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A concise enantioselective synthesis of 1,4-dideoxy-1,4-imino-D-arabinitol using Co(III)(salen)-catalyzed hydrolytic kinetic resolution of a two-stereocentered *anti*-azido epoxide

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ABSTRACT

A concise enantioselective synthesis of 1,4-dideoxy-1,4-imino-D-arabinitol, (+)-DAB-1, has been described in good overall yield (18.1%) and with high enantiomeric purity (up to 98% ee) starting from a simple raw material, *cis*-2-butene-1,4-diol. The Co-catalyzed hydrolytic kinetic resolution of a two-stereocentered racemic azido epoxide followed by asymmetric dihydroxylation of the alkene and 'one pot' reductive cyclisation of the azido diol are key reactions in the synthetic sequence.

1. Introduction

Polyhydroxylated pyrrolidines and piperidines have inspired the design of novel potential glycosyltransferase inhibitors.[1,2] The field of the therapeutic applications of such compounds seems promisingly broad since they could be involved in the treatment of fungal infections (chitin synthase inhibition), inflammatory processes, xenotransplant rejection or tumor growth (α-1,3-fucosyltransferase inhibition), and glycosphingolipid storage disorders (ceramide glucosyltransferase inhibition). 1,4-Dideoxy-1,4-imino-D-arabinitol (DAB-1) **1** is one such naturally occurring pyrrolidine alkaloid found in *Arachniodes standishii*[3] and *Angylocalyx boutiqueanus*,[4] which is a specific inhibitor of glycosidase and potential inhibitor of HIV replication.[5] The structural complexity (three contiguous stereocenters) and biological importance of both DAB-1 **1** and its antipode LAB-1 **2** (Fig. 1) have attracted considerable interest toward their synthesis. The reported methods of their synthesis, however, largely rely upon chiral pool resources[6] and invariably involve multiple steps while asymmetric version involving enzymatic or kinetic resolution strategy is rather limited in terms of its utility.[7] Recently, we reported the Co-catalyzed hydrolytic kinetic resolution of racemic *anti*-azido epoxides with two consecutive stereocenters to generate the corresponding diols and epoxides with high enantiomeric purity (97–99% ee) in a single step.[8] As part of our research program aimed at developing the enantioselective synthesis of biologically active molecules,[9] we herein report a concise synthesis of (+)-DAB-1 **1** that utilizes a two-stereocentered hydrolytic kinetic resolution of racemic azido epoxide **4** as the key reaction (Schemes 2 and 3).

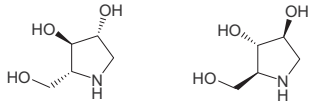

Figure 1. Structure of both the enantiomers of 1,4-dideoxy-1,4-iminoarabinitol.

2. Results and discussion

The retrosynthetic plan of 1,4-dideoxy-1,4-imino-D-arabinitol, (+)-DAB-1 **1**, is shown in Scheme 1. We thus envisioned the pyrrolidine formation at the final stage of the synthesis by reductive cyclization of azido diol **2**. Azido diol **2** was in turn visualized from diol **3** by a series of simple reaction sequences (oxidation, Wittig reaction and dihydroxylation). The key intermediate diol **3** could be readily obtained from racemic azido epoxide **4** by utilizing the Co-catalyzed two-stereocentered hydrolytic kinetic resolution of racemic azido epoxide. The formation of racemic azido epoxide **4** was planned from *cis*-2-butene-1,4-diol **5** by following standard azido bromination and epoxidation reaction sequences.

