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N-Heterocyclic Carbene-Catalyzed Benzoin Strategy for Divergent Synthesis of Cyclitol Derivatives from Alditols

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Abstract: A divergent synthesis of cyclitol derivatives has been developed utilizing an N-heterocyclic carbene-catalyzed benzoin-type cyclization of C_2-symmetrical dialdoses. The resulting inososes are versatile intermediates, which are readily converted into not only inositols but also amino-, deoxy-, *O*-methyl- and *C*-methyl-inositols.

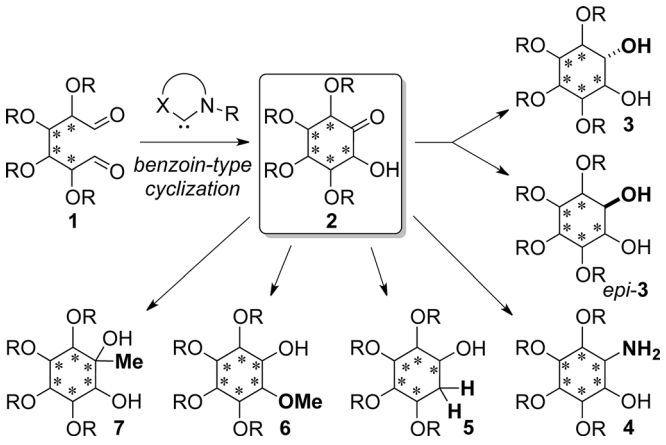
Keywords: benzoin reaction; cyclitol derivatives; N-heterocyclic carbenes

Introduction

Cyclitols, which are poly-hydroxylated cycloalkanes, have attracted attention, especially as building blocks for natural product synthesis.[1] In addition, interesting bioactivities of cyclitols have recently been reported.[2] Despite the utilities, cyclitols are not readily available in nature. Hence, many synthetic methods have been developed.[3] In addition to fermentative approaches,[4] various reactions have been applied to make cycloalkanes from oxygenated carbon chains, including Ferrier carbocyclization,[5] cyclization of malonates,[6] nitronate,[7] enolate,[8] or α,α-dithio carbanion,[9] Mukaiyama aldol reactions,[10] Horner–Wadsworth–Emmons reactions,[11] pinacol coupling,[12] ring-closing metathesis,[13] cycloaddition,[14] and Claisen rearrangement.[15]

The benzoin condensation, which occurs between two molecules of aldehydes to give α-hydroxy ketones,[16] is a well-known N-heterocyclic carbene (NHC)-catalyzed reaction.[17,18] Because the products are simple homo-dimeric compounds, the original reaction has a limited utility. Therefore, efforts have been made to develop so-called cross-benzoin reactions. In particular, an intramolecular cross-benzoin reaction between aldehydes and ketones[19] has been utilized for natural product synthesis.[20] In contrast, an intramolecular benzoin reaction of dialdehydes has been less explored,[21] probably due to difficulty in controlling chemoselectivity[22] and the lack of attention to products derived from simple symmetrical dialdehydes.[19c,21] However, we expected that an intramolecular benzoin-type cyclization of dialdose should provide a new divergent access to a variety of cyclitol derivatives.

Our strategy is based on the availability of various dialdoses **1** and the versatility of inososes **2** as a synthetic intermediate (Scheme 1). Benzoin-type cyclization of **1**, which is available from the corresponding alditols, should give **2**. Stereoselective reduction of **2** affords cyclitols **3** and *epi*-**3**. Moreover, other derivatives, such as amino-, deoxy-, and *O*-methyl- and *C*-methylcyclitols **4**, **5**, **6**, and **7** should also be available from **2**. Herein, we report the syntheses of cyclitol de-



Scheme 1. Divergent strategy for cyclitol derivatives *via* NHC-catalyzed benzoin-type cyclization.

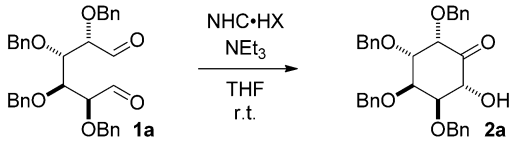
rivatives based on this strategy using C_2-symmetrical dialdoses.[23]

Results and Discussion

NHC-Catalyzed Benzoin-Type Cyclization of C_2-Symmetric Dialdoses to give Inososes

First, tetrabenzyl dialdose **1a**, which was prepared from D-mannitol, was subjected to an NHC-catalyzed benzoin-type cyclization reaction (Table 1). A THF solution of **1a** was added to a solution of thiazolium salt **8**[24] (Figure 1; 25 mol%) and DBU (20 mol%) in THF. After stirring at room temperature for 4 h, TLC monitoring indicated that **1a** was completely consumed, and *allo*-2-inosose **2a** was produced as a single diastereomer in 19% yield after purification by silica gel column chromatography (entry 1).[25] The stereochemistry of the newly formed hydroxy group was determined by the *trans*-diaxial coupling ($J = 9.5$ Hz)[26]

Table 1. Optimization of the reaction conditions for **1a**.[a]



Entry	NHC·HX	Solvent	Time [h]	Yield [%][b]
1	**8** 25 mol%[c]	THF	4	19
2	**9a** 25 mol%	THF	24	<1
3	**9b** 25 mol%[c]	THF	24	<1
4	**9c** 25 mol%	THF	10	58
5	**10** 10 mol%	THF	2.5	78
6	*ent*-**10** 25 mol%	THF	24	0 (quant)
7	**10** 5 mol%	THF	24	39 (11)
8	**10** 5 mol%	MeCN	12	83
9	**10** 5 mol%	CH_2Cl_2	0.5	81
10	**10** 5 mol%	toluene	0.75	88
11[d]	**10** 5 mol%	toluene	1	90

[a] 20 mol% of Et_3N was used in entries 1–4 and 6, while the same amount of Et_3N as NHC·HX was used in entries 5 and 7–11.
[b] **1a** was completely consumed unless the recovery yield is presented in parentheses.
[c] DBU was used instead of Et_3N.
[d] 6.0 g of **1a** (11 mmol) were used.

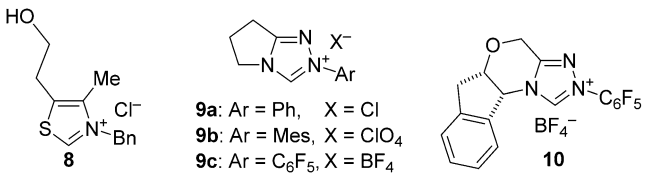


Figure 1. Structures of the NHC precursors.

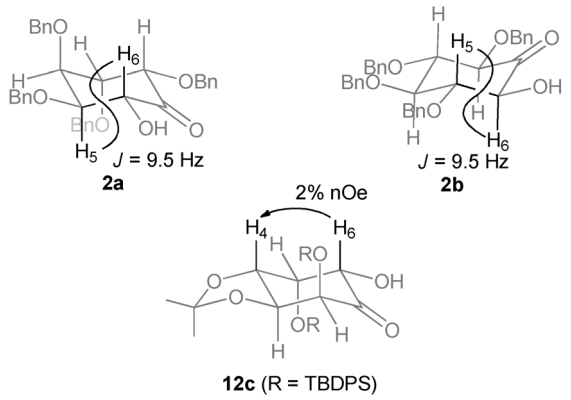


Figure 2. Determination of the stereochemistry of inososes.

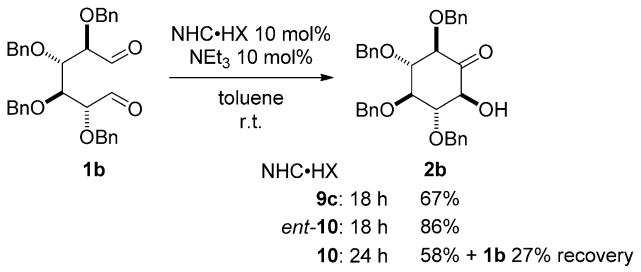
between the carbinol and the adjacent methine protons (H-5 and H-6; Figure 2).

Use of triazolium salt **9a**[27] or **9b**[28] instead of **8** gave a complex mixture, and **2a** was not obtained (entries 2 and 3). Because several formyl protons were observed in the ^{1}H NMR spectra of the crude mixtures, it is speculated that aldol-type side reactions occur due to the basicity of the utilized NHCs. Using more acidic triazolium salt **9c**[27] with a pentafluorophenyl group suppressed the side reactions, and **2a** was obtained in 58% yield after 10 h (entry 4).

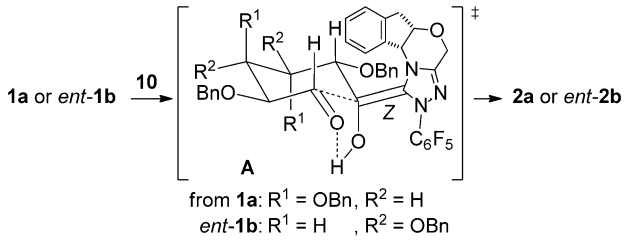
To our delight, using chiral triazolium salt **10**[27] drastically accelerated the reaction, which was completed after 2.5 h even with a lower catalyst loading (10 mol%) and an improved yield of **2a** (78%; entry 5). Interestingly, when the antipode of **10** was used as a catalyst, the reaction did not proceed, and **1a** was recovered quantitatively after 24 h (entry 6).

Other solvents were tested for the reaction using 5 mol% of **10**. In acetonitrile, the reaction proceeded more cleanly, and **2a** was obtained in a higher yield (83% after 12 h; entry 8) than that in THF (39% after 24 h; entry 7). The reaction was much faster in dichloromethane, and **2a** was obtained in 81% yield after 30 min (entry 9). Among the tested solvents, toluene gave the best results (88% yield after 45 min; entry 10). It is noteworthy that the reaction with 6.0 g **1a** proceeded without problems to give 5.4 g **2a** (entry 11).

Next, the reaction was conducted with another C_2-symmetrical dialdose **1b**, which was derived from L-iditol (Scheme 2). Although the reaction with **9c** gave **2b** in a moderate yield along with unidentified by-products, the reaction with *ent*-**10** (10 mol%) afforded *myo*-inosose **2b** as a single diastereomer in 86% yield. In contrast to the reaction with **1a**, which has the opposite stereochemistry at the α-positions, **1b** and **10** had a mismatched stereochemistry, giving **2b** in 58% yield after 24 h along with 27% recovery of **1b**. The stereochemistry of **2b** was determined based on the coupling constant similar to that of **2a** (Figure 2).



Scheme 2. Reaction with **1b**.



Scheme 3. Rationale for the stereochemical outcomes of the reaction with **1a** or **1b** (*ent*-**1b** is depicted for clarity).

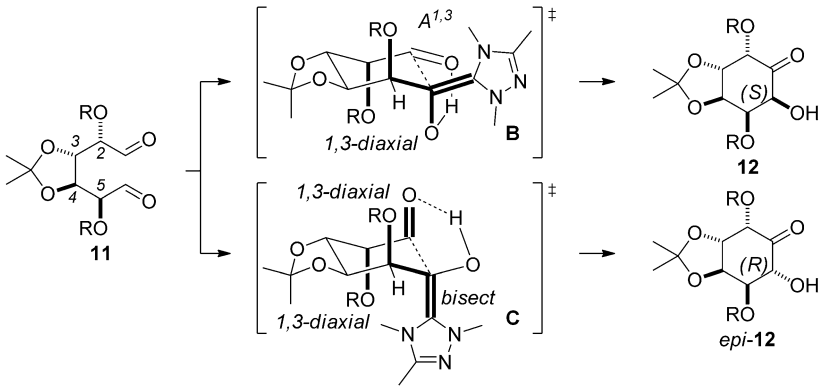
The observed stereoselectivity in the benzoin-type cyclization of dialdoses **1a** and **1b** can be explained as follows (Scheme 3; for simplicity, *ent*-**1b** and **10** are considered instead of **1b** and *ent*-**10**). Breslow intermediate **A**,[18] which is generated from **10** and dialdose **1a** or *ent*-**1b**, undergoes cyclization through the chair conformation, where the benzyloxy group next to the nucleophilic enamine carbon is in the equatorial position to minimize $A^{1,3}$ strain. The nucleophilic attack then occurs from the *si*-face of the aldehyde moiety, which leads to hydrogen bonding between the carbonyl and the hydroxy group, resulting in the *R*-configuration in the newly formed stereochemistry.

The observed stereochemical outcome and match–mismatch with **10** and *ent*-**10** likely indicate that the reaction better proceeds through the Breslow intermediate with the *Z*-geometry; otherwise the reaction would occur from the hindered face of the enamine moiety. This model contradicts Houk's model, where a Breslow intermediate derived from *N*-phenyltriazolylidene prefers the *E*-geometry in the transition state of a benzoin reaction.[29] Recently, however, Rovis' group also reported evidence of the *Z*-preference for a Breslow intermediate derived from *N*-pentafluorophenyltriazolylidene.[30] The preferred geometry of Breslow intermediates likely depends on the nitrogen-substituent of the NHC.

The above speculation led us to envision that changing the protective groups would alter the stereochemistry in the cyclization (Scheme 4). If the 3- and 4-hydroxy groups are protected as an acetonide as shown in **11**, the reaction should proceed *via* chair conformation **B** or **C**. In **B**, there are one repulsive 1,3-diaxial interaction and one non-minimum $A^{1,3}$ strain, while **C** has two repulsive 1,3-diaxial interactions and an unfavorable bisect allylic conformation. If **B** is more stable than **C**, then inosose **12** with a hydroxy group in the *S*-configuration should be produced.

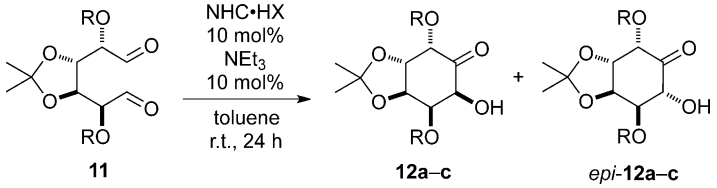
Thus, the reaction was performed with dialdose **11a**, which has TIPSO groups at the 2- and 5-positions with acetonide as a protective group for the 3- and 4-hydroxy groups. As expected, with **9c** as an NHC precursor, **12a** was formed preferentially over *epi*-**12a** (74:26), and **12a** and *epi*-**12a** were produced in 53% combined yield (Table 2, entry 3). With **10** or *ent*-**10**, the reaction was much slower, giving an almost 1:1 mixture of **12a** and *epi*-**12a** in 13 and 7% combined yield, respectively (entries 1 and 2). This is probably because the bulky NHCs enforce the $A^{1,3}$ strain in transition state **B** as well as the 1,3-diaxial interaction in **C** (Scheme 4).

The axially oriented substituents at the 2,5-positions significantly influence the selectivity. The product ratio was reduced to 57:43 in the reaction with **11b**, which has less bulky benzyloxy groups (entry 4), while **12c** was produced with perfect selectivity (>99:1) when the reaction was conducted using **11c**, which bears more bulky TBDPSO groups (entry 5).



Scheme 4. Transition states **B** and **C** leading to **12** and *epi*-**12**, respectively.

Table 2. Reactions of **11a–c** protected with acetonide.



