Synthesis of Aminocyclitols by Intramolecular Reductive Coupling of Carbohydrate Derived δ- and ϵ-Functionalized Oxime Ethers Promoted by Tributyltin Hydride or Samarium Diiodide†

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The intramolecular reductive coupling of a series of simple or polyoxygenated oxime ethers δ- or ϵ-functionalized with bromide, α,β-unsaturated ester, aldehyde, or ketone groups is reported. The cyclization of a nitrile-tethered aldehyde is also studied. These reductive couplings are promoted by tributyltin hydride or samarium diiodide. The reactions proceed under mild conditions, in good chemical yield, and with high stereoselectivity. When applied to highly functionalized substrates derived from carbohydrates, this approach provides a selective entry to enantiomerically pure aminocyclitols of varying regio- and stereochemistry. In particular, the reductive coupling reaction of carbonyl-tethered oxime ethers promoted by samarium diiodide can be performed in a one-pot sequence, following a Swern oxidation step, allowing the direct transformation of hydroxyl-tethered oxime ethers into the corresponding aminocyclitols. Moreover, the resultant *O*-benzylhydroxylamine products of these cyclizations can be further reduced *in situ* with excess samarium diiodide, in the presence of water, to the corresponding amino alcohols in excellent yields. Some transformations of these compounds are discussed.

Introduction

Polyhydroxylated aminocyclopentanes are structural motifs present in a growing number of natural products and pharmacologically important drugs that show interesting biological properties. Well known members of this group are the carbocyclic glycosidase inhibitors mannostatin A (**1**),[1] trehazolin (**2**),[2] allosamidin (**3**),[3] and the carbocyclic nucleosides aristeromycin (**4**),[4] neplanocin A (**5**),[5] and analogs such as *epi*-5′-nor-aristeromycin (**6**)[6] (Figure 1). Polyhydroxylated aminocyclohexanes have also attracted much attention due to their therapeutic applications.[7] Different strategies have been employed for the synthesis of such densely functionalized carbocycles,[1−3] but one of the most successful involves the transformation of carbohydrates.[8] Following this ap-

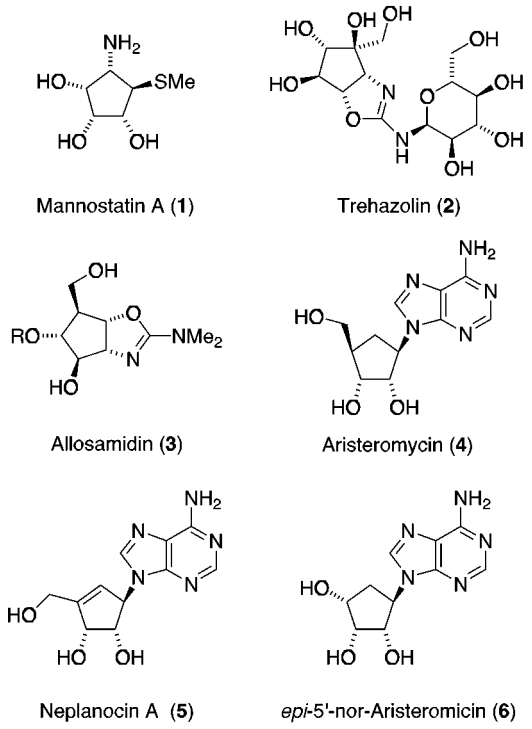

Figure 1. Aminocyclopentitol-derived natural products.

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† Dedicated to the memory of Prof. Eldiberto Fernández-Alvarez (deceased August 23, 1996).

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(1) Recent syntheses: (a) Knapp, S.; Dhar, T. G. M. *J. Org. Chem.* **1991**, *56*, 4096. (b) Trost, B. M.; Van Kranken, D. L. *J. Am. Chem. Soc.* **1993**, *115*, 444, and references cited therein. (c) King, S. B.; Ganem, B. *J. Am. Chem. Soc.* **1994**, *116*, 562, and references cited therein. (d) Li, C.; Fuchs, P. L. *Tetrahedron Lett.* **1994**, *35*, 5121. (e) Ogawa, S.; Kimura, H.; Uchida, C.; Ohashi, T. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1695, and references cited therein.

(2) Recent syntheses of trehazoline and its aglycon: (a) Kobayashi, Y.; Miyazaki, H.; Shiozaki, M. *J. Org. Chem.* **1994**, *59*, 813, and references therein. (b) Uchida, C.; Yamagishi, T.; Ogawa, S. *J. Chem. Soc., Perkin Trans. 1* **1994**, 589, and references cited therein. (c) Knapp. S.; Purandare, A.; Rupitz, K.; Withers, S. G. *J. Am. Chem. Soc.* **1994**, *116*, 7461. (d) Ledford, B. E.; Carreira, E. M. *J. Am. Chem. Soc.* **1995**, *117*, 11811.