The complete synthetic sequence for obtaining the key chiral diol intermediate **3** via hydrolytic kinetic resolution commencing from commercially available *cis*-2-butene-1,4-diol **5** is outlined in Scheme 2. The azidobromination of **5** using *N*-bromosuccinimide

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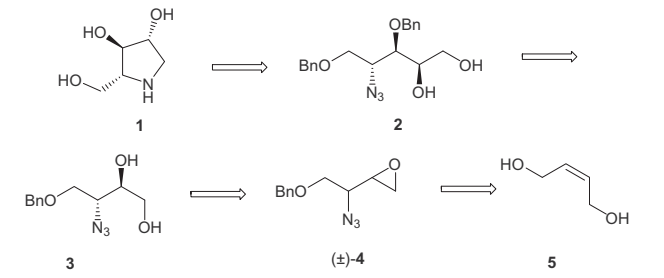
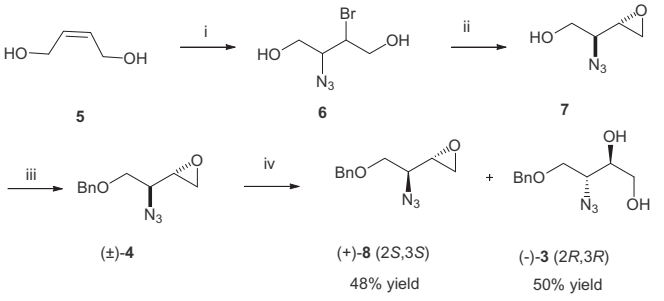


Scheme 1. Retrosynthetic plan for (+)-DAB-1 **1**.



Scheme 2. Reagents and conditions: (i) NBS (1.1 equiv), NaN_3 (2 equiv), CH_3CN:H_2O (3:1), 0 °C, 4 h, 89%; (ii) NaOH powder, THF, 0 °C, 1 h, 84%; (iii) BnBr (1.1 equiv), NaH (1.5 equiv), DMF, 0–25 °C, 92%; (iv) (*S*,*S*)-salen-cobalt(III)OAc (1 mol %), H_2O (0.5 equiv), 0 °C, 14 h.

(NBS) and sodium azide (NaN_3) in CH_3CN:H_2O afforded azido diol product **6** in 89% isolated yield. The azido diol **6** thus obtained was readily transformed into racemic *anti*-azido epoxy alcohol **7** (84% yield) under basic conditions. The free-hydroxyl group was then protected as its benzyl ether **4** (92% yield). The racemic azido epoxide **4** was subjected to hydrolytic kinetic resolution with (*S*,*S*)-salen Co(III)OAc complex (0.5 mol %) and H_2O (0.49 equiv), which produced the corresponding azido diol (−)-**3** (48%, 99% ee) and chiral epoxide (+)-**8** (50%, 97% ee) with high enantiomeric purity. The key diol intermediate (−)-**3** was readily separated from epoxide (+)-**8** by simple flash column chromatographic purification over silica gel. The enantiomeric purity of azido diol (−)-**3** was determined by chiral HPLC analysis as 99% ee.

Scheme 3 presents the remaining steps in order to obtain the target molecule **1** from chiral diol intermediate **3**. Firstly, the primary hydroxyl group was regioselectively protected as its silyl ether to afford **9** in 92% yield. Protection of the secondary hydroxyl group as its benzyl ether followed by deprotection of silyl ether was carried out to give azido alcohol **10** in 84% yield. Pyridinium chlorochromate mediated oxidation of alcohol **10** resulted in the formation of the aldehyde, which was immediately subjected to one carbon homologation to give olefin **11** in 81% yield over two steps. The asymmetric dihydroxylation of alkene **11** using AD-mix-α gave the corresponding diol **2** with high diastereoselectivity (dr = 14:1; *anti:syn*), which was smoothly separated using flash column chromatography.[10] Finally, the primary hydroxyl group of diol **2** was selectively protected as its tosylate using Bu_2SnO and tosyl chloride. The crude tosylate, without purification, was then subjected to catalytic hydrogenation [10% Pd/C, H_2 (1 atm) MeOH] under strongly acidic conditions (6 M HCl) for 24 h, which resulted in the reduction of the azide group to the amine, concomitant nucleophilic displacement of the tosylate moiety by in situ formed amine[10] and global deprotection of benzyl groups, all occurring in a 'one pot' operation to afford the target molecule (+)-DAB-1 **1** in 90% yield. The ^1H and ^{13}C NMR as well as other spectroscopic data of **1** were in complete agreement with the values reported in the literature.[10]