Entry	11	R	NHC·HX	12	Yield [%][a]	Ratio 12:*epi*-12[b]
1	**11a**	TIPS	**10**	**12a**	13 (61)	48:52
2	**11a**	TIPS	*ent*-**10**	**12a**	7 (47)	49:51
3	**11a**	TIPS	**9c**	**12a**	53 (31)	74:26
4	**11b**	Bn	**9c**	**12b**	30 (3)	57:43
5	**11c**	TBDPS	**9c**	**12c**	49 (29)	>99:1
6	**11c**	TBDPS	**9c**[c]	**12c**	55[d] (4)	>99:1

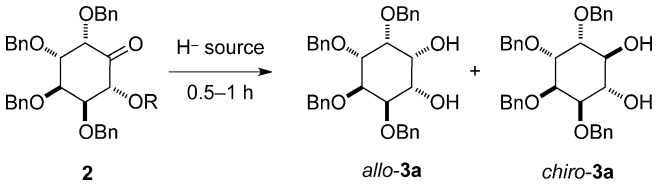
[a] Combined yield of **12** and *epi*-**12** determined by ^{1}H NMR with Ph_3CH as an internal standard. Number in parentheses is the recovery yield of **11**.
[b] Determined by ^{1}H NMR of the crude mixture.
[c] 20 mol%.
[d] Isolated yield.

This observation indicates that the two 1,3-diaxial repulsions in **C** are predominant over the $A^{1,3}$ strain in **B** (Scheme 4). Finally, using 20 mol% of **9c**, **12c** was obtained in 55% yield as a single diastereomer (entry 6). The stereochemistry of **12c** was determined by the NOE experiment (Figure 2).

Stereoselective Reduction of Inososes to Give Inositols

To selectively obtain *allo*- and *chiro*-inositols from **2a**, the conditions for stereoselective reduction were investigated (Table 3). Treating **2a** with $NaBH_4$ in methanol gave *allo*-insitol derivative *allo*-**3a** in 81% yield as a single diastereomer (entry 1). The stereochemistry was determined by X-ray crystallography. Thus, conditions to produce *chiro*-**3a** were examined. Although neither reduction using $NaBH(OAc)_3$ nor BH_3·THF produced *chiro*-**3a**, reduction with BH_3·SMe_2 gave *chiro*-**3a** as a minor diastereomer (entry 2). The proportion of *chiro*-**3a** in the product increased to 30% and 56% when BH_3·NH_3 and *t*-$BuNH_2$·BH_3[31] were used as hydride source, respectively (entries 3 and 4).

Table 3. Selectivity in the reduction of **2a** and **2c–f**.[a]



Entry	2	R	H^- source	Solvent	Yield	*dr*
1	**2a**	H	$NaBH_4$	MeOH	81%[b]	>99:1
2	**2a**	H	BH_3·SMe_2	THF	quant	92:8
3	**2a**	H	BH_3·NH_3	THF	96%	70:30
4	**2a**	H	*t*-$BuNH_2$·BH_3	THF	98%	44:56
5	**2c**	TBDPS	*t*-$BuNH_2$·BH_3	toluene	93%[b]	33:67
6	**2d**	TBDMS	*t*-$BuNH_2$·BH_3	toluene	96%	19:81
7	**2e**	TES	*t*-$BuNH_2$·BH_3	toluene	87%[c]	10:90
8	**2f**	TMS	*t*-$BuNH_2$·BH_3	toluene	88%	16:84

[a] Yield and *dr* (ratio of *allo*- and *chiro*-**3a**) were determined by ^{1}H NMR using Ph_3CH as an internal standard unless otherwise noted.
[b] Isolated yield.
[c] Isolated yield over two steps from **2a**.

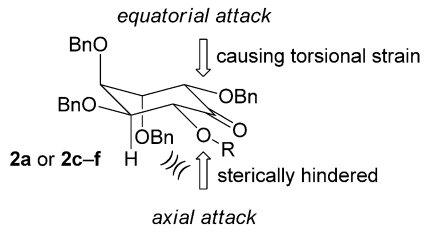


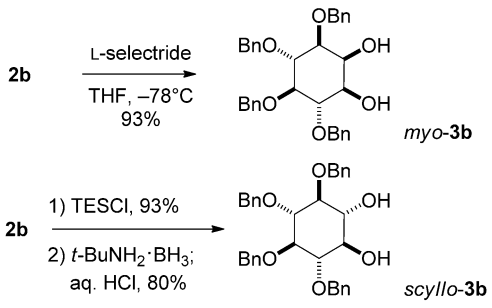
Figure 3. Rationale for stereoselectivity in Table 3.

The observed selectivity can be explained as follows. Hydride reduction of inososes generally occurs from the less hindered side,[5f] due to the electronegative substituents of inosose, which enhance the electrophilicity of the carbonyl group and induce an early transition state. Consequently, steric hindrance becomes a controlling factor. When an amine–borane complex is used as a hydride source, its relatively low reducing ability causes a later transition state. Consequently, torsional strain becomes more important (Figure 3).

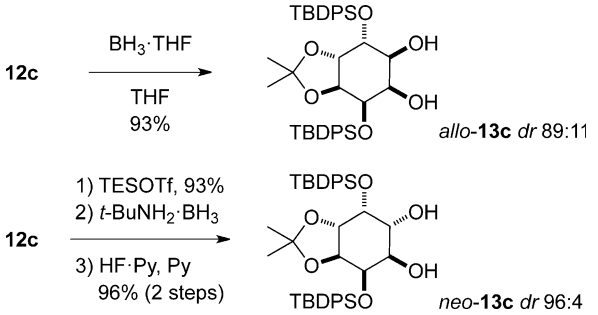
Based on the above speculation, the α-hydroxy group of **2a** was protected with a bulky silyl group to increase the torsional strain. As expected, the selectivity was further improved to 67–90% (entries 5–8). The TES group gave the best result, and *chiro*-**3a** was obtained with a high diastereoselectivity (90:10) in 87% yield after treatment with TBAF (entry 7). The two epimers were easily separated by silica gel column chromatography.

A similar selectivity was observed in the reduction of **2b** (Scheme 5). Reduction by $NaBH_4$ occurred preferentially from the equatorial direction to give *myo*-**3b** with a slightly lower selectivity (98:2) than that of **2a**, probably due to the reduced steric hindrance of the axial side. The use of L-selectride afforded *myo*-**3b** as a single diastereomer. Protection with a TES group and reduction using *t*-$BuNH_2{\cdot}BH_3$ exclusively produced *scyllo*-**3b** after protodesilylation.

With **12c**, $BH_3{\cdot}THF$ was used for the reduction from the equatorial direction to give an *allo*-rich mixture (89:11) of **13c** in 93% yield (Scheme 6). In contrast, $NaBH_4$ gave the opposite selectivity, and reduction from the axial direction was slightly preferred to give a 75:25 mixture of *neo*- and *allo*-**13c**. This preference is attributable to the steric hindrance by the axial TBDPSO group at the α-position. Reduction with *t*-$BuNH_2{\cdot}BH_3$ after TES protection gave *neo*-**13c** with a high diastereoselectivity (*neo*:*allo* = 96:4).



Scheme 5. Stereoselective reduction of **2b**.



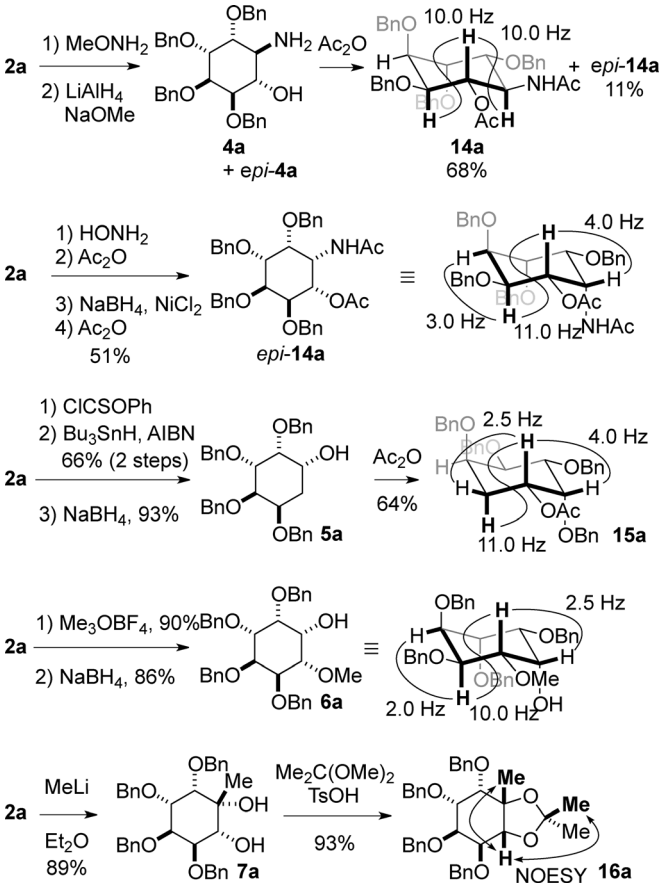
Scheme 6. Stereoselective reduction of **12c**.

Synthesis of Other Cyclitol Derivatives and Deprotection

To show the utility of the inososes **2** as synthetic intermediates, several transformations of **2a** were demonstrated (Scheme 7). Amino sugar **4a** was obtained along with minor diastereomer *epi*-**4a** by $LiAlH_4$/NaOMe reduction of the *O*-methyl oxime[32] derived from **2a**. The stereoselectivity of the reduction was reversed when the *O*-acetyl oxime was reduced with $NaBH_4/NiCl_2$,[33] and *epi*-**14a** was obtained as a sole diastereomer after acetylation. Deoxygenation of **2a** *via* thiocarbonate and subsequent reduction of the carbonyl group afforded deoxyinositol, *talo*-quercitol derivative **5a**. The stereochemistries of **4a**, *epi*-**4a**, and **5a** were determined after acetylation on the basis of the coupling constants (**14a**, *epi*-**14a**, and **15a**).

Treatment of **2a** with the Meerwein reagent and subsequent reduction gave *O*-methylinositol, *epi*-D-pinitol derivative **6a**. Reaction of **2a** with methyllithium provided *C*-methylinositol **7a** as the sole diastereomer. The stereochemistry of **6a** was confirmed by the coupling constants, while that of **7a** was determined by NOESY after conversion into acetonide **16a**.

As reported with *allo*-**3a**,[23] the benzyl groups were easily removed. Hydrogenolysis of **2a** and *chiro*-**3a** using Pd/C under a hydrogen atmosphere gave *allo*-2-inosose and D-*chiro*-inositol in 84% and 81% yields, respectively (Scheme 8). Deprotection of acetonide *neo*-**13c** was reported in the literature.[12c] By analogy, the other compounds should be deprotected in similar manners.



Scheme 7. Conversion of **2a** into other derivatives.

Conclusions

We have developed a divergent method to synthesize cyclitol derivatives utilizing NHC-catalyzed benzoin-type cyclization of C_2-symmetrical dialdose. With tetrabenzyl-protected dialdose, the key for efficient cyclization is the chiral triazolylidene catalyst. Acetonide protection at the 3,4-positions inverts the selectivity in the cyclization of the mannitol-derived dialdose. In the stereoselective reduction, employing *t*-$BuNH_2{\cdot}BH_3$ as a hydride source with α-*O*-TES protection of inosose is highly effective to overcome the inherent preference for reduction from the axial direction. The inosose products are versatile intermediates, which can be converted into various cyclitol derivatives. These results testify to the validity of our strategy in Scheme 1. Future investigations include broadening the scope of the methodology to non-C_2-symmetrical dialdoses.

Experimental Section

General Methods

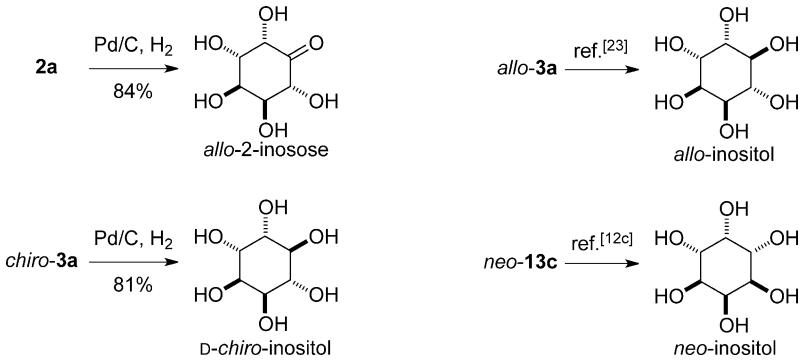
All melting points are uncorrected. NMR (500 and 125 MHz for ^1H and ^{13}C, respectively) spectra were measured in $CDCl_3$ unless otherwise mentioned. Abbreviations are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. ^{13}C NMR peak multiplicity assignments were made based on DEPT. Quadrupole, double-focusing magnetic sector, and TOF mass spectrometers were used for EI-, FAB-, and ESI-MS, respectively. Silica gel was used for column chromatography. Reactions were conducted under argon atmospheres unless otherwise noted.

Materials

Triazoliums **9c**, **10**, and *ent*-**10** were prepared as reported.[34] $(COCl)_2$, Et_3N, 2,6-lutidine, TMSCl, and CH_2Cl_2 were purchased and distilled prior to use. Other starting materials, reagents and solvents were purchased and used as supplied unless a literature method for the preparation is cited. Commercially available anhydrous solvents were used as reaction solvents, except that the MeOH and CH_2Cl_2, DMSO and pyridine utilized in reactions were anhydrous grade.

2,3,4,5-Tetra-*O*-benzyl-D-*manno*-hexodialdose (1a; Table 1)

A solution of $(COCl)_2$ (0.25 mL, 2.9 mmol) in CH_2Cl_2 (1.5 mL + 0.5 mL wash) was added to a solution of DMSO (0.21 mL, 2.9 mmol) in CH_2Cl_2 (4.5 mL) cooled at −78 °C. After 2 min, a solution of 2,3,4,5-tetra-*O*-benzyl-D-mannitol[35] (621 mg, 1.14 mmol) in CH_2Cl_2 (3 mL + 1 mL wash × 2)



Scheme 8. Deprotection of the products.

was added over 5 min. After 1.5 h, Et_3N (1.6 mL, 11 mmol) was added, and the mixture was stirred for additional 10 min before the cooling bath was removed. The mixture was allowed to warm to room temperature and concentrated under vacuum. The resulting white solids were suspended in a 1:1 mixture of pentane and EtOAc (20 mL), filtered, and washed with the mixed solvent (20 mL×2). The combined filtrate was concentrated under vacuum to give a 58:28:14 mixture of the title compound, EtOAc, and DMSO as a pale yellow oil; yield: 682 mg (quant): IR (neat): ν=3441, 3062, 3031, 2861, 1728, 1496, 1458, 1373, 1258, 1211, 1096, 910, 741, 702, 602, 455, 463 cm^{-1}; ^1H NMR: δ=4.05 (br s, 2H), 4.12 (br s, 2H), 4.43 (d, J=12.0 Hz, 2H), 4.51 (d, J=11.0 Hz, 2H), 4.60 (d, J=11.0 Hz, 2H), 4.65 (d, J=12.0 Hz, 2H), 7.20–7.36 (m, 20H) 9.70 (d, J=1.5 Hz, 2H); ^{13}C NMR: δ=72.5 (CH_2), 73.7 (CH_2), 80.0 (CH), 83.2 (CH), 127.9 (CH), 127.97 (CH), 128.00 (CH), 128.1 (CH), 128.3 (CH), 128.4 (CH), 136.9 (C), 137.1 (C), 201.0 (C); FAB-MS: m/z= 561 (M+Na). This oil was used for the next reaction without further purification.