(3) Recent syntheses of allosamidine and its aglycon: (a) Nakata, M.; Akazawa, S.; Kitamura, S.; Tatsuta, K. *Tetrahedron Lett.* **1991**, *32*, 5363. (b) Takahashi, S.; Terayama, H.; Kuzuhara, H. *Tetrahedron Lett.* **1992**, *33*, 7565, and references cited therein. (c) Simpkins, N. S.; Stokes, S.; Whittle, A. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2471, and references cited therein. (d) Kitahara, T.; Suzuki, N.; Koseki, K.; Mori, K. *Biosci., Biotechnol., Biochem.* **1993**, *57*, 1906. (e) Maloisel, J.-L.; Vasella, A.; Trost, B. M.; Van Vranken, D. L. *Helv. Chim. Acta* **1992**, *75*, 1515. (f) Goering, B. K.; Ganem, B. *Tetrahedron Lett.* **1994**, *35*, 6997. (g) Blattner, R.; Furneaux, R. H.; Kemmit, T.; Tyler, P. C.; Ferrier, R.; Tidén, A.-K. *J. Chem. Soc., Perkin Trans. 1* **1994**, 3411. (h) Griffith, D. A.; Danishefsky, S. *J. Am. Chem. Soc.* **1996**, *118*, 9526, and references cited therein. See also ref 1b.

(4) For a review, see: Quinkert, E., Ed. *Synform* **1989**, *7*, 192.

(5) For a review, see: Quinkert, E., Ed. *Synform* **1989**, *7*, 225.

(6) (a) Siddiqi, S. M.; Chen, X.; Schneller, S. W. *J. Med. Chem.* **1994**, *37*, 1382. (b) Siddiqi, S. M.; Chen, X.; Schneller, S. W. *J. Med. Chem.* **1994**, *37*, 551, and references cited therein.

(7) *Aminoglycoside antibiotics*; Umezawa, H., Hooper, I. R., Eds.; Springer-Verlag: New York, 1982.

(8) For a recent review on the use of carbohydrate templates for the preparation of carbocycles, see: Ferrier, R. J.; Middleton, S. *Chem. Rev.* **1993**, *93*, 2779.

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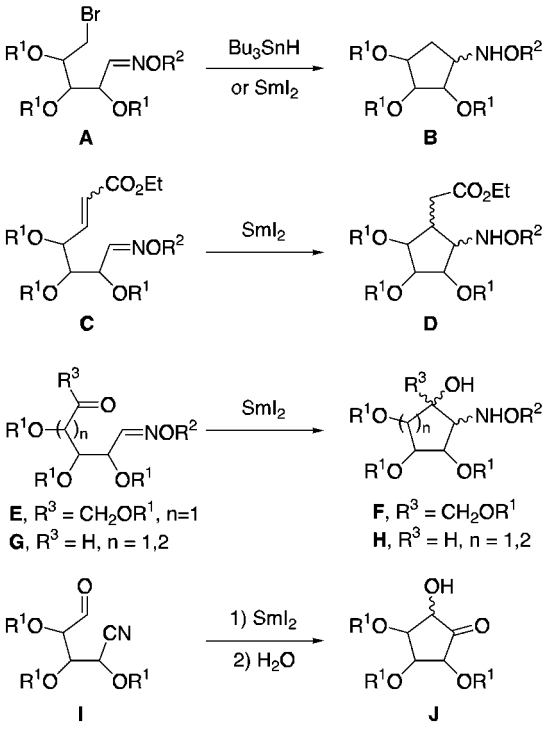
Scheme 1



proach, a series of carbocyclization methods have been developed, a particularly interesting process being the intramolecular trapping of a radical by an oxime ether[9] or by a hydrazone.[10] The efficiency of these reactions lies in the additional stabilization of the intermediate aminyl radical by a lone pair in the adjacent oxygen or nitrogen atom.[11] Our particular effort in this area during the last few years has resulted in several new methodologies for the synthesis of enantiomerically pure polyhydroxylated cyclopentanes and cyclohexanes using radical cyclizations promoted by tributyltin hydride[12] or by samarium diiodide.[13,14]

In this paper we report in full our recent results in the field, showing the scope and generality of some of these protocols. In particular, we have investigated the carbocyclizations outlined in Scheme 1. To this end, we have prepared a series of simple or polyhydroxylated and enantiomerically pure oxime ethers (Figure 2), δ- or ϵ-functionalized with a bromide (**7a**−**e**, **8**), an α,β-unsaturated ester (**9**), an aldehyde (**11**−**16**), or a ketone group (**17**−**20**). All these compounds have been submitted to typical conditions for carbocyclization promoted by tributyltin hydride or samarium diiodide. The cyclization of a nitrile-tethered aldehyde (**10**) has been also investigated.