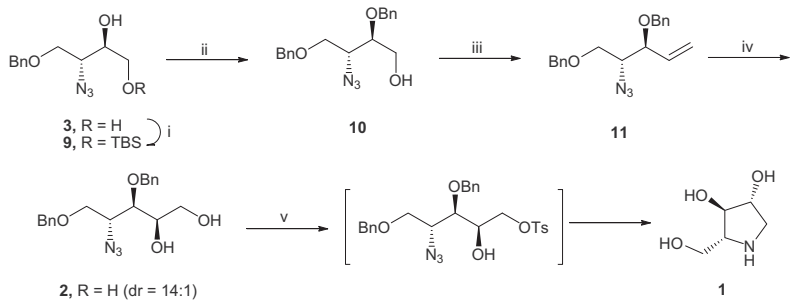
3. Conclusion

In conclusion, an efficient and straightforward enantioselective synthesis of (+)-DAB 1 **1** with reasonably good overall yield (18.1%) and high enantioselectivity (ee ~99%) has been described. The initial Co-catalyzed hydrolytic kinetic resolution of the two-stereocentered racemic azido epoxide **4** for the induction of chirality and the subsequent dihydroxylation constitute as the key reactions for obtaining three contiguous stereocenters in the desired fashion. We believe that the synthetic strategy described herein has significant potential for further extension to other stereoisomers and related analogues of multi-functionalized pyrrolidine alkaloids owing to the flexible synthesis of racemic azido epoxides with different stereochemical combinations and with different substituents.

4. Experimental section

4.1. General

Solvents were purified and dried by standard procedures before use. Optical rotations were measured using sodium D line on a JASCO-181 digital polarimeter. The ^1H NMR and ^{13}C NMR spectra were recorded on Bruker AC-200 spectrometer unless mentioned otherwise. Elemental analysis was carried out on a Carlo Erba CHNS-O analyzer. IR spectra were recorded on a Perkin-Elmer model 683 B and absorption is expressed in cm^{-1}. Purification was done using column chromatography (230–400 mesh).



Scheme 3. Reagents and conditions: (i) TBSCl (1.1 equiv), imidazole (1.5 equiv), CH_2Cl_2, 25 °C, 92%; (ii) (a) BnBr (1.1 equiv), NaH (1.5 equiv), DMF, 0 °C to 25 °C; (b) CSA (10 mol %), CH_2Cl_2:MeOH (1:1), 84% (over 2 steps); (iii) (a) PCC, CH_2Cl_2, 4 Å MS, 25 °C; (b) CH_3PPh_3I (1.1 equiv), *n*-BuLi (1.5 equiv), THF, 0–25 °C, 81% (over 2 steps) (iv) AD-mix-α, ^tBuOH:H_2O (1:1), 25 °C, 6 h, 88%; (v) (a) Bu_2SnO (2 equiv), *p*-TsCl (1.1 equiv), Et_3N (2 equiv), DMAP (10 mol %), CH_2Cl_2, 0–25 °C; (b)10% Pd/C, 6 M HCl, MeOH, H_2 (1 atm), 25 °C, 12 h, 90%.

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4.2. 2-Azido-3-bromobutane-1,4-diol 6

A mixture of *cis*-2-butene-1,4-diol **5** (10 g, 113.63 mmol) and NaN_3 (14.77 g, 227.27 mmol) were taken in CH_3CN/H_2O (180:60 mL) after which NBS (24.13 g, 136.36 mmol) was added slowly via solid addition funnel with stirring at 0 °C while the progress of the reaction was monitored by TLC. After completion of the reaction (monitored by TLC), CH_3CN was evaporated, the reaction mixture was diluted with EtOAc (80 mL), and the aq. layer was extracted with EtOAc (3 × 30 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give a crude product, which was purified by column chromatography using petroleum ether: ethyl acetate (50:50) to afford pure product **6** as a colorless solid in 89% yield. Yield: 89% (21.1 g) colorless solid, mp: 52 °C; IR: (neat, cm^{-1}): ν_{max} 1035, 1267, 2104, 3361; ^1H NMR (200 MHz, $CDCl_3$ + DMSO-d_6): δ 3.74–3.95 (m, 5H), 4.12–4.20 (m, 1H), 4.43–4.54 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$ + DMSO-d_6): δ 54.3, 62.4, 63.3, 63.4; Anal. Calcd for $C_4H_8BrN_3O_2$ requires C, 22.87; H, 3.84; N, 20.01; found C, 22.80; H, 3.82; N, 20.06.