(2*S*,3*S*,4*R*,5*R*,6*R*)-2,3,4,5-Tetrakis(benzyloxy)-6-hydroxycyclohexanone (2a) (entry 10)

EtOAc was removed from the above mixture of **1a** (174 mg, 0.290 mmol) by evaporation with toluene (5 mL×3), and the residue was dissolved in toluene (3 mL). To a suspension of triazolium salt **10** (6.8 mg, 0.015 mmol) in toluene (5.5 mL), a 1% v/v solution of Et_3N in toluene (0.20 mL, 0.015 mmol) was added, and after 30 min, the above solution of **1a** was added (1.5 mL toluene wash×2). After 45 min, the mixture was concentrated under vacuum, and the residue was purified by column chromatography (toluene/EtOAc 40/1 to 20/1) to give the title compound as a colorless oil; yield: 138 mg (88%); $[\alpha]_D^{25}$: −65.1 (c 1.00, $CHCl_3$): IR (neat): ν= 3472, 3032, 2924, 2878, 1736, 1636, 1497, 1458, 1366, 1327, 1211, 1111, 910, 741, 702, 463 cm^{-1}; ^1H NMR (C_6D_6): δ= 3.76 (br s, 1H), 3.86 (dd, J=3.5, 4.0 Hz, 1H), 3.96 (dd, J= 3.0, 9.5 Hz, 1H), 4.02 (t, J=4.0 Hz, 1H), 4.05 (d, J=9.5 Hz, 1H), 4.37 (d, J=12.0 Hz, 1H), 4.43 (d, J=12.0 Hz, 1H), 4.50 (d, J=12.0 Hz, 1H), 4.55 (dd, J=1.5, 3.0 Hz, 1H), 4.76 (br d, J=12.0 Hz, 3H), 4.81 (d, J=11.5 Hz, 1H), 4.95 (d, J= 12.0 Hz, 1H), 7.31–7.34 (m, 4H), 7.27–7.35 (m, 16H); ^{13}C NMR: δ=72.6 (CH_2), 73.4 (CH_2), 73.5 (CH_2), 73.7 (CH_2), 75.0 (CH), 76.5 (CH), 77.7 (CH), 80.3 (CH), 82.3 (CH), 127.6 (CH), 127.72 (CH), 127.74 (CH), 127.8 (CH), 127.9 (CH), 128.29 (CH), 128.32 (CH), 128.35 (CH), 128.40 (CH), 137.5 (C), 137.7 (C), 137.8 (C), 138.3 (C), 205.1 (C); EIMS: m/z=538 (M^+); HR-MS-FAB (m/z): m/z=561.2249 $[M+Na]^+$, calcd. for $C_{34}H_{34}NaO_6$: 561.2253. The stereochemistry was determined based on the *trans*-diaxial coupling (J=9.5 Hz) between 5-H and 6-H (3.96 and 4.05 ppm, respectively) as shown in Figure 2.

(2*S*,3*S*,4*R*,5*R*,6*R*)-2,3,4,5-Tetrakis(benzyloxy)-6-hydroxycyclohexanone (2a) (entry 11)

To a solution of DMSO (2.2 mL, 31 mmol) in CH_2Cl_2 (60 mL) cooled at −78 °C, a solution of $(COCl)_2$ (2.5 mL, 29 mmol) in CH_2Cl_2 (20 mL) was added over 20 min. After 2 min, a solution of 2,3,4,5-tetra-*O*-benzyl-D-mannitol (6.0 g, 11 mmol) in CH_2Cl_2 (20 mL+10 mL wash) was added over 30 min. After 1.5 h, Et_3N (10 mL, 72 mmol) was added, and the mixture was stirred for additional 15 min before the cooling bath was removed. The mixture was allowed to warm to room temperature and evaporated. The resulting white solids were suspended in a 1:1 mixture of pentane and EtOAc (20 mL), filtered, and washed with the mixed solvent (5 mL×2). The combined filtrate was concentrated under vacuum to give a mixture of **1a** and DMSO as an orange oil. The oil was dissolved in toluene (240 mL) and added to a premixed suspension of triazolium salt **10** (240 mg, 0.51 mmol) and Et_3N (80 μL, 0.58 mmol) in toluene (200 mL). After 1 h, the mixture was evaporated, and the residue was purified by column chromatography (hexane/EtOAc 3/1) to give the title compound as a pale yellow oil; yield: 5.4 g (90%).

2,3,4,5-Tetra-*O*-benzyl-L-*ido*-hexodialdose (1b; Scheme 2)

The same procedure as **1a** using 2,3,4,5-tetra-*O*-benzyl-L-iditol[36] (331 mg, 0.611 mmol) in place of 2,3,4,5-tetra-*O*-benzyl-D-mannitol gave a 71:29 mixture of the title compound, and DMSO as yellow oil; yield: 349 mg (quant.). ^1H and ^{13}C NMR were identical to those reported.[37] This oil was used for the next reaction, without further purification.

(2*R*,3*S*,4*R*,5*S*,6*S*)-2,3,4,5-Tetrakis(benzyloxy)-6-hydroxycyclohexanone (2b)

To a suspension of triazolium salt *ent*-**10** (14 mg, 30 μmol) in toluene (6 mL), a 10% v/v solution of Et_3N in toluene (41 μL, 29 μmol) was added at room temperature. After 30 min, **1b**[37] (160 mg, 0.297 mmol) in toluene (3 mL+1.5 mL wash×2) was added. After 18 h, the mixture was concentrated under vacuum. The residue was purified by column chromatography (toluene/EtOAc 19/1) to give the title compound as a white solid; yield: 137 mg (86%); mp 159–161 °C (decomp); $[\alpha]_D^{25}$: +24.4 (c 1.00, $CHCl_3$). IR (KBr): ν=3435, 1730 cm^{-1}; ^1H NMR: δ=3.42 (t, J=9.5 Hz, 1H), 3.47 (d, J=4.5 Hz, 1H), 3.65 (t, J=9.5 Hz, 1H), 3.89 (t, J=9.5 Hz, 1H), 4.30 (dd, J=2.0, 9.5 Hz, 1H), 4.37 (ddd, J=2.0, 4.5, 9.5 Hz, 1H), 4.58 (d, J=11.5 Hz, 1H), 4.790 (d, J=11.0 Hz, 1H), 4.794 (d, J=11.0 Hz, 1H), 4.86–4.91 (m, 3H), 4.91 (d, J=11.5 Hz, 1H), 4.96 (d, J=11.0 Hz, 1H), 7.20–7.40 (m, 20H); ^{13}C NMR: δ=73.5 (CH_2), 75.4 (CH_2), 76.1 (CH_2), 77.3 (CH), 81.4 (CH), 81.7 (CH), 83.2 (CH), 83.6 (CH), 127.7 (CH), 127.78 (CH), 127.80 (CH), 127.9 (CH), 128.0 (CH), 128.09 (CH), 128.13 (CH), 128.4 (CH), 128.5 (CH), 137.0 (C), 137.9 (C), 138.0 (C), 138.1 (C), 204.1 (C). IR, and ^1H and ^{13}C NMR data were in good agreement with those reported.[38]

3,4-*O*-Isopropylidene-2,5-bis-*O*-triisopropylsilyl-D-*manno*-hexodialdose (11a; Table 2)

To a solution of DMSO (0.19 mL, 2.3 mmol) in CH_2Cl_2 (4 mL) cooled at −78 °C, a solution of $(COCl)_2$ (0.21 mL, 2.5 mmol) in CH_2Cl_2 (2 mL+1 mL wash) was added. The resulting mixture was stirred for 2 min before a solution of 3,4-*O*-isopropylidene-2,5-bis-*O*-triisopropylsilyl-D-mannitol[12c] (535 mg, 1.00 mmol) in CH_2Cl_2 (3 mL+0.5 mL wash×2) was added over 5 min. After 1.5 h, Et_3N (1.4 mL, 10 mmol) was added, and the mixture was stirred for addi-

tional 10 min. After addition of pentane (20 mL), the cooling bath was removed, and the mixture was allowed to warm to room temperature. The resulting suspension was filtered, and the filtered solids were washed with a 1:1 mixture of pentane and EtOAc (20 mL×2). The volume of combined filtrate was reduced to *ca.* 10 mL by evaporation, and the resulting suspension was further diluted with pentane (10 mL). The whole was filtered, and the filtered solids were washed with the mixed solvent (10 mL×2). The combined filtrate was concentrated under vacuum to give a 63:30:6 mixture of the title compound, EtOAc, and DMSO as a yellow oil; yield: 570 mg (98%). IR (neat): ν=2943, 2866, 1736, 1466, 1381, 1238, 1219, 1153, 1107, 1072, 1045, 1015, 999, 883, 760 cm^{-1}; ^{1}H NMR: δ=1.00–1.20 (m, 42H), 1.35 (s, 6H), 4.21 (br s, 2H), 4.42 (br s, 2H), 9.68 (d, J=1.5 Hz, 2H); ^{13}C NMR: δ=12.2 (CH), 17.8 (CH_3), 26.9 (CH_3), 76.9 (CH), 77.8 (CH), 109.8 (C), 202.7 (CH); HR-MS-ESI: m/z=553.3352 $[M+Na]^+$, calcd. for $C_{27}H_{54}NaO_6Si_2$, 553.3351. This oil was used for the next reaction without further purification.

2,5-Di-*O*-Benzyl-3,4-*O*-isopropylidene-D-*manno*-hexodialdose (11b)[12c]

To a solution of $(COCl)_2$ (0.26 mL, 3.0 mmol) in THF (3.5 mL) cooled at −19 °C, was added a 1 M solution of DMSO in THF (3.1 mL, 3.1 mmol) at such a rate that the temperature did not rise above −18 °C. After 2 min, the mixture was cooled at −78 °C and stirred for additional 10 min. A solution of 2,5-di-*O*-benzyl-3,4-*O*-isopropylidene-D-mannitol[12c] (402 mg, 1.00 mmol) in THF (7 mL+1 mL wash) was added over 5 min. After 30 min, Et_3N (1.4 mL, 10 mmol) was added. After 10 min, the cooling bath was removed, and the mixture was allowed to warm to room temperature. After addition of pentane (10 mL), the resulting suspension was filtered, and the filtered solids were washed with a 1:1 mixture of pentane and EtOAc (15 mL×2). The volume of the combined filtrate was reduced by evaporation to *ca.* 10 mL, and the resulting suspension was further diluted with pentane (5 mL) and filtered. The filtered solids were washed with the mixed solvent (15 mL×2). Concentration of the filtrate gave a 39:31:30 mixture of the title compound, DMSO, and EtOAc as a yellow oil; yield: 510 mg (97%). IR (neat): ν=3256, 3090, 3063, 3032, 2986, 2932, 2874, 2723, 1736, 1454, 1381, 1138, 1084, 1026, 914, 868, 810, 748 cm^{-1}; ^{1}H NMR: δ=1.36 (s, 6H), 3.87 (dd, J=2.0, 3.0 Hz, 1H), 3.88 (dd, J=2.0, 3.0 Hz, 1H), 4.33 (d, J=3.0 Hz, 1H), 4.34 (d, J=3.0 Hz, 1H), 4.57 (d, J=12.0 Hz, 2H), 4.64 (d, J=12.0 Hz, 2H), 7.27–7.37 (m, 10H), 9.58 (d, J=2.0 Hz, 2H); ^{13}C NMR: δ=26.6 (CH_3), 73.3 (CH_2), 77.4 (CH), 83.0 (CH), 110.8 (C), 128.4 (CH), 128.6 (CH), 136.5 (C), 201.4 (CH); HR-MS-ESI: m/z=421.1625 $[M+Na]^+$, calcd. for $C_{23}H_{26}NaO_6$: 421.1622. This oil was used for the next reaction without further purification.

2,5-Bis-*O*-*tert*-butyldiphenylsilyl-3,4-*O*-isopropylidene-D-*manno*-hexodialdose (11c)[12c]

The same procedure as **11a** using 3,4-*O*-isopropylidene-2,5-bis-*O*-*tert*-butyldiphenylsilyl-D-mannitol[12c] (1.02 g, 1.46 mmol) in place of 3,4-*O*-isopropylidene-2,5-bis-*O*-triisopropylsilyl-D-mannitol gave a 52:37:11 mixture of the title compound, EtOAc, and DMSO as a pale yellow oil; yield: 1.11 g (98%). IR (neat): ν=3071, 3051, 2959, 2932, 2859, 1740, 1474, 1427, 1381, 1234, 1111, 1076, 999, 822, 760, 741 cm^{-1}; ^{1}H NMR: δ=1.07 (s, 18H), 1.30 (s, 6H), 3.75 (br s, 2H), 4.27 (br s, 2H), 7.25–7.39 (m, 12H), 7.54–7.60 (m, 8H), 9.25 (s, 2H); ^{13}C NMR: δ=14.2 (C), 26.8 (CH_3), 76.1 (CH), 78.5 (CH), 110.1 (C), 127.8 (CH), 127.9 (CH), 130.0 (CH), 130.2 (CH), 132.27 (C), 132.28 (C), 135.75 (CH), 135.77 (CH), 202.0 (CH); HR-MS-ESI: m/z=717.3028 $[M+Na]^+$, calcd. for $C_{41}H_{50}NaO_6Si_2$: 717.3038. The oil was used for the next reaction without further purification.

(2*S*,3*S*,4*R*,5*R*,6*S*)- and (2*S*,3*S*,4*R*,5*R*,6*R*)-3,4-Isopropylidenedioxy-2,5-bis(triisopropylsiloxy)-6-hydroxycyclohexanone (12a and *epi*-12a) (entry 3)

EtOAc was removed from the above mixture of **11a** (212 mg, 0.365 mmol) by evaporation with toluene (5 mL×3), and the residue was dissolved in toluene (6.5 mL). To a suspension of triazolium salt **9c** (13 mg, 37 μmol) in toluene (7 mL), a 1% v/v solution of Et_3N in toluene (0.51 mL, 37 μmol) was added, and after 30 min, the above solution of **11a** was added (2 mL toluene wash). After 24 h, the mixture was concentrated under vacuum to give a crude product. The yield (53%) and diastereomeric ratio (74:26) of the title compounds, and the recovery yield of **11a** (31%) were determined by area integration of the ^{1}H NMR signals at 4.75 (**12a**), 4.13 (*epi*-**12a**), and 9.67 (**11a**) ppm with Ph_3CH (5.55 ppm) as an internal standard. The diastereomers were separated by column chromatography (toluene/hexane 5:1) to give **12a** as a pale yellow solid; mp 48–50 °C; $[\alpha]_D^{25}$: +6.2 (*c* 1.0, $CHCl_3$) and *epi*-**12a** as a pale yellow oil, containing *ca.* 10% unidentified impurity. The stereochemistry was tentatively assigned by analogy with that of **12c**.