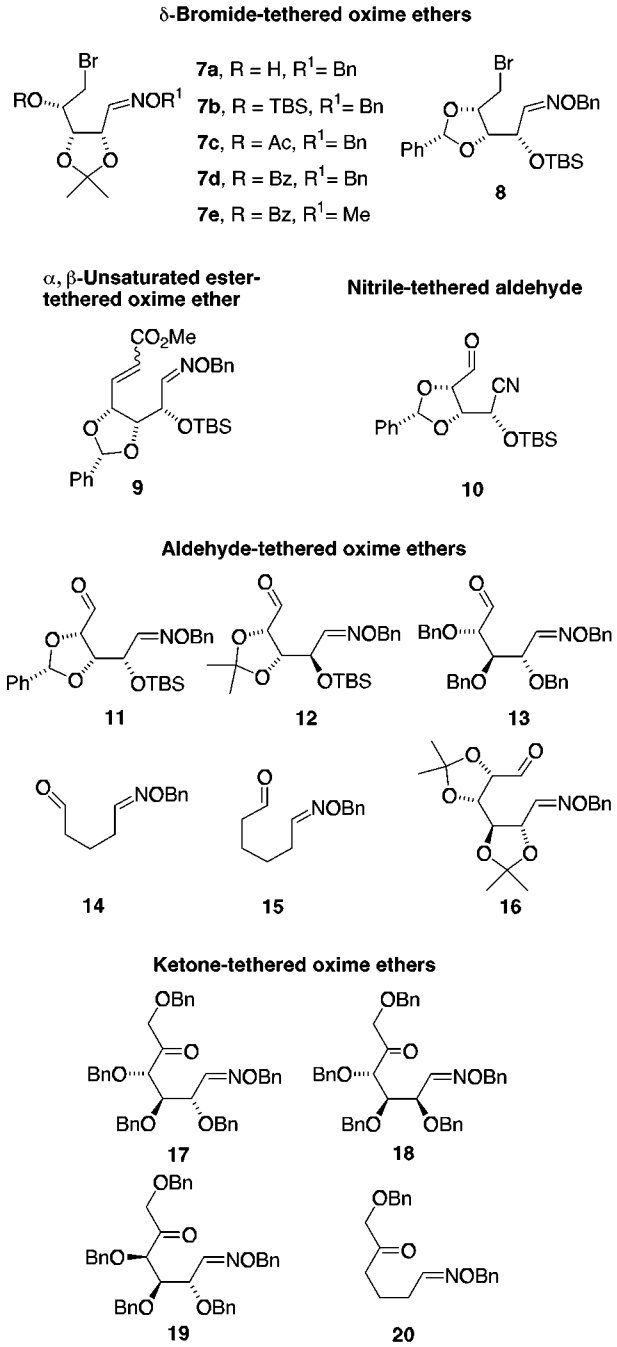


Figure 2.

Results and Discussion

A. Tributyltin Hydride Cyclization of δ-Bromo Oxime Ethers. The 5-*exo-trig* free radical cyclization of 5-bromo-5-deoxy-D-ribose derivatives, using an α,β-unsaturated ester as radical trap, was first reported by

(9) (a) Hart, D. J.; Seely, F. L. *J. Am. Chem. Soc.* **1988**, *110*, 1631. (b) Bartlett, P. A.; McLaren, K. L.; Ting, P. C. *J. Am. Chem. Soc.* **1988**, *110*, 1633. For recent examples, see: Booth, S. E.; Jenkins, P. R.; Swain, C. J.; Sweeney, J. B. *J. Chem. Soc., Perkin Trans. 1* **1994**, 3499, and references cited therein.

(10) (a) Kim, S.; Kee, I. S. *Tetrahedron Lett.* **1993**, *34*, 4213. (b) Sturino, C. F.; Fallis, A. G. *J. Am. Chem. Soc.* **1994**, *116*, 7447. (c) Sturino, C. F.; Fallis, A. G. *J. Org. Chem.* **1994**, *59*, 6514. (d) Bowman, W. R.; Stephenson, P. T.; Terrett, N. K.; Young, A. R. *Tetrahedron Lett.* **1994**, *35*, 6369.