4.3. *rac*-2-Azido-2-(oxiran-2-yl)ethanol 7

Azido bromide **6** (8 g, 38.27 mmol) was taken in THF (50 mL) and NaOH powder (1.83 g, 45.75 mmol) was added slowly with stirring at 0 °C for 2 h. After completion of the reaction (monitored by TLC), the reaction mixture was diluted with EtOAc (60 mL) and water (50 mL). The organic layer was further separated and the aq. layer extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give a crude product, which was then purified by column chromatography using petroleum ether:ethyl acetate (8:2) as eluents to afford **7** in 84% yield as a colorless oil. Yield: 84% (4.14 g) colorless oil; IR ($CHCl_3$, cm^{-1}): ν_{max} 1264, 2104, 2931, 3383; ^1H NMR (200 MHz, $CDCl_3$): δ 2.18 (br s, 1H), 2.80–2.90 (m, 2H), 3.09–3.15 (m, 1H), 3.44–3.52 (m, 1H), 3.65–3.90 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 44.2, 49.9, 61.8, 62.9; Anal. Calcd for $C_4H_7N_3O_2$ requires C, 37.21; H, 5.46; N, 32.54; found C, 37.28; H, 5.56; N, 32.46.

4.4. *rac*-2-(1-Azido-2-(benzyloxy)ethyl)oxirane 4

To a suspension of sodium hydride (1.1 g, 42.63 mmol) in DMF (50 mL), a solution of epoxy alcohol **7** (5 g, 38.75 mmol) in DMF (10 mL) was added. To this, BnBr (7.25 g, 42.63 mmol) was added slowly and the stirring was continued for 2 h at -40 °C. After completion of the reaction (monitored by TLC), it was quenched with saturated NH_4Cl and extracted with EtOAc (3 × 50 mL). The combined organic layer was separated and dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography over silica gel using petroleum ether:ethyl acetate (95:5) to give product **4** in 92% yield. Yield: 92% (7.81 g), colorless oil; IR ($CHCl_3$, cm^{-1}): ν_{max} 1264, 1453, 2102, 2864; ^1H NMR (200 MHz, $CDCl_3$): δ 2.74–2.83 (m, 2H), 3.05–3.11 (m, 1H), 3.44–3.52 (m, 1H), 3.57–3.73 (m, 2H), 4.59 (s, 2H), 7.28–7.39 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 45.0, 50.5, 61.7, 69.9, 73.5, 127.6, 127.8, 128.4, 137.4; Anal. Calcd for $C_{11}H_{13}N_3O_2$ requires C, 60.26; H, 5.98; N, 19.17; found C, 60.24; H, 5.90; N, 19.20.

4.5. 3-Azido-4-(benzyloxy)butane-1,2-diol (−)-3

To a solution of (*S*,*S*)-Co-*salen* (0.027 g, 0.5 mol %) in toluene (2 mL), AcOH (0.02 g, 0.36 mmol) was added. The solution was then allowed to stir at 25 °C in open air for 30 min. During this time, the color changed from orange-red to a dark brown; it was then dried under vacuum. To this racemic azido epoxide (2 g, 9.13 mmol), H_2O (0.08 mL, 4.47 mmol) was added at 0 °C. The reaction was then allowed to stir for 12 h at 25 °C. After completion of the reaction (monitored by TLC), the crude product was purified by column chromatography over silica gel to give chiral azido epoxide (+)-**8**, [solvent system; petroleum ether:ethyl acetate (95:5)] and chiral azido diol (−)-**3** [solvent system; petroleum ether:ethyl acetate (6:4)] in pure form.