12a: IR (KBr): ν=3510, 2943, 2866, 1736, 1466, 1381, 1369, 1227, 1165, 1138, 1069, 1049, 1018, 883, 864, 849, 822, 799 cm^{-1}; ^{1}H NMR: δ=1.00–1.20 (m, 42H), 1.44 (s, 3H), 1.46 (s, 3H), 3.17 (br d, J=7.0 Hz, 1H), 3.98 (dd, J=2.5, 9.5 Hz, 1H), 4.45 (dd, J=2.0, 9.5 Hz, 1H), 4.65 (d, J=2.5 Hz, 1H), 4.67 (dd, J=3.0, 7.0 Hz, 1H), 4.75 (dd, J=2.0, 3.0 Hz, 1H); ^{13}C NMR: δ=11.9 (CH), 12.6 (CH), 17.6 (CH_3), 17.7 (CH_3), 17.9 (CH_3), 18.0 (CH_3), 26.8 (CH_3), 27.1 (CH_3), 70.2 (CH), 73.7 (CH), 73.8 (CH), 74.2 (CH), 75.4 (CH), 112.5 (C), 207.2 (C); HR-MS-ESI: m/z=553.3351 $[M+Na]^+$, calcd. for $C_{27}H_{54}NaO_6Si_2$: 553.3351.

epi-**12a:** IR (neat): ν=3507, 2943, 2870, 1736, 1466, 1381, 1227, 1134, 1057, 1042, 1015, 883, 853, 826, 760 cm^{-1}; ^{1}H NMR: δ=1.00–1.20 (m, 42H), 1.44 (s, 3H), 1.47 (s, 3H), 3.68 (d, J=8.5 Hz, 1H), 4.00 (ddd, J=1.0, 3.0, 8.5 Hz, 1H), 4.13 (dd, J=3.0, 10.0 Hz, 1H), 4.45 (d, J=3.0, 10.0 Hz, 1H), 4.49 (t, J=3.0 Hz, 1H), 4.66 (dd, J=1.0, 3.0 Hz, 1H); ^{13}C NMR: δ=12.0 (CH), 12.2 (CH), 17.5 (CH_3), 17.65 (CH_3), 17.68 (CH_3), 17.8 (CH_3), 26.9 (CH_3), 27.1 (CH_3), 70.6 (CH), 73.3 (CH), 74.3 (CH), 77.5 (CH), 80.5 (CH), 112.1 (C), 203.7 (C); HR-MS-ESI: m/z=553.3351 $[M+Na]^+$, calcd. for $C_{27}H_{54}NaO_6Si_2$: 553.3351.

(2*S*,3*S*,4*R*,5*R*,6*S*)- and (2*S*,3*S*,4*R*,5*R*,6*R*)-2,5-Bis(benzyloxy)-3,4-isopropylidenedioxy-6-hydroxycyclohexanone (12b and *epi*-12b) (entry 4)

EtOAc was removed from the above mixture of **11b** (148 mg, 0.280 mmol) by evaporation with toluene (5 mL × 3), and the residue was dissolved in toluene (3.5 mL). To a suspension of triazolium salt **9c** (10 mg, 28 μmol) in toluene (5 mL), a 1% v/v solution of Et_3N in toluene (0.39 mL, 28 μmol) was added, and after 30 min, the above solution of **11b** was added (1 mL toluene wash). After 24 h, the mixture was concentrated under vacuum to give a crude product. The yield (30%) and diastereomeric ratio (57:43) of the title compounds, and the recovery yield of **11b** (3%) were determined by area integration of the ^{1}H NMR signals at 4.14 (**12b**), 4.26–4.33 (*epi*-**12b**, 2H), and 9.58 (**11b**) ppm with Ph_3CH (5.55 ppm) as an internal standard. The diastereomers were separated by column chromatography (hexane/EtOAc 8/1 to 4/1). The stereochemistry was tentatively assigned by analogy with that of **12c**.

12b: colorless oil; $[\alpha]_D^{20}$: −4.8 (*c* 1.4, $CHCl_3$); IR (neat): ν = 3464, 3090, 3063, 3032, 2986, 2932, 2874, 1736, 1497, 1454, 1381, 1346, 1231, 1169, 1126, 1069, 1057, 1026, 972, 910, 849, 802, 741 cm^{-1}; ^{1}H NMR: δ = 1.49 (s, 3H), 1.54 (s, 3H), 3.12 (br s, 1H), 4.14 (dd, *J* = 2.5, 10.0 Hz, 1H), 4.38 (d, *J* = 2.5 Hz, 1H), 4.41 (dd, *J* = 2.0, 4.0 Hz, 1H), 4.55 (dd, *J* = 2.0, 10.0 Hz, 1H), 4.57 (d, *J* = 11.5 Hz, 1H), 4.60 (br d, *J* = 4.0 Hz, 1H), 4.69 (d, *J* = 12.5 Hz, 1H), 4.72 (d, *J* = 12.5 Hz, 1H), 4.87 (d, *J* = 11.5 Hz, 1H), 7.27–7.38 (m, 10H); ^{13}C NMR (C_6D_6): δ = 26.8 (CH_3), 26.9 (CH_3), 73.0 (CH_2), 74.1 (CH), 74.50 (CH_2), 74.54 (CH), 75.5 (CH), 75.6 (CH), 80.0 (CH), 112.4 (C), 127.76 (CH), 127.78 (CH), 127.9 (CH), 128.52 (CH), 128.53 (CH), 128.6 (CH), 137.5 (C), 138.7 (C), 205.7 (C); HR-MS-ESI: *m*/*z* = 421.1622 $[M+Na]^+$, calcd. for $C_{23}H_{26}NaO_6$: 421.1622.

epi-**12b:** white solid; mp 121–124 °C; $[\alpha]_D^{20}$: +11.5 (*c* 1.82, $CHCl_3$); IR (neat): ν = 3329, 3090, 3063, 3028, 2982, 2932, 2909, 2882, 1744, 1497, 1454, 1396, 1381, 1242, 1219, 1180, 1150, 1123, 1096, 1049, 1022, 968, 914, 976, 845, 795, 752, 733 cm^{-1}; ^{1}H NMR: δ = 1.50 (s, 3H), 1.52 (s, 3H), 3.40 (br d, *J* = 6.5 Hz, 1H), 3.97 (dt, *J* = 8.0, 1.5 Hz, 1H), 4.20 (br m, 1H), 4.26–4.33 (m, 2H), 4.40 (dd, *J* = 1.5, 4.0 Hz, 1H), 4.73 (d, *J* = 11.5 Hz, 1H), 4.74 (d, *J* = 11.5 Hz, 1H), 4.86 (d, *J* = 11.5 Hz, 1H), 4.88 (d, *J* = 11.5 Hz, 1H), 7.27–7.37 (m, 8H), 7.43 (d, *J* = 7.5 Hz, 2H); ^{13}C NMR (C_6D_6): δ = 26.5 (CH_3), 27.2 (CH_3), 72.3 (CH_2), 74.3 (CH_2), 74.8 (CH), 75.7 (CH), 76.8 (CH), 77.0 (CH), 81.8 (CH), 112.6 (C), 127.68 (CH), 127.74 (CH), 127.9 (CH), 128.0 (CH), 128.5 (CH), 128.6 (CH), 138.3 (C), 138.5 (C), 205.2 (C); HR-MS-ESI: *m*/*z* = 421.1622 $[M+Na]^+$, calcd. for $C_{23}H_{26}NaO_6$: 421.1622.

(2*S*,3*S*,4*R*,5*R*,6*S*)-2,5-Bis(*tert*-butyldiphenylsiloxy)-3,4-isopropylidenedioxy-6-hydroxycyclohexanone (12c) (entry 6)

EtOAc was removed from the above mixture of **11c** (367 mg, 0.474 mmol) by evaporation with toluene (5 mL × 2), and the residue was dissolved in toluene (7.5 mL). To a suspension of triazolium salt **9c** (34 mg, 95 μmol) in toluene (9.5 mL), a 10% v/v solution of Et_3N in toluene (0.13 mL, 95 μmol) was added, and after 30 min, the above solution of **11c** was added (1 mL toluene wash × 2). After 24 h, the mixture was concentrated under vacuum to give a crude product as a yellow oil; yield: 469 mg. The yield was estimated to be 57% by area integration of the ^{1}H NMR signals at 4.57–4.66 (4H) with Ph_3CH (5.55 ppm) as an internal standard. The above oil was purified by column chromatography (DIOL silica gel, hexane to hexane/EtOAc 98:2) to give **12c** as a white solid; yield: 181 mg (55%); mp 156–157 °C; $[\alpha]_D^{25}$: +12.6 (*c* 3.03, $CHCl_3$); IR (neat): ν = 3510, 3071, 3051, 2954, 2932, 2893, 2859, 1732, 1589, 1470, 1427, 1369, 1227, 1169, 1130, 1111, 1068, 1049, 968, 937, 864, 821, 799, 753, 741, 702 cm^{-1}; ^{1}H NMR: δ = 1.02 (s, 9H), 1.04 (s, 9H), 1.46 (s, 3H), 1.51 (s, 3H), 2.72 (d, *J* = 7.5 Hz, 1H), 4.12 (dd, *J* = 8.5, 10.0 Hz, 1H), 4.59 (dd, *J* = 1.5, 10.0 Hz, 1H), 4.62–4.65 (m, 2H), 4.66 (d, *J* = 2.5 Hz, 1H), 7.30–7.46 (m, 12H), 7.50 (m, 2H), 7.53 (m, 2H), 7.70 (m, 2H), 7.77 (m, 2H); ^{1}H NMR (C_6D_6): δ = 1.09 (s, 9H), 1.18 (s, 9H), 1.41 (s, 3H), 1.45 (s, 3H), 3.02 (d, *J* = 7.0 Hz, 1H), 4.08 (dd, *J* = 2.5, 10.0 Hz, 1H), 4.34 (dd, *J* = 1.0, 10.0 Hz, 1H), 4.67 (d, *J* = 3.5, 7.0 Hz, 1H), 4.60 (dd, *J* = 1.0, 3.5 Hz, 1H), 4.73 (d, *J* = 2.5 Hz, 1H), 7.13–7.28 (m, 12H), 7.61–7.69 (m, 4H), 7.77–7.83 (m, 2H), 7.94–7.99 (m, 2H); ^{13}C NMR: δ = 19.3 (C), 19.6 (C), 26.75 (CH_3), 26.84 (CH_3), 26.9 (CH_3), 27.1 (CH_3), 70.8 (CH), 73.6 (CH), 73.9 (CH), 74.6 (CH), 75.7 (CH), 112.8 (C), 127.48 (CH), 127.52 (CH), 127.7 (CH), 127.8 (CH), 129.5 (CH), 129.9 (CH), 130.0 (CH), 130.2 (CH), 131.9 (C), 132.0 (C), 132.1 (C), 134.1 (C), 135.7 (CH), 135.9 (CH), 136.7 (CH), 206.1 (C); HR-MS-FAB: *m*/*z* = 717.3033 $[M+Na]^+$, calcd. for $C_{41}H_{50}NaO_6Si_2$: 717.3038. The relative configuration was determined by 2% nOe between 4-H and 6-H (4.34 and 4.67 ppm in C_6D_6, respectively) as shown in Figure 2.

(2*S*,3*S*,4*S*,5*S*,6*R*)-2,3,4,5-Tetrakis(benzyloxy)-6-(*tert*-butyldiphenylsiloxy)cyclohexanone (2c; Table 3)

To a solution of **2a** (108 mg, 0.201 mmol), imidazole (27 mg, 0.40 mmol), and DMAP (5 mg, 0.4 mmol) in DMF (0.4 mL) was added TBDPSCl (62 μL, 0.24 mmol) at room temperature. After 8.5 h, TBDPSCl (41 μL, 0.16 mmol) was added. After 2.5 h, water (1 mL) was added, and the whole was extracted with toluene (8 mL × 3). The combined organic layers were washed three times with water and with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by column chromatography (toluene/hexane 3:1 and then hexane/EtOAc 9:1) to give a colorless oil. The oil was dissolved in EtOAc (2 mL), and washed with saturated aqueous $NaHCO_3$ (2 mL). The aqueous layer was extracted with EtOAc, and the combined organic layers were dried over Na_2SO_4 and evaporated under reduced pressure to yield the title compound as a colorless oil; yield: 94 mg (60%); $[\alpha]_D^{25}$: −58.6 (*c* 1.35, $CHCl_3$); IR (neat): ν = 3067, 3028, 2932, 2859, 1748, 1497, 1454, 1427, 1389, 1362, 1215, 1161, 1111, 1080, 1049, 822, 756 cm^{-1}; ^{1}H NMR: δ = 1.18 (s, 9H), 3.74 (dd, *J* = 3.0, 4.0 Hz, 1H), 3.79 (dd, *J* = 3.0, 4.0 Hz, 1H), 3.84 (d, *J* = 12.0 Hz, 1H), 3.91 (dd, *J* = 3.0, 10.0 Hz, 1H), 4.08 (d, *J* = 3.0 Hz, 1H), 4.37 (d, *J* = 12.5 Hz, 1H), 4.43 (d, *J* = 11.5 Hz, 1H), 4.45 (d, *J* = 11.5 Hz, 1H), 4.56 (d, *J* = 11.5 Hz, 1H), 4.67 (d, *J* = 12.0 Hz, 1H), 4.69 (d, *J* = 12.5 Hz, 1H), 4.74 (d, *J* = 10.0 Hz, 1H), 4.79 (d, *J* = 11.5 Hz, 1H), 7.04–7.14 (m, 6H), 7.21–7.38 (m, 20H), 7.72–7.75 (m, 4H); ^{13}C NMR: δ = 19.6 (C), 27.2 (CH_3), 72.0 (CH_2), 73.3 (CH_2), 73.6 (CH_2), 73.9 (CH_2), 75.3 (CH), 77.6

(CH), 78.0 (CH), 80.5 (CH), 82.2 (CH), 127.2 (CH), 127.5 (CH), 127.57 (CH), 127.59 (CH), 127.64 (CH), 127.7 (CH), 128.0 (CH), 128.2 (CH), 128.3 (CH), 129.3 (CH), 129.4 (CH), 133.8 (C), 134.2 (C), 136.1 (CH), 136.6 (CH), 137.8 (C), 138.0 (C), 138.2 (C), 138.3 (C), 201.9 (C); FAB-MS: $m/z = 799$ (M+Na), 91 (Bn); HR-MS-FAB: $m/z = 799.3431$ $[M+Na]^+$, calcd. for $C_{50}H_{52}NaO_6Si$: 799.3426.

