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Regio- and Stereoselective Synthesis of Aminoinositols and 1,2-Diaminoinositols from Conduritol B Epoxide

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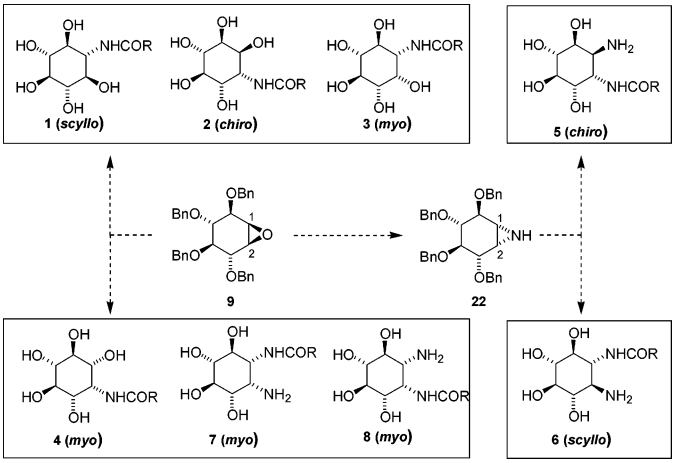

A systematic approach to the regio- and stereoselective synthesis of aminoinositols and 1,2-diaminoinositols arising from tetra-*O*-benzylconduritol B epoxide (**9**) and its aziridine analogue **22**, respectively, is described. In all cases, the synthetic methodologies rely on the regio- and stereocontrolled azidolysis of the starting precursors to give the corresponding trans regioadducts. Subsequent functional group manipulation under strict configurational control affords the isomeric cis adducts. Chemoselective functionalization of the diamine moiety in 1,2-diaminoinositol derivatives can be achieved by the proper design of the reaction sequence and choice of reagents. The described protocols allow efficient access to each of the eight possible configurations of the 1,2-diamino and 1,2-amino alcohol moieties from chemical modifications of the epoxide moiety on the common precursor **9**.

Aminoinositols constitute a wide group of natural products with interesting biological properties. In particular, the aminocyclitol family of antibiotics[1] has stimulated the development of synthetic methodologies in the search for analogues with an enhanced pharmacological profile,[2] as well as studies on the chemistry of the amino sugar moiety[3−5] and their use as synthetic intermediates in natural products chemistry.[6] In addition, aminocyclitol analogues have also gained relevance as glycomimetics,[7] as enzyme inhibitors with multiple biomedical applications,[8] and also as pharmacological tools for the study of

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(1) Ogawa, S. In *Carbohydrates in Drug Design*; Witczak, Z., Nieforth, K., Eds.; Dekker: New York, 1997; pp 433−469.

(2) For examples of synthesis of cyclitol derivatives, see: (a) Gravier-Pelletier, C.; Maton, W.; Dintinger, T.; Tellier, C.; Le Merrer, Y. *Tetrahedron* **2003**, *59*, 8705−8720. (b) Miyabe, H.; Nishiki, A.; Naito, T. *Chem. Pharm. Bull.* **2003**, *51*, 100−103. (c) Gomez, A. M.; Moreno, E.; Valverde, S.; Lopez, J. C. *Tetrahedron Lett.* **2002**, *43*, 7863−7866. (d) Marco-Contelles, J.; Rodriguez-Fernandez, M. *C. R. Acad. Sci. Ser. II C* **2001**, *4*, 443−452. (e) Sellier, O.; Van de Weghe, P.; Le Nouen, D.; Strehler, C.; Eustache, J. *Tetrahedron Lett.* **1999**, *40*, 853−856.

(3) Eguchi, T.; Sasaki, S.; Huang, Z.; Kakinuma, K. *J. Org. Chem.* **2002**, *67*, 3979−3984.

(4) Agnelli, T.; Sucheck, S. J.; Marby, K. A.; Rabuka, D.; Yao, S. L.; Sears, P. S.; Liang, F. S.; Wong, C. H. *Angew. Chem., Int. Ed.* **2004**, *43*, 1562−1566.

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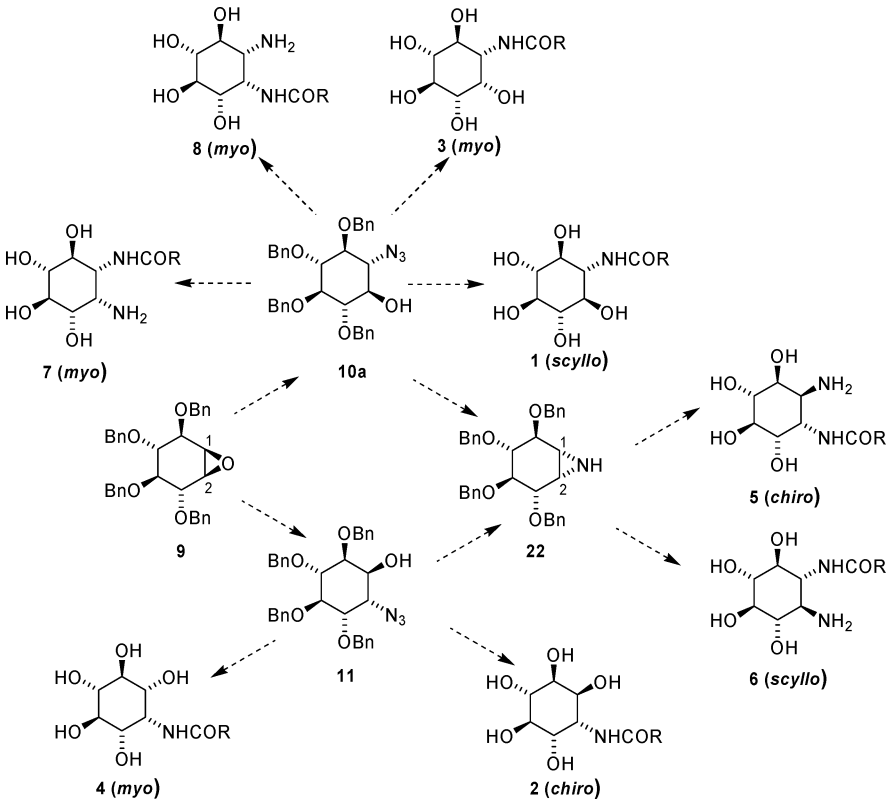
SCHEME 1. Amino- and 1,2-Diaminoinositols Synthesized in This Work



the inositol phosphate cycle and related processes.[9] On the other side, albeit not so deeply explored, the 1,2-diaminoinositol framework has also been incorporated into new salen asymmetric catalysts[10,11] and also into new water-soluble antitumor platinum complexes[12,13] and other chelating agents.[14] Moreover, amides derived from the simple *trans*-1,2-cyclohexanediamine have been described as "universal" gelling agents.[15] However, there are few general chemo- and stereoselective synthetic protocols leading to *N*,*N*′-1,2-diaminoinositols, and most of the described procedures afford identically *trans*-*N*,*N*′-disubstituted compounds.[16] Examples of cis derivatives are scarce and the synthetic protocols described so far also lead to identically bis-functionalized *N*,*N*′-diamino adducts.[17,18]

In the context of our current research on the synthesis and enzyme inhibitory studies of inositol derivatives,[19] we were interested in the development of a versatile synthetic approach for the chemo-, regio-, and stereoselective synthesis of *N*-octanoyl derivatives of amino- and 1,2-diaminoinositols, as pharmacological tools for our current biochemical studies. Synthesis of the target inositol derivatives has been devised from chemical

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(6) (a) Schilling, S.; Rinner, U.; Chan, C.; Ghiviriga, I.; Hudlicky, T. *Can. J. Chem.* **2001**, *79*, 1659−1667. (b) Frontier, A. J.; Raghavan, S.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2000**, *122*, 6151−6159. (c) Suzuki, T.; Tanaka, S.; Yamada, I.; Koashi, Y.; Yamada, K.; Chida, N. *Org. Lett.* **2000**, *2*, 1137−1140.

(7) *Carbohydrate Mimics, Concepts and Methods*; Chapleur, Y., Ed.; Wiley-VCH: Weinheim, 1998.

(8) For recent examples of inositol derivatives as enzyme inhibitors see: (a) Bashir-Uddin Surfraz, M.; Miller, D. J.; Gani, D.; Allemann, R. K. *Tetrahedron Lett.* **2003**, *44*, 7677−7679. (b) Mills, S. J.; Potter, B. V. L. *Bioorg. Med. Chem.* **2003**, *11*, 4245−4253. (c) Mills, S. J.; Backers, K.; Erneux, C.; Potter, B. *Org. Biomol. Chem.* **2003**, *1*, 3546−3556. (d) Chang, Y.; Choi, G.; Bae, Y.; Burdett, M.; Moon, H.; Lee, J.; Gray, N.; Schultz, P.; Meijer, L.; Chung, S.; Choi, K.; Suh, P.; Ryu, S. *ChemBioChem* **2002**, *3*, 897−901. (e) Ahn, Y.; Chung, S. *Bull. Korean Chem. Soc.* **2002**, *23*, 515−517.

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(16) For *trans*-1,2-diaminocyclitols from N-tosyl or N-acyl aziridines see: (a) Reference 7. (b) Paul, B. J.; Martinot, T. A.; Willis, J.; Hudlicky, T. *Synthesis−Stuttgart* **2001**, 952−956. (c) Paulsen, H.; Mielke, B. *Liebigs Ann. Chem.* **1990**, 169−180. (d) Kresze, G.; Melzer, H. *Liebigs Ann. Chem.* **1981**, 1874−1879. From reaction of a *trans*-1,2-dimesylate with sodium azide, see: (e) De Almeida, M. V.; Figueiredo, R. M.; Dos Santos, H. F.; Da Silva, A. D.; De Almeida, W. B. *Tetrahedron Lett.* **2001**, *42*, 2767−2769. For general synthesis of *trans*-1,2-diaminocyclohexane derivatives from *N*-substituted aziridinecyclohexane derivatives, see: (f) Watson, I. D.; Yudin, A. K. *J. Org. Chem.* **2003**, *68*, 5160−5167. (g) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew Chem., Int. Ed.* **2001**, *40*, 2004−2021. (h) Karpf, M.; Trussardi, R. *J. Org. Chem.* **2001**, *66*, 2044−2051. (i) Mitchell, J. M.; Finney, N. S. *Tetrahedron Lett.* **2000**, *41*, 8431−8434.

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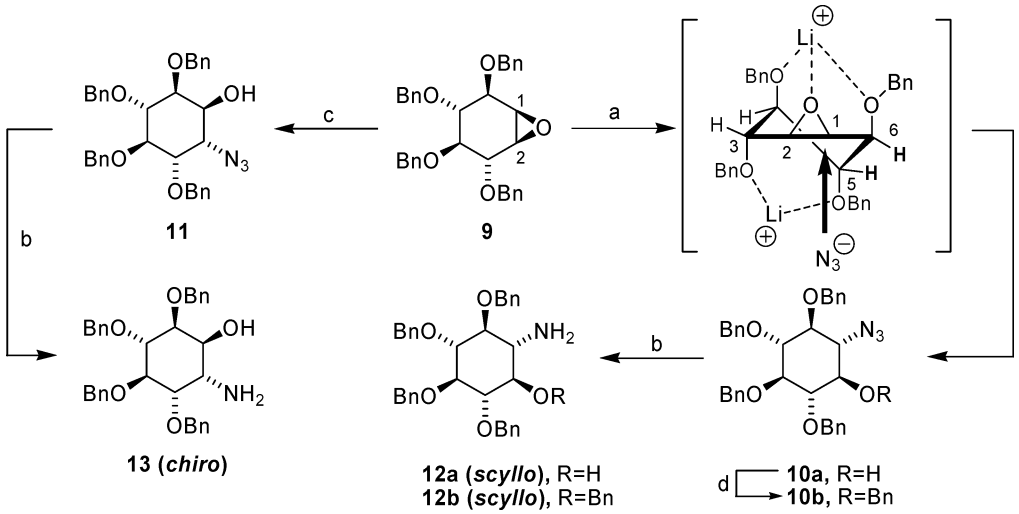
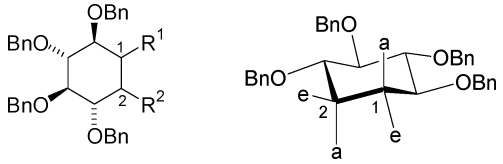
SCHEME 2[a]



[a] Reagents and conditions: (a) NaN_3, CH_3CN, 2 N $LiClO_4$ (91%); (b) $LiAlH_4$, THF (92−99%) from **10a**, **10b**, and **11**; (c) NaN_3, 1.2 N NH_4Cl (MeOH/H_2O) (89%); (d) NaH, BnCl, THF (95%).