4.6. (2*R*,3*R*)-3-Azido-4-(benzyloxy)butane-1,2-diol (−)-3

Yield: 50% (1.08 g), colorless oil; $[\alpha]_D^{25} = -37.8$ (*c* 1, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): ν_{max} 1271, 1453, 2099, 2870, 2929, 3384; ^1H NMR (200 MHz, $CDCl_3$): δ 1.60 (br s, 1H), 2.81 (br s, 1H), 3.59–3.83 (m, 6H), 4.59 (s, 2H), 7.34 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 62.0, 63.4, 69.9, 71.4, 73.5, 127.7, 127.9, 128.5, 137.3; Anal. Calcd for $C_{11}H_{15}N_3O_3$ requires C, 55.69; H, 6.37; N, 17.71; found C, 55.70; H, 6.48; N, 17.65; enantiomeric purity: 99% ee determined from HPLC analysis (Chiral OD-H column, *n*-hexane/ 2-propanol (90:10), 0.5 mL/min, 254 nm) Retention time: t_{major} = 21.25 and t_{minor} = 24.82 min.

4.7. (*S*)-2-((*S*)-1-Azido-2-(benzyloxy)ethyl)oxirane (+)-8

Yield: 48% (0.96 g), colorless oil; $[\alpha]_D^{25} = +29.3$ (*c* 1, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): ν_{max} 1264, 1453, 2102, 2864; ^1H NMR (200 MHz, $CDCl_3$): δ 2.74–2.83 (m, 2H), 3.05–3.11 (m, 1H), 3.44–3.52 (m, 1H), 3.57–3.73 (m, 2H), 4.59 (s, 2H), 7.28–7.39 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 45.0, 50.5, 61.7, 69.9, 73.4, 127.6, 127.8, 128.4, 137.4; Anal. Calcd for $C_{11}H_{13}N_3O_2$ requires C, 60.26; H, 5.98; N, 19.17; found C, 60.24; H, 5.90; N, 19.20; enantiomeric purity: 99% ee determined from HPLC analysis (Chiral OD-H column, *n*-hexane/2-propanol (95:5), 0.5 mL/min, 254 nm) Retention time: t_{minor} = 13.51 and t_{major} = 16.20 min.

4.8. (2*R*,3*R*)-3-Azido-4-(benzyloxy)-1-((*tert*-butyldimethylsilyl)oxy)butan-2-ol 9

To a stirred solution of azido diol **3** (2 g, 8.43 mmol) in CH_2Cl_2 (25 mL) were added TBSCl (1.52 g, 10.11 mmol) and imidazole (1.15 g, 16.86 mmol) at 25 °C. The resulting solution was stirred at same temperature for 3 h, then quenched with water and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give the crude product. Column chromatographic purification with silica gel using petroleum ether:ethyl acetate (95:5) as the eluent gave pure mono-TBS ether **9** as a colorless oil in 92% yield (2.72 g). Yield: 92%, colorless oil; $[\alpha]_D^{25} = +33.3$ (*c* 1, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): ν_{max} 1464, 1593, 2102, 2864, 3414; ^1H NMR (200 MHz, $CDCl_3$): δ 0.00 (d, *J* = 1.8 Hz, 6H), 0.81 (s, 9H), 2.47 (d, *J* = 6.1 Hz, 1H), 3.40–3.69 (m, 5H), 3.71–3.83 (m, 1H), 4.50 (s, 2H), 7.24 (s, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): −5.4, 25.7, 25.9, 62.0, 63.7, 70.5, 70.8, 73.5, 127.6, 127.8, 128.5, 137.7; HRMS (ESIMS): calcd for $C_{17}H_{29}SiN_3O_3$+Na]$^+$ 374.1876, found 374.1875.