(2*S*,3*S*,4*S*,5*S*,6*R*)-2,3,4,5-Tetrakis(benzyloxy)-6-(*tert*-butyldimethylsiloxy)cyclohexanone (2d)

To a solution of **2a** (106 mg, 0.197 mmol) and imidazole (74 mg, 1.1 mmol) in DMF (1 mL) was added TBDMSCl (50 mg, 0.33 mmol) at room temperature. After 4 h, TBDMSCl (50 mg, 0.33 mmol) was added, and the mixture was stirred for 11 h. After addition of water (1 mL), the whole was extracted with toluene. The organic layer was washed with water three times and with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by column chromatography (hexane/EtOAc 15:1) to yield the title compound as a yellow oil; yield: 118 mg (92%); $[\alpha]_D^{25}$: −24.1 (*c* 1.20, $CHCl_3$); IR (neat): $\nu = 3088$, 3063, 3030, 2951, 2928, 2857, 1746, 1497, 1454, 1389, 1362, 1254, 1207, 1155, 1101, 1051, 1028, 837, 781, 737 cm^{-1}; ^1H NMR: $\delta = 0.05$ (s, 3H), 0.17 (s, 3H), 0.96 (s, 9H), 3.70 (dd, $J = 3.0$, 4.0 Hz, 1H), 3.83 (dd, $J = 3.0$, 9.5 Hz, 1H), 3.85 (dd, $J = 3.0$, 4.0 Hz, 1H), 4.37 (d, $J = 12.5$ Hz, 1H), 4.40 (d, $J = 12.5$ Hz, 1H), 4.42 (dd, $J = 1.0$, 3.0 Hz, 1H), 4.47 (d, $J = 12.0$ Hz, 1H), 4.51 (d, $J = 12.0$ Hz, 1H), 4.56 (d, $J = 1.0$, 9.5 Hz, 1H), 4.64 (d, $J = 12.5$ Hz, 1H), 4.75 (d, $J = 12.5$ Hz, 1H), 4.80 (d, $J = 12.0$ Hz, 1H), 4.85 (d, $J = 12.0$ Hz, 1H), 7.07–7.15 (m, 4H), 7.23–7.35 (m, 16H); ^{13}C NMR: $\delta = -5.2$ (CH_3), −4.7 (CH_3), 18.6 (C), 25.8 (CH_3), 72.4 (CH_2), 73.2 (CH_2), 73.7 (CH_2), 74.0 (CH_2), 75.4 (CH), 77.5 (CH), 78.0 (CH), 80.6 (CH), 81.8 (CH), 127.55 (CH), 127.63 (CH), 127.67 (CH), 127.71 (CH), 127.8 (CH), 127.9 (CH), 128.2 (CH), 128.27 (CH), 128.33 (CH), 128.34 (CH), 137.9 (C), 138.00 (C), 138.04 (C), 138.5 (C), 203.0 (C); FAB-MS: $m/z = 675$ (M+Na), 91 (Bn); HR-MS-FAB: $m/z = 675.3118$ $[M+Na]^+$, calcd. for $C_{40}H_{48}NaO_6Si$: 675.3113.

(2*S*,3*S*,4*S*,5*S*,6*R*)-2,3,4,5-Tetrakis(benzyloxy)-6-(triethylsiloxy)cyclohexanone (2e)

To a solution of **2a** (237 mg, 0.440 mmol) and pyridine (0.14 mL, 1.8 mmol) in CH_2Cl_2 (0.8 mL), was added TESOTf (0.20 mL, 0.88 mmol) at −78 °C. After 2 h, saturated aqueous $NaHCO_3$ (2 mL) was added, and the organic layer was separated. The aqueous layer was extracted with toluene (2 mL × 5). The combined organic layers were washed with water (10 mL × 5) and brine (10 mL), dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by column chromatography (hexane/EtOAc 96:4) to yield the title compound as a colorless oil; yield: 246 mg (86%); $[\alpha]_D^{20}$: −37.2 (*c* 0.445, $CHCl_3$); IR (neat): $\nu = 3086$, 3063, 3032, 2955, 2936, 2913, 2874, 1748, 1454, 1385, 1362, 1238, 1207, 1157, 1111, 1084, 1053, 1026, 914, 814, 737 cm^{-1}; ^1H NMR: $\delta = 0.58$–0.78 (m, 6H), 0.99 (t, $J = 8.0$ Hz, 9H), 3.71 (dd, $J = 3.0$, 4.0 Hz, 1H), 3.82 (dd, $J = 3.0$, 9.5 Hz, 1H), 3.86 (dd, $J = 3.0$, 4.0 Hz, 1H), 4.37 (d, $J = 12.0$ Hz, 1H), 4.41 (d, $J = 12.0$ Hz, 1H), 4.43 (dd, $J = 1.0$, 3.0 Hz, 1H), 4.48 (d, $J = 12.0$ Hz, 1H), 4.52 (d, $J = 12.0$ Hz, 1H), 4.59 (dd, $J = 1.0$, 9.5 Hz, 1H), 4.65 (d, $J = 12.0$ Hz, 1H), 4.76 (d, $J = 12.0$ Hz, 1H), 4.81 (d, $J = 12.0$ Hz, 1H), 4.86 (d, $J = 12.0$ Hz, 1H), 7.06–7.16 (m, 4H), 7.23–7.35 (m, 16H); ^{13}C NMR: $\delta = 4.9$ (CH_2), 6.8 (CH_3), 72.4 (CH_2), 73.2 (CH_2), 73.7 (CH_2), 74.0 (CH_2), 75.4 (CH), 77.5 (CH), 77.9 (CH), 80.6 (CH), 81.9 (CH), 127.5 (CH), 127.68 (CH), 127.69 (CH), 127.72 (CH), 127.8 (CH), 128.18 (CH), 128.24 (CH), 128.3 (CH), 137.9 (C), 138.0 (C), 138.1 (C), 138.6 (C), 203.1 (C); FAB-MS: $m/z = 675$ (M+Na), 91 (Bn); HR-MS-ESI: $m/z = 675.3118$ $[M+Na]^+$, calcd. for $C_{40}H_{48}NaO_6Si$: 675.3113.

(2*S*,3*S*,4*S*,5*S*,6*R*)-2,3,4,5-Tetrakis(benzyloxy)-6-(trimethylsiloxy)cyclohexanone (2f)

To a solution of **2a** (87 mg, 0.16 mmol) and Et_3N (90 μL, 0.64 mmol) in CH_2Cl_2 (0.5 mL) was added TMSCl (41 μL, 0.32 mmol) at 0 °C. After 1.5 h, Et_3N (45 μL, 0.32 mmol) and TMSCl (21 μL, 0.16 mmol) were added. After 1.5 h, saturated aqueous $NaHCO_3$ (4 mL) was added, and the organic layer was separated. The aqueous layer was extracted with EtOAc (4 mL × 3). The combined organic layers were washed with water (12 mL) and brine (12 mL), dried over Na_2SO_4, and evaporated to give a crude product as a pale yellow oil. ^1H NMR: $\delta = 0.31$ (s, 9H), 3.87 (dd, $J = 3.0$, 4.0 Hz, 1H), 4.07 (dd, $J = 3.0$, 4.0 Hz, 1H), 4.11 (dd, $J = 3.0$, 9.5 Hz, 1H), 4.21 (d, $J = 12.0$ Hz, 1H), 4.40 (d, $J = 12.0$ Hz, 1H), 4.42 (d, $J = 12.0$ Hz, 1H), 4.45 (d, $J = 12.0$ Hz, 1H), 4.62 (dd, $J = 1.0$, 3.0 Hz, 1H), 4.75 (d, $J = 12.0$ Hz, 1H), 4.76 (d, $J = 12.0$ Hz, 1H), 4.83 (d, $J = 12.0$ Hz, 1H), 4.88 (dd, $J = 1.0$, 9.5 Hz, 1H), 4.92 (d, $J = 12.0$ Hz, 1H), 7.03–7.37 (m, 20H). Remaining EtOAc was removed by evaporation with toluene (5 mL). The resulting pale yellow oil was used in the reduction without purification.

(1*R*,2*S*,3*R*,4*R*,5*R*,6*R*)-3,4,5,6-Tetrakis(benzyloxy)-cyclohexane-1,2-diol (*allo*-3a) (entry 1)

To a solution of **2a** (38 mg, 71 μmol) in MeOH (0.5 mL) was added $NaBH_4$ (4 mg, 0.1 mmol) at 0 °C. After 30 min, saturated aqueous $NaHCO_3$ (1 mL) was added, and the whole was extracted with $CHCl_3$. The organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated under vacuum. The residue was purified by column chromatography (hexane/EtOAc 3:1) to yield the title compound as a colorless solid; yield: 31 mg (81%); mp 96–98 °C; $[\alpha]_D^{20}$: −20.2 (*c* 1.00, $CHCl_3$); IR (neat): $\nu = 3441$, 3063, 3028, 2874, 1497, 1454, 1273, 1092, 1068, 1026, 910 cm^{-1}; ^1H NMR (55 °C): $\delta = 2.67$ (br s, 1H), 3.47 (br s, 1H), 3.86–3.92 (br m, 5H), 4.15 (br s, 1H), 4.50–4.70 (m, 8H), 7.20–7.35 (m, 20H); ^{13}C NMR: $\delta = 73.2$ (CH_2), 77.1 (CH), 78.7 (CH), 127.7 (CH), 127.8 (CH), 127.9 (CH), 128.3 (CH), 128.36 (CH), 128.44 (CH), 128.5 (CH), 137.9 (C), 138.4 (C); HR-MS-ESI: $m/z = 563.2404$ $[M+Na]^+$, calcd. for $C_{34}H_{36}NaO_6$: 563.2405. Recrystallization from hexane/EtOAc provided colorless needles suitable for X-ray crystallographic analysis; monoclinic $P2_1$, $a = 11.3487(9)$ Å, $b = 7.9412(6)$ Å, $c = 16.2792(13)$ Å, $\alpha = 90.0000°$, $\beta = 99.4718(19)°$, $\gamma = 90.0000°$, $Z = 2$, $R_1 = 0.1000$, $wR_2 = 0.1548$; which determined the stereochemistry. CCDC 1009954 contains the supplementary crystallographic data of this compound. These data can be obtained free of

charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

(1*S*,2*S*,3*R*,4*R*,5*R*,6*R*)-3,4,5,6-Tetrakis(benzyloxy)-cyclohexane-1,2-diol (*chiro*-3a) (entry 7)

To a solution of **2a** (174 mg, 0.323 mmol) and pyridine (0.11 mL, 1.3 mmol) in CH_2Cl_2 (0.5 mL) was added TESCl (0.15 mL, 0.65 mmol) at −78 °C. After 2 h, saturated aqueous $NaHCO_3$ (2 mL) was added, and the organic layer was separated. The aqueous layer was extracted with toluene (2 mL × 4), and the combined organic layers were washed with water (8 mL × 5) and brine (8 mL), dried over Na_2SO_4, and evaporated under reduced pressure to give crude *O*-TES inosose **2e** as a yellow oil (yield: 230 mg). After removal of residual EtOAc by evaporation with toluene (5 mL), the crude product was dissolved in toluene (2 mL), and *t*BuNH$_2$·BH$_3$ (73 mg, 0.81 mmol) was added at room temperature. After 30 min, 10% HCl (4 mL) and EtOAc (2 mL) were added, and the mixture was vigorously stirred for 2 h. The aqueous layer was separated and extracted with EtOAc (4 mL × 2). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (12 mL) and brine (12 mL), dried over Na_2SO_4, and concentrated. The *dr* (90:10) was determined by the area integration of the ^{1}H NMR signals at 4.39 (*chiro* 2H) and 3.86–3.93 (*chiro* 2H + *allo* 5H) ppm. The residue was purified by column chromatography (hexane/EtOAc 5:2 to 1:1) to yield the title compound as a colorless oil; yield: 136 mg (78%); $[\alpha]_D^{25}$: +2.0 (*c* 1.0, $CHCl_3$); IR (neat): ν = 3410, 3063, 3028, 2916, 2870, 1493, 1454, 1273, 1096, 1057, 1026, 999, 914 cm^{-1}; ^{1}H NMR (55 °C): δ = 2.52 (br s, 2H), 3.68 (br d, *J* = 7.0 Hz, 2H), 3.74 (br s, 2H), 3.91 (m, 2H), 4.39 (d, *J* = 12.0 Hz, 2H), 4.54 (d, *J* = 12.0 Hz, 2H), 4.60 (d, *J* = 12.0 Hz, 2H), 4.61 (d, *J* = 12.0 Hz, 2H), 7.18–7.19 (m, 4H), 7.25–7.33 (m, 16H); ^{13}C NMR: 72.6 (CH), 72.8 (CH_2), 73.1 (CH_2), 74.3 (CH), 78.2 (CH), 127.70 (CH), 127.72 (CH), 127.8 (CH), 128.0 (CH), 128.3 (CH), 128.4 (CH), 138.16 (C), 138.23 (C); FAB-MS: *m*/*z* = 563 (M + Na); HR-MS-FAB: *m*/*z* = 563.2411 $[M+Na]^+$, calcd. for $C_{34}H_{36}NaO_6$, 563.2404. The stereochemistry was determined after the conversion into D-*chiro*-inositol. *allo*-**3a** (yield: 16 mg, 9%) was also obtained as the less polar product.

(1*R*,2*S*,3*S*,4*R*,5*R*,6*S*)-3,4,5,6-Tetrakis(benzyloxy)-cyclohexane-1,2-diol (*myo*-3b; Scheme 5)

To a solution of **2b** (20 mg, 37 μmol) in THF (1 mL) was added a 1 M solution of L-selectride in THF (74 μL, 74 μmol) at −78 °C. After 30 min, water (1 mL) was added, and the mixture was allowed to warm to room temperature. The whole was extracted with EtOAc (2 mL × 3), and the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography (hexane/EtOAc 2:1) to yield the title compound as a white solid; yield: 18.7 mg (93%); mp 142–143 °C; $[\alpha]_D^{20}$: −22.3 (*c* 1.60, $CHCl_3$); IR (neat): ν = 3588, 3345, 3086, 3063, 3028, 2913, 1497, 1454, 1385, 1358, 1211, 1134, 1088, 1069, 1026, 729 cm^{-1}; ^{1}H NMR: δ = 2.43 (br d, *J* = 4.5 Hz, 1H), 2.52 (br s, 1H), 3.45–3.50 (m, 3H), 3.86 (t, *J* = 9.5 Hz, 1H), 3.97 (t, *J* = 9.5 Hz, 1H), 4.20 (t, *J* = 2.5 Hz, 1H), 4.70 (d, *J* = 11.5 Hz, 1H), 4.71 (d, *J* = 11.5 Hz, 1H), 4.75 (d, *J* = 11.0 Hz, 1H), 4.84 (d, *J* = 11.0 Hz, 1H), 4.85 (d, *J* = 10.5 Hz, 1H), 4.91 (d, *J* = 11.0 Hz, 1H), 4.92 (d, *J* = 10.5 Hz, 1H), 4.95 (d, *J* = 11.0 Hz, 1H), 7.26–7.35 (m, 20H); ^{13}C NMR: δ = 69.1 (CH), 71.7 (CH), 72.7 (CH_2), 75.6 (CH_2), 75.7 (CH_2), 75.9 (CH_2), 80.0 (CH), 81.3 (CH), 81.6 (CH), 83.2 (CH), 127.6 (CH), 127.8 (CH), 127.88 (CH), 127.93 (CH), 128.0 (CH), 128.36 (CH), 128.39 (CH), 128.5 (CH), 128.6 (CH), 137.7 (C), 138.5 (C), 138.6 (C); HR-MS-ESI: *m*/*z* = 563.2404 $[M+Na]^+$, calcd. for $C_{34}H_{36}NaO_6$: 563.2404. The melting point, specific rotation, and ^{1}H and ^{13}C NMR were in good agreement with those reported {mp 140–142 °C; $[\alpha]_D^{20}$: −25 (*c* 2.7, $CHCl_3$)}.[39]

(1*R*,2*R*,3*S*,4*R*,5*R*,6*S*)-3,4,5,6-Tetrakis(benzyloxy)-cyclohexane-1,2-diol (*scyllo*-3b)