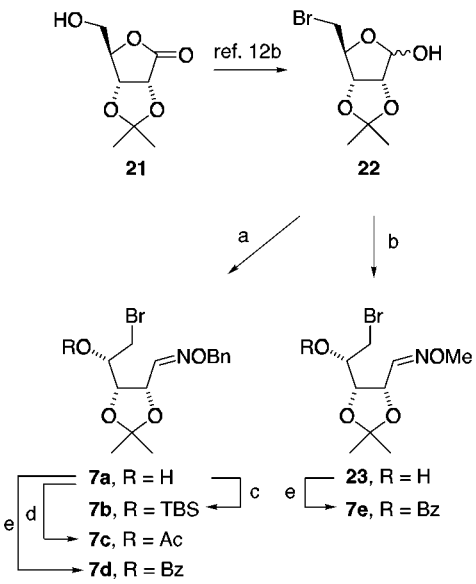
(11) Kim, S.; Yoon, K. S.; Kim, Y. S. *Tetrahedron* **1997**, *53*, 73.

(12) (a) Marco-Contelles, J.; Martínez, L.; Martínez-Grau, A. *Tetrahedron: Asymmetry* **1991**, *2*, 961. (b) Marco-Contelles, J.; Ruiz, P.; Martínez, L.; Martínez-Grau, A. *Tetrahedron* **1993**, *49*, 6669. For a later report on exactly the same methodology, see: Ingall, A. H.; Moore, P. R.; Roberts, S. M. *Chem. Commun.* **1994**, 83 (corrigendum: *Chem. Commun.* **1994**, 675). (c) Marco-Contelles, J.; Sánchez, B. *J. Org. Chem.* **1993**, *58*, 4293. (d) Marco-Contelles, J.; Destabel, C.; Gallego, P.; Chiara, J. L.; Bernabé, M. *J. Org. Chem.* **1996**, *61*, 1354. (e) Marco-Contelles, J. In *Carbohydrate Mimics: Concepts and Methods*; Chapleur, Y., Ed.; VCH: Weinheim, in press.

(13) (a) Chiara, J. L.; Martín-Lomas, M. *Tetrahedron Lett.* **1994**, *35*, 2969. (b) Chiara, J. L.; Valle, N. *Tetrahedron: Asymmetry* **1995**, *6*, 1547. (c) Chiara, J. L.; Marco-Contelles, J.; Khiar, N.; Gallego, P.; Destabel, C.; Bernabé, M. *J. Org. Chem.* **1995**, *60*, 6010. (d) Chiara, J. L.; Martínez, S.; Bernabé, M. *J. Org. Chem.* **1996**, *61*, 6488. (e) Chiara, J. L. In *Carbohydrate Mimics: Concepts and Methods*; Chapleur, Y., Ed.; VCH: Weinheim, in press.

(14) For recent reviews on applications of samarium diiodide in organic synthesis, see: (a) Molander, G. A. *Chem. Rev.* **1996**, *96*, 307. (b) Molander, G. A. *Org. React.* **1994**, *46*, 211. (c) Imamoto, T. *Lanthanides in Organic Synthesis*; Academic Press: London, 1994.

Scheme 2[a]



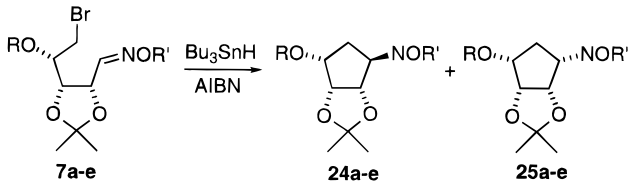
[a] Reagents and conditions: (a) $BnONH_2$·HCl, py, CH_2Cl_2, reflux (95%); (b) $MeONH_2$·HCl, py, CH_2Cl_2, reflux (81%); (c) *t*-$BuMe_2SiCl$, imidazole, DMF, rt (41%); (d) Ac_2O, py, rt (76%); (e) PhCOCl, py, rt (**7a** → **7d**: 54%; **23** → **7e:** 78%);

Wilcox in a seminal paper published in 1985.[15] After this report, Bartlett[9b] described the use of oxime ethers as efficient radical traps, compared to aldehydes,[16] for similar ring closures. These reports encouraged us to explore the synthesis and carbocyclization of 5-bromo-5-deoxy-2,3-*O*-isopropylidene-D-ribose *O*-benzyl oxime ether derivatives.[12] This protocol should provide a simple and ready access to chiral 4-amino-1,2,3-cyclopentanetriols (**B**; Scheme 1), a structural motive found in interesting, recently discovered antiviral agents such us **6**.[6]

Compound **7a**[12b] and related 4-*O*-substituted derivatives (**7b**−**e**)[12a] were prepared from commercially available D-ribonolactone derivative **21**, following standard methodologies (Scheme 2). These compounds were obtained as inseparable mixtures of *syn* and *anti* isomers in 70:30 ratio, respectively, as determined by ^{1}H NMR [H-1 (*syn*): 7.30 ppm, d, J = 7.3 Hz; H-1 (*anti*): 6.80 ppm, d, J = 5.5 Hz)].