TABLE 1. NMR Data of Azido Amines 23, 24, 28, and 30



entry	compound	R^1 (a/e)[a]	R^2 (a/e)[a]	relative stereochemistry	C*H*-N_3	C*H*-NH_2	J $_{H1-H2}$	*C*-N_3 (calcd)[b]	*C*-NH_2 (calcd)[b]
1	**23**	N_3 (a)	NH_2 (a)	trans	4.21	3.41	3.9	63.1 (63.2)	50.9 (49.0)
2	**24**	NH_2 (e)	N_3 (e)	trans	3.26	2.68	10.2	67.0 (69.6)	53.9 (55.3)
3	**28**	NH_2 (e)	N_3 (a)	cis	4.07	2.61	3.0	63.5 (66.9)	52.5 (52.8)
4	**30**	N_3 (e)	NH_2 (a)	cis	3.38	4.21	3.0	68.8 (65.9)	63.2 (51.5)

[a] (a/e) denotes the axial or equatorial disposition of the R group. [b] Calculated from ref 39.

manipulation of a suitably protected conduritol B epoxide (**9**) (Scheme 1).[20]

The stereoselective opening of epoxycyclohexane derivatives with nucleophiles to give the corresponding trans adducts has been extensively reported in the literature.[21] However, examples on cyclitol epoxides are less abundant and, in general, the regioselectivity of the process is determined by conformational grounds that can be modulated by proper choice of reaction conditions. Closely related to our previous work[22] on the role of chelating Lewis acids on the regioselective opening of these systems,[23] azidolysis of **9** in the presence of 2 N $LiClO_4$ led to the C1 trans adduct **10a** through a putative "all-axial" conformation (Scheme 2).[24] Further azide reduction afforded aminoinositol **12**, a representative of the 1-amino-1-deoxy-*scyllo*-inositol series. Stereochemical assignment in this series was unambiguously confirmed by the simplification of the NMR pattern of fully benzylated azide **10b**, due to the inherent symmetry of the resulting derivative.

Conversely, azidolysis under acidic "nonchelating" conditions (MeOH/1.2 N NH_4Cl (4:1), 80 °C) afforded the regioisomeric C2 trans adduct **11** as precursor of the 1-amino-1-deoxy-*chiro*-inositol **13**. The assigned stereochemistry was inferred from the downfield chemical shift for the C(*H*)N_3 proton (around 4.05−4.10 ppm), as observed in related amino azide **23** (see Table 1).[25] This reaction outcome is consistent with the expected epoxide opening under the above conditions.[26]

Installation of the cis stereochemistry leading to amino-deoxy-*myo*-inositol derivatives (Scheme 1) was

(20) For the sake of simplicity, the synthetic methodology described in this work has been carried out from the easily available racemic tetra-*O*-benzylconduritol B epoxide **9**, obtained from (±)-conduritol B by epoxidation (MCPBA, MeOH) followed by benzylation (BnBr, NaH, DMF). For the synthesis of enantiopure **9**, see ref 22. For general syntheses of enantiopure conduritol B epoxide derivatives from the chiral pool, see: (a) Falshaw, A.; Hart, J. B.; Tyler, P. C. *Carbohydr. Res.* **2000**, *329*, 301−308. (b) Takahashi, H.; Iimori, T.; Ikegami, S. *Tetrahedron Lett.* **1998**, *39*, 6939−6942. (c) Watanabe, Y.; Mitani, M.; Ozaki, S. *Chem. Lett.* **1987**, 123−126. Enantiopure conduritol B from deracemization of conduritol B tetracarbonate: Trost, B. M.; Patterson, D. E.; Hembre, E. J. *Chem. Eur. J.* **2001**, *7*, 3768−3775.

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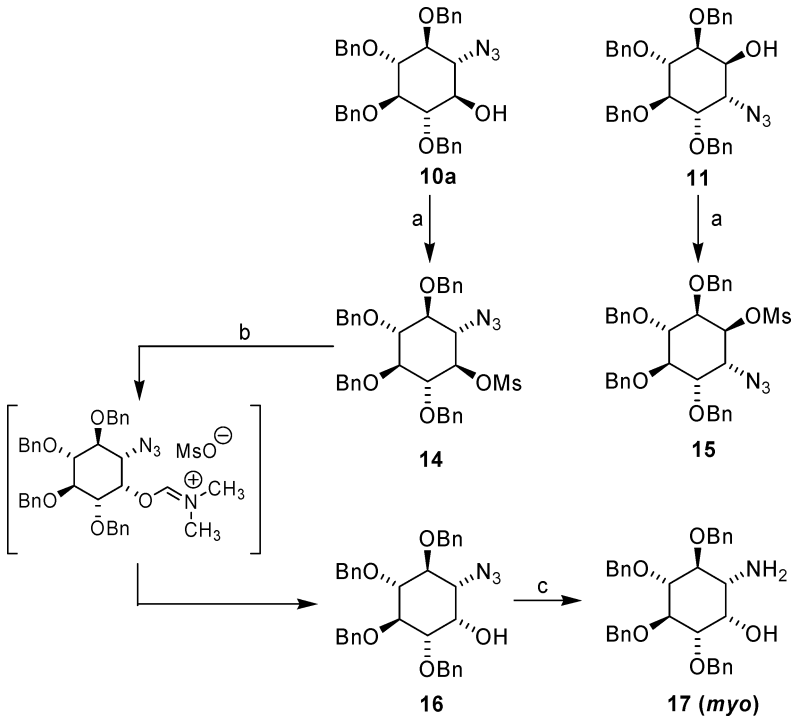
(22) Serrano, P.; Llebaria, A.; Delgado, A. *J. Org. Chem.* **2002**, *67*, 7165−7167.

(23) For the use of chelation-controlled aminolysis and azidolysis of 1,2-epoxycyclohexanes bearing remote polar groups, see Calvani, F.; Crotti, P.; Gardelli, C.; Pineschi, M. *Tetrahedron* **1994**, *50*, 12999−13022 and references therein.

(24) A theoretical study of this reaction has been carried out. Serrano, P.; Llebaria, A.; Vazquez, J.; de Pablo, J.; Anglada, J. M.; Delgado, A. *Chem. Eur. J.* **2005**, *11*, 4465−4472.

SCHEME 3[a]



[a] Reagents and conditions: (a) MsCl, Et_3N, THF (88−92%); (b) DMF, 140 °C, sealed tube (82%); (c) $LiAlH_4$, THF (87%).

attempted by stereochemical inversion of mesylate **14** arising from azido alcohol **10a**. Thus, we were pleased to observe that treatment of mesylate **14** in DMF in a sealed tube at 140 °C for prolonged reaction times cleanly afforded *cis*-azido alcohol **16** with exquisite stereocontrol (Scheme 3).[27] Again, the stereochemical assigment was carried out by NMR, in particular the chemical shifts and coupling constants of the vicinal C(*H*)N_3 and C(*H*)OH protons. Thus, C(*H*)N_3 shows one large (J = 10 Hz) and one small J value (J' = 2.5 Hz) in agreement with its axial disposition. On the other side, C(*H*)OH appears as an apparent triplet of small coupling constants ($J = J'$ = 2.5 Hz). The stereochemical outcome of this transformation can be rationalized by assuming a S_N2 mesylate displacement by DMF with formation of an intermediate imidate ester salt, leading ultimately to azido alcohol **16**.[28,29] This transformation seems strongly dependent on the configuration of the starting azido alcohol, since regioisomeric *trans*-azido mesylate **15** was recovered unaltered under otherwise identical reaction conditions (Scheme 3).[30] If we assume that conformational equilibrium is frozen in **14** and **15** by the "all-equatorial" disposition of the OBn groups, azido mesylate **15** could be expected to react faster than **14** due to the axial disposition of the mesyloxy group.[31] However, the observed results are in agreement with the operation of singular stereoelectronic effects, as described in related systems.[32] Finally, reduction of the azide group in **16** afforded 1-amino-1-deoxy-*myo*-inositol derivative **17**.

Synthesis of regioisomeric 2-amino-2-deoxy-*myo*-inositol was next attempted from *N*-Boc amino alcohol mesylate **19** (Scheme 4), configurationally equivalent to the above azido mesylate **15**. This alternative approach relied on the configurational inversion of the carbon atom bearing the mesyloxy group through a stereospecific in situ intramolecular oxazolidinone formation, as described

(25) In all cases, the major conformation is assumed to be that imposed by the "all-equatorial" disposition of the OBn groups.

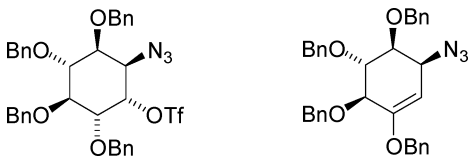
(26) For epoxide opening under nonchelating conditions, see, inter alia: (a) Uzan, R.; Letellier, P.; Ralainairina, R.; Beaupère, D. *Synthesis* **1994**, 925−930. (b) Nakata, M.; Chong, C.; Niwata, Y.; Toshima, K.; Tatsuta, K. *J. Antibiot.* **1993**, *46*, 1919−1922. (c) Letellier, P.; Rallainirina, R.; Uzan, R.; Beaupère, D. *Tetrahedron Lett.* **1994**, *35*, 4555−4558. (d) Ogawa, S.; Chida, N.; Suami, T. *J. Org. Chem.* **1983**, *48*, 1203−1207.

(27) Formation of minor amounts of azido alcohol **16** had already been observed in reaction of mesylate **14** with other nucleophiles in DMF (unpublished results from our group).

(28) Imidate esters salts have been proposed as reaction intermediates for the conversion of alcohols into formate esters. See, for example: (a) Barluenga, J.; Campos, P. J.; González-Núñez, E.; Asensio, G. *Synthesis* **1985**, 426−428. (b) Riley, A. M.; Jenkins, D. J.; Potter, B. V. L. *Carbohydr. Res.* **1998**, *314*, 277−281. Although we have never observed the corresponding formate ester, its formation and in situ hydrolysis along the reaction course cannot be ruled out.

(29) It is worth mentioning that this transformation is independent of the water content, since identical results have been obtained by using DMF systems containing variable amounts of water. For a similar transformation, in a DMF−H_2O system, see: Angyal, S. J.; Odier, L. *Carbohydr. Res.* **1980**, *80*, 203−206.

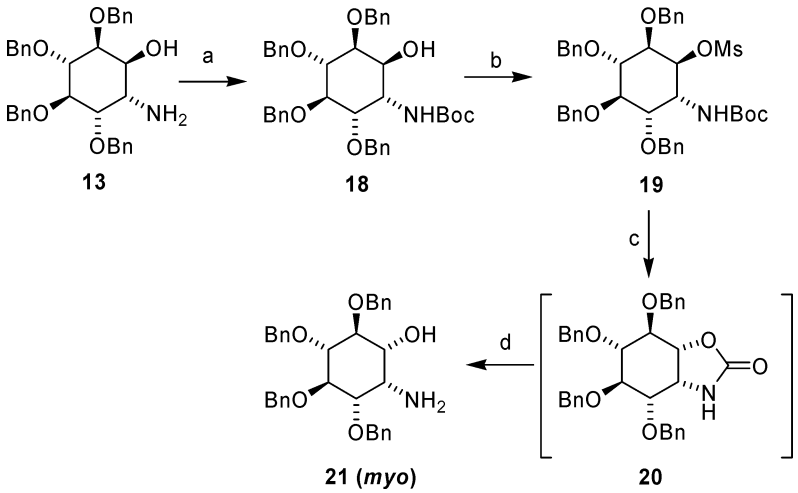
(30) Mesylate **15** also failed to react with other nucleophiles, such as sodium azide, potassium phthalimide (see text), or benzoic acid/CsF, whereas the corresponding triflate **A** gave the anti elimination adduct **B**.



(31) Eliel, E.; Ro, R. S. *J. Am. Chem. Soc.* **1957**, *79*, 5995−6000.

