*R*,7a*S*)-7-azido-3a,4,7,7a-tetrahydro-2,2-dimethylbenzo[*d*][1,3]dioxol-4-ol (22a). as colorless oil. R_f = 0.45 (silica gel, EtOAc : hexane = 1 : 3); $[\alpha]_D^{25}$ = -36.7° (*c* 0.8, $CHCl_3$); IR (film) ν_{max} 3442, 2109, 1649, 1380, 1260, 1213, 1063, 872 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.90 (ddd, *J*=10.0, 2.8, 2.8 Hz, 1H), 5.66 (ddd, *J*=10.0, 2.8, 2.8 Hz, 1H), 4.22-4.18 (m, 1H), 4.17-4.10 (m, 2H), 3.95-3.92 (m, 1H), 2.45 (d, *J*=4.8 Hz, 1H), 1.48 (s, 3H), 1.36 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 132.8, 126.1, 110.0, 79.8, 77.5, 70.9, 61.4, 27.0, 24.7; HRMS (EI, magnetic sector) m/z: $[M]^+$ calcd for $C_9H_{13}N_3O_3$ 211.0957; found 211.0951.

(3a*S*,7*R*,7a*S*)-7-azido-tetrahydro-2,2-dimethylbenzo[*d*][1,3]dioxol-4(3a*H*)-one (22c). as colorless oil. R_f = 0.48 (silica gel, EtOAc : hexane = 1 : 3); $[\alpha]_D^{25}$ = -75° (*c* 0.04, $CHCl_3$); IR (film) ν_{max} 2106, 1733, 1221, 1053, 1034 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.44-4.41 (m, 1H), 4.37 (d, *J*=6.0 Hz, 1H), 4.02 (dd, *J*=8.8, 3.6 Hz, 1H), 2.65-2.56 (m, 1H), 2.43 (ddd, *J*=16.0, 5.2, 5.2 Hz, 1H), 2.25-2.16 (m, 1H), 2.10-2.03 (m, 1H), 1.44 (s, 3H), 1.37 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz,

$CDCl_3$): δ 206.2, 111.0, 78.8, 77.8, 58.6, 34.3, 27.0, 25.7, 24.3; HRMS (EI, magnetic sector) m/z: $[M]^+$ calcd for $C_9H_{13}N_3O_3$ 211.0957; found 211.0954.

(1*S*,2*R*,3*R*,6*R*)-6-acetamidocyclohex-4-ene-1,2,3-triyl triacetate: tetraacetyl conduramine C-4 (23). A solution of azido alcohol **22b** (10 mg, 0.047 mmol, 1.0 equiv.) in anhydrous ether (1.5 mL) was dropwisely added to a 0 °C suspension consisting of $LiAlH_4$ (8.9 mg, 0.24 mmol, 5.0 equiv.) in anhydrous ether (1.5 mL). After stirring 1 hour at 0 °C, a small amount of water is carefully added to destroy the excess $LiAlH_4$, and then a solution of HOAc : H_2O (4 : 1, 2 mL) was added and stirred at 110 °C for 22 h. The mixture was evaporated in *vacuo* to give conduramine C-4, which was characterized as its tetraacetate. To the residue was added pyridine (0.6 mL) and Ac_2O (0.3 mL) at room temperature. After stirring 16 hours at room temperature, the reaction mixture was concentrated in *vacuo*, diluted with EtOAc (5 mL), filtered through a pad of Celite and poured into satd aq. Na_2CO_3 (3 mL). The aqueous layer was extracted with EtOAc (2×5 mL) and the combined organic phases were dried over $MgSO_4$, concentrated. The obtained residue was purified by silica gel column chromatography using EtOAc as eluents to give conduramine C-4 tetraacetate **23** as white soild (8.6 mg, 58%). R_f = 0.40 (silica gel, EtOAc); $[\alpha]_D^{25}$ = -130° (*c* 0.1, $CHCl_3$); IR (film) ν_{max} 2106, 1733, 1221, 1053, 1034 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.72 (dd, *J*=9.2, 2.4 Hz, 1H), 5.56-5.54 (m, 4H), 5.04 (d, *J*=9.2 Hz, 1H), 4.99-4.95 (m, 1H), 2.13 (s, 3H), 2.05 (s, 3H), 2.01 (s, 3H), 1.96 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 171.0, 170.4, 170.1, 169.9, 130.0, 125.5, 70.8, 69.4, 68.0, 48.1, 23.3, 20.8 (2C), 20.7; HRMS (EI, magnetic sector) m/z: $[M]^+$ calcd for $C_{14}H_{19}NO_7$ 313.1161; found 313.1165.