With these precursors in hand, we tried the tributyltin hydride promoted cyclization. The reaction proceeded in moderate to good yield and excellent diastereoselectivity under standard conditions [for comparative purposes we have also included the data for compound **7a**; see Table 1, entry 1]. For compounds **7b**,**c**, exclusively exo-cyclized products **24b**,**c** were obtained, with the *O*-alkylhydroxyamino group predominantly in *trans* relative orientation with respect to the vicinal alkoxy substituent.[17a] For compounds **7d** or **7e** (see Table 1, entries 4 and 5) the minor *cis* isomers **25d** and **25e** could be detected in an increased amount, but we were unable to isolate the major isomers pure. Compounds **24b** and **24d**/**25d** (91:9 mixture) were transformed by mild acid hydrolysis and sodium methoxide treatment, respectively, into **24a**,

Table 1. Tributyltin Hydride Mediated Cyclization of Precursors 7a−e



entry	radical precursor	R	R	product ratios **24**/**25**[a]	yield (%)[b]
1[c]	**7a**	H	Bn	>95:5	75
2	**7b**	TBS	Bn	>95:5	53
3	**7c**	Ac	Bn	>95:5	52
4	**7d**	Bz	Bn	89:11	58
5	**7e**	Bz	Me	80:20	71

[a] Product ratios computed from NMR analysis of crude mixtures. [b] Isolated yield of cyclized products. [c] Reference 12b.

confirming the assigned absolute configuration at C-4 in these carbocycles.

Since we were unable to separate the *syn* and *anti* isomers of compounds **7a**−**e**, we could not analyze independently the stereochemical outcome of their radical cyclization. In principle, each isomer could yield a different *trans*/*cis* ratio of cyclic products. However, according to previous reports,[9b] no significant differences should be expected between the cyclizations of each oxime isomer. The stereochemical results obtained in the cyclization of these radical precursors can be rationalized in terms of the model proposed by Wilcox for the cyclization of analogous α,β-unsaturated esters.[15a] According to Beckwith,[18] 5-hexenyl radical species prefer chairlike conformations in the transition state with most substituents in pseudoequatorial position. In our case, conformation **S2** (Scheme 3) presents unfavorable 1,3-steric interactions between substituents at C-2 and C-4. This effect makes conformation **S1** the most favorable and, accordingly, isomers **24a**−**e** should be formed preferentially. Comparison of the cyclizations of compounds **7d** and **7e** with those of **7a**−**c** suggest a probable influence of electronic effects of the aryl ester.[12a]

From a practical perspective, the cyclization of precursor **7a** could be scaled up to ∼4 mmol without loss of chemical yield (∼80%).[12b] With compound **24a** in hand, we tried several chemical manipulations directed toward the synthesis of carbocyclic nucleosides. Thus, treatment of **24a** with a THF solution of SmI_2[19] at room temperature cleanly gave the amino alcohol **26** (Scheme 4). Unfortunately, subsequent reaction of **26** with 5-amino-4,6-dichloropyrimidine to give the carbocyclic nucleoside **27**,[20] followed by reaction with triethyl orthoformate and acid hydrolysis, afforded **28**[20] in very poor overall yield (7%), and this approach was abandoned.

(15) (a) Wilcox, C. S.; Thomasco, L. M. *J. Org. Chem.* **1985**, *50*, 546. For a similar cyclization using samarium diiodide, see: (b) Zhou, Z.; Bennett, S. M. *Tetrahedron Lett.* **1997**, *38*, 1153. See also: (c) RajanBabu, T. V. *J. Org. Chem.* **1988**, *53*, 4522.

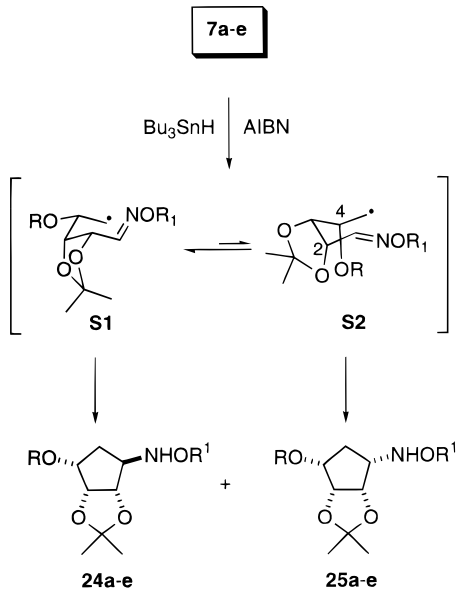
(16) Yeung, B, W.; Alonso, R.; Vité, G. D.; Fraser-Reid, B. *J. Carbohydr. Chem.* **1989**, *8*, 413, and references cited therein.