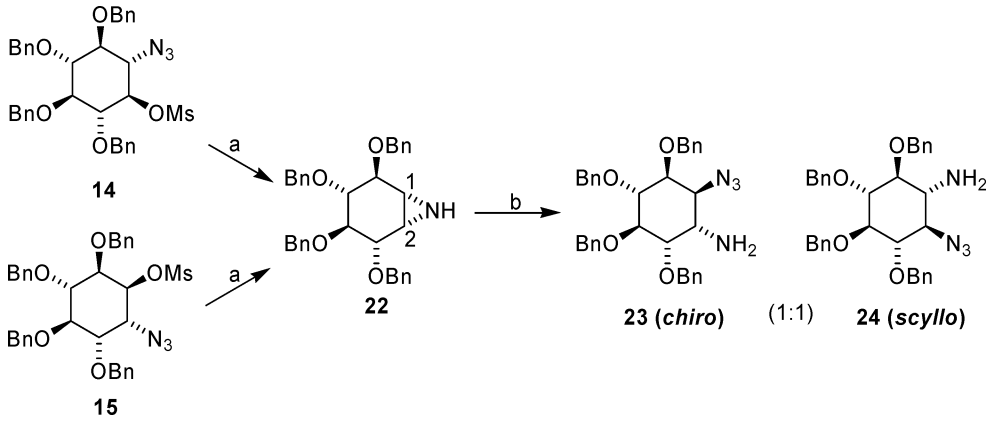
(32) For related examples of the effect of stereoelectronic effects on the reactivity of inositol derivatives, see: (a) Guidot, J. P.; Legall, T. *J. Org. Chem.* **1993**, *58*, 5271−5273. (b) Shing, T. K.; Wan, L. H. *J. Org. Chem.* **1996**, *61*, 8468−8479.

SCHEME 4[a]



[a] Reagents and conditions: (a) $(Boc)_2O$, acetone (78%); (b) MsCl, Et_3N, THF (84%); (c) DMF, 120 °C, 16 h; (d) 1 N NaOH−MeOH, 80 °C, 24 h (65%).

SCHEME 5[a]



[a] Reagents and conditions: (a) $LiAlH_4$, THF, 0 °C (90%); (b) NaN_3 (20 equiv); NH_4Cl (1 equiv), MeOH:H_2O (9:1), 80 °C (82%).

for related vicinal *N*-Boc amino alcohol mesylates.[33] Thus, aminoinositol **13** was converted into *N*-Boc aminocyclitol mesylate **19**, which, under thermal conditions (DMF, 120 °C) followed by in situ hydrolysis, afforded the required 2-amino-2-deoxy-*myo*-inositol derivative **21**, presumably through a putative oxazolidinone **20** intermediate, as shown in Scheme 4. Stereochemical assignment of amino alcohol **21** was corroborated from comparison with regioisomeric amino alcohol **17**, in particular the C(*H*)NH_2 proton chemical shifts. Thus, while this proton is observed at 2.64 ppm in **17**, it is found around 1.0 ppm downfield shifted in **21**, in agreement with its expected equatorial disposition.[25]

Diamino derivatives of the *chiro* and *scyllo* series, showing a trans relationship between both nitrogen atoms, have been obtained from the hitherto unprecedented aziridine **22** (Scheme 5). This was obtained, in turn, by reduction of azido mesylates **14** or **15**, followed by in situ intramolecular displacement of the transient amino mesylates. Opening of aziridine **22** with sodium azide under acid catalysis afforded a 1:1 mixture of azido amines **23** (*chiro*) and **24** (*scyllo*),[34] which could be easily separated by flash chromatography.

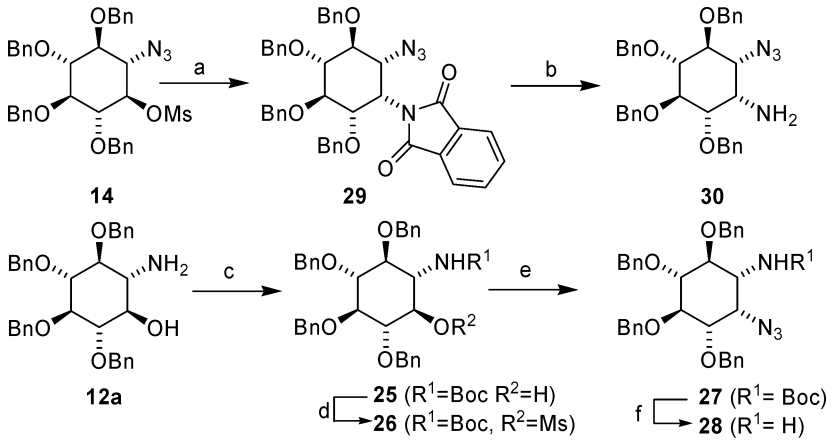
Regioselective synthesis of 1,2-diamino-1,2-dideoxy-*myo*-inositol derivatives, showing a cis relationship between both nitrogen atoms, was first envisaged from azido mesylate **14**. Thus, nucleophilic displacement of the mesyloxy group in **14** with potassium phthalimide (DMF, 140 °C, 48 h) afforded adduct **29** with complete configurational inversion (Scheme 6).[35] Hydrazinolysis of **29** afforded cis azido amine **30**, a key synthetic precursor of the 1,2-diamino-*myo*-inositol series. Access to the regioisomeric cis azido amine **28** was first attempted following a similar procedure from mesylate **15**. However, treatment of **15** with excess (3 equiv/mol) potassium phthalimide led to the recovery of the starting material, even

(33) Benedetti, F.; Norbedo, S. *Tetrahedron Lett.* **2000**, *41*, 10071−10074.

(34) For a similar process, see: Rohloff, J. C.; Kent, K. M.; Postich, M. J.; Becker, M. W.; Chapman, H. H.; Kelly, D. E.; Lew, W.; Louie, M. S.; McGee, L. R.; Prisbe, E. J.; Schultze, L. M.; Yu, R. H.; Zhang, L. J. *J. Org. Chem.* **1998**, *63*, 4545−4550.

(35) The reactivity of mesylate **14** with nonanionic nitrogen nucleophiles was somewhat sluggish. Thus, no reaction was observed with butylamine or diethylamine under forcing conditions (10 equiv, DMF, 90 °C, 48 h, sealed tube). On the contrary, reaction of **14** with sodium azide (DMF, 100 °C) afforded the expected *cis*-diazide, whose spectroscopic data matched those described in the literature (ref 18).

SCHEME 6[a]



[a] Reagents and conditions: (a) potassium phthalimide, DMF, 140 °C, 72 h (56%); (b) N_2H_4, THF, 80 °C, (79%); (c) $(Boc)_2O$, acetone, rt (78%); (d) MsCl, DCM, TEA, rt (84%); (e) NaN_3, DMF, 120 °C (75%) from **26**; (f) HCl:AcOEt (1:20), rt (95%).

under forcing conditions (DMF, 140 °C, 72 h).[30] This result is illustrative of the dramatic influence of stereoelectronic effects in the reactivity of inositol derivatives. On the other hand, attempts to exploit the reactivity of **29** by reducing the azide group to the corresponding amine were unsuccessful under a variety of conditions (catalytic hydrogenation, Zn/NH_4Cl or $NaBH_4$).

As an alternative approach, we turned our attention to trans amino alcohol **12**, whose transformation into cis azido amine **28** is outlined in Scheme 6. Protection of the amino group, to give carbamate **25**, followed by hydroxyl group activation to mesylate **26**, followed by azide displacement[36,37] and *N*-Boc removal, afforded the desired amino azide intermediate **28**.

Stereochemical assignments on the diamino-inositol series were also carried out by NMR methods by comparison of C(1)H and C(2)H chemical shifts and coupling constants of azido amines **23**, **24**, **28**, and **30** (see Table 1).[38] The observed results are in agreement with a major or exclusive conformation with an "all-equatorial" disposition of the OBn groups. It is worth mentioning the strong deshielding effect (between 0.8 and 1.5 ppm) observed for C*H*-N_3 and C*H*-NH_2 equatorial protons compared with their axial counterparts. Moreover, a large H_1-H_2 coupling constant (around 10.2 Hz) is also observed for **24**, in agreement with the *trans*-diaxial disposition for these protons. Concerning ^{13}CNMR data, an excellent fit between observed and calculated chemical shifts for *C*-N_3 and *C*-NH_2 carbon atoms was found. The only exception was observed in compound *cis*-**30** (entry 4), where *C*-NH_2 carbon atom was deshielded by around 12 ppm with respect to the expected value.

With protected aminoinositols **12**, **13**, **17**, **21** and 1-amino-2-azidoinositols **23**, **24**, **28**, and **30** in hand, synthesis of our target inositols was next envisaged. Acyl aminoinositols required acylation of the amino group and final OBn deprotection. However, while acylation with *n*-octanoyl chloride was straightforward, deprotection was rather cumbersome and required a thorough examination. Initial experiments were carried out on amide **31** under standard hydrogenolysis conditions in the presence of $Pd(OH)_2$ or Pd−C as catalysts in MeOH as solvent. In both cases, the reaction progress was very slow and required several days for completion.[40] Catalytic transfer hydrogenation with formic acid as hydrogen source[41] in a mixture of *t*-BuOH/THF (1:1) at 40°C was also considered. Although amide **31** could be deprotected in good yield under these conditions after 72 h, the reaction was too sluggish for practical purposes. Gratifyingly, benzyl removal could be efficiently achieved with BCl_3 in CH_2Cl_2 at −78°C. Under these conditions, fully deprotected 1-(*N*-octanoylamino)-*scyllo*-inositol hydrochloride **1** was obtained in excellent yield after a simple workup. The above sequence of *N*-acylation and deprotection was used for the remaining aminoinositol members **2**−**4**, as shown in Scheme 7.

Diaminoinositol derivatives were similarly obtained from 1-amino-2-azidoinositols **23**, **24**, **28**, and **30** (Scheme 8). It is worth mentioning the efficient, chemoselective reduction of the azide group in tetra-*O*-benzyl *N*-acyl derivatives **35**, **37**, **39**, and **41** by catalytic hydrogenation under mild conditions. In this case, the above-mentioned poisonous effect of polybenzylated aminoinositols toward benzyl ether hydrogenolysis[40] was crucial for the success of this transformation.[42]

In summary, the herein described methodology represents a versatile approach to the regio-, and stereoselective synthesis of *N*-acyl derivatives of amino- and 1,2-

(36) The relative configuration present in mesylates **14** and **26**, in which the mesyloxy group shows a trans relationship with respect to both of the substituents on the adjacent carbon atoms, seems to be the only one operative for intermolecular substitution with anionic nitrogen nucleophiles. Compare, for example, the reactivity of the above mesylates with that of diastereomeric mesylate **15** (see text) or triflate **A**, as indicated in ref 30.

(37) For a similar sequence leading to differently functionalized *N*,*N*′-*cis*-1,2-diaminocyclohexane derivatives, see: Govindaraju, T.; Gonnade, R. G.; Bhadbhade, M. M.; Kumar, V. A.; Ganesh, K. N. *Org. Lett.* **2003**, *5*, 3013−3016.

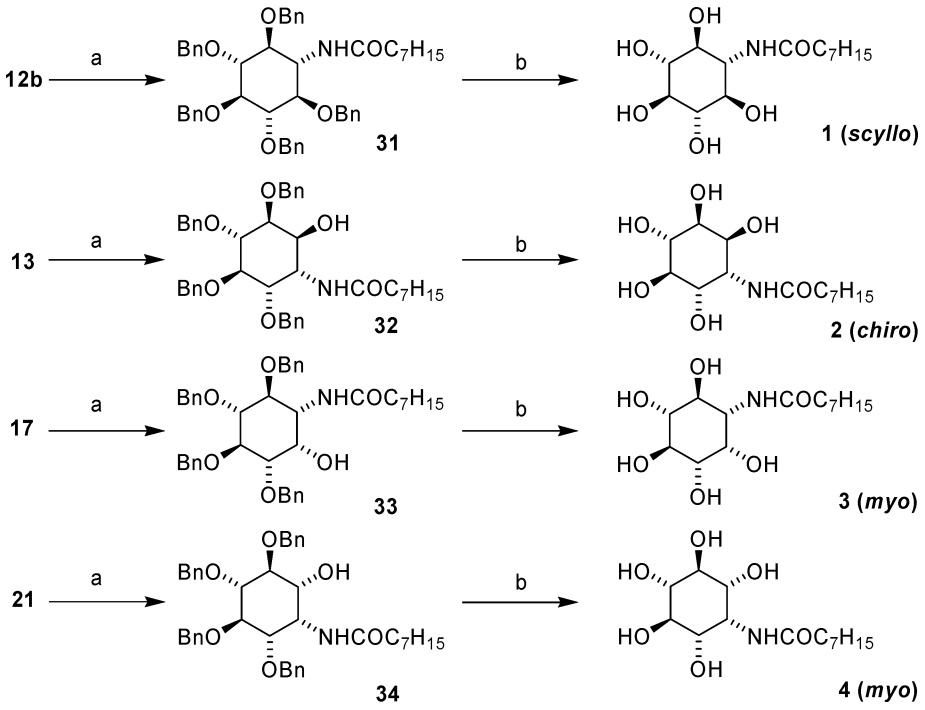
(38) Bidimensional nOe experiments from azido *N*-octanoyl derivative **35** were also in agreement with the stereochemical assignment for precursor azido amine **23** (see Supporting Information).