To a solution of **2b** (38 mg, 70 μmol) and imidazole (24 mg, 0.35 mmol) in DMF (0.2 mL) cooled in an ice-water bath, was added TESCl (29 μL, 0.17 mmol). After removal of the cooling bath, the mixture was stirred for 2 h, and water (1 mL) was added to the mixture. The whole was extracted with Et_2O (1 mL × 3), and the combined organic layers were washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by column chromatography (hexane/EtOAc 14:1) to yield *O*-TES inosose as a white solid; yield: 42.4 mg (93%); mp 89–91 °C; $[\alpha]_D^{20}$: −40 (*c* 0.06, $CHCl_3$); IR (KBr): ν = 3032, 2955, 2920, 2878, 1736, 1458, 1408, 1385, 1366, 1261, 1238, 1211, 1134, 1069, 1026, 814, 737 cm^{-1}; ^{1}H NMR: δ = 0.59–0.70 (m, 6H), 0.96 (t, *J* = 8.0 Hz, 9H), 3.48 (t, *J* = 10.0 Hz, 1H), 3.61 (t, *J* = 10.0 Hz, 1H), 3.84 (t, *J* = 10.0 Hz, 1H), 4.14 (dd, *J* = 1.5, 10.0 Hz, 1H), 4.34 (dd, *J* = 1.5, 10.0 Hz, 1H), 4.55 (d, *J* = 11.0 Hz, 1H), 4.76 (d, *J* = 11.0 Hz, 1H), 4.77 (d, *J* = 11.0 Hz, 1H), 4.84 (d, *J* = 11.0 Hz, 1H), 4.87 (d, *J* = 11.0 Hz, 1H), 4.89 (d, *J* = 11.0 Hz, 1H), 4.91 (d, *J* = 11.0 Hz, 1H), 4.92 (d, *J* = 11.0 Hz, 1H), 7.18–7.22 (m, 2H), 7.25–7.33 (m, 16H), 7.35–7.39 (m, 2H); ^{13}C NMR: δ = 4.9 (CH_2), 6.8 (CH_3), 73.2 (CH_2), 75.9 (CH_2), 75.97 (CH_2), 76.04 (CH_2), 78.7 (CH), 81.6 (CH), 82.2 (CH), 82.8 (CH), 83.3 (CH), 127.57 (CH), 127.62 (CH), 127.7 (CH), 127.81 (CH), 127.83 (CH), 127.9 (CH), 128.0 (CH), 128.1 (CH), 128.26 (CH), 128.31 (CH), 128.34 (CH), 128.4 (CH), 137.3 (C), 138.2 (C), 138.3 (C), 202.5 (C); FAB-MS: *m*/*z* = 675 (M + Na), 91 (Bn); HR-MS-ESI: *m*/*z* = 675.3112 $[M+Na]^+$, calcd. for $C_{40}H_{48}NaO_6Si$: 675.3113.

To a solution of the above solid (24.5 mg, 37.5 μmol) in toluene (0.25 mL) was added *t*-BuNH$_2$·BH$_3$ (8 mg, 0.09 mmol) at room temperature. After 1 h, 10% HCl (2 mL) and THF (2 mL) were added, and the mixture was vigorously stirred for 15 min. The volume of the mixture was reduced to *ca.* 2 mL by evaporation, and the mixture was extracted with EtOAc. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography (hexane/EtOAc 2:1) to yield the title compound as a white solid; yield: 16.3 mg (80%); mp 120–123 °C; $[\alpha]_D^{20}$: −4 (*c* 0.1, $CHCl_3$); IR (KBr): ν = 3372, 3275, 3063, 3005, 2913, 1454, 1400, 1385, 1354, 1261, 1126, 1088, 1069, 1053, 1022, 802, 748 cm^{-1}; ^{1}H NMR: δ = 2.53 (br s, 2H), 3.43 (br m, 2H), 3.49 (br m, 2H), 3.58 (br m, 2H), 4.78 (d, *J* = 11.0 Hz, 2H), 4.88 (s, 4H), 4.92 (d, *J* = 11.0 Hz, 2H), 7.26–7.33 (m, 20H); ^{13}C NMR: δ = 73.8 (CH), 75.5 (CH_2), 75.9 (CH_2), 82.3 (CH), 83.1 (CH), 127.7 (CH), 127.8

(CH), 127.89 (CH), 127.94 (CH), 128.4 (CH), 128.6 (CH), 138.3 (C), 138.4 (C); HR-MS-ESI: $m/z = 563.2404$ $[M+Na]^+$, calcd. for $C_{34}H_{36}NaO_6$: 563.2404. ^1H and ^{13}C NMR were in good agreement with those reported.[12a,40]

(1*R*,2*S*,3*R*,4*S*,5*S*,6*R*)-3,6-Bis(*tert*-butyldiphenylsiloxy)-4,5-(isopropylidenedioxy)cyclohexane-1,2-diol (*allo*-13c; Scheme 6)

To a solution of **12c** (20 mg, 29 μmol) in THF (0.5 mL) cooled in an ice-water bath, was added a 1 M solution of BH_3·THF in THF (60 μL, 60 μmol). After 7 h, another portion of a 1 M solution of BH_3·THF in THF (15 μL, 15 μmol) was added. After 1.5 h, water (2 mL) was added, and the whole was extracted with EtOAc (2 mL × 3). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated. The borane-derived impurities were removed by column chromatography (hexane/EtOAc 19:1) to yield a mixture of the title compound with *neo*-**13c** as a colorless oil (yield: 19 mg, 93%); $[\alpha]_D^{20}$: −20 (*c* 0.74, $CHCl_3$); IR (neat): $\nu = 3549$, 3530, 3071, 3051, 2959, 2897, 1474, 1427, 1381, 1369, 1227, 1142, 1111, 1072, 1045, 1007, 880, 849, 822, 795, 760 cm^{-1}; ^1H NMR: $\delta = 1.04$ (s, 9H), 1.10 (s, 9H), 1.43 (s, 3H), 1.46 (s, 3H), 1.89 (d, $J = 10.5$ Hz, 1H), 2.81 (d, $J = 9.0$ Hz, 1H), 3.43 (dt, $J = 8.5$, 3.0 Hz, 1H), 3.76 (dt, $J = 10.0$, 3.0 Hz, 1H), 4.08 (dd, $J = 2.0$, 10.0 Hz, 1H), 4.33 (dd, $J = 2.5$, 10.0 Hz, 1H), 4.44 (t, $J = 3.0$ Hz, 1H), 4.71 (br t, $J = 3.0$ Hz, 1H), 7.30–7.50 (m, 14H), 7.61 (m, 2H), 7.70–7.80 (m, 4H); ^{13}C NMR: $\delta = 19.2$ (C), 19.4 (C), 26.9 (CH_3), 27.07 (CH_3), 27.12 (CH_3), 68.3 (CH), 69.8 (CH), 72.5 (CH), 74.1 (CH), 74.4 (CH), 75.7 (CH), 111.0 (C), 127.5 (CH), 127.6 (CH), 127.8 (CH), 127.9 (CH), 129.8 (CH), 130.0 (CH), 130.1 (CH), 132.0 (C), 132.7 (C), 133.4 (C), 133.6 (C), 135.7 (CH), 136.0 (CH), 136.1 (CH), 136.5 (CH); HR-MS-ESI: $m/z = 719.3195$ $[M+Na]^+$, calcd. for $C_{41}H_{52}NaO_6Si_2$: 719.3195. The *dr* (89:11) was determined by the integration area of ^1H NMR signals at 4.71 and 4.58 ppm. The stereochemistry was tentatively assigned as drawn.

(1*R*,2*R*,3*R*,4*S*,5*S*,6*R*)-4,5-(Isopropylidenedioxy)-3,6-bis(*tert*-butyldiphenylsiloxy)cyclohexane-1,2-diol (*neo*-13c)

To a solution of **12c** (235 mg, 0.338 mmol) and 2,6-lutidine (0.20 mL, 1.7 mmol) in CH_2Cl_2 (0.5 mL) cooled at −78 °C, was added TESOTf (0.23 mL, 1.0 mmol). After 14.5 h, water (2 mL) was added, and the mixture was allowed to warm to room temperature. The aqueous layer was separated and extracted with $CHCl_3$ (2 mL × 3). The combined organic layers were washed with water (6 mL × 3), dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography (hexane/EtOAc 98:2) to yield 6*O*-TES inosose as a white solid; yield: 254 mg (93%); mp 78–80 °C; $[\alpha]_D^{20}$: −20.5 (*c* 1.00, $CHCl_3$); IR (neat): $\nu = 3075$, 3051, 2955, 2932, 2878, 2859, 1751, 1474, 1462, 1427, 1381, 1369, 1231, 1180, 1134, 1115, 1059, 1049, 1022, 8445, 822, 741 cm^{-1}; ^1H NMR: $\delta = 0.14$ (q, $J = 8.0$ Hz, 6H), 0.61 (t, $J = 8.0$ Hz, 9H), 0.99 (s, 9H), 1.10 (s, 9H), 1.41 (s, 3H), 1.47 (s, 3H), 4.19 (dd, $J = 2.5$, 10.0 Hz, 1H), 4.53 (dd, $J = 2.0$, 10.0 Hz, 1H), 4.58 (dd, $J = 2.0$, 3.5 Hz, 1H), 4.61 (d, $J = 2.5$ Hz, 1H), 4.64 (d, $J = 3.5$ Hz, 1H), 7.29–7.45 (m, 12H), 7.59–7.64 (m, 4H), 7.67–7.72 (m, 4H); ^{13}C NMR: $\delta = 4.0$ (CH_2), 6.5 (CH_3), 19.3 (C), 19.9 (C), 26.81 (CH_3), 26.84 (CH_3), 27.0 (CH_3), 27.2 (CH_3), 71.9 (CH), 74.2 (CH), 74.6 (CH), 75.4 (CH), 75.7 (CH), 112.7 (C), 126.9 (CH), 127.3 (CH), 127.5 (CH), 127.6 (CH), 129.0 (CH), 129.5 (CH), 129.9 (CH), 130.0 (CH), 132.3 (C), 132.7 (C), 133.1 (C), 135.9 (CH), 136.2 (CH), 136.4 (CH), 136.6 (CH), 203.9 (C); HR-MS-ESI: $m/z = 831.3903$ $[M+Na]^+$, calcd. for $C_{47}H_{64}NaO_6Si_3$: 831.3903.

To a solution of the above solid (20 mg, 25 μmol) in toluene (0.15 mL), was added *t*-$BuNH_2$·BH_3 (6 mg, 0.06 mmol) at room temperature. After 30 min, the mixture was evaporated to give a crude material as a cloudy oil. The oil was dissolved in a 1:1 mixture of THF/pyridine (0.8 mL) cooled in an ice-water bath, HF·pyridine complex (0.2 mL) was added. The cooling bath was removed and the mixture was stirred for 45 min. The mixture was cooled in the ice-water bath, and the reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (2 mL). The whole was extracted with EtOAc (2 mL × 3), and the combined organic layers were washed with brine (6 mL), dried over Na_2SO_4, and concentrated under vacuum. The residual pyridine was removed by evaporation with toluene (10 mL × 2). The *dr* (96:4) was determined by area integration of the ^1H NMR signals at 4.58 and 4.71 ppm. The residue was purified by column chromatography (hexane/EtOAc 95:5) to give a 96:4 diastereomeric mixture of the title compound as a white solid; yield: 16.6 mg (96%); mp 46–48 °C; $[\alpha]_D^{25}$: (*c* 0.83, $CHCl_3$) {lit:[12c] mp 61–64 °C, $[\alpha]_D$ +13.7 (*c* 1.0, $CHCl_3$)}; IR (neat): $\nu = 3549$, 3071, 3051, 3013, 2986, 2969, 2932, 2859, 1427, 1381, 1369, 1219, 1157, 1111, 1042, 1007, 837, 760 cm^{-1}; ^1H NMR: $\delta = 1.08$ (s, 18H), 1.42 (s, 6H), 3.66 (br s, 2H), 4.12 (br s, 2H), 4.58 (br s, 2H), 7.33–7.45 (m, 12H), 7.66 (m, 4H), 7.78 (m, 4H); ^{13}C NMR: $\delta = 19.6$ (C), 27.06 (CH_3), 27.13 (CH_3), 67.0 (CH), 72.8 (CH), 74.5 (CH), 111.4 (C), 127.5 (CH), 127.7 (CH), 129.8 (CH), 129.9 (CH), 132.6 (C), 134.1 (C), 136.0 (CH), 136.5 (CH). EI-MS; $m/z = 639$ (M−*t*-Bu). ^1H and ^{13}C NMR data were in good agreement with those reported.[12c]

(1*S*,2*R*,3*R*,4*R*,5*S*,6*R*)-2-Acetamido-3,4,5,6-tetrakis-(benzyloxy)cyclohexyl acetate (14a; Scheme 7)

To a stirred solution of **2a** (161 mg, 0.299 mmol) in EtOH (1.5 mL), were added pyridine (0.16 mL, 2.0 mmol) and $MeONH_2$·HCl (125 mg, 1.50 mmol) at room temperature. After 30 min, the solution was diluted with EtOAc, washed with H_2O and brine, dried over Na_2SO_4, and concentrated under vacuum. From the residue, the remaining pyridine was removed by three-time evaporation with toluene to give crude *O*-methyl oxime as a yellow oil (yield: 178 mg).

The above oil was dissolved in THF (0.5 mL + 0.25 mL wash × 2) and added to a suspension of NaOMe (162 mg, 3.00 mmol) and $LiAlH_4$ (170 mg, 4.48 mmol) at −78 °C. After 30 min, the cooling bath was removed, and the mixture was allowed to warm up to room temperature. After 30 min, the mixture was heated at 65 °C for 30 min and then cooled to room temperature. To the mixture, H_2O was dropwise added until no gas evolution occurred. The whole was filtered through celite, which was successively washed with $CHCl_3$. The combined filtrate was concentrated under vacuum to give a crude mixture of **4a** and *epi*-**4a** as a yellow oil.

The above oil was dissolved in CH_2Cl_2 (3 mL), and pyridine (0.48 mL, 5.9 mmol), Ac_2O (0.57 mL, 6.0 mmol), and DMAP (4 mg, 0.03 mmol) were added. The mixture was stirred at room temperature for 1.5 h and diluted with EtOAc. The mixture was washed with 10% HCl, H_2O, sat aqueous $NaHCO_3$, and brine, dried over Na_2SO_4, and concentrated under vacuum. The resulting oil was purified by column chromatography (hexane/EtOAc 3:2 to 4:6) to give the title compound as a yellow oil; yield: 127 mg (68%); $[\alpha]_D^{20}$: +23 (*c* 0.33, $CHCl_3$); IR (neat): ν = 3294, 3063, 3028, 2924, 2870, 1736, 1667, 1551, 1524, 1497, 1454, 1373, 1234, 1103, 1072, 1026, 756 cm^{-1}; ^1H NMR: δ = 1.86 (s, 3H), 2.01 (s, 3H), 3.57 (dd, *J* = 1.5, 10.0 Hz, 1H), 3.67 (br m, 1H), 3.71 (br m, 1H), 3.90 (dd, *J* = 2.5, 10.0 Hz, 1H), 4.32 (br d, *J* = 12.0 Hz, 1H), 4.36–4.42 (m, 2H), 4.45–4.57 (m, 4H), 4.67 (d, *J* = 12.0 Hz, 1H), 4.68 (d, *J* = 12.0 Hz, 1H), 5.12 (t, *J* = 10.0 Hz, 1H), 5.12 (br s, 1H), 7.15–7.19 (m, 4H), 7.25–7.36 (m, 16H); ^{13}C NMR: δ = 20.9 (CH_3), 23.4 (CH_3), 71.8 (CH_2), 73.0 (CH), 73.1 (CH_2), 73.2 (CH_2), 73.5 (CH_2), 73.6 (CH), 75.0 (CH), 76.5 (CH), 77.2 (CH), 127.65 (CH), 127.73 (CH), 127.8 (CH), 127.9 (CH), 128.1 (CH), 128.31 (CH), 128.34 (CH), 128.37 (CH), 128.43 (CH), 138.0 (C), 138.2 (C), 170.1 (C), 171.3 (C); HR-MS-ESI: *m*/*z* = 662.2518 $[M+K]^+$, calcd. for $C_{38}H_{41}KNO_7$: 662.2515. The stereochemistry was determined based on the *trans*-diaxial couplings of 1-H (5.12 ppm) with 2-H and 6-H (both *J* = 10 Hz) as shown in Scheme 7. In addition, *epi*-**14a** (*vide infra*) was isolated as a minor product; yield: 20 mg (11%).