(17) (a) This assignment was evident after ^{1}H NMR detailed analysis of these compounds: a $^3J_{3,4} = 0$ Hz clearly suggested a *trans* relative stereochemistry for these carbons, establishing as *R* the absolute configuration at the new stereocenter. (b) The absolute configuration at the new stereocenters was established by detailed ^{1}H NMR and 2D NOESY studies (see the Supporting Information). (c) A detailed analysis of the ^{1}H NMR spectrum of **36a** showed a $^3J_{HC(NHOBn)-HC(OTBS)} = 9.4$ Hz; this value strongly suggets a *trans* arrangement between these vicinal protons, establishing as *R* the absolute configuration at the new stereocenter.

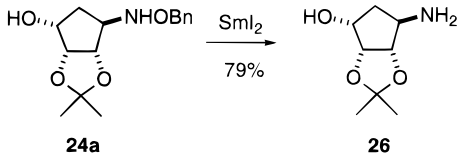
(18) (a) Beckwith, A. L. J.; Schiesser, C. H. *Tetrahedron* **1985**, *41*, 3925. (b) Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073 and references therein.

(19) (a) Chiara, J. L.; Destabel, C.; Gallego, P.; Marco-Contelles, J. *J. Org. Chem.* **1996**, *61*, 359. (b) Keck, G. E.; McHardy, S. F.; Wager, T. T. *Tetrahedron Lett.* **1995**, *36*, 7419.

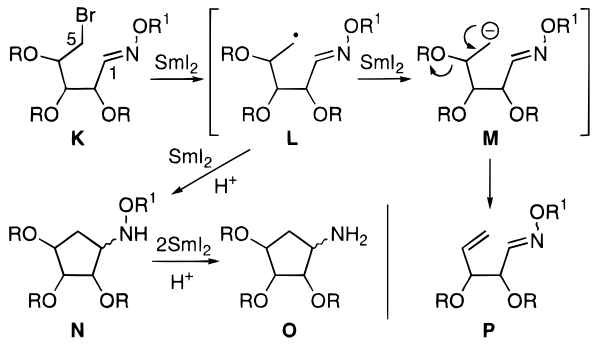
Scheme 3



Scheme 4

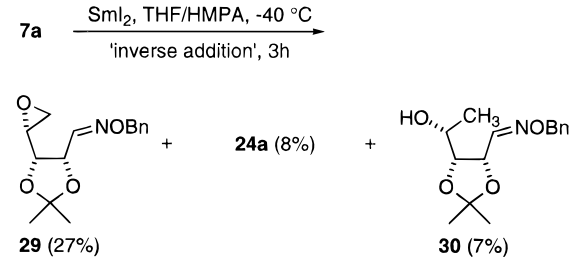


Scheme 5

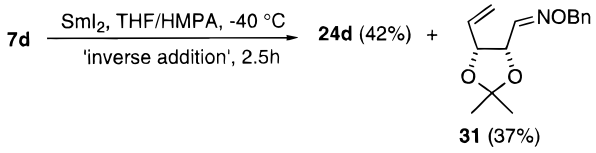


At this point, we considered the use of SmI_2 as reductive promotor in these carbocyclizations (Scheme 5). Intramolecular Barbier-type reactions promoted by samarium diiodide are known[14] but, to our knowledge, have never been applied to such highly functionalized substrates as those derived from sugars. Besides, the first examples of aza-Barbier couplings promoted by samarium diiodide have been reported recently, but only for simple substrates.[10b,c] Two questions attracted also our interest at this point: (a) Will cyclization compete favorably with other possible side-reactions such as the

Scheme 6



Scheme 7

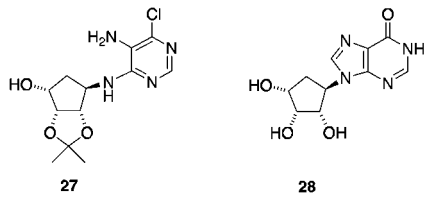


β-elimination **M** → **P** (Scheme 5) that could take place after reduction of the initial radical **L** to an organosamarium intermediate **M**?; (b) is the stereochemical outcome of the cyclization dependent on the reagent Bu_3SnH or SmI_2 used for the reaction? Both questions have been answered, and our results are as follows.