(39) Pretsch, E.; Clerc, T.; Seibl, J.; Simon, W. *Tablas para la determinación estructural por métodos espectroscópicos*; Springer-Verlag Ibérica: Barcelona, 1998.

(40) Polybenzylated aminocyclitols have been reported to be poisonous for the Pd/C catalysed hydrogenolysis of benzyl ethers (Surfraz, M. B. U.; Akhtar, M.; Allemann, R. K. *Tetrahedron Lett.* **2004**, *45*, 1223−1226).

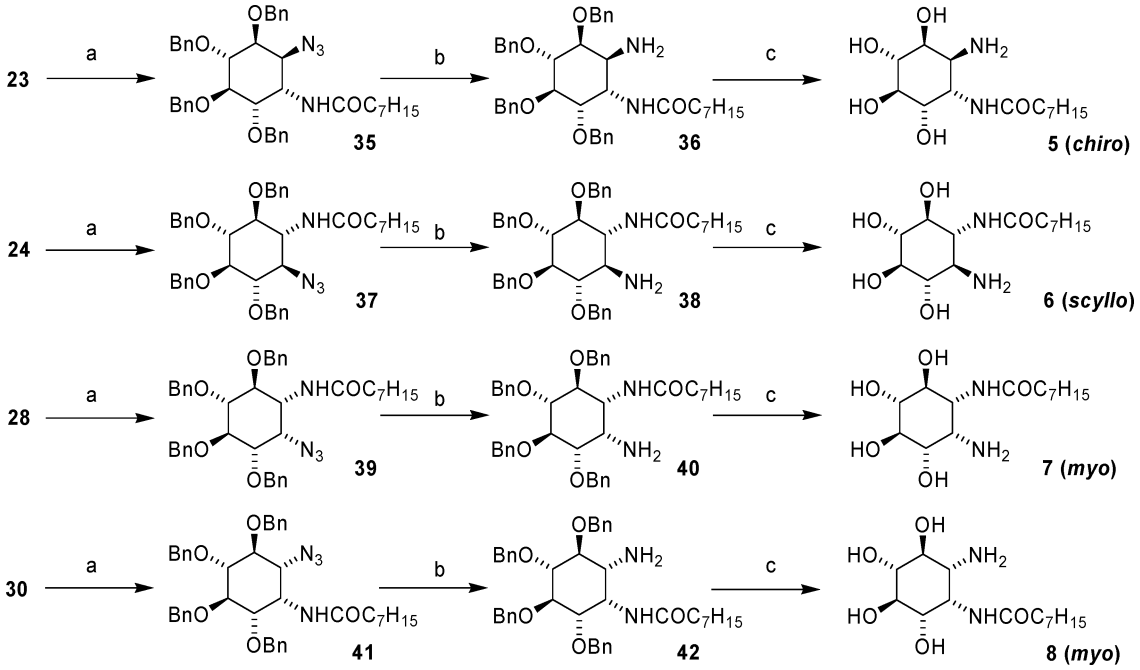
(41) Elamin, B.; Anantharamaiah, G. M.; Royer, G. P.; Means, G. E. *J. Org. Chem.* **1979**, *44*, 3442−3444.

SCHEME 7[a]



[a] Reagents and conditions: (a) $C_7H_{15}COCl$, CH_2Cl_2, Et_3N (78−90%); (b) 1 M in heptane BCl_3, CH_2Cl_2 (65−83%).

SCHEME 8[a]



[a] Reagents and conditions: (a) $C_7H_{15}COCl$, CH_2Cl_2, Et_3N (79−87%); (b) H_2, Pd/C, THF, rt; (c) 1 M in heptane BCl_3, CH_2Cl_2 (70−76%).

diaminoinositols derived from conduritol B epoxide as a common precursor. Described protocols allow the "on demand" access to each of the configurations of the diamino and amino alcohol moieties present in these systems. Interestingly, 2-azido-1-aminoinositols **23**, **24**, **28**, and **30** are suitable synthetic intermediates for the chemoselective functionalization of each of the nitrogen atoms. These findings open new opportunities for the synthesis of inositol analogues and the study of their biological profiles.

Experimental Section

For General Methods, see the Supporting Information.

(1*RS*,2*RS*,3*SR*,4*RS*,5*RS*,6*SR*)-2-Azido-3,4,5,6-tetrakis-benzyloxycyclohexanol (10a). A solution of the starting epoxide **9** (500 mg, 0.96 mmol) in CH_3CN (17 mL) was added

dropwise under argon over $LiClO_4$ (160 mg, 1.50 mmol) at room temperature. A solution of 624 mg (9.6 mmol) of NaN_3 in CH_3CN (4 mL) was added next and the reaction mixture was stirred at 80 °C under argon. After 18 h, the reaction mixture was cooled to room temperature, quenched with H_2O (10 mL), extracted with CH_2Cl_2 (3 × 20 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation afforded crude azido alcohol, which was purified by filtration through a plug of silica and elution with hexanes/EtOAc (1:1) to afford 492 mg (0.87 mmol, 91%) of **10a**. IR (film): 3331, 3057, 2107, 1489, 1457, 1359, ^{13}C NMR (75 MHz): 66.4, 72.6, 75.7, 75.9, 75.8, 76.0, 81.1, 82.4, 82.6, 83.4, 127.6−128.5, 137.5−138.1; ^1H NMR (300 MHz): 3.40−3.44 (m, 4H), 3.50−3.69 (m, 2H), 4.75−4.96 (m, 8H), 7.26−7.35 (m, 20H). Anal. Calcd for $C_{34}H_{35}N_3O_5$: C, 72.19; H, 6.24; N, 7.43 Found: C, 72.23; H, 6.22; N, 7.39.

(1*RS*,2*RS*,3*SR*,4*SR*,5*RS*,6*SR*)-1-azido-2,3,4,5,6-pentakisbenzyloxycyclohexane (10b). A solution of alcohol **10a** (1.4 g, 3.0 mmol) in anhydrous THF (20 mL) was added dropwise over an ice-cooled suspension of sodium hydride (60% dispersion in mineral oil, 270 mg, 11.25 mmol), previously washed with hexane (3 × 10 mL) in tetrahydrofuran (25 mL) under an atmosphere of argon. Stirring was continued until complete gas evolution, and benzyl chloride (0.45 mL, 3.79 mmol) was added next. The reaction mixture was stirred at room temperature for 24 h, quenched with water (10 mL), and extracted with diethyl ether (3 × 25 mL). The combined organic layers were washed with brine (20 mL), dried, and concentrated. The resulting oil was purified by flash chromatography using a mixture of hexane/ethyl acetate (4:1) as eluent to afford azide **10b** (95%); oil; IR (film): 3031, 2909, 2107, 1496, 1454, 1359; ^1H NMR (300 MHz): 3.34−3.38 (2H, m, 2 × C*H*), 3.46−3.58 (4 H, m, 4 × C*H*), 4.84−4.90 (10H, m, 5 × OC*H*$_2$Ph), 7.2−7.4 (25H, m, Ar). ^{13}C NMR (75 MHz): 53.2, 66.9, 73.5 (2×), 75.9 (2×), 82.4, 83.1 (4×), 127.7−128.4, 137.7, 138.1. Anal. Calcd for $C_{41}H_{41}N_3O_5$: C, 75.09; H, 6.30; N, 6.41. Found: C, 75.18; H, 6.27; N, 6.56.

(1*RS*,2*RS*,3*RS*,4*SR*,5*SR*,6*RS*)-2-Azido-3,4,5,6-tetrakisbenzyloxycyclohexanol (11). A solution of the starting epoxide **9** (260 mg, 0.5 mmol) in a 4:1 mixture of MeOH/aqueous 1.2 N NH_4Cl (10 mL) was treated with NaN_3 (325 mg, 5 mmol). The reaction mixture was stirred at 80 °C for 20 h, cooled to room temperature, diluted with H_2O (10 mL), extracted with Et_2O (4 × 15 mL), and dried over anhydrous. Na_2SO_4. Filtration and evaporation afforded crude azido alcohol, which was purified by filtration through a plug of silica and elution with hexanes/EtOAc (1:1) to afford 475 mg (0.84 mmol, 89%) of **11**; IR (film): 3342, 3090, 3036, 2980, 2106, 1497, 1369. ^{13}C NMR (125 MHz): 61.2, 68.7, 73.6, 73.7, 76.1, 76.2, 79.7 (2×, 79.8, 81.6, 127.8−128.8, 137.2−138.0. ^1H NMR (500 MHz): 3.70 (dd, J = 4.0, 8.0 Hz, 1H, H6), 3.78 (t, J = 9.0 Hz, 1H, H4), 3.87 (t, J = 9.5 Hz, 1H, H5), 3.97 (t, J = 3.5 Hz, 1H, H1), 4.05−4.10 (m, 2H, H2, H3), 4.65 (d, J = 11 Hz, 1H), 4.74−4.92 (m, 9H), 7.22−7.39 (m, 20H). Anal. Calcd for $C_{34}H_{35}N_3O_5$: C, 72.19; H, 6.24; N, 7.43. Found: C, 72.09; H, 6.30; N, 7.48.

General Method for Azide Reduction: Synthesis of Amino Alcohols 12a, 12b, 13, and 17. A solution of the corresponding azido alcohol (0.4 mmol) in THF (2.5 mL) was added to a suspension of $LiAlH_4$ (19 mg, 0.5 mmol) in THF (2.5 mL) at 0 °C. The reaction mixture was stirred for 2 h and EtOAc (2 mL) was added at 0 °C. The resulting suspension was diluted with H_2O (10 mL), extracted with Et_2O (4 × 10 mL), and dried to afford the crude amino alcohol, which was purified by flash chromatography using a mixture of hexane: EtOAc/TEA (2:1/2% vol).

(1*RS*,2*RS*,3*SR*,4*RS*,5*RS*,6*SR*)-2-Amino-3,4,5,6-tetrakisbenzyloxycyclohexanol (12a) (99%). IR (film): 3331, 3062, 3031, 2907, 1580, 1496, 1456, 1406. ^{13}C NMR (75 MHz): 56.8, 74.5, 75.5−76.5 (4×), 81.0, 81.5, 82.5, 83.2, 127.6−128.5, 138.3. ^1H NMR (300 MHz): 2.97 (*t*, J = 9.9 Hz, 1H), 3.35 (m, 2H), 3.62 (m, 3H), 4.68−5.01 (m, 10H), 7.24−7.40 (m, 20H). Anal. Calcd for $C_{34}H_{37}NO_5$: C, 75.67; H, 6.91; N, 2.60. Found: C, 75.73; H, 7.12; N, 2.58.

(1*RS*,2*SR*,3*RS*,4*SR*,5*SR*,6*RS*)-2,3,4,5,6-pentakisbenzyloxycyclohexylamine (12b) (99%). IR (film): 3331, 3062, 3031, 2907, 1580, 1496, 1456, 1406. ^{13}C NMR (75 MHz): 56.8, 74.5, 75.5−76.5 (4×), 81.0, 81.5, 82.5, 83.2, 127.6−128.5, 138.3.^1H NMR (300 MHz): 2.94 (t, J = 9.9 Hz, 1H), 3.35 (t, J = 9.0 Hz, 2H), 3.60−3.70 (m, 3H), 4.68−5.01(m, 10H), 7.24−7.34 (m, 25H). Anal. Calcd for $C_{41}H_{43}NO_5$: C, 78.19; H, 6.88; N, 2.22. Found: C, 78.24; H, 6.76; N, 2.21.

(1*RS*,2*RS*,3*RS*,4*SR*,5*SR*,6*RS*)-2-Amino-3,4,5,6-tetrakisbenzyloxycyclohexanol (13) (92%). IR (film): 3300, 3222, 3029, 2936, 1488, 1466, 1412. ^{13}C NMR (125 MHz): 42.5, 61.8, 72.2, 75.5, 76.1, 76.2, 80.7, 83.3, 84.3, 85.3, 127.9−128.8, 138.5, 138.6, 138.9. ^1H NMR (500 MHz): 2.52 (t, 10.0 Hz, 1H), 2.66 (m, 1H), 2.76 (m, 1H), 3.41 (t, J = 9.0 Hz, 1H), 3.47 (t, J = 9.9 Hz, 1H), 3.49 (t, J = 9.0 Hz, 1H), 3.58 (t, J = 9.5 Hz, 1H), 3.3.64 (t, J = 9.0 Hz, 1H), 4.70−5.02 (m, 8H), 7.24−7.34 (m, 20H); Anal. Calcd for $C_{34}H_{37}NO_5$: C, 75.67; H, 6.91; N, 2.60. Found: C, 75.72; H, 6.79; N, 2.63.