4.9. (2*R*,3*R*′)-3-Azido-2,4-bis(benzyloxy)butan-1-ol 10

To a stirred solution of alcohol **9** (2.5 g, 7.11 mmol) in DMF (40 mL) was added sodium hydride (0.256 g, 10.66 mmol) at 0 °C followed by the addition of benzyl bromide (1.33 g, 7.82 mmol). After stirring for 1 h, the reaction mixture was quenched by the addition of ice. The aqueous layer was extracted with EtOAc (3 × 50 mL) and the combined organic layers were washed with water, brine, and dried over anhyd Na_2SO_4, after which the solvent was distilled off under reduced pressure to give the crude benzyl ether. The crude product was dissolved in MeOH (30 mL) after

which camphor sulfonic acid (10 mol %, 0.165 mg) was added and the mixture stirred at room temperature. After completion of the reaction as monitored by TLC, MeOH was evaporated and water (30 mL) was added. The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with water, brine, and dried over anhyd Na_2SO_4, after which the solvent was distilled off under reduced pressure to give the crude product, which was purified by column chromatography over silica gel using EtOAc/Pet. ether as eluent (5:95) to give pure alcohol **10** in 1.95 g (84%). Yield: 84%, colorless oil; $[\alpha]_D^{25}$ = +26.3 (*c* 1, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): ν_{max} 745, 1364, 1553, 2100, 2864, 3342; ^1H NMR (200 MHz, $CDCl_3$): δ 2.00 (br s, 2H), 3.54–3.81 (m, 7H), 4.56 (d, *J* = 6.1 Hz, 4H), 7.32 (s, 10H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 60.6, 60.8, 69.2, 72.2, 73.1, 78.2, 127.4, 127.5, 127.6, 128.2, 137.4, 137.4; HRMS (ESIMS): calcd for $C_{18}H_{21}N_3O_3$+Na]+ 350.1481, found 350.1489.

4.10. ((((2*R*,3*S*)-2-Azidopent-4-ene-1,3-diyl)bis(oxy))bis(methylene))dibenzene 11

To a stirred solution of alcohol **10** (1.0 g, 3.05 mmol) in CH_2Cl_2 (20 mL) was added PCC (0.78 g, 3.66 mmol) at 25 °C. The reaction mixture was allowed to stir at the same temperature for 3 h. After completion (as monitored by TLC), the reaction mixture was filtered and water (20 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with water, brine and dried over anhyd Na_2SO_4, after which the solvent was distilled off under reduced pressure to give the crude product. In a separate round bottomed flask, one carbon Wittig salt (ICH_3PPh_3) (1.47 g, 3.66 mmol) in THF was added *n*-BuLi (390 mg, 6.1 mmol, 3.85 mL of 1.6 M solution in THF) at 0 °C, which gave a yellow solution of the Wittig ylide. The above crude aldehyde was added to this reaction mixture and allowed to stir at 25 °C for 8 h. After completion of the reaction, as monitored by TLC, the reaction mixture was quenched with ice followed by the addition of water. The THF layer was concentrated and the resultant aqueous layer was extracted with EtOAc (3 × 40 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and the solvent was distilled off under reduced pressure to give the crude product, which was purified by flash column chromatography over silica gel using EtOAc/Pet. ether as eluent (5:95) to give alkene **11** in 0.80 g (81%). Yield: 81%, colorless oil; $[\alpha]_D^{25}$ = −22.3 (*c* 1, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): ν_{max} 760, 1259, 2102, 2864, 2937; ^1H NMR (200 MHz, $CDCl_3$): δ 3.50–3.72 (m, 3H), 3.96 (dd, *J* = 7.8, 5.1 Hz, 1H), 4.33–4.68 (m, 5H), 5.27–5.47 (m, 2H), 5.71–5.96 (m, 1H), 7.21–7.44 (m, 12H): ^{13}C NMR (50 MHz, $CDCl_3$): δ 61.4, 62.7, 70.6, 78.6, 118.6, 127.0, 127.2, 127.4, 127.5, 136.7, 136.8; HRMS (ESIMS): calcd for $C_{19}H_{21}N_3O_2$+Na]$^+$ 346.1526, found 346.1524.