(1*S*,2*S*,3*R*,4*R*,5*S*,6*R*)-2-Acetamido-3,4,5,6-tetrakis-(benzyloxy)cyclohexyl acetate (*epi*-14a)

To a solution of **2a** (109 mg, 0.203 mmol) in pyridine (2 mL), was added $HONH_2$·HCl (71 mg, 1.0 mmol), and the solution was stirred at room temperature for 1.5 h. The solution was diluted with EtOAc (20 mL), washed with H_2O (20 mL × 3) and brine, dried over Na_2SO_4, and concentrated under vacuum to give crude oxime as a pale brown oil; yield: 139 mg.

The above oil was dissolved in CH_2Cl_2 (2 mL), and pyridine (0.33 mL, 4.1 mmol), DMAP (3 mg, 0.02 mmol), and Ac_2O (0.38 mL, 4.0 mmol) were added to the stirred solution cooled in an ice-water bath. The mixture was stirred for 1 h, and the reaction was quenched by the addition of H_2O (10 mL). The whole was extracted with $CHCl_3$ (20 mL × 3), and the combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, and concentrated under vacuum. The residual pyridine was removed by three-time evaporation with toluene (10 mL × 3) to give crude *O*-acetyl oxime as a yellow oil; yield: 131 mg.

The above oil was dissolved in EtOH (2 mL), and $NiCl_2$·$6H_2O$ (97 mg, 0.41 mmol) was added. To the mixture cooled in an ice-water bath, $NaBH_4$ (78 mg, 2.1 mmol) was portion-wise added, and the cooling bath was removed. After 1.5 h, the mixture was cooled in an ice-water bath, and $NaBH_4$ (78 mg, 2.1 mmol) was portion-wise added again. The mixture was stirred at room temperature for 2 h and diluted with EtOAc (20 mL). After addition of H_2O (20 mL), the whole was filtered through celite pad, which was successively washed with EtOAc. The organic layer was separated, and the aqueous layer was extracted with EtOAc (20 mL × 3). The combined organic layers were washed with H_2O and brine, dried over Na_2SO_4, and concentrated under vacuum to give crude *epi*-**4a** as a pale yellow oil; yield: 115 mg.

The above oil was dissolved in CH_2Cl_2 (2 mL), and pyridine (0.16 mL, 2.0 mmol), Ac_2O (0.19 mL, 2.0 mmol), and DMAP (2 mg, 0.02 mmol) were added to the stirred solution cooled in an ice-water bath. After 1.5 h, the reaction was quenched by the addition of H_2O (5 mL), and the whole was extracted with $CHCl_3$ (10 mL × 3). The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum to give crude product as a pale brown oil; yield: 128 mg. This oil was purified by column chromatography (hexane/EtOAc 2:1) to give the title compound as a colorless oil; yield: 64.9 mg (51%); $[\alpha]_D^{20}$: −18.2 (*c* 1.00, $CHCl_3$); IR (neat): ν = 3410, 3028, 3009, 2924, 2870, 1734, 1674, 1512, 1497, 1454, 1369, 1323, 1234, 1099, 1053, 1026, 914, 802, 752 cm^{-1}; ^1H NMR (−20 °C): δ = 1.81 (s, 3H), 2.04 (s, 3H), 3.78 (dd, *J* = 3.0, 4.0 Hz, 1H), 3.84 (dd, *J* = 3.0, 11.0 Hz, 1H), 3.86 (m, 1H), 3.94 (dd, *J* = 3.0, 4.5 Hz, 1H), 4.36 (d, *J* = 11.5 Hz, 1H), 4.46 (d, *J* = 11.0 Hz, 1H), 4.47 (d, *J* = 12.0 Hz, 1H), 4.52 (d, *J* = 12.0 Hz, 1H), 4.62 (d, *J* = 12.0 Hz, 1H), 4.66 (d, *J* = 11.5 Hz, 1H), 4.67 (d, *J* = 11.0 Hz, 1H), 4.68 (d, *J* = 12.0 Hz, 1H), 5.04 (ddt, *J* = 1.0, 9.0, 4.5 Hz, 1H), 5.22 (dd, *J* = 4.0, 11.0 Hz, 1H), 6.90 (d, *J* = 9.0 Hz, 1H), 7.18–7.21 (m, 4H), 7.29–7.40 (m, 16H); ^{13}C NMR: δ = 21.0 (CH_3), 23.4 (CH_3), 48.1 (CH), 70.7 (CH_2), 70.8 (CH), 71.7 (CH), 73.0 (CH_2), 73.5 (CH_2), 74.1 (CH_2), 74.5 (CH), 74.8 (CH), 79.1 (CH), 127.5 (CH), 127.57 (CH), 127.60 (CH), 127.7 (CH), 127.8 (CH), 128.1 (CH), 128.27 (CH), 128.30 (CH), 128.32 (CH), 128.5 (CH), 137.5 (C), 137.87 (C), 137.90 (C), 138.4 (C), 170.4 (C), 170.5 (C); FAB-MS: *m*/*z* = 624 (M+H), 91 (Bn); HR-MS-FAB: *m*/*z* = 624.2949 $[M+H]^+$, calcd. for $C_{38}H_{42}NO_7$: 624.2956. The stereochemistry was determined based on the *trans*-diaxial coupling (*J* = 11.0 Hz) between 2-H and 3-H (3.84 and 5.22 ppm, respectively) as shown in Scheme 7.

(1*R*,2*R*,3*R*,4*R*,5*R*)-2,3,4,5-Tetrakis(benzyloxy)-cyclohexanol (5a)

To a solution of **2a** (540 mg, 1.00 mmol), DMAP (18 mg, 0.15 mmol), and pyridine (0.28 mL, 3.5 mmol) in CH_2Cl_2 (10 mL) cooled in an ice-water bath, was added *O*-phenyl chlorothioformate (0.42 mL, 3.0 mmol). After 2.5 h, MeOH (2 mL) was added, and the mixture was stirred for another 10 min and evaporated. To the residue, EtOAc and water were added, and the aqueous layer was separated and extracted 3 times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The resulting orange oil (1.1 g), containing *O*-phenoxythiocarbonyl inosose, was used in the next reaction without purification. The crude inosose was purified by column chromatography (hexane/EtOAc 95:5) to provide a pale yellow solid; mp 88–90 °C; $[\alpha]_D^{20}$: −53.0 (*c* 1.21, $CHCl_3$); IR (neat): ν = 3086, 3063, 3028, 2920, 2874, 1751, 1589, 1493, 1454, 1362, 1285, 1223, 1207, 1107, 1049, 1045, 1026, 1003, 914, 864, 818, 752 cm^{-1}; ^1H NMR: δ = 3.82 (dd, *J* = 3.0, 4.0 Hz, 1H), 3.93 (dd, *J* = 3.0, 4.0 Hz, 1H), 4.19 (dd, *J* = 3.0, 11.0 Hz, 1H), 4.40 (d, *J* = 12.0 Hz, 1H), 4.43 (d, *J* = 12.0 Hz, 1H), 4.50 (d, *J* = 12.0 Hz, 1H), 4.53 (d, *J* = 12.0 Hz, 1H), 4.62 (d, *J* = 3.0 Hz, 1H), 4.71 (d, *J* = 12.0 Hz, 1H), 4.73 (d, *J* = 12.0 Hz, 1H), 4.78 (d, *J* = 12.0 Hz, 1H),

4.90 (d, $J=12.0$ Hz, 1H), 6.15 (d, $J=11.0$ Hz, 1H), 7.09–7.44 (m, 25H); ^{13}C NMR: $\delta=72.8$ (CH_2), 73.7 (CH_2), 73.8 (CH_2), 73.9 (CH_2), 74.9 (CH), 77.5 (CH), 78.8 (CH), 80.9 (CH), 85.6 (CH), 121.9 (CH), 126.6 (CH), 127.76 (CH), 127.78 (CH), 127.83 (CH), 127.9 (CH), 128.0 (CH), 128.3 (CH), 128.4 (CH), 128.5 (CH), 129.5 (CH), 137.5 (C), 137.7 (C), 153.6 (C), 194.8 (C), 197.0 (C); FAB-MS: $m/z=697$ (M+Na), 91 (Bn); HR-MS-ESI: $m/z=697.2233$ $[M+Na]^+$, calcd. for $C_{41}H_{38}NaO_7S$, 697.2231.

To a solution of the above crude material in toluene (10 mL), were added Bu_3SnH (0.40 mL, 1.5 mmol) and AIBN (16 mg, 0.097 mmol), and the solution was heated at 80 °C. After 2 h, another portion of AIBN (16 mg, 0.097 mmol) was added. After 1.5 h, AIBN (16 mg, 0.097 mmol) and Bu_3SnH (0.40 mL, 1.5 mmol) were added again. After 1 h, the mixture was evaporated, and the resulting yellow oil was purified by column chromatography (hexane to hexane/EtOAc 95:5) to yield deoxyinososе as a pale yellow oil; yield: 345 mg (66% in 2 steps); $[\alpha]_D^{20}$: −61.3 (*c* 0.45, $CHCl_3$); IR (neat): $\nu=3086$, 3063, 3028, 2924, 2870, 1732, 1496, 1454, 1366, 1327, 1312, 1265, 1215, 1111, 1026, 1003, 914, 802, 752 cm^{-1}; ^{1}H NMR: $\delta=2.75$ (ddd, $J=1.5$, 5.0, 13.0 Hz, 1H), 2.84 (dd, $J=11.0$, 13.0 Hz, 1H), 3.93 (ddd, $J=1.5$, 2.5, 5.0 Hz, 1H), 3.99 (dd, $J=3.5$, 5.0 Hz, 1H), 4.06 (ddd, $J=2.5$, 5.0, 11.0 Hz, 1H), 4.431 (d, $J=12.0$ Hz, 1H), 4.433 (d, $J=3.5$ Hz, 1H), 4.44 (d, $J=12.0$ Hz, 1H), 4.47 (d, $J=12.0$ Hz, 1H), 4.52 (d, $J=12.0$ Hz, 1H), 4.55 (d, $J=12.0$ Hz, 1H), 4.74 (d, $J=12.0$ Hz, 1H), 4.75 (d, $J=12.0$ Hz, 1H), 4.87 (d, $J=12.0$ Hz, 1H), 7.16–7.19 (m, 4H), 7.27–7.37 (m, 16H); ^{13}C NMR: $\delta=42.2$ (CH_2), 71.4 (CH_2), 72.6 (CH_2), 73.4 (CH_2), 73.5 (CH_2), 75.7 (CH), 75.8 (CH), 78.1 (CH), 81.5 (CH), 127.5 (CH), 127.68 (CH), 127.73 (CH), 127.76 (CH), 127.79 (CH), 128.3 (CH), 128.38 (CH), 128.42 (CH), 137.8 (C), 138.0 (C), 138.05 (C), 138.14 (C), 204.6 (C); HR-MS-ESI: $m/z=545.2299$ $[M+Na]^+$, calcd. for $C_{34}H_{34}NaO_5$: 545.2299.

To a solution of the above oil (9.0 mg, 17 μmol) in MeOH (0.2 mL) cooled in an ice-water bath, was added $NaBH_4$ (1.7 mg, 45 μmol), and the mixture was stirred for 40 min. After addition of saturate aqueous NH_4Cl, the whole was extracted with EtOAc (1.5 mL×4). The combined organic layers were washed with brine (4.5 mL), dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography (hexane/EtOAc 9:2) to give the title compound as a pale yellow solid; yield: 8.3 mg (93%); mp 91–92.5 °C; $[\alpha]_D^{20}$: −24 (*c* 0.30, $CHCl_3$); IR (KBr): $\nu=3314$, 3086, 3063, 3028, 2955, 2928, 2855, 2878, 2758, 2739, 2677, 1496, 1454, 1435, 1315, 1261, 1207, 1150, 1099, 1084, 1065, 1026, 1084, 914, 868, 802, 745 cm^{-1}; ^{1}H NMR (60 °C): $\delta=1.85$–1.95 (br s, 1H), 1.98 (ddd, $J=3.5$, 7.5, 11.5 Hz, 1H), 3.86–3.88 (m, 2H), 3.95 (dd, $J=2.5$, 7.5 Hz, 1H), 3.97 (br s, 1H), 4.09 (br s, 1H), 4.55–4.72 (m, 7H), 4.77 (br s, 1H), 7.21–7.35 (m, 20H); ^{13}C NMR: $\delta=32.4$ (CH_2), 71.5 (CH_2), 72.5 (CH), 73.0 (CH_2), 73.9 (CH_2), 79.4 (CH), 127.6 (CH), 127.66 (CH), 127.72 (CH), 127.8 (CH), 127.9 (CH), 128.39 (CH), 128.41 (CH), 128.49 (CH), 128.51 (CH), 138.7 (C), 138.8 (C), 138.9 (C); HR-MS-ESI: $m/z=547.2453$ $[M+Na]^+$, calcd. for $C_{34}H_{36}NaO_5$, 547.2455. The stereochemistry was determined at the stage of **15a**.

(1*R*,2*R*,3*S*,4*R*,5*R*)-2,3,4,5-Tetrakis(benzyloxy)cyclohexyl acetate (15a)

To a solution of **5a** (5.9 mg, 11 μmol), DMAP (1 mg, 8 μmol), and Et_3N (0.01 mL, 0.07 mmol) in CH_2Cl_2 (0.1 mL) cooled in an ice-water bath, was added Ac_2O (0.01 mL, 0.1 mmol), and the mixture was stirred for 1 h. After addition of water (2 mL), the whole was extracted three times with $CHCl_3$. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under vacuum. The residue was purified by column chromatography (hexane/EtOAc 95:5) to give the title compound as a pale yellow oil; yield: 4.0 mg (64%); $[\alpha]_D^{20}$: −3.9 (*c* 1.00, $CHCl_3$); IR (neat): $\nu=3088$, 3063, 3030, 2933, 2903, 2868, 1738, 1497, 1454, 1368, 1346, 1240, 1207, 1159, 1094, 1070, 1051, 1026, 735 cm^{-1}; ^{1}H NMR (60 °C): $\delta=1.93$–2.05 (m, 2H), 1.97 (s, 3H), 3.91–3.94 (m, 2H), 3.98 (dd, $J=2.5$, 9.0 Hz, 1H), 4.12 (br m, 1H), 4.64 (d, $J=11.5$ Hz, 1H), 4.66 (s, 2H), 4.67 (d, $J=11.5$ Hz, 1H), 4.69 (d, $J=11.5$ Hz, 1H), 4.71 (d, $J=11.5$ Hz, 1H), 4.76 (d, $J=11.5$ Hz, 1H), 4.81 (d, $J=11.5$ Hz, 1H), 5.12 (ddd, $J=2.5$, 4.0, 11.0 Hz, 1H), 7.23–7.35 (m, 20H); ^{13}C NMR: $\delta=21.3$ (CH_3), 28.4 (CH_2), 69.9 (CH), 71.6 (CH_2), 72.5 (CH), 73.0 (CH_2), 73.3 (CH_2), 74.4 (CH_2), 76.9 (CH), 79.1 (CH), 79.4 (CH), 127.45 (CH), 127.49 (CH), 127.54 (CH), 127.7 (CH), 127.82 (CH), 127.84 (CH), 128.27 (CH), 128.33 (CH), 128.4 (CH), 138.6 (C), 139.0 (C), 139.1 (C), 139.2 (C), 170.6 (C); HR-MS-ESI: $m/z=605.2300$ $[M+K]^+$, calcd. for $C_{36}H_{38}KO_6$: 605.2300. The stereochemistry was determined based on the coupling constant (2.5, 4.0, and 11.0 Hz) of the methine proton that the AcO group attaches on, indicating an equatorial orientation of the AcO group and axial orientation of the adjacent BnO groups, as shown in Scheme 7.