(1*RS*,2*SR*,3*RS*,4*SR*,5*SR*,6*RS*)-2-Amino-3,4,5,6-tetrakisbenzyloxycyclohexanol (17) (87%). IR (film): 3329, 3031, 2987, 1502, 1446, 1421. ^{13}C NMR (125 MHz): 52.1, 68.9, 72.1, 75.0, 75.2, 75.3, 80.7, 81.3, 81.4, 84.0, 127.6−128.8, 138.3−139.0. ^1H NMR (500 MHz): 2.64 (dd, J = 2.5, 10 Hz, 1H), 3.49 (m, 2H), 3.63 (t, J = 9.5 Hz, 1H), 3.96 (t, J = 10 Hz, 1H), 4.11−4.18 (broad, 1H), 4.60−5.03 (m, 8H), 7.24−7.34 (m, 20H). Anal. Calcd for $C_{34}H_{37}NO_5$: C, 75.67; H, 6.91; N, 2.60. Found: C, 75.46; H, 6.81; N, 2.55.

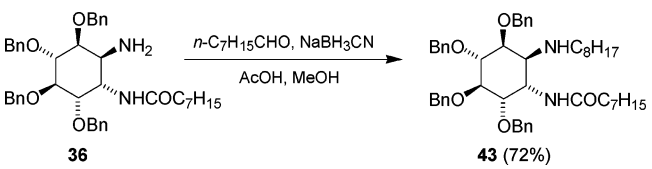
Synthesis of Azido Mesylates 14 and 15. A solution of the starting azido alcohol **10a** or **11** (277 mg, 0.49 mmol) and TEA (0.5 mL) in THF (20 mL) was treated with MsCl (58 mg, 0.51 mmol). The reaction mixture was stirred at room temperature for 20 h, diluted with H_2O (10 mL), extracted with Et_2O (4 × 15 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation afforded crude azido mesylates which were purified by filtration through a plug of silica and elution with hexanes/EtOAc (2:1).

(1′*RS*,2′*SR*,3′*SR*,4′*RS*,5′*SR*,6′*RS*)-(2-Azido-3,4,5,6-tetrakisbenzyloxy)cyclohexyl methanesulfonate ester (14) (289 mg, 0.45 mmol, 92%). IR (film): 3029, 2919, 2870, 2109, 1496, 1454, 1363. ^{13}C NMR (75 MHz): 39.3, 64.6, 75.9, 76.0, 76.1, 76.2, 80.2, 80.7, 80.8, 82.1, 82.9, 127.7−128.7, 137.2−137.9. ^1H NMR (300 MHz): 3.05 (s, 3H), 3.50 (t, J = 9 Hz, 1H), 3.58−3.70 (m, 4H), 4.48 (t, J = 9 Hz, 1H), 4.80−5.00 (m, 8H), 7.23−7.35 (m, 20H). Anal. Calcd for $C_{35}H_{37}N_3O_7S$: C, 65.30; H, 5.79; N, 6.53. Found: C, 65.58; H, 5.68; N, 6.70.

(1′*RS*,2′*SR*,3′*RS*,4′*SR*,5′*RS*,6′*SR*)-(2-Azido-3,4,5,6-tetrakisbenzyloxy)cyclohexyl methanesulfonate ester (15) (277 mg, 0.43 mmol, 88%). IR (film): 3031, 2920, 2870, 2109, 1469, 1454, 1354. ^{13}C NMR (75 MHz): 38.68, 60.0, 73.8, 73.9, 75.9, 76.1, 76.7, 77.1, 79.2, 80.8, 81.4, 127.7−128.7, 137.2−138.4. ^1H NMR (500 MHz): 2.95 (s, 3H), 3.74 (t, J = 10 Hz, 1H), 3.80 (dd, J = 3.0,10.0 Hz, 1H), 3.88 (t, J = 9.0 Hz, 1H), 4.02 (dd, J = 3.0,9.5 Hz, 1H), 4.10 (t, J = 4.0 Hz), 4.71−5.02 (m, 9H), 7.23−7.35 (m, 20H). Anal. Calcd for $C_{35}H_{37}N_3O_7S$: C, 65.30; H, 5.79; N, 6.53. Found: C, 65.21; H, 5.59; N, 6.73.

(1*RS*,2*SR*,3*RS*,4*SR*,5*SR*,6*RS*)-2-Azido-3,4,5,6-tetrakisbenzyloxycyclohexanol (16). A solution of **14** (100 mg, 0.15 mmol) in DMF (4 mL) was stirred at 140 °C in a sealed tube for 96 h. After the solvent was removed under reduced pressure, the resulting crude was taken up in Et_2O (5 mL), washed with H_2O (3 × 2 mL), treated with brine, and dried

(42) This unexpected chemoselectivity can be used for the selective functionalization of the amino group. The reductive amination of **36** with *n*-octanal to afford amino amide **43** (see below) is illustrative.



36 **43** (72%)

over anhydrous Na_2SO_4. Evaporation under reduced pressure afforded a crude, which was purified by flash chromatography on hexanes/EtOAc (1:1) to give **16** (76 mg, 82%); IR (film): 3298, 3050, 3036, 2970, 2105, 1489, 1369. ^{13}C NMR (125 Hz): 63.6, 69.2, 73.3, 76.1, 76.2, 76.3, 80.2, 80.5, 81.5, 84.2, 127.9−128.9, 137.7−138.6. ^{1}H NMR (500 MHz): 3.36 (dd, J = 2.5, 10.0 Hz, 1H, H2), 3.48 (dd, J = 3.0, 10.5 Hz, H6), 3.55 (t, J = 9.5 Hz, 1H, H4), 3.97 (t, J = 9.5 Hz, 1H, H5), 4.03 (t, J = 10.0 Hz, 1H, H3), 4.17 (t, J = 2.5 Hz, 1H, H1), 4.70−4.97 (m, 10H), 7.24−7.36 (m, 20H). Anal. Calcd for $C_{34}H_{35}N_3O_5$: C, 72.19; H, 6.24; N, 7.43. Found: C, 71.98; H, 6.14; N, 7.51.

(1*RS*,2*RS*,3*SR*,4*SR*,5*RS*,6*RS*)-*N*-(2,3,4,5-Tetrakisbenzyloxy-6-hydroxycyclohexyl) Carbamic Acid *tert*-Butyl Ester (18). A solution of **13** (97 mg, 0.18 mmol) in acetone (4 mL) was treated with $(Boc)_2O$ (42 mg, 0.24 mmol). The reaction mixture was stirred at room temperature overnight. Evaporation afforded crude **18**, which was purified flash chromatography on hexanes/EtOAc (5:1) to afford 89 mg (0.14 mmol, 78%) of carbamate **18**. IR (film): 3342, 3063, 3030, 2976, 2901, 1687, 1534, 1497, 1453, 1365. ^{13}C NMR (125 MHz): 28.2, 50.5 (broad), 60.3, 72.1, 72.6, 75.6, 77.2 (2×, 72.3, 79.8, 80.6, 81.4, 127.8−128.8, 138.1−138.9, 156.3. ^{1}H NMR (500 MHz): 1.49 (s, 9H), 2.59 (bb, 1H), 3.62 (t, J = 9.0 Hz, 1H), 3.74 (dd, J = 3.0, 9.0 Hz, 1H), 3.91 (t, J = 9.5 Hz, 1H), 4.14 (dd, J = 4.5, 9.9 Hz, 1H), 4.29 (m, 1H), 4.53 (m, 1H), 4.60−4.98 (m, 8H), 7.24−7.38 (m, 20H). ESP(+): (M + Na) 662.3. Anal. Calcd for $C_{39}H_{45}NO_7$: C, 73.22; H, 7.09; N, 2.19. Found: C, 73.43; H, 7.21; N, 2.24.

(1′*RS*,2′*SR*,3′*RS*,4′*SR*,5′*RS*,6′*SR*)-(2,3,4,5-Tetrakisbenzyloxy-6-*tert*-butoxycarbonylamino)cyclohexyl Methanesulfonate Ester (19). A solution of the starting carbamate **18** (96 mg, 0.15 mmol) and TEA (0.1 mL) in CH_2Cl_2 (5 mL) was treated with MsCl (22 mg, 0.19 mmol). The reaction mixture was stirred at room temperature for 18 h, diluted with H_2O (5 mL), extracted with Et_2O (4 × 10 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation afforded crude **19**, which was purified by filtration through a plug of silica and elution with hexanes/EtOAc (9:1) to give 90 mg (0.12 mmol, 84%) of **19**. IR (film): 3068, 2982, 2932, 1809, 1757, 1477, 1458, 1395. ^{13}C NMR (125 MHz): 28.3, 38.9, 72.5, 73.1 (broad), 75.7 (broad), 75.8 (broad), 76.5, 76.8, 80.2, 127.9−128.8, 138.1−138.9, 156.4. ^{1}H NMR (500 MHz): 1.49 (s, 9H), 3.01 (s, 3H), 3.65 (t, J = 9.5 Hz, 1H), 3.85 (m, 2H), 4.05 (m, 1H), 4.22 (broad, 1H), 4.70−5.00 (m, 9H), 5.78 (bb, 1H), 7.24−7.38 (m, 20H). ESP(+): (M + Na) 740.3. Anal. Calcd for $C_{40}H_{47}NO_9S$: C, 66.93; H, 6.60; N, 1.95. Found: C, 66.51; H, 6.49; N, 1.89.

(1*RS*,2*SR*,3*SR*,4*RS*,5*RS*,6*SR*)-2-Amino-3,4,5,6-tetrakisbenzyloxycyclohexanol (21). A solution of carbamate **19** (50 mg, 0.096 mmol) in anhydrous DMF (2 mL) was heated at 120 °C. After the solution was stirred for 16 h, the solvent was removed under reduced pressure and the resulting crude was taken up in Et_2O (10 mL), washed with H_2O (2 × 5 mL), treated with brine, and dried over anhydrous Na_2SO_4. The resulting residue was treated with 1 N methanolic NaOH at 80 °C for 24 h. Then, methanol was removed under reduced pressure and the resulting residue was extracted with Et_2O (3 × 5 mL). The combined organic phases were washed with H_2O, treated with brine, dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure. Crude amino alcohol was purified by flash chromatography using a mixture of hexane:EtOAc/Et_3N (2:1/2% vol) to furnish **21** (34 mg, 0.063 mmol, 65%). IR (film): 3311, 3087, 3059, 3029, 2946, 1574, 1499, 1439. ^{13}C NMR (125 MHz): 51.3, 71.9, 72.7, 75.7, 75.8, 76.1, 81.0, 81.4, 82.0, 84.1, 127.8−128.9, 138.5−139.0. ^{1}H NMR (500 MHz): 3.50−3.56 (m, 3H), 3.69 (t, J = 3.5 Hz, 1H), 4.05 (t, J = 9.5 Hz, 1H), 4.17 (t, J = 9.5 Hz), 4.72−5.04 (m, 8H), 7.24−7.38 (m, 20H). Anal. Calcd for $C_{34}H_{37}NO_5$: C, 75.67; H, 6.91; N, 2.60. Found: C, 75.92; H, 7.02; N, 2.54.

(1*RS*,2*SR*,3*RS*,4*RS*,5*SR*,6*SR*)-2,3,4,5-Tetrakisbenzyloxy-7-azabicyclo[4.1.0]heptane (22). A solution of the starting azido mesylates **14** or **15** (315 mg, 0.49 mmol) in THF (3 mL) was added to a suspension of $LiAlH_4$ (30 mg, 0.79 mmol) in THF (3 mL) at 0 °C. The reaction mixture was stirred for 2 h and EtOAc (2 mL) was added at 0 °C. The suspension was diluted with water (10 mL), extracted with Et_2O (4 × 10 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation afforded crude aziridine, which was chromatographed on silica gel using a mixture of hexane/EtOAc (2:1) in the presence of TEA (3%) to afford 229 mg (0.41 mmol, 90%) of **22**. IR (film): 3292, 3062, 3031, 2920, 1858, 1488, 1454, 1365; ^{13}C NMR (75 MHz): 34.2, 72.7 (broad), 72.8, 75.2, 75.7, 79.5, 79.7, 81.2, 84.2 (broad), 127.3−128.3, 138.0−138.9. ^{1}H NMR (300 MHz): 2.36 (m, 1H), 2.51 (bb, 1H), 3.44 (dd, J = 7.8,10.2 Hz, 1H), 3.65 (t, J = 9.3 Hz, 1H), 3.83−3.90 (m, 2H), 4.65−4.95 (m, 8H), 7.24−7.34 (m, 20H). ESP(+): (M + H) 522.4. Anal. Calcd for $C_{34}H_{35}NO_4$: C, 78.28; H, 6.76; N, 2.69;. Found: C, 78.45; H, 6.97; N, 2.81.