First of all, we observed that cyclization with the bromide precursors did not proceed in the absence of HMPA.[10b] After extensive experimentation, compound **7a** gave in the best conditions a mixture of products **29**, **24a**, and **30** (Scheme 6). Compound **30** is the reduced, uncyclized material accompanied with minor amounts of the cyclized *trans* isomer **24a** and epoxide **29**, isolated as a *syn*/*anti* mixture of oxime ethers, but diastereomerically pure at C-4.[21] We then turned our attention to precursor **7d**, where epoxide formation would be prevented. Under the same experimental conditions, we isolated the cyclic product **24d** as a single diastereoisomer together with almost an equimolar amount of the reductive elimination product **31** (Scheme 7). Although no epoxide was formed, elimination of the benzoate group upon reduction of the initial radical by SmI_2 competes with cyclization. Very significantly, performing the reaction at −78 °C prevents formation of **31** giving a mixture of cyclized products **24d**/**25d** in very poor yield (16%) and lower stereoselectivity (70/30, respectively).

From these experiments we conclude that the tin-mediated radical cyclization of 5-bromo-oxime ethers derived from carbohydrates is clearly superior to the corresponding SmI_2-mediated reaction. In the latter case, side reactions such as reductive elimination of the alkoxide group at C-4, epoxide formation, or simple dehalogenation of the substrate compete with cyclization. The low yield of carbocycles is probably due also to partial N−O reductive cleavage by excess SmI_2 (see below).[22] These problems probably could be overcome if precursors with an iodide instead of bromide group were used. However, this possibility was discarded since, in our previous experience, this type of compound is rather

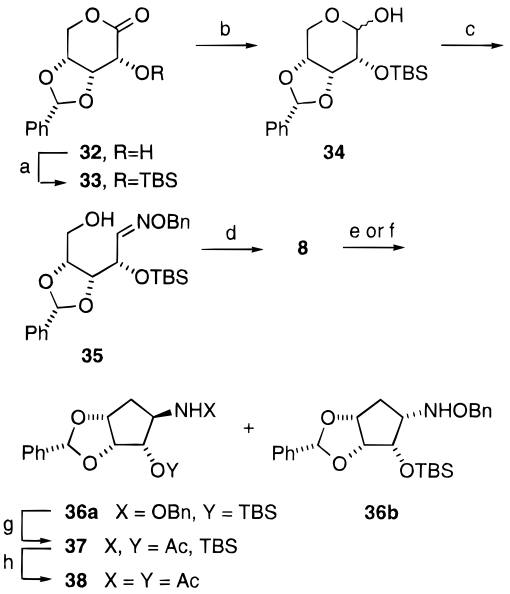
(20) **27**: yellowish foam; ^{1}H NMR ($CDCl_3$) δ 8.16 (s, 1H), 4.83 (d, J = 4.4 Hz, 1H), 4.59 (m, 2H), 4.29 (m, 2H), 3.50 (br s, 2H), 2.54 (br s, 1H), 2.25−1.98 (m, 2H), 1.54 (s, 3H), 1.36 (s, 3H). **28**: white solid; ^{1}H NMR ($CDCl_3$) δ 8.28 and 8.23 (2s, 2H), 5.18 (m, 1H), 4.71 (m, 2H), 4.33 (t, J = 4.2 Hz, 1H), 2.55 (m, 2H).



(21) The last product probably arises from a samarium(III) alkoxide intermediate via intramolecular bromide displacement. This alkoxysamarium could be formed by deprotonation of **7a** by the intermediate anions formed from **7a** in the reaction, although direct reduction of the hydroxyl group of **7a** by the SmI_2/HMPA complex to the samarium(III) alkoxide with release of H_2 cannot be discarded.

(22) In fact, in these reactions we detect always benzyl alcohol that results from the N−O reductive cleavage. The presence of HMPA made troublesome to isolate, for instance, the corresponding amino alcohol **26** (Scheme 4).

Scheme 8[a]



[a] Reagents and conditions: (a) *t*BuMe$_2$SiCl, imidazole, DMF (99%); (b) DIBALH, -78 °C (98%); (c) BnONH$_2$·HCl, py, CH$_2$Cl$_2$ (80%); (d) CBr$_4$, py (48%); (e) SmI$_2$, THF/HMPA, -40 °C, 1 h (**36a**: 40 %, **36b**: traces); (f) Bu$_3$SnH, AIBN, toluene, 110 °C (**36a**/**36b**: 1.8/1; 80%); (g) SmI$_2$, then Ac$_2$O, py (78%); (h) i. TBAF, THF, ii. Ac$_2$O, py (81%, 2 steps).