(1*R*,2*R*,3*R*,4*R*,5*R*,6*S*)-2,3,4,5-Tetrakis(benzyloxy)-6-methoxycyclohexanol (6a)

To a solution of **2a** (107 mg, 0.198 mmol) and proton sponge (85 mg, 0.40 mmol) in CH_2Cl_2 (2 mL), was added $Me_3O{\cdot}BF_4$ (59 mg, 0.40 mmol) at room temperature. After 14 h, water (8 mL) was added, and the whole was extracted with $CHCl_3$ (8 mL×2). The combined organic layers were washed with brine (16 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (hexane/EtOAc 5:1) to yield *O*-methylinososе as a colorless oil; yield: 103 mg (90%); $[\alpha]_D^{20}$: −39.0 (*c* 1.00, $CHCl_3$); IR (neat): $\nu=3395$, 3086, 3062, 3028, 3086, 3005, 2920, 2873, 1743, 1654, 1543, 1497, 1454, 1385, 1366, 1323, 1026, 1150, 1111, 1026, 957, 918, 737 cm^{-1}; ^{1}H NMR: $\delta=3.58$ (s, 3H), 3.75 (dd, $J=3.5$, 4.0 Hz, 1H), 3.88 (dd, $J=3.0$, 4.0 Hz, 1H), 3.90 (dd, $J=3.5$, 10.0 Hz, 1H), 4.18 (dd, $J=1.0$, 10.0 Hz, 1H), 4.36 (d, $J=12.0$ Hz, 1H), 4.43 (d, $J=12.0$ Hz, 1H), 4.48 (dd, $J=1.0$, 3.0 Hz, 1H), 4.49 (d, $J=12.0$ Hz, 1H), 4.53 (d, $J=12.0$ Hz, 1H), 4.68 (d, $J=12.0$ Hz, 1H), 4.73 (d, $J=12.0$ Hz, 1H), 4.80 (d, $J=12.0$ Hz, 1H), 4.88 (d, $J=12.0$ Hz, 1H), 7.08–7.16 (m, 4H), 7.25–7.36 (m, 16H); ^{13}C NMR: $\delta=59.9$ (CH_3), 72.5 (CH_2), 73.3 (CH_2), 73.7 (CH_2), 74.0 (CH_2), 75.3 (CH), 77.2 (CH), 80.6 (CH), 80.7 (CH), 85.7 (CH), 127.6 (CH), 127.71 (CH), 127.73 (CH), 127.8 (CH), 127.9 (CH), 128.2 (CH), 128.3 (CH), 128.4 (CH), 137.7 (C), 137.8 (C), 137.9 (C), 138.5 (C), 202.8 (C); FAB-MS: $m/z=575$ (M+Na), 329, 136, 91 (Bn); HR-MS-

FAB: $m/z = 575.2415$ $[M+Na]^+$, calcd. for $C_{35}H_{36}NaO_6$, 575.2404.

To a solution of the above oil (9.7 mg, 18 μmol) in MeOH (0.2 mL) cooled in an ice-water bath, was added $NaBH_4$ (2 mg, 0.05 mmol). After 30 min, saturated aqueous NH_4Cl (1.5 mL) was added, and the whole was extracted with EtOAc (1.5 mL × 5). The combined organic layers were washed with brine (8 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (hexane/EtOAc 2:1) to yield the title compound as a colorless oil; yield: 8.4 mg (86%); $[\alpha]_D^{20}$: −13 (*c* 0.42, $CHCl_3$); IR (neat): $\nu = 3502$, 3028, 3009, 2924, 2874, 1497, 1454, 1358, 1261, 1215, 1092, 1041, 1026, 910, 802, 748 cm^{-1}; ^1H NMR (−20 °C): $\delta = 3.50$ (dd, $J = 2.5$, 10.0 Hz, 1H), 3.57 (s, 3H), 3.64 (br s, 1H), 3.66 (br s, 1H), 3.77 (br s, 1H), 3.94 (dd, $J = 2.0$, 10.0 Hz, 1H), 4.34 (d, $J = 12.0$ Hz, 1H), 4.37 (d, $J = 12.0$ Hz, 1H), 4.45 (d, $J = 12.0$ Hz, 1H), 4.47 (br s, 1H), 4.52 (d, $J = 12.0$ Hz, 1H), 4.58 (d, $J = 12.0$ Hz, 1H), 4.63 (d, $J = 12.0$ Hz, 1H), 4.68 (d, $J = 12.0$ Hz, 1H), 4.82 (d, $J = 12.0$ Hz, 1H), 7.05–7.45 (m, 20H); ^{13}C NMR (−20 °C): $\delta = 58.0$ (CH_3), 68.6 (CH), 70.4 (CH_2), 72.9 (CH), 73.2 (CH_2), 73.6 (CH_2), 74.8 (CH), 75.7 (CH), 77.8 (CH), 79.8 (CH), 127.5 (CH), 127.6 (CH), 127.7 (CH), 127.78 (CH), 127.84 (CH), 127.9 (CH), 128.0 (CH), 128.29 (CH), 128.34 (CH), 128.4 (CH), 137.0 (C), 137.8 (C), 137.9 (C), 138.7 (C); HR-MS-ESI: $m/z = 577.2568$ $[M+Na]^+$, calcd. for $C_{35}H_{38}NaO_6$: 577.2561. The stereochemistry was determined based on the *trans*-diaxial coupling ($J = 10.0$ Hz) between 5-H and 6-H (3.94 and 3.50 ppm, respectively) as shown in Scheme 7.

(1*R*,2*R*,3*R*,4*R*,5*S*,6*S*)-3,4,5,6-Tetrakis(benzyloxy)-1-methylcyclohexane-1,2-diol (7a)

A 1.5 M solution of MeLi·LiBr in THF (0.23 mL, 0.35 mmol) was diluted with Et_2O (0.4 mL) and cooled at −78 °C. A solution of **2a** (62 mg, 0.12 mmol) in Et_2O (0.4 mL + 0.2 mL wash × 2) was added, and the cooling bath was replaced with an ice-water bath. After 2 h, saturated aqueous NH_4Cl (2 mL) was added, and the whole was extracted with EtOAc (2 mL × 4). The combined organic layers were washed with brine (8 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (hexane/EtOAc 3:1 to 2:1) to yield the title compound as a colorless oil; yield: 57 mg (89%); $[\alpha]_D^{20}$: +15.8 (*c* 1.00, $CHCl_3$); IR (neat): $\nu = 3483$, 3086, 3063, 3028, 3005, 2982, 2932, 2870, 1655, 1605, 1543, 1497, 1420, 1385, 1366, 1331, 1250, 1207, 1142, 1099, 1065, 1026, 964, 914, 802, 748 cm^{-1}; ^1H NMR: $\delta = 1.34$ (s, 3H), 2.41 (br s, 1H), 3.49 (br s, 1H), 3.60–3.78 (m, 4H), 3.82 (br s, 1H), 4.43–4.42 (m, 2H), 4.45–4.63 (m, 5H), 4.71 (d, $J = 12.0$ Hz, 1H), 7.09–7.19 (m, 4H), 7.23–7.39 (m, 16H); ^{13}C NMR: $\delta = 22.1$ (CH_3), 72.9 (CH_2), 73.1 (CH_2), 73.2 (CH_2), 73.7 (CH_2), 74.2 (CH), 76.4 (CH), 77.2 (CH), 77.9 (CH), 99.8 (C), 127.6 (CH), 127.7 (CH), 127.9 (CH), 128.0 (CH), 128.1 (CH), 128.35 (CH), 128.42 (CH), 128.5 (CH), 137.1 (C), 137.7 (C), 138.2 (C), 138.5 (C); FAB-MS: $m/z = 577$ (M + Na), 525, 481, 437, 393, 349, 305, 243, 183, 91 (Bn); HR-MS-FAB: $m/z = 577.2565$ $[M+Na]^+$, calcd. for $C_{35}H_{38}NaO_6$: 577.2561. The stereochemistry was determined at the stage of **16a**.

(1*R*,2*R*,3*R*,4*R*,5*S*,6*S*)-3,4,5,6-Tetrakis(benzyloxy)-1,2-isopropylidenedioxy-1-methylcyclohexane (16a)

To a solution of **7a** (66 mg, 0.12 mmol) in 2,2-dimethoxypropane (2.0 mL, 16 mmol) was added $TsOH \cdot H_2O$ (5 mg, 0.03 mmol) at room temperature. The mixture was stirred for 2 h, and saturated aqueous $NaHCO_3$ (10 mL) was added. The whole was extracted with EtOAc (10 mL × 3), and the combined organic layers were washed with brine (30 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (hexane/EtOAc 96:4) to yield the title compound as a colorless oil; yield: 66 mg (93%); $[\alpha]_D^{25}$: −27.2 (*c* 1.44, $CHCl_3$); IR (neat): $\nu = 3086$, 3062, 3028, 3005, 2982, 2932, 2889, 2878, 1497, 1454, 1377, 1308, 1258, 1242, 1211, 1188, 1115, 1088, 1072, 1026, 984, 918, 864, 752, 733 cm^{-1}; ^1H NMR: $\delta = 1.36$ (s, 3H), 1.38 (s, 3H), 1.39 (s, 3H), 3.65 (d, $J = 3.0$ Hz, 1H), 3.87 (dd, $J = 3.0$, 6.5 Hz, 1H), 4.08 (d, $J = 5.0$ Hz, 1H), 4.10 (dd, $J = 3.5$, 6.5 Hz, 1H), 4.19 (dd, $J = 3.5$, 5.0 Hz, 1H), 4.57 (s, 2H), 4.65 (d, $J = 12.0$ Hz, 1H), 4.67 (d, $J = 12.0$ Hz, 1H), 4.68 (d, $J = 12.0$ Hz, 1H), 4.72 (d, $J = 12.0$ Hz, 1H), 4.74 (d, $J = 12.0$ Hz, 1H), 4.76 (d, $J = 12.0$ Hz, 1H), 7.23–7.37 (m, 20H); ^{13}C NMR: $\delta = 26.0$ (CH_3), 27.0 (CH_3), 27.6 (CH_3), 72.3 (CH_2), 72.89 (CH_2), 72.92 (CH_2), 74.7 (CH_2), 76.5 (CH), 76.9 (CH), 77.2 (CH), 81.0 (CH), 81.2 (C), 82.2 (CH), 109.7 (C), 127.31 (CH), 127.32 (CH), 127.34 (CH), 127.4 (CH), 127.49 (CH), 127.52 (CH), 127.6 (CH), 128.07 (CH), 128.11 (CH), 128.15 (CH), 128.18 (CH), 138.6 (C), 138.7 (C), 138.8 (C); FAB-MS: $m/z = 617$ (M + Na), 329, 176, 91 (Bn); HR-MS-FAB: $m/z = 617.2873$ $[M+Na]^+$, calcd. for $C_{38}H_{42}NaO_6$: 617.2874. The relative configuration was determined by NOESY correlation between angular CH_3 (1.36 ppm) and H (4.05 ppm) as shown in Scheme 7.

(2*R*,3*S*,4*R*,5*S*,6*S*)-2,3,4,5,6-Pentahydroxycyclohexanone (*allo*-2-inosose; Scheme 8)

To a solution of **2a** (819 mg, 1.52 mmol) in MeOH (10 mL), was added 10% Pd/C (wetted with 55% water, 485 mg, 0.20 mmol), and the mixture was stirred under an H_2 atmosphere at room temperature for 24 h. After addition of H_2O (10 mL) and activated charcoal (500 mg), the mixture was stirred for 20 min and filtered through filter paper, which was washed with H_2O (10 mL × 3). The combined filtrate was concentrated under vacuum to give the title compound as colorless blocks; yield: 228 mg (84%); mp 180–182 °C (H_2O/*i*-PrOH); $[\alpha]_D^{20}$: +75.1 (*c* 1.04, H_2O) {lit:[41] mp 195–197 °C, $[\alpha]_D^{20}$: +68.6 (*c* 1, H_2O)}; ^1H NMR (DMSO-d_6): $\delta =$ 3.56 (br m, 1H), 3.82 (br s, 1H), 3.92 (br s, 1H), 4.15 (br d, $J = 6.5$ Hz, 1H), 4.39 (br s, 1H), 4.71 (br s, 1H), 4.91 (br s, 1H), 5.00 (br s, 1H), 5.10 (br s, 1H), 5.28 (br s, 1H); ^{13}C NMR (DMSO-d_6): $\delta = 71.1$ (CH), 73.3 (CH), 73.6 (CH), 74.2 (CH), 75.7 (CH), 208.0 (C); HR-MS-ESI: $m/z =$ 201.0378 $[M+Na]^+$, calcd. for $C_6H_{10}NaO_6$: 201.0370. ^1H and ^{13}C NMR data were in good agreement with those reported.[41]

D-*chiro*-Inositol

To a solution of *chiro*-**3a** (195 mg, 0.361 mmol) in MeOH (2 mL), was added 10% Pd/C (wetted with 55% water, 193 mg, 82 μmol), and the mixture was stirred under an H_2 atmosphere at room temperature for 10 h. After addition of

H_2O (5 mL), the whole was filtered through filter paper, which was washed with H_2O (5 mL × 3). The combined filtrate was concentrated under vacuum to give the title compound as a slightly brown solid; yield: 53 mg (81%); mp 231–235 °C (H_2O/EtOH); $[\alpha]_D^{20}$: +65.2 (*c* 1.05, H_2O) {lit: $[\alpha]_D^{24}$: +85.5 (*c* 0.1, H_2O);[5f] mp 238–242 °C, $[\alpha]_D^{20}$: +63.2 (*c* 1, H_2O)[41]}; ^{1}H NMR (D_2O): δ = 3.52 (m, 4H), 3.70 (m, 4H), 3.96 (br s, 4H); ^{13}C NMR (D_2O): δ = 71.0 (CH), 72.3 (CH), 73.3 (CH); HR-MS-ESI: *m*/*z* = 203.0532 $[M+Na]^+$, calcd. for $C_6H_{12}NaO_6$: 203.0526. ^{1}H and ^{13}C NMR data were in good agreement with those reported.[5f,41]

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