Synthesis of 2-Azido-1-amino Cyclitols 23 and 24 by Ring Opening of Aziridine 22. A solution of the starting aziridine **22** (250 mg, 0.48 mmol) and NH_4Cl (0.48 mmol) in a 4:1 mixture of MeOH/H_2O (10 mL) was treated with NaN_3 (650 mg, 10 mmol). The reaction mixture was stirred at 80 °C until the starting material could not be detected by TLC, cooled to room temperature, diluted with H_2O (10 mL), extracted with Et_2O (4 × 15 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation afforded a 1:1 mixture of azidoaminocyclitols **23** and **24**, which were isolated by flash chromatography on elution with hexanes/EtOAc (2:1) in the presence of TEA (2%).

(1*RS*,2*RS*,3*RS*,4*SR*,5*SR*,6*RS*)-2-Azido-3,4,5,6-tetrakisbenzyloxycyclohexylamine (23) (112 mg, 0.20 mmol, 42%). IR (film): 3043, 3039, 3045, 3032, 2922, 2876, 2103, 1476, 1359. ^{13}C NMR (75 MHz): 50.9, 63.1, 72.9, 73.5, 75.7, 75.8, 79.3, 79.4, 81.1 (broad), 81.9 (broad), 127.5−128.4, 138.1−138.8; ^{1}H NMR (300 MHz): 3.41 (t, J = 3.9 Hz, 1H, H1), 3.72 (dd, J = 3.9, 9.0 Hz, 1H), 3.79 (t, J = 3.9 Hz, 1H), 3.84−3.89 (m, 2H), 4.21 (dd, J = 3.3, 9 Hz, 1H, H2), 4.60−5.00 (m, 8H), 7.23−7.34 (m, 20H). HRMS: calcd for $C_{34}H_{36}N_4O_4$ (M + H^+), 565.2737; found, 565.2759.

(1*RS*,2*RS*,3*SR*,4*RS*,5*RS*,6*SR*)-2-Azido-3,4,5,6-tetrakisbenzyloxycyclohexylamine (24) (109 mg, 0.19 mmol, 40%). IR (film): 3081, 3035, 2939, 2910, 2106, 1496, 1457. ^{13}C NMR (75 MHz): 53.9, 67.0, 75.8, 75.9, 77.0, 77.2, 82.5, 83.1, 83.9 (2×, 127.6−128.6, 137.5−138.2. ^{1}H NMR (500 MHz): 2.68 (t, J = 9.9 Hz, 1H, H1), 3.26 (t, J = 10.2 Hz, 1H, H2), 3.33 (t, J = 9, 3 Hz, 1H), 3.50 (t, J = 9.9 Hz, 1H), 3.56−3.67 (m, 2H), 4.68−5.05 (m, 8H), 7.29−7.38 (m, 20H). HRMS: calcd for $C_{34}H_{36}N_4O_4$ (M + H^+), 565.2737; found, 565.2748.

(1′*RS*,2′*SR*,3′*RS*,4′*RS*,5′*SR*,6′*RS*)-*N*-(2,3,4,5-Tetrakisbenzyloxy-6-hydroxycyclohexyl) carbamic Acid *tert*-Butyl Ester (25). A solution of **12a** (97 mg, 0.18 mmol) in acetone (4 mL) was treated with $(Boc)_2O$ (42 mg, 0.24 mmol). The reaction mixture was stirred at room temperature overnight. Evaporation afforded crude **25** which was purified by silica flash chromatography on hexanes/EtOAc (5:1) to afford 89 mg (0.14 mmol, 78%) of carbamate **25**. IR (film): 3342, 3063, 3030, 2976, 2901, 1687, 1534, 1497, 1453, 1365. ^{13}C NMR (125 MHz): 28.6, 56.8, 73.4, 75.8, 76.0, 76.1, 79.2, 80.4, 82.8 84.1, 84.3, 127.8−128.8, 138.2−138.8, 157.0. ^{1}H NMR (500 MHz): 1.48 (s, 9H), 3.18 (bs, 1H), 3.42−3.68 (m, 5H), 4.53 (d, J = 7 Hz, 1H), 4.70 (d, J = 11 Hz, 1H), 4.87−4.94 (m, 9H), 7.24−7.40 (m, 20H). HRMS: calcd for $C_{39}H_{45}NO_7$ (M + Na), 662.3094; found, 662.3117

(1′*RS*,2′*RS*,3′*SR*,4′*RS*,5′*SR*,6′*SR*)-(2,3,4,5-Tetrakisbenzyloxy-6-*tert*-butoxycarbonylamino)cyclohexyl Methanesulfonic Ester (26). A solution of the starting carbamate **25** (96 mg, 0.15 mmol) and TEA (0.1 mL) in CH_2Cl_2 (5 mL) was treated with MsCl (22 mg, 0.19 mmol). The reaction mixture was stirred at room temperature for 18 h, diluted with H_2O (5 mL), extracted with Et_2O (4 × 10 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation afforded crude **26**, which was purified by filtration through a plug of silica and elution with hexanes/EtOAc (9:1) to give 90 mg (0.12 mmol, 84%) of **26**. IR (film): 3068, 2974, 2862, 2105, 1698,

1463. ^{13}C NMR (125 MHz): 28.6, 39.1, 54.7, 75.7, 75.9, 76.1, 76.3, 79.2, 80.3, 80.9, 81.3, 82.6, 83.8, 127.9−128.7, 137.9−138.4, 155.8. ^{1}H NMR (500 MHz): 1.48 (s, 9H), 2.87 (s, 3H), 3.50−3.70 (m, 4H), 3.78 (q, J = 9 Hz, 1H), 4.58 (m, 1H), 4.70−4.98 (m, 10 H), 7.22−7.38 (m, 20 H). HRMS: calcd for $C_{40}H_{47}NO_9S$ (M + Na), 740.2870; found, 740.2847.

(1′*RS*,2′*SR*,3′*SR*,4′*RS*,5′*RS*,6′*SR*)-*N*-(2-Azido-3,4,5,6-tetrakisbenzyloxycyclohexyl)carbamic Acid *tert*-Butyl Ester (27). A solution of **26** (108 mg, 0.15 mmol) in DMF (2 mL) was treated with NaN_3 (49 mg, 0.75 mmol) and the reaction mixture was stirred at 120 °C. After 16 h, the reaction was cooled to room temperature, diluted with H_2O (10 mL), extracted with Et_2O (4 × 15 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation afforded crude azido carbamate **27**, which was purified by filtration through a plug of silica and elution with hexanes/EtOAc (1:1) to afford 75 mg (0.11 mmol, 75%) of **27**. IR (film): 3340, 3031, 2912, 2101, 1684, 1526, 1357. ^{13}C NMR (125 MHz): 28.6, 51.6, 62.7, 73.4, 75.6, 76.1, 76.3, 79.2, 80.2, 81.1, 81.7, 84.3, 127.8−128.7, 137.7−138.6. ^{1}H NMR (300 MHz): 1.43 (s, 9H), 3.51 (m, 2H), 3.70 (m, 2H), 3.89 (t, J = 9.5 Hz, 1H), 4, 18 (m, 1H), 4.60−4.98 (m, 8H), 7.24−7.38 (m, 20 H). HRMS: Calcd for $C_{39}H_{44}N_4O_6$ (M + Na), 687.3159; found, 687.3178.

(1*RS*,2*SR*,3*SR*,4*RS*,5*RS*,6*SR*)-(2-Azido-3,4,5,6-tetrakisbenzyloxy)cyclohexylamine (28). Compound **27** (66.5 mg, 0.10 mmol) was solved in 2 mL of a 20:1 mixture of EtOAc: aqueous 1 N HCl. The reaction mixture was stirred at room temperature until the starting material could not be detected. A solution of aqueous 1 N NaOH (5 mL) was then added, and the reaction mixture was extracted with Et_2O (4 × 15 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation afforded a residue, which was purified by filtration through a plug of silica and elution on hexanes/EtOAc (2:1) in the presence of TEA (2%) to afford 54 mg (0.095 mmol, 95%) of azido amine **28**. IR (film): 3377, 3063, 3030, 2914, 2101, 1697, 1585, 1496, 1454. ^{13}C NMR (125 MHz): 52.5, 63.5, 73.4, 76.0, 76.13, 76.3, 81.6, 82.3, 82.7, 84.7, 127.9−128.88, 137.8−138.7; ^{1}H NMR (300 MHz): 2.61 (dd, J = 3, 9.5 Hz, 1H, H1), 3.42 (t, J = 9.5 Hz, 1H), 3.48 (t, J = 9.5 Hz, 1H), 3.66 (dd, J = 3, 9.5 Hz, 1H), 3.98 (t, J = 9.5 Hz, 1H), 4.07 (t, J = 3 Hz, 1H, H2), 4.65−5.00 (m, 8H), 7.24−7.38 (m, 20 H). HRMS: calcd for $C_{34}H_{36}N_4O_4$ (M + H^+), 565.2737; found, 565.2751.

(1′*RS*,2′*SR*,3′*RS*,4′*SR*,5′*SR*,6′*RS*)-2-(2-Azido-3,4,5,6-tetrakisbenzyloxycyclohexyl)isoindole-1,3-dione (29). A solution of azido mesylate **14** (244 mg, 0.38 mmol) in DMF (10 mL) was treated with potassium phthalimide (203 mg, 1.1 mmol). The reaction mixture was stirred at 140 °C for 72 h, diluted with H_2O (10 mL), extracted with Et_2O (4 × 15 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation afforded a residue, which was purified by flash chromatography on hexanes/EtOAc (9:1) to give 147 mg (0.21 mmol, 56%) of **29**. IR (film): 3063, 2925, 2858, 2107, 1715, 1495, 1459, 1370; ^{13}C NMR (125 MHz): 48.5, 62.3, 73.3, 75.9, 76.0, 76.1, 78.5, 82.7, 83.3, 84.7, 123.9, 127.6−128.6, 134.6, 137.4, 138.1, 139.0, 169.4. ^{1}H NMR (500 MHz): 3.63 (t, J = 9.5 Hz, 1H), 3.82−3.86 (m, 2H), 4.48−4.57 (m, 3H), 4.67 (d, J = 10.8 Hz, 1H), 4.80−5.02 (m, 6H), 5.25 (t, J = 11.5 Hz, 1H), 7.24−7.40 (m, 20H), 7.78 (dd, J = 3.5, J = 6.0 Hz, 2H), 7.92 (dd, J = 3.5, J = 6.0 Hz, 2H). HRMS: calcd for $C_{42}H_{38}N_4O_6$ (M + H^+); 695.2791; found, 695.2768.

(1*RS*,2*SR*,3*RS*,4*SR*,5*SR*,6*RS*)-(2-Azido-3,4,5,6-tetrakisbenzyloxy)cyclohexylamine (30). A solution of **29** (69.5 mg, 0.1 mmol) in THF (4 mL) was treated with 2 mL of hydrazine (1 N solution in THF). The reaction mixture was stirred at 80 °C until the starting material could not be detected. Evaporation afforded crude **30**, which was purified by flash chromatography on elution with hexanes/EtOAc (2:1) in the presence of TEA (2%) to give 44.8 mg (0.079 mmol, 79%) of **30**. IR (film): 3053, 2919, 2861, 2099, 1454, 1364. ^{13}C NMR (125 MHz): 63.2, 68.8, 73.2, 76.1, 76.2, 76.3, 80.1, 80.5, 81.5, 84.2, 127.9−128.9, 137.9, 138.1, 138.9. ^{1}H NMR (500 MHz): 3.38 (dd, J = 3.0, 10 Hz, 1H, H2), 3.50 (dd, J = 3.0, 10 Hz, 1H), 3.58 (t, J = 9.5 Hz, 1H), 4.01 (t, J = 9.0 Hz, 1H), 4.07 (t, J = 10 Hz, 1H), 4.21 (t, J = 2.5 Hz, 1H, H1), 4.70−4.80 (m, 2H), 4.88−5.00 (m, 6H), 7.24−7.40 (m, 20H). HRMS: calcd for $C_{34}H_{36}N_4O_4$ (M + H^+), 565.2737; found, 565.2744.

General Method for Reduction of the Azide Group. To a solution of the corresponding azido amide (0.03 mmol) in THF was added 8 mg of Degussa E196R/W Pd−C catalyst. The reaction mixture was stirred at room temperature under H_2 (3 atm) until the presence of the azido group could not be detected by IR analysis. The solutions were filtered through Celite, and the catalyst was washed with MeOH (2 × 2 mL). Evaporation afforded pure amino amides.