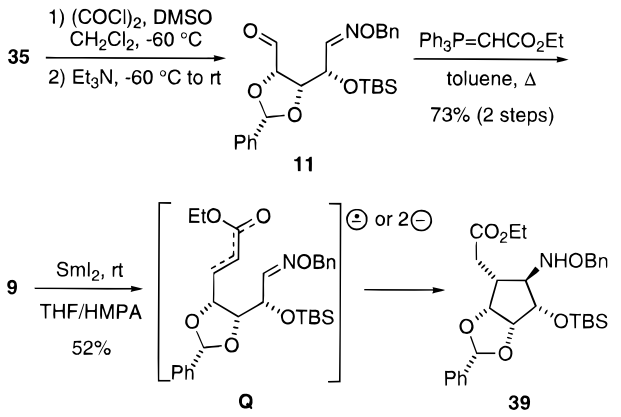
unstable, and the chemical yields in the Bu$_3$SnH mediated cyclization are considerably lower.[12b]

Finally, we performed a comparative study of the Bu$_3$SnH and SmI$_2$ mediated ring closure of compound **8**, a D-ribose derivative with a slightly different arrangement of protecting groups. This substrate was obtained from the protected D-ribonolactone **32**[23] after standard manipulations, and it was submitted to cyclization as shown in Scheme 8. The samarium diiodide ring closure gave, in 40% total yield (61% taking into account the recovered starting material), the major *trans* product **36a**[17c] with traces of the *cis* isomer **36b**. The analogous cyclization with tributyltin hydride gave compounds **36a**/**36b** in a 1.8:1 ratio, in 80% yield. Finally, samarium diiodide reductive cleavage of the N−O bond[19] followed by acetylation in situ gave a mixture of silyl-migrated compounds **37** (78%) which, after desilylation and acetylation, gave finally the acetamide **38**.

B. Samarium Diiodide Cyclization of Oxime Ethers *δ*-Functionalized with an α,*β*-Unsaturated Ester. Although the SmI$_2$ cyclization of sugar-derived α,*β*-unsaturated esters tethered to carbonyl groups is known,[24] the similar protocol using oxime ethers has not been described yet.[25] This process, if successful, would result in a simple entry into branched aminocyclitols of type **D** from acyclic sugar derivatives **C** (Scheme 1).

To this end, we prepared the precursor **9** from alcohol **35** by standard manipulations (Scheme 9). Compound

Scheme 9



9 was obtained as the *E* isomer at the C=C double bond and as a mixture of *syn*/*anti* oxime isomers in 3:1 ratio, respectively. We were unable to separate these isomers that were submitted together to cyclization. When a solution of **9** in THF was added to SmI$_2$ (3 mol equiv) in THF and HMPA (15 mol equiv) at room temperature, compound **39** was formed after 3 h in 52% yield, as a single isomer.[17b] When the reaction was performed at −40 °C, a mixture of products resulted from which **39** could be isolated in a lower yield, together with other uncharacterized products. Although no mechanistic studies were performed, we hypothesize that this reaction takes place via a homoenolate reactive species **Q** (Scheme 9), formed after one- (radical-anion) or two- (dianion) electron transfers from SmI$_2$, that attacks the oxime ether. Some reports are also in support of this hypothesis.[26]

C. Samarium Diiodide Mediated Cyclization of Oxime Ethers *δ*- or *ϵ*-Functionalized with a Carbonyl Group. We have previously reported on a new approach to highly functionalized chiral aminocyclopentitols via the intramolecular reductive cross-coupling of oxime ethers with aldehydes or ketones prepared from readily available carbohydrate precursors.[13c] We now report in full our recent results using this strategy, including an example of cyclization to give a six-membered ring. The first example of intramolecular reductive cross-coupling of oxime ethers with carbonyl compounds was described by Corey.[27] More recently, this reaction has been performed using electroreduction[28] or tributyltin hydride.[29] Samarium diiodide has also been used for the intermolecular coupling of aldehydes and ketones with *O*-benzylformaldoxime[30] and, more recently, for the corresponding intramolecular coupling with diphenylhydrazones.[10b,c] In both cases, the addition of HMPA was found to be essential for a successful reaction. Although the reported intermolecular cross-coupling with *O*-benzylformaldoxime failed completely with other aldoximes, we set out to study an intramolecular version of this reaction with the hope that its lower entropic barrier could make the process feasible. This process could provide a straightforward access to branched (**F**)

(23) Shen, S. Y.; Jouillé, M. M. *J. Org. Chem.* **1984**, *49*, 2168. Bagget, N.; Buchanan, J. G.; Fatah, M. Y.; Lachut, C. H.; McCullough, K. J.; Webber, J. M.; *J. Chem. Soc., Chem. Commun.* **1985**, 1826.

(24) (a) Enholm, E. J.; Trivellas, A. *J. Am. Chem. Soc.* **1989**, *111*, 6463. (b) Enholm, E. J.; Satici, H.; Trivellas, A. *J. Org. Chem.* **1989**, *54*, 5841. (c) Enholm, E. J.; Trivellas