(3a*S*,4*R*,7*S*,7a*S*)-7-azido-2,2-dimethyl-3a,4,7,7a-tetrahydrobenzo[*d*][1,3]dioxol-4-yl benzoate (25). A solution of 1,4-azido alcohol **24**[7a] (100 mg, 0.47 mmol, 1.0 equiv.) in anhydrous THF (3 mL) was added a stirred solution of PPh_3 (triphenylphosphine) (206 mg, 1.18 mmol, 2.5 equiv.) in anhydrous THF (2 mL) at room temperature followed by benzoic acid (144 mg, 1.18 mmol, 2.5 equiv.) and DEAD (diethyl azodicarboxylate) (196 mg, 1.13 mmol, 2.4 equiv.) in THF (2 mL) were added and continued the stirring for 2 hours until TLC analysis indicated disappearance of starting materials (EtOAc : hexane = 1 : 2, R_f startng metarial : product = 0.3 : 0.8). Upon completion, The solvent was removed under reduced pressure and the residue was purified by normal phase silica gel column with eluted by EtOAc : hexane = 1 : 10 to give compound as colorless oil **25** (131 mg, 87%). R_f = 0.66 (silica gel, EtOAc : hexane = 1 : 4); $[\alpha]_D^{25}$ = -48° (*c* 2.0, $CHCl_3$); IR (film) ν_{max} 2101, 1718, 1601, 1267, 1115, 1092, 848, 711cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.07-8.05 (m, 2H), 7.58-7.54 (m, 1H), 7.45-7.41 (m, 2H), 5.87-5.86 (m, 2H), 5.70 (d, *J*=8.8 Hz, 1H), 4.49 (dd, *J*=4.0, 4.0 Hz, 1H), 4.22 (dd, *J*=10.0, 8.8 Hz, 1H), 3.80 (dd, *J*=10.0, 4.0 Hz, 1H), 1.53 (s, 3H), 1.49 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 165.9, 133.3, 131.3, 129.9, 129.6, 128.4, 125.8, 111.7, 76.5, 73.9, 73.3, 56.4, 27.0, 26.4; HRMS (EI, magnetic sector) m/z: $[M]^+$ calcd for $C_{16}H_{17}N_3O_4$ 315.1219; found 315.1214.

(1*S*,2*S*,3*R*,6*S*)-6-acetamidocyclohex-4-ene-1,2,3-triyl triacetate: tetraacetyl *ent*-conduramine F-1 (26). A solution of azido **25** (79 mg, 0.25 mmol, 1.0 equiv.) in anhydrous ether (3.5 mL) was dropwisely added to a 0 °C suspension consisting of $LiAlH_4$ (48 mg, 1.25 mmol, 5.0 equiv.) in anhydrous ether (4.4 mL). After stirring 1 hour at 0 °C, a small amount of water is carefully added to destroy the excess $LiAlH_4$, and then a solution of HOAc : H_2O (4 : 1, 7.9 mL) was added and stirred at 50 °C for 22 h. The mixture was evaporated in *vacuo* to give *ent*-conduramine F-1, which was characterized as its tetraacetate. To the residue was added pyridine (4.7 mL) and Ac_2O (2.4 mL) at room temperature. After stirring 16 hours at room temperature, the reaction mixture was concentrated in *vacuo*, diluted with EtOAc (10 mL), filtered through a pad of Celite and poured into satd aq. Na_2CO_3 (5 mL). The aqueous layer was extracted with EtOAc (2×10 mL) and the combined organic phases were dried over $MgSO_4$, concentrated. The obtained residue was purified by silica gel column chromatography using EtOAc as eluents to give tetraacetyl *ent*-conduramine F-1 **26** as white soild (70 mg, 89%). Spectroscopic data was identical to that reported previously.[13a] R_f = 0.51 (silica gel, EtOAc); $[\alpha]_D^{25}$ = -8.6° (*c* 0.5, $CHCl_3$) [lit.[13a] $[\alpha]_D^{25}$ = -7.1° (*c* = 0.15, $CHCl_3$)]; IR (film) ν_{max} 3283, 1746, 1655, 1226, 1034 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.81 (ddd, *J*=10.0, 4.8, 1.6 Hz, 1H), 5.73 (ddd, *J*=10.8, 2.8, 0.4 Hz, 1H), 5.55 (d, *J*=8.8 Hz, 1H), 5.37 (dd, *J*=10.0, 6.8 Hz, 1H), 5.31-5.28 (m, 1H), 5.06 (dd, *J*=10.0, 4.8 Hz, 1H), 4.99 (ddd, *J*=9.2, 4.8, 4.8 Hz, 1H), 2.05 (s, 3H), 2.04 (s, 3H), 2.00 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.2, 170.1, 169.9, 169.8, 128.0, 127.5, 77.2, 71.8, 68.7, 45.4, 23.3, 20.9, 20.8, 20.7; HRMS (EI, magnetic sector) m/e calcd for $C_{14}H_{19}NO_7$ 313.1161; found 313.1165.

(3a*S*,4*S*,5*S*,7a*S*)-5-azido-3a,4,5,7a-tetrahydro-2,2-dimethylbenzo[*d*][1,3]dioxol-4-ol (28). To a stirred solution of bromohydrin **27**[\h] (320 mg, 1.28 mmol, 1.0 equiv.) in anhydrous DMF (5.0 mL) was added sodium azide (125 mg, 1.92 mmol, 1.5 equiv.). After stirring 12 hour at room temperature until TLC indicated disappearance of starting material (EtOAc : hexane = 1 : 4, R_f startng metarial : product = 0.3 : 0.2). Upon completion, it was diluted with EtOAc (15 mL) and washed with water (6 mL) and then brine. The aqueous layer was extracted with EtOAc (2×10 mL) and the combined organic phases were dried over $MgSO_4$, concentrated in *vacuo*. The resulting residue was purified by silica gel column chromatography using EtOAc : hexane (1 : 2) as eluents to give azido **28** as colorless oil (246 mg, 91%). R_f = 0.49 (silica gel, EtOAc : hexane = 1 : 2); $[\alpha]_D^{25}$ = -153.4° (*c* 3.2, $CHCl_3$); IR (film) ν_{max} 3450, 2987, 2102, 1377, 1229, 1168, 1117, 1085, 858 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.32 (ddd, *J*=10.0, 2.4, 2.4 Hz, 1H), 5.60 (dddd, *J*=10.0, 2.4, 2.4, 1.2 Hz, 1H), 4.67-4.61 (m, 2H), 3.95-3.92 (m, 1H), 3.50 (dd, *J*=8.8, 1.6 Hz, 1H), 2.65 (d, *J*=2.4 Hz, 1H), 1.47 (s, 3H), 1.44 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 129.3, 124.7, 111.0, 79.5, 71.0, 68.1, 61.1, 26.8, 26.3; HRMS (EI, magnetic sector) m/e calcd for $C_9H_{13}N_3O_3$ 211.0957; found 211.0950.

(1*S*,2*R*,3*S*,6*S*)-6-acetamidocyclohex-4-ene-1,2,3-triyl triacetate: tetraacetyl *ent*-conduramine C-1 (29). A

solution of azido **28** (155 mg, 0.73 mmol, 1.0 equiv.) in anhydrous ether (7 mL) was dropwisely added to a 0 °C suspension consisting of $LiAlH_4$ (139 mg, 3.65 mmol, 5.0 equiv.) in anhydrous ether (8.5 mL). After stirring 1 hour at 0 °C, a small amount of water is carefully added to destroy the excess $LiAlH_4$, and then a solution of HOAc : H_2O (4 : 1, 15.5 mL) was added and stirred at 50 °C for 22 h. The mixture was evaporated in *vacuo* to give *ent*-conduramine C-1, which was characterized as its tetraacetate. To the residue was added pyridine (9.3 mL) and Ac_2O (4.7 mL) at room temperature. After stirring 16 hours at room temperature, the reaction mixture was concentrated in *vacuo*, diluted with EtOAc (15 mL), filtered through a pad of Celite and poured into satd aq. Na_2CO_3 (8 mL). The aqueous layer was extracted with EtOAc (2×15 mL) and the combined organic phases were dried over $MgSO_4$, concentrated. The obtained residue was purified by silica gel column chromatography using EtOAc as eluents to give tetraacetyl *ent*-conduramine C-1 **29** as white soild (156 mg, 68%). Spectroscopic data was identical to that reported previously.[7c,11] R_f = 0.48 (silica gel, EtOAc); $[\alpha]_D^{25}$ = +187° (*c* 1.4, CH_2Cl_2) [lit.[11] enantiomer $[\alpha]_D^{25}$ = -181° (*c* 1.0, CH_2Cl_2), lit.[7c] enantiomer $[\alpha]_D$ = -178° (*c* 0.995, CH_2Cl_2)]; IR (film) ν_{max} 3285, 1747, 1659, 1226 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.72 (d, *J*=10.4 Hz, 1H), 5.63-5.59 (m, 2H), 5.52 (bs, 2H), 5.13 (d, *J*=7.6 Hz, 1H), 5.05 (dd, *J*=5.6, 2.8 Hz, 1H), 2.11 (s, 3H), 2.05 (s, 3H), 2.01 (s, 3H), 1.96 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.4, 170.0, 169.7, 169.2, 129.1, 126.4, 71.5, 70.0, 68.9, 46.3, 23.2, 21.0, 20.9, 20.8; HRMS (EI, magnetic sector) m/z: $[M]^+$ calcd for $C_{14}H_{19}NO_7$ 313.1162; found 313.1164.

(3a*S*,7*S*,7a*S*)-7-azido-7,7a-dihydro-2,2-dimethylbenzo[*d*][1,3]dioxol-4(3a*H*)-one (30). To a stirred solution of 1,2-azido alcohol **28** (135 mg, 0.64 mmol, 1.0 equiv.) in anhydrous CH_2Cl_2 (4.5 mL) was added trifluoroacetic acid (0.5 M in CH_2Cl_2, 51 µL, 0.026 mmol, 0.040 equiv.) at 0 °C and stirred for an additional 2 hours at 10 °C until TLC indicated disappearance of starting material (EtOAc : hexane = 1 : 2, R_f startng metarial : allylic alcohol = 0.5 : 0.3). Upon completion, the reaction mixture was added Dess-Martin periodinane (406 mg, 0.96 mmol, 1.5 equiv.) at 0 °C and stirred for an additional 30 minutes at 0 °C until TLC indicated disappearance of starting material (EtOAc : hexane = 1 : 2, R_f allylic alcohol : product = 0.3 : 0.5). Upon completion, the solution was filtered through a pad of Celite, concentrated. The obtained residue was purified by silica gel column chromatography using EtOAc : hexane (1 : 3) as eluents to give α,β-unsaturated ketone **30** as colorless oil (88 mg, 66%). R_f = 0.47 (silica gel, EtOAc : hexane = 1 : 2); $[\alpha]_D^{25}$ = +183° (*c* 0.3, $CHCl_3$); IR (film) ν_{max} 2103, 1684, 1649, 1377, 1229, 1109, 1066, 1046, 838, 773 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.81 (ddd, *J*=10.4, 2.4, 2.4 Hz, 1H), 6.22 (dd, *J*=10.4, 2.4 Hz, 1H), 4.79 (ddd, *J*=6.8, 2.4, 2.4 Hz, 1H), 4.35-4.32 (m, 1H), 4.31 (d, *J*=5.2 Hz, 1H), 1.42 (s, 3H), 1.34 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 194.5, 144.4, 129.8, 111.1, 75.7, 75.2, 55.5, 27.2, 26.0; HRMS (EI, magnetic sector) m/z: $[M]^+$ calcd for $C_9H_{11}N_3O_3$ 209.0801; found 209.0806.

(3aR,4R,7S,7aS)-7-azido-3a,4,7,7a-tetrahydro-2,2-dimethylbenzo[d][1,3]dioxol-4-ol (31). To a stirred solution of ketone **30** (49 mg, 0.23 mmol, 1.0 equiv.) in anhydrous MeOH (3.0 mL) was added $CeCl_3{\cdot}7H_2O$ (131 mg, 0.35 mmol, 1.5 equiv.). Then, the reaction mixture was cooled to -78 °C and $NaBH_4$ (10.2 mg, 0.47 mmol, 2.0 equiv.) was added. After stirring for an additional 1 hours at –78 °C until TLC indicated disappearance of starting material (EtOAc : hexane = 1 : 2, R_f startng metarial : allylic alcohol = 0.5 : 0.1). Upon completion, the reaction mixture was quenched with satd aq. NH_4Cl, diluted with EtOAc (10 mL) and washed with satd aq. NH_4Cl (3 mL) and then brine. The combined organic layers were dried over $MgSO_4$, filtered and concentrated in *vacuo*. The resulting residue was purified by silica gel column chromatography using EtOAc : hexane (1 : 1.5) as eluents to give alcohol **31** as white soild (45 mg, 91%). R_f = 0.45 (silica gel, EtOAc : hexane = 1 : 1); $[\alpha]_D^{25}$ = -37.5° (*c* 0.4, $CHCl_3$); IR (film) ν_{max} 3420, 2105, 1649, 1381, 1080, 1250, 1211, 1167, 857 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.91-5.87 (m, 1H), 5.77-5.73 (m, 1H), 4.64 (ddd, *J*=7.6, 4.0, 2.0 Hz, 1H), 4.55 (ddd, *J*=7.6, 4.4, 2.0 Hz, 1H), 3.96 (ddd, *J*=10.8, 4.8, 2.4 Hz, 1H), 3.56 (dd, *J*=2.8, 2.8 Hz, 1H), 2.55 (d, *J*=10.8 Hz, 1H), 1.38 (s, 3H), 1.36 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 133.8, 124.8, 110.2, 75.6, 75.5, 66.7, 56.7, 25.5, 24.7; HRMS (EI, magnetic sector) m/z: $[M]^+$ calcd for $C_9H_{13}N_3O_3$ 211.0957; found 211.0950.

(1*S*,2*R*,3*R*,6*S*)-6-acetamidocyclohex-4-ene-1,2,3-triyl triacetate: tetraacetyl conduramine D-1 (32). A solution of azido **31** (35 mg, 0.17 mmol, 1.0 equiv.) in anhydrous ether (2 mL) was dropwisely added to a 0 °C suspension consisting of $LiAlH_4$ (31.5 mg, 0.83 mmol, 5.0 equiv.) in anhydrous ether (3.3 mL). After stirring 1 hour at 0 °C, a small amount of water is carefully added to destroy the excess $LiAlH_4$, and then a solution of HOAc : H_2O (4 : 1, 5.3 mL) was added and stirred at 110 °C for 22 h. The mixture was evaporated in *vacuo* to give conduramine D-1, which was characterized as its tetraacetate. To the residue was added pyridine (3.2 mL) and Ac_2O (1.6 mL) at room temperature. After stirring 16 hours at room temperature, the reaction mixture was concentrated in *vacuo*, diluted with EtOAc (10 mL), filtered through a pad of Celite and poured into satd aq. Na_2CO_3 (5 mL). The aqueous layer was extracted with EtOAc (2×10 mL) and the combined organic phases were dried over $MgSO_4$, concentrated. The obtained residue was purified by silica gel column chromatography using EtOAc as eluents to give tetraacetyl conduramine D-1 **32** as white soild (32 mg, 62%). Spectroscopic data was identical to that reported previously, but the optical rotation value is not identical.[7c,9] So, we have provided corrected optical rotation value. R_f = 0.36 (silica gel, EtOAc); $[\alpha]_D^{25}$ = -50° (*c* 0.4, $CHCl_3$) [lit.[9] enantiomer $[\alpha]_D^{25}$ +14.13° (c 1.0, $CHCl_3$)]; IR (film) ν_{max} 3361, 1741, 1651, 1229 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.84 (ddd, *J*=10.0, 4.4, 2.0 Hz, 1H), 5.74-5.68 (m, 2H), 5.55-5.52 (m, 1H), 5.49 (bs, 1H), 5.20 (dd, *J*=5.6, 2.0 Hz, 1H), 4.98 (ddd, *J*=10.0, 5.6, 5.6 Hz, 1H), 2.12 (s, 3H), 2.04 (s, 3H), 2.03 (s, 3H), 1.99 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.7, 169.5, 169.3, 169.2, 128.7, 126.3, 68.9, 67.0, 66.7, 44.7, 23.3, 20.9,

20.7, 20.6; HRMS (EI, magnetic sector) m/z: $[M]^+$ calcd for $C_{14}H_{19}NO_7$ 313.1162; found 313.1151.

(3a*S*,4*S*,7*R*,7a*S*)-3a,4,7,7a-tetrahydro-4-hydroxy-2,2-dimethylbenzo[*d*][1,3]dioxol -7-yl benzoate (33). To a stirred solution of $Pd(PPh_3)_4$ [tetrakis(triphenylphosphine) palladium(0)] (40.5 mg, 0.035 mmol, 0.020 equiv.) and benzoic acid (144 mg, 1.18 mmol, 2.5 equiv.) in anhydrous THF (5 mL) was added at 0 °C a solution of allylic epoxide **10**[10h] (295 mg, 1.75 mmol, 1.0 equiv.) in anhydrous THF (5 mL). After stirring 30 minutes at 0 °C until TLC indicated disappearance of starting material (EtOAc : hexane = 1 : 4, R_f startng metarial : product = 0.6 : 0.2). Upon completion, it was diluted with EtOAc (20 mL) and washed with water (6 mL) and then brine. The aqueous layer was extracted with EtOAc (2×15 mL) and the combined organic phases were dried over $MgSO_4$, concentrated in *vacuo*. The resulting residue was purified by silica gel column chromatography using EtOAc : hexane (1 : 2) as eluents to give alcohol **33** (484 mg, 95%). R_f = 0.34 (silica gel, EtOAc : hexane = 1 : 2); $[\alpha]_D^{25}$ = -64° (*c* 2.0, $CHCl_3$); IR (film) ν_{max} 3473, 1721, 1601, 1270, 1090, 849, 817, 713 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.07-8.04 (m, 2H), 7.57-7.52 (m, 1H), 7.44-7.40 (m, 2H), 6.00 (ddd, *J*=10.0, 5.2, 5.2, 2.0 Hz, 1H), 5.84 (dd, *J*=10.0, 2.0 Hz, 1H), 5.74-5.70 (m, 1H), 4.58 (dd, *J*=4.0, 4.0 Hz, 1H), 4.25 (dd, *J*=10.0, 8.8 Hz, 1H), 3.62 (dd, *J*=10.0, 3.6 Hz, 1H), 2.47 (bs, 1H), 1.48 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.0, 133.2, 130.6, 129.9, 129.8, 128.8, 128.3, 111.2, 76.9, 73.6, 73.1, 64.1, 27.1, 26.7; HRMS (ESI, magnetic sector) m/z: $[M+H]^+$ calcd for $C_{16}H_{20}O_5$ 291.1227; found 291.1218.

(3a*S*,4*R*,7*R*,7a*S*)-4-azido-3a,4,7,7a-tetrahydro-2,2-dimethylbenzo[*d*][1,3]dioxol-7-yl benzoate (35). To a stirred solution of allylic alcohol **33** (138 mg, 0.48 mmol, 1.0 equiv.) in anhydrous DMF (2.0 mL) was added Et_3N (0.12 mL, 0.71 mmol, 1.5 equiv.) and MsCl (methanesulfonyl chloride) (44 µL, 0.57 mmol, 1.2 equiv.) at 0 °C and stirred for an additional 20 minutes at 0 °C until TLC indicated disappearance of starting material (EtOAc : hexane = 1 : 4, R_f startng metarial : allylic alcohol = 0.2 : 0.7). Upon completion, the reaction mixture was added sodium azide (62 mg, 0.95 mmol, 2 equiv.) at 0 °C and then allowed to stir to room temperature for 2 hours until TLC indicated disappearance of starting material (EtOAc : hexane = 1 : 4, R_f startng metarial : allylic alcohol = 0.7 : 0.65). Upon completion, it was diluted with EtOAc (15 mL) and washed with water (6 mL) and then brine. The aqueous layer was extracted with EtOAc (2×10 mL) and the combined organic phases were dried over $MgSO_4$, concentrated in *vacuo*. The resulting residue was purified by silica gel column chromatography using EtOAc : hexane (1 : 10) as eluents to give azido **35** as white soild (132 mg, 88%). R_f = 0.65 (silica gel, EtOAc : hexane = 1 : 4); $[\alpha]_D^{25}$ = -231° (*c* 2.0, $CHCl_3$); IR (film) ν_{max} 2104, 1722, 1602, 1269, 1134, 1096, 1026, 974, 851, 712 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.07-8.04 (m, 2H), 7.58-7.54 (m, 1H), 7.45-7.41 (m, 2H), 5.84 (ddd, *J*=10.0, 2.0, 2.0 Hz, 1H), 5.80-5.76 (m, 1H), 5.72 (ddd, *J*=10.0, 2.0, 2.0 Hz, 1H), 4.24 (ddd, *J*=8.8, 4.8, 2.4 Hz, 1H), 3.89 (dd, *J*=10.0, 8.8 Hz, 1H), 3.70 (dd, *J*=9.2, 9.2 Hz, 1H), 1.48 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 165.8, 133.3, 129.8, 129.6, 129.2, 128.4, 127.7, 112.1, 78.3, 77.7, 72.7, 61.2, 26.9(2C); HRMS (EI, magnetic sector) m/z: $[M]^+$ calcd for $C_{16}H_{17}N_3O_4$ 315.1220; found 315.1216.

(1S,2S,3R,6R)-6-acetamidocyclohex-4-ene-1,2,3-triyl triacetate: tetraacetyl conduramine B-1 (36). A solution of azido **35** (50 mg, 0.16 mmol, 1.0 equiv.) in anhydrous ether (2 mL) was dropwisely added to a 0 °C suspension consisting of $LiAlH_4$ (30 mg, 0.79 mmol, 5.0 equiv.) in anhydrous ether (3 mL). After stirring 1 hour at 0 °C, a small amount of water is carefully added to destroy the excess $LiAlH_4$, and then a solution of HOAc : H_2O (4 : 1, 5 mL) was added and stirred at 50 °C for 22 h. The mixture was evaporated in *vacuo* to give conduramine B-1, which was characterized as its tetraacetate. To the residue was added pyridine (3 mL) and Ac_2O (1.5 mL) at room temperature. After stirring 16 hours at room temperature, the reaction mixture was concentrated in *vacuo*, diluted with EtOAc (10 mL), filtered through a pad of Celite and poured into satd aq. Na_2CO_3 (5 mL). The aqueous layer was extracted with EtOAc (2×10 mL) and the combined organic phases were dried over $MgSO_4$, concentrated. The obtained residue was purified by silica gel column chromatography using EtOAc as eluents to give tetraacetyl conduramine B-1 **36** as white soild (33.3 mg, 67%). Spectroscopic data was identical to that reported previously.[8a] R_f = 0.53 (silica gel, EtOAc); $[\alpha]_D^{25}$ =-156° (*c* 0.6, $CHCl_3$) [lit.[8a] $[\alpha]_D$ = -169°]; IR (film) ν_{max} 3283, 1751, 1659, 1224 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.71 (d, *J*=8.4 Hz, 1H), 5.67-5.58 (m, 2H), 5.54-5.51 (m, 1H), 5.35 (dd, *J*=10.8, 8.0 Hz, 1H), 5.05 (dd, *J*=10.8, 9.2 Hz, 1H), 4.87-4.81 (m, 1H), 2.03 (s, 6H), 2.01 (s, 3H), 1.93 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 171.1, 170.3, 169.9, 169.6, 129.7, 125.9, 71.9, 71.7, 71.4, 50.9, 23.1, 20.8, 20.6, 20.5; HRMS (EI, magnetic sector) m/z: $[M]^+$ calcd for $C_{14}H_{19}NO_7$ 313.1162; found 313.1165.

***N*-((3a*S*,4*R*,7*S*,7a*S*)-7-hydroxy-2,2-dimethyl-3a,4,7,7a-tetrahydrobenzo[*d*][1,3]dioxol-4-yl)-4-methylbenzenesulfonamide (34)**. To a stirred solution of $Pd(PPh_3)_4$ [tetrakis(triphenylphosphine) palladium(0)] (34 mg, 0.029 mmol, 0.050 equiv.), NaNHTs (172 mg, 0.89 mmol, 1.5 equiv.) and NH_2Ts (102 mg, 0.59 mmol, 1.0 equiv.) in anhydrous THF (4 mL) was added at 0 °C a solution of allylic epoxide **10**[7h] (100 mg, 0.59 mmol, 1.0 equiv.) in anhydrous THF (5 mL). The reaction mixture allowed to stir to room temperature for 30 hours until TLC indicated disappearance of starting material (EtOAc : hexane = 1 : 4, R_f startng metarial : product : side product = 0.6 : 0 : 0.2). Upon completion, it was diluted with EtOAc (15 mL) and washed with satd aq. NH_4Cl (5 mL) and then brine. The aqueous layer was extracted with EtOAc (2×10 mL) and the combined organic phases were dried over $MgSO_4$, concentrated in *vacuo*. The resulting residue was purified by silica gel column chromatography using EtOAc : hexane (1 : 1) as eluents to give (tosylamide product **34** as slight yellow soild 139 mg, 69% and side protuct as white soild **34a** 7.9 mg, 8%). R_f = 0.15 (silica gel, EtOAc : hexane = 1 : 1); $[\alpha]_D^{25}$ = +35° (*c* 0.6 , $CHCl_3$); IR (film) ν_{max} 3445, 3284, 2986, 2899, 1631, 1599, 1451, 1374, 1330, 1230, 1159, 1135, 1088, 815 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, *J*=8.4 Hz, 2H), 7.26 (d, *J*=8.4 Hz, 2H), 5.81 (ddd, *J*=10.0, 5.2, 2.4 Hz,

1H), 5.54 (dd, *J*=10.0, 2.0 Hz, 1H), 5.19 (d, *J*=8.8 Hz, 1H), 4.43 (ddd, *J*=5.2, 3.2, 3.2 Hz, 1H), 4.02 (dd, *J*=8.8, 8.8 Hz, 1H), 3.69 (dd, *J*=9.6, 9.6 Hz, 1H), 3.36 (dd, *J*=9.6, 3.2 Hz, 1H), 2.62 (bs, 1H), 2.40(s, 3H), 1.33 (s, 3H), 1.28 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 143.3, 138.1, 132.3, 129.4, 128.2, 127.2, 110.7, 77.6, 73.6, 63.8, 55.9, 27.0, 26.4, 21.5; HRMS (ESI, magnetic sector) m/z: $[M+H]^+$ calcd for $C_{16}H_{22}NO_5S$ 340.1213; found 340.1200.

(3a*S*,4*S*)-2,2-dimethyl-3a,4-dihydrobenzo[*d*][1,3]dioxol-4-ol (34a). R_f = 0.24 (silica gel, EtOAc : hexane = 1 : 4); $[\alpha]_D^{25}$ = +416 (*c* 1.1 , $CHCl_3$); IR (film) ν_{max} 3420, 1685, 1650, 1386, 1223, 1073 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.16 (dd, *J*=9.6, 5.6 Hz, 1H), 5.71-5.67 (m, 1H), 5.04 (dd, *J*=5.2, 2.0 Hz, 1H), 4.66 (ddd, *J*=5.2, 1.6, 0.8 Hz, 1H), 4.21-4.17 (m, 1H), 1.81 (d, *J*=4.4 Hz, 1H), 1.61 (s, 3H), 1.51 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 154.1, 129.5, 117.0, 114.4, 87.9, 77.9, 62.8, 26.7, 24.6; HRMS (EI, magnetic sector) m/z: $[M]^+$ calcd for $C_9H_{12}O_3$ 168.0786; found 168.0776.

(1*S*,2*S*,3*S*,6*R*)-6-acetamidocyclohex-4-ene-1,2,3-triyl triacetate : tetraacetyl *ent*-conduramine F-4 (40). Small pieces of sodium (72 mg, 3.2 mmol, 10 equiv.) were added to a solution of tosylamide **34** (112 mg, 0.33 mmol, 1.0 equiv.) in THF (2 mL) and liquid ammonia (10 mL) at −78 °C until the blue color persisted. The mixture was stirred for 45 minutes at - 78 °C, and a small amount of NH_4Cl (100 mg) was then carefully added to destroy the excess amount of sodium. The reaction mixture was slowly warmed to room temperature for overnight and then concentrated *in vacuo* and then a solution of HOAc : H_2O (4 : 1, 5 mL) was added and stirred at 50 °C for 18 h. The mixture was evaporated in *vacuo* to give *ent*-conduramine F-4, which was characterized as its tetraacetate. To the residue was added pyridine (4 mL), Ac_2O (2 mL) and DMAP (4-dimethylaminopyridine) (10 mg, 0.080 mmol, 0.25 equiv.) at room temperature. After stirring 18 hours at room temperature, the reaction mixture was concentrated in *vacuo*, diluted with EtOAc (20 mL), filtered through a pad of Celite and poured into satd aq. $NaHCO_3$ (5 mL). The aqueous layer was extracted with EtOAc (2×10 mL) and the combined organic phases were dried over $MgSO_4$, concentrated. The obtained residue was purified by silica gel column chromatography using EtOAc as eluents to give tetraacetyl *ent*-conduramine F-4 **40** as white soild (85 mg, 82%). Spectroscopic data was identical to that reported previously.[14c] R_f = 0.46 (silica gel, EtOAc); $[\alpha]_D^{25}$ = +86° (*c* 0.06, $CHCl_3$) [lit.[14c] $[\alpha]_D^{25}$ = +81° (*c* 1.0, $CHCl_3$)]; IR (film) ν_{max} 3380, 1744, 1658, 1543, 1371, 1226, 1043 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.80-5.79 (m, 2H), 5.72 (d, *J*=8.4 Hz, 1H), 5.61 (dd, *J*=3.6, 3.6 Hz, 1H), 5.27 (dd, *J*=11.2, 8.4 Hz, 1H), 5.16 (dd, *J*=11.2, 4.0 Hz, 1H), 4.76 (dd, *J*=8.4, 8.4 Hz, 1H), 2.07 (s, 3H), 2.06 (s, 3H), 2.00 (s, 3H), 1.96 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 171.4, 170.1, 169.9, 169.6, 132.9, 123.9, 69.5, 68.8, 66.0, 51.5, 23.2, 20.9, 20.8, 20.6; HRMS (ESI, magnetic sector) m/z: $[M+H]^+$ calcd for $C_{14}H_{20}NO_7$ 314.1234; found 314.1217.

(3a*S*,5*R*,7a*S*)-3a,4,5,7a-tetrahydro-2,2-dimethyl-4-oxobenzo[*d*][1,3]dioxol-5-yl benzoate (37). To a stirred solution of allylic alcohol **33** (649 mg, 2.25 mmol, 1.0 equiv.) in anhydrous CH_2Cl_2 (20.0 mL) was added trifluoroacetic acid (0.5 M in CH_2Cl_2, 0.27 mL, 0.14 mmol, 0.060 equiv.) and stirred for an additional 30 hours at 50 °C until TLC indicated disappearance of starting material (EtOAc : hexane = 1 : 2, R_f startng metarial : alcohol = 0.34 : 0.3). Upon completion, the reaction mixture was added Dess-Martin periodinane (5.73 mg, 13.5 mmol, 5 equiv.) at 0 °C and stirred for an additional 15 hours at room temperature until TLC indicated disappearance of starting material (EtOAc : hexane = 1 : 2, R_f allylic alcohol : product = 0.3 : 0.5). Upon completion, the solution was filtered through a pad of Celite, concentrated. The obtained residue was purified by silica gel column chromatography using EtOAc : hexane (1 : 3) as eluents to give ketone **37** as white soild (455 mg, 71%). R_f = 0.45 (silica gel, EtOAc : hexane = 1 : 2); $[\alpha]_D^{25}$ = -30.8° (*c* 0.8, $CHCl_3$); IR (film) ν_{max} 1756, 1724, 1646, 1282, 1245, 1123, 1093, 1067, 711 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.10-8.08 (m, 2H), 7.60-7.55 (m, 1H), 7.46-7.42 (m, 2H), 6.18-6.11 (m, 2H), 6.07-6.04 (m, 1H), 5.16 (ddd, *J*=7.2, 3.6, 1.6 Hz, 1H), 4.89 (d, *J*=6.8 Hz, 1H), 1.51 (s, 3H), 1.42 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 197.3, 165.2, 133.4, 130.5, 129.8, 128.9, 128.3, 126.0, 112.0, 77.7, 77.1, 72.6, 26.9, 25.7; HRMS (EI, magnetic sector) m/z: $[M]^+$ calcd for $C_{16}H_{16}O_5$ 288.0998; found 288.0992.

(3a*S*,5*R*,7a*S*)-2,2-dimethyl-5,7a-dihydro-3aH-spiro[benzo[*d*][1,3]dioxole-4,2'-oxirane]-5-yl benzoate (38). To a stirred solution of ketone **37** (82 mg, 0.28 mmol, 1.0 equiv.) in anhydrous MeOH (5.0 mL) at room temperature was added CH_2N_2 in ether until the reaction mixture converted to yellow color and stirred for an additional 20 minutes. The solvent was removed under reduced pressure and the obtained residue was purified by silica gel column chromatography using EtOAc : hexane (1 : 10) as eluents to give epoxide **38** as white soild (60 mg, 70%). R_f = 0.41 (silica gel, EtOAc : hexane = 1 : 5); $[\alpha]_D^{25}$ = -137.5° (*c* 0.8, $CHCl_3$); IR (film) ν_{max} 1719, 1650, 1601, 1262, 1111, 1058, 824, 711 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.03-8.00 (m, 2H), 7.57-7.53 (m, 1H), 7.44-7.40 (m, 2H), 6.06-5.97 (m, 2H), 5.37-5.36 (m, 1H), 4.87-4.85 (m, 1H), 4.07 (d, *J*=6.4 Hz, 1H), 3.10 (d, *J*=4.8 Hz, 1H), 3.01 (d, *J*=4.8 Hz, 1H), 1.52 (s, 3H), 1.39 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 165.6, 133.2, 129.8(2C), 129.7, 128.4, 126.7, 111.0, 75.1, 72.7, 68.3, 56.0, 49.6, 27.4, 26.1; HRMS (EI, magnetic sector) m/z: $[M]^+$ calcd for $C_{17}H_{18}O_5$ 302.1155; found 302.1151.

(1R,2S,3S,4S)-2-methylcyclohex-5-ene-1,2,3,4-tetraol (39). A solution of epoxide **38** (60 mg, 0.20 mmol, 1.0 equiv.) in anhydrous ether (1.5 mL) was dropwisely added to a 0 °C suspension consisting of $LiAlH_4$ (38 mg, 0.99 mmol, 5.0 equiv.) in anhydrous ether (1 mL). After stirring 1 hour at 0 °C, a small amount of water is carefully added to destroy the excess $LiAlH_4$, and then a solution of HOAc : H_2O (4 : 1, 2 mL) was added and stirred at 110 °C for 22 h. The solution was filtered through a pad of Celite, washed with MeOH (3×5 mL), concentrated. The obtained residue was purified by silica gel column chromatography using MeOH : CH_2Cl_2 (1 : 5) as eluents to give tetraol **39** as white soild (29 mg, 91%). Spectroscopic data was identical to that reported previously.[17a] R_f = 0.52 (silica gel, MeOH : EtOAc = 1 : 3); $[\alpha]_D^{25}$ = +20° (*c* 0.2, CH_3OH) [lit.[17a] $[\alpha]_D^{25}$ = +15.5° (*c* 2.6, CH_3OH)]; IR (film) ν_{max} 3420, 1699, 1650, 1095, 1032 cm^{-}

[1]; ^{1}H NMR (400 MHz, CD_3OD): δ 5.74 (ddd, *J*=10.4, 3.2, 1.6 Hz, 1H), 5.70-5.66 (m, 1H), 4.33-4.30 (m, 1H), 3.76-3.74 (m, 1H), 3.58 (dd, *J*=4.8, 0.8 Hz, 1H), 1.31 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, CD_3OD): δ 131.1, 129.5, 75.2, 74.2, 74.1, 68.0, 20.8; HRMS (EI, magnetic sector) m/z: $[M]^+$ calcd for $C_7H_{12}O_4$ 160.0736; found 160.0733.

ASSOCIATED CONTENT

Supporting Information: The Supporting Information is available free of charge on the ACS publications website http://pubs.acs.org. (Copies of NMR spectra for all new compound).

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Notes

The authors declare no competing financial interest.

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