(1′*RS*,2′*RS*,3′*RS*,4′*SR*,5′*SR*,6′*RS*)-*N*-(2-Amino-3,4,5,6-tetrakisbenzyloxy cyclohexyl)octanamide (36) (18 mg, 0.027 mmol, 82%). IR (film): 3291, 3029, 2925, 2853, 1638, 1557. ^{13}C NMR (125 MHz): 14.3, 22.8, 26.2, 29.3, 29.5, 31.9, 37.5, 49.6, 50.9, 72.3, 72.4 (2×), 72.5, 75.4, 75.7, 79.7 (2×), 127.9−128.7, 138.0−138.9, 174.4. ^{1}H NMR (500 MHz): 0.89 (t, J = 6.9 Hz, 3H), 1.20−1.40 (m, 8H), 1.59 (m, 2H), 2.1 (t, J = 7.5 Hz, 2H), 3.60 (t, J = 8.5 Hz, 1H), 3.7 (dd, J = 4.0, 8.5 Hz, 1H), 3.83 (t, J = 4 Hz, 1H), 4.00 (t, J = 8.0 Hz, 1H), 4.25 (dd, J = 4.0, 8.5 Hz, 1H), 4.34 (dd, J = 5.0, 10 Hz), 4.55−4.66 (m, 5H), 4.77−4.86 (m, 4H), 5.61 (d, J = 5.0 Hz, 1H), 7.24−7.40 (m, 20 H). HRMS: calcd for $C_{42}H_{52}N_2O_5$ (M + H^+), 665.3876; found, 665.3895.

(1′*RS*,2′*RS*,3′*SR*,4′*RS*,5′*RS*,6′*SR*)-*N*-(2-Amino-3,4,5,6-tetrakisbenzyloxy-cyclohexyl)octanamide (38) (17 mg, 0.026 mmol, 87%). IR (film): 3301, 3054, 3037, 2955, 2849, 1678, 1499. ^{13}C NMR (125 MHz): 14.3, 22.8, 26.2, 29.3, 29.5, 31.9, 37.5, 49.6, 50.9, 72.4, 72.5, 75.2, 75.6, 75.7, 77.2, 79.7, 127.9−128.7, 138.0−138.9, 174.4. ^{1}H NMR (500 MHz): 0.89 (t, J = 6.9 Hz, 3H), 1.20−1.40 (m, 8H), 1.59 (m, 2H), 2.10 (t, J = 7.5 Hz, 2H), 3.60 (t, J = 8.5 Hz, 1H), 3.70 (dd, J = 4.0, 8.5 Hz, 1H), 3.83 (t, J = 4 Hz, 1H), 4.00 (t, J = 8.0 Hz, 1H), 4.25 (dd, J = 4.0, 8.5 Hz, 1H), 4.34 (dd, J = 5.0, 10 Hz) 4.55−4.66 (m, 5H), 4.77−4.86 (m, 4H), 5.61 (d, J = 5.0 Hz, 1H), 7.24−7.40 (m, 20H). HRMS: calcd for $C_{42}H_{52}N_2O_5$ (M + H^+), 665.3876; found, 665.3891.

(1′*RS*,2′*SR*,3′*SR*,4′*RS*,5′*RS*,6′*SR*)-*N*-(2-Amino-3,4,5,6-tetrakisbenzyloxy-cyclohexyl)octanamide (40) (16 mg, 0.025 mmol, 87%). IR (film): 3301, 3033, 2956, 2925, 2847, 1657, 1540, 1469. 1453. ^{13}C NMR (125 MHz): 14.2, 22.8, 25.9, 29.2, 29.5−29.9 (rotamers), 31.9, 37.0, 49.4, 52.3, 72.6, 74.7, 75.8, 78.1, 81.0, 84.1, 127.8−129.0, 138.2−138.8, 173.5. ^{1}H NMR (500 MHz): 0.89 (t, J = 6.9 Hz, 3H), 1.22−1.40 (m, 10H), 1.95 (m, 2H), 3.61 (m, 2H), 3.71 (t, J = 1.5 Hz, 1H), 3.82−3.90 (m, 2H), 3.94 (t, J = 9, 0 Hz, 1H), 4.62 (s, 2H), 4.81−4.88 (m, 6H), 5.49 (d, J = 6.5 Hz, 1H), 7.24−7.40 (m, 20H). RMS. calcd for $C_{42}H_{52}N_2O_5$ (M + H^+), 665.3876; found: 665.3861.

(1′*RS*,2′*SR*,3′*RS*,4′*SR*,5′*SR*,6′*RS*)-*N*-(2-Amino-3,4,5,6-tetrakisbenzyloxy-cyclohexyl)octanamide (42) (17 mg, 0.026 mmol, 87%). IR (film): 3291, 3030, 2940, 2851, 1666, 1537. ^{13}C NMR (125 MHz): 14.0, 22.5, 25.7, 29.3−29.5 (rotamers), 31.7, 32.2, 36.8, 63.1, 72.7, 74.5, 74.7, 78.2, 80.0, 127.7−128.3, 137.6−138.4, 173.0. ^{1}H NMR (500 MHz): 0.89 (t, J = 6.9 Hz, 3H), 1.25−1.45 (m, 8H), 1.59 (bs), 1.98 (m, 2H), 2.58 (t, J = 3.9 Hz, 1H), 2.83 (m, 1H), 3.36 (t, J = 3.0 Hz, 1H), 3.28−3.77 (m, 5H), 4.58−4.98 (m, 8H), 6.40 (d, J = 5.5 Hz, 1H), 7.24−7.40 (m, 20H); RMS. calcd for $C_{42}H_{52}N_2O_5$ (M + H^+), 665.3876; found, 665.3888.

General Method for the Synthesis of *N*-octanoyl Benzylaminoinositols (31−35, 37, 39, 41). A solution of the corresponding aminocyclitol (0.1 mmol) and TEA (0.1 mL) in CH_2Cl_2 (2 mL) was treated with octanoyl chloride (0.12 mmol). The reaction mixture was stirred at room temperature until the staring material could not be detected. Dilution with H_2O (5 mL), extraction with CH_2Cl_2, drying over anhydrous Na_2SO_4, and evaporation afforded a crude, which was purified by flash chromatography on elution with hexanes/EtOAc (10:1 to 4:1).

(1′*RS*,2′*SR*,3′*RS*,4′*RS*,5′*SR*,6′*RS*)-*N*-(2,3,4,5,6-Pentakisbenzyloxycyclohexyl)octanamide (31) (65 mg, 86%). IR

(film): 3269, 3089, 3065, 3030, 2925, 2854, 1644, 1565, 1497, 1454. ^{13}C NMR (75 MHz): 14.1, 22.7, 25.6, 29.3, 29.7, 31.9, 37.1, 53.8 (broad), 55.5, 74.9, 75.7, 75.8, 78.9, 82.7, 84.9, 127.6−128.3, 138.4, 173.5; ^{1}H NMR (300 MHz): 0.89 (t, J = 6.7 Hz, 3H). 1.20−1.42 (m, 8H), 1.52 (m, 2H), 1.98 (t, J = 7.5 Hz, 2H), 3.60−3.67 (m, 4H), 3.88 (m, 2H), 4.65−4.98 (m, 10H), 5. 43 (d, J = 5.4 Hz, 1H), 7.24−7.34 (m, 25H). Anal. Calcd for $C_{49}H_{57}NO_6$: C, 77.85; H, 7.60; N, 1.85. Found: C, 78.23; H, 7.45; N, 1.91.

(1′*RS*,2′*RS*,3′*SR*,4′*SR*,5′*RS*,6′*RS*)-*N*-(2,3,4,5-Tetrakisbenzyloxy-6-hydroxycyclohexyl)octanamide (32) (57 mg, 86%). IR (film): 3309, 3080, 3059, 2931, 1667, 1464. ^{13}C NMR (125 MHz): 14.3, 22.8, 25.9, 29.2, 29.5, 31.9, 37.5, 50.0, 67.5, 72.4, 72.9, 75.7, 75.9, 79.6 (2×), 80.5, 81.4, 127.9−128.5, 137.9−139.7, 174.6. ^{1}H NMR (500 MHz): 0.90 (t, J = 6.5 Hz, 3H), 1.20−1.38 (m, 8H), 1.61 (m, 2H), 2.17 (t, J = 8.0 Hz, 1H), 2.65 (bb, 1H), 3.62 (t, J = 8.5 Hz, 1H), 3.65 (d, J = 8.5 Hz, 1H), 3.91 (t, J = 9.0 Hz, 1H), 4.15 (dd, J = 4.0, 9.0 Hz, 1H), 4.52 (m, 1H), 4.60−4.90 (m, 8H), 5.90 (d, J = 4.0 Hz, 1H), 7.28−7.34 (m, 20H). Anal. Calcd for $C_{42}H_{51}NO_6$: C, 75.76; H, 7.72; N, 2.10. Found: C, 76.29; H, 7.81; N, 2.14.

(1′*RS*,2′*SR*,3′*RS*,4′*RS*,5′*SR*,6′*SR*)-*N*-(2,3,4,5-Tetrakisbenzyloxy-6-hydroxycyclohexyl)octanamide (33) (52 mg, 78%). IR (film): 3309, 3080, 3059, 2931, 1667, 1464. ^{13}C NMR (125 MHz): 14.3, 22.9, 25.9, 29.3, 29.5, 31.9, 37.1, 51.2, 69.2, 73.2, 75.4, 76.2, 79.1, 80.6, 81.5, 84.4, 127.9−128.9, 137.9−138.8, 173.3. ^{1}H NMR (500 MHz): 0.89 (t, J = 7.5 Hz, 3H), 1.20−1.38 (m, 8H), 1.56 (m, 2H), 2.05 (t, J = 8.5 Hz, 1H), 3.57 (dd, J = 3.0, 9.6 Hz, 1H), 3.61 (t, J = 9.0 Hz, 1H), 3.77 (t, J = 10.5 Hz, 1H), 3.89 (t, J = 9.0 Hz), 4.08 (m, 1H), 4.13 (t, J = 3.0 Hz), 4.65−4.98 (m, 8H), 5.64 (d, J = 9.0 Hz), 7.28−7.34 (m, 20H). Anal. Calcd for $C_{42}H_{51}NO_6$: C, 75.76; H, 7.72; N, 2.10. Found: C, 76.16; H, 7.83; N, 2.01.

(1′*RS*,2′*RS*,3′*SR*,4′*SR*,5′*RS*,6′*SR*)-*N*-(2,3,4,5-Tetrakisbenzyloxy-6-hydroxycyclohexyl)octanamide (34) (60 mg, 90%). IR (film): 3321, 3069, 3030, 2982, 2935, 1678, 1556, 1424. 1401. ^{13}C NMR (125 MHz): 14.3, 22.8, 26.0, 29.3, 29.4, 31.9, 37.9, 51.7, 72.3, 72.5, 75.1, 75.5, 75.6, 77.6, 80.9, 81.3, 81.7, 127.8−128.8, 137.4−138.8, 176.3. ^{1}H NMR (500 MHz): 0.89 (t, J = 6.9 Hz, 3H), 1.20−1.38 (m, 8H), 1.65 (m, 2H), 2.28 (t, J = 7.0 Hz, 2H), 3.56 (t, J = 8.0 Hz, 1H), 3.66 (t, J = 8.0 Hz, 1H), 3.72 (m, 2H), 3.78 (dd, J = 4.0, 8.5 Hz, 1H), 4.57 (m, 1H), 4.59 (m, 2H), 4.78−4.98 (m, 6H), 5.64 (d, J = 9.0 Hz), 5.90 (d, J = 5.0 Hz, 1H), 7.28−7.34 (m, 20H). Anal. Calcd for $C_{42}H_{51}NO_6$: C, 75.76; H, 7.72; N, 2.10. Found: C, 75.99; H, 7.59; N, 1.99.

(1′*RS*,2′*RS*,3′*RS*,4′*SR*,5′*SR*,6′*RS*)-*N*-(2-Azido-3,4,5,6-tetrakisbenzyloxycyclohexyl)octanamide (35) (60 mg, 0.087 mmol, 87%). IR (film):3327, 3035, 2933, 2913, 2860, 2106, 1736, 1707, 1653, 1536, 1454; ^{13}C NMR (75 MHz): 14.0, 22.6, 25.7, 29.0, 29.2, 31.7, 35.2, 49.3, 58.5, 72.3, 72.8, 75.8, 76.0, 78.9, 80.6, 81.6, 127.7−128.5, 137.3−138.4, 174.4; ^{1}H NMR (300 MHz): 0.89 (t, J = 6.9 Hz, 3H), 1.22−1.40 (m, 8H), 1.61 (m, 2H), 2.15 (m, 2H), 3.54 (t, J = 9.9 Hz, 1H), 3.75 (dd, J = 3.9, 9.3 Hz, 1H), 3.87−3.97 (m, 2H), 4.26 (dd, J = 1.5, 2.4 Hz), 4.58−4.98 (m, 9H), 5.55 (d, J = 4.2 Hz, 1H), 7.24−7.40 (m, 20H). HRMS: calcd for $C_{42}H_{50}N_4O_5$ (M + H$^+$), 691.3781; found, 691.3804.