4.11. (2*R*,3*R*,4*R*)-4-Azido-3,5-bis(benzyloxy)pentane-1,2-diol 2

To a stirred solution of $K_3Fe(CN)_6$ (1.52 g, 4.65 mmol), K_2CO_3 (641 mg, 4.65 mmol), $MeSO_2$-NH_2 (441 mg, 4.65 mmol), and $(DHQ)_2$-PHAL (60 mg, 0.077 mmol) were added *t*-BuOH and water (1:1, 50 ml). The mixture was stirred at 0 °C for 5 min, and then to this solution was added $K_2OsO_4{\cdot}2H_2O$ (5.74 mg, 1 mol %) immediately followed by the addition of alkene **11** (0.5 g, 1.55 mmol). The reaction was stirred vigorously at 0 °C for 2–18 h. Ethyl acetate was then added to the reaction mixture followed by quenching with solid sodium sulfite. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine and then dried over Na_2SO_4. After concentration, the crude mixture was purified by column chromatography over silica gel using EtOAc/Pet. ether as eluent (4:6) to give diol **2** in 0.484 g (88%). Yield: 88%, colorless oil; $[\alpha]_D^{25}$ = −36.3 (*c* 1, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): ν_{max} 698, 737, 1100, 1453, 2098, 2924, 3438; ^1H NMR (200 MHz, $CDCl_3$): δ 1.98 (s, 1H), 2.83 (br s, 1H), 3.73–3.94 (m, 7H), 4.58–4.73 (m, 4H), 7.35 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 62.0, 63.3, 69.4, 71.3, 73.4, 73.9, 79.2, 127.7, 127.9, 128.0, 128.2, 128.5, 137.4, 137.5; HRMS (ESIMS): calcd for $C_{19}H_{23}N_3O_4$+Na]$^+$ 380.1581, found 380.1580.

4.12. 1,4-Dideoxy-1,4-imido-D-arabinitol 1

To a stirred solution of diol **2** (0.3 g, 0.58 mmol) in CH_2Cl_2 were added Bu_2SnO (291 mg, 1.174 mmol), *p*-TsCl (122 mg, 0.64 mmol), Et_3N (1.174 mmol, 0.16 ml) and DMAP (10 mol %, 7.1 mg) at 0 °C. The reaction mixture was allowed to stir at 25 °C for 3 h. After completion, the reaction mixture was quenched with water and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4. After concentration, to the crude mixture in MeOH (20 mL) was added a solution of aqueous 6 M HCl (4 mL) and 10% Pd/C (0.1 g, 0.1 mmol). The reaction mixture was allowed to stir under an H_2 atmosphere (1 atm) for 36 h. The resulting mixture was filtered through a Celite pad and concentrated in vacuo. The residue was purified by column chromatography to afford 90 mg (90%) of 1,4-dideoxy-1,4-imino-D-arabinitol **1** as its hydrochloride salt, a colorless solid. Yield: 90%, colorless solid; R_f = 0.30 (CH_2Cl_2/MeOH/EtOH/30%NH_4OH 5:2:2:1); mp: 112–114 °C; $[\alpha]_D^{25}$ = +39.2 (*c* 0.5, D_2O); lit.[11] $[\alpha]_D^{25}$ = +40.1 (*c* 0.5, D_2O); ^1H NMR (500 MHz, D_2O) δ 3.03–3.09 (m, *J* = 11.9 Hz, 1H), 3.23–3.39 (m, 2H), 3.62–3.68 (m, *J* = 11.7 Hz, 1H), 3.96–4.29 (m, 3H); ^{13}C NMR (125 MHz, D_2O): δ 50.5, 60.5, 66.1, 75.6, 77.6; HRMS (ESIMS): Calcd for $C_5H_{12}NO_3$ [M+H+] 134.0812, found 134.0814.

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