(1′*RS*,2′*RS*,3′*SR*,4′*RS*,5′*RS*,6′*SR*)-*N*-(2-Azido-3,4,5,6-tetrakisbenzyloxy-cyclohexyl)octanamide (37). (54 mg, 0.079 mmol, 79%). IR (film): 3056, 3028, 2929, 2862, 2107, 1713, 1694, 1459, 1362. ^{13}C NMR (125 MHz): 14.3, 22.8, 25.8, 29.3, 29.5, 31.9, 37.3, 44.7, 54.8, 64.0, 75.4, 76.0, 76.1, 79.1, 82.4, 83.4, 84.0, 128.0−128.7, 137.9−138.4, 174.0. ^{1}H NMR (500 MHz): 0.89 (t, J = 7.0 Hz, 3H), 1.22−1.32 (m, 10H), 2.09 (m, 2H), 3.41 (m, 2H), 3.55 (t, J = 9.5 Hz, 1H), 3.62 (t, J = 9.5 Hz, 1H), 3.85 (t, J = 10.0 Hz, 1H), 4.62 (d, J = 11 Hz, 1H), 4.86−4.98 (m, 9H), 5.40 (d, J = 8.0 Hz, 1H), 7.24−7.40 (m, 20H). HRMS: calcd for $C_{42}H_{50}N_4O_5$ (M + H$^+$): 691.3781; found; 691.3796.

(1′*RS*,2′*SR*,3′*SR*,4′*RS*,5′*RS*,6′*SR*)-*N*-(2-Azido-3,4,5,6-tetrakis-benzyloxy-cyclohexyl)octanamide (39). (61 mg, 0.089 mmol, 89%). IR (film): 3282, 3064, 30 20, 2953, 2924, 2854, 210 3, 1646, 1546, 1453, 1357; ^{13}C NMR (125 MHz): 14.3, 22.8, 22.9, 25.8, 29.2−29.5 (rotamers), 31.9, 36.9, 50.4, 61.6, 73.3, 75.1, 76.2, 76.3, 78.1, 80.9, 81.6, 84.3, 127.9−129.0 0, 137.7−138.6, 173.6. ^{1}H NMR (500 MHz): 0.89 (t, J = 6.9 Hz, 3H), 1.22−1.40 (m, 10H), 1.95 (m, 2H), 3.55−3.62 (m, 2H), 3.73 (dd, J = 3.5, 9.5 Hz, 1H), 3.90−3.97 (m, 2H), 4.28 (t, J = 3.5 Hz, 1H), 4.60−4.98 (m, 8H), 5.22 (d, J = 7.5 Hz, 1H), 7.24−7.40 (m, 20H); HRMS: calcd for $C_{42}H_{50}N_4O_5$ (M + H$^+$): 691.3781; found, 691.3784.

(1′*RS*,2′*SR*,3′*RS*,4′*SR*,5′*SR*,6′*RS*)-*N*-(2-Azido-3,4,5,6-tetrakisbenzyloxycyclohexyl)octanamide (41). (59 mg, 0.086 mmol, 86%). IR (film): 3068, 2974, 2862, 2105, 1698, 1463. ^{13}C NMR (125 MHz): 14.0, 22.7, 24.8, 25.9, 29.0, 29.2, 31.7, 47.2, 62.4, 72.0, 76.2 (2×), 76.3, 78.2, 80.8, 81.4, 83.4, 127.9−128.6, 137.5−138.2 (4×), 174.1; ^{1}H NMR (300 MHz): 0.89 (t, J = 6.8 Hz, 3H), 1.20−1.40 (m, 8H), 1.60−1.68 (m, 3H), 2.15 (m, 2H), 2.18 (t, J = 7.5 Hz, 1H), 3.55−3.65 (m, 5H), 4.52 (d, J = 7.5 Hz, 1H), 4.72−4.95 (m, 7H), 5.0 5(m, 1H), 5.41 (d, J = 9.0 Hz), 7.24−7.40 (m, 20H). HRMS: calcd for $C_{42}H_{50}N_4O_5$ (M + H$^+$), 691.3781; found, 691.3794.

***N*-(1′*RS*,2′*RS*,3′*SR*,4′*SR*,5′*RS*,6′*RS*)-(2,3,4,5-tetrakisbenzyloxy-6-octylaminocyclohexyl)octanamide (43).** To a solution of **36** (33 mg, 0.05 mmol) in MeOH (2 mL) were added AcOH (0.05 mmol) and $NaBH_3CN$ (4,5 mg, 0.07 mmol). After 10 min, octanaldehyde (7.7 mg, 0.06 mmol) was added and the reaction mixture was stirred at room temperature. After 16 h, the solvent was evaporated and the residue diluted with H_2O (5 mL), extracted with Et_2O (3 × 5 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation afforded crude amide **43**, which was purified by filtration through a plug of silica and elution with hexane/EtOAc (10:1) to give 27 mg (0.036 mmol, 72%) of **43**. IR: 3067, 3022, 2956, 2920, 1679, 1547, 1495. ^{1}H NMR (500 MHz): 0.89 (m, 6H), 1.23−1.35 (broad, 22 H), 1.55−1.62 (m, 2H), 2.19 (t, J = 6.5 Hz, 2H), 2.35 (t, J = 6.5 Hz, 1H), 2.59 (m, 1H), 2.66 (m, 1H), 3.49 (t, J = 3.0 Hz, 1H), 3.57 (t, J = 9.0 Hz, 1H), 3.69 (dd, J = 4.0 Hz, 9.5 Hz, 1H), 3.92 (t, J = 9.0 Hz, 1H), 4.24 (dd, J = 5.0, 9.5 Hz, 1H), 4.54 (m, 1H), 4.57−4.64 (m, 4H), 4.80−4.94 (m, 4H), 5.59 (d, J = 6.0 Hz, 1H), 7.24−7.39 (m, 20H). HRMS: calcd for $C_{50}H_{68}N_2O_5$ (M + H$^+$), 777.5206; found: 777.5190.

General Method for the *O*-Debenzylation: Synthesis of *N*-Octanoylaminoinositols (1−8). A solution of the corresponding amide (0.05 mmol) in CH_2Cl_2 (1 mL) at −78 °C was treated with 1 M BCl_3 in heptane (2 equiv per OBn group). The reaction mixture was allowed to warm to room temperature and stirred for an additional 16 h. The mixture was then cooled to −78 °C and quenched with methanol (0.5 mL). Solvents were then removed under reduced pressure and EtOAc (2 mL) was added next to the oily residue. After sonication in an ultrasonic bath for 1 min, the suspended solid was collected by filtration. Following this protocol, inositols **5**−**8** were obtained as the corresponding hydrochloride salts.

(1′*rs*,2′*RS*,3′*SR*,4′*sr*,5′*RS*,6′*SR*)-*N*-(2,3,4,5,6-Pentahydroxycyclohexyl)octanamide (1) (12.0 mg, 76%). ^{1}H NMR (500 MHz, MeOD): 0.91 (t, J = 7.0 Hz, 3H), 1.22−1.40 (m, 8H), 1.61 (m, 2H), 2.26 (t, J = 8 Hz, 2H), 3.25 (m, 4H), 3.59 (t, J = 8.5 Hz, 1H), 3.68 (dd, J = 4.5, 5.5 Hz, 1H). HRMS. calcd for $C_{14}H_{27}NO_6$ (M + H$^+$), 306.1917; found, 306.1939.

(1′*RS*,2′*SR*,3′*SR*,4′*SR*,5′*RS*,6′*SR*)-*N*-(2,3,4,5,6-Pentahydroxycyclohexyl)octanamide (2) (11.5 mg, 75%). ^{1}H NMR (500 MHz, MeOD): 0.91 (t, J = 7.0 Hz, 3H), 1.22−1.40 (m, 8H), 1.60 (m, 2H), 2.27 (t, J = 8 Hz, 2H), 3.55 (m, 2H), 3.63 (t, J = 9.0 Hz, 1H), 3.94 (m, 2H), 4.31 (m, 1H). HRMS calcd for $C_{14}H_{27}NO_6$ (M + H$^+$), 306.1917; found, 306.1951.

(1′*RS*,2′*RS*,3′*SR*,4′*RS*,5′*RS*,6′*RS*)-*N*-(2,3,4,5,6-Pentahydroxycyclohexyl)octanamide (3) (9.8 mg, 65%). ^{1}H NMR (500 MHz, MeOD): 0.91 (t, J = 7.0 Hz, 3H), 1.22−1.40 (m, 8H), 1.65 (m, 2H), 2.27 (t, J = 7.5 Hz, 2H), 3.23 (t, J = 9.5 Hz, 1H), 3.42 (dd, J = 3.0, 9.0 Hz, 1H), 3.60 (m, 2H), 3.76 (dd, J = 2.0, 9.0 Hz, 1H), 3.90 (m, 1H). HRMS calcd for $C_{14}H_{27}NO_6$ (M + H$^+$), 306.1917; found, 306.1932.

(1′*rs*,2′*RS*,3′*SR*,4′*rs*,5′*RS*,6′*SR*)-*N*-(2,3,4,5,6-Pentahydroxycyclohexyl)octanamide (4) (12.7 mg, 83%). ^{1}H NMR (500 MHz, MeOD): 0.91 (t, J = 6.5 Hz, 3H), 1.22−1.40 (m, 8H), 1.62 (m, 2H), 2.32 (t, 7.5 Hz, 2H), 3.18 (t, J = 9.0 Hz, 1H, H4), 3.47 (t, J = 10 Hz, 2H, H3−H3′), 3.55 (dd, J = 4.5, 10 Hz, 2H, H2−H2′), 4.53 (t, J = 4.5 Hz, 1H, H1). HRMS. calcd for $C_{14}H_{27}NO_6$ (M + H$^+$): 306.1917; found, 306.1931.

(1′*RS*,2′*RS*,3′*RS*,4′*SR*,5′*SR*,6′*RS*)-*N*-(2-Amino-3,4,5,6-tetrahydroxycyclohexyl)octanamide (5) (HCl salt, 12.9 mg, 76%). ^{1}H NMR (500 MHz, MeOD−D_2O): 0.92 (t, 3H), 1.33−1.36 (m, 8H), 1.65 (m, 2H), 2.32−2.35 (m, 2H), 3.58−3.71 (m, 2H), 3.88−4.01 (m, 3H), 4.59 (m, 1H). HRMS. Calcd for $C_{14}H_{28}N_2O_5$ (M + H$^+$), 305.2076; found, 305.2079.

(1′*RS*,2′*RS*,3′*SR*,4′*RS*,5′*RS*,6′*SR*)-*N*-(2-amino-3,4,5,6-tetrahydroxycyclohexyl)octanamide (6) (HCl salt, 12.2 mg, 72%). ^{1}H NMR (500 MHz, MeOD−D_2O): 0.93 (t, 3H), 1.25−1.41 (m, 8H), 1.75 (m, 2H), 2.21 (m, 2H), 3.30−3.85 (m, 6H). HRMS: calcd for $C_{14}H_{28}N_2O_5$ (M + H$^+$), 305.2076; found, 305.2081.

(1′*RS*,2′*SR*,3′*SR*,4′*RS*,5′*RS*,6′*SR*)-*N*-(2-Amino-3,4,5,6-tetrahydroxycyclohexyl)octanamide (7) (HCl salt, 11.9 mg, 70%). ^{1}H NMR (500 MHz, MeOD−D_2O): 0.94 (t, 3H), 1.28−1.39 (m, 8H), 1.70 (m, 2H), 2.36 (m, 2H), 3.40−3.90 (m, 6H). HRMS: calcd for $C_{14}H_{28}N_2O_5$ (M + H$^+$, 305.2076; found, 305.2082.

(1′*RS*,2′*SR*,3′*RS*,4′*SR*,5′*SR*,6′*RS*)-*N*-(2-Amino-3,4,5,6-tetrahydroxycyclohexyl)octanamide (8) (HCl salt, 12.5 mg, 73%). ^{1}H NMR (500 MHz, MeOD−D_2O): 0.91 (t, 3H), 1.26−1.32 (m, 8H), 1.71 (m, 2H), 1.91 (m, 2H), 3.32−3.36 (m, 4H), 3.63−3.66 (m, 2H), 7.91 (m, 1H), 8.21 (m, 1H). HRMS: calcd for $C_{14}H_{28}N_2O_5$ (M + H$^+$), 305.2076; found, 305.2085.

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Supporting Information Available: NMR spectra for all the compounds described in this work. This material is available free of charge via the Internet at http://pubs.acs.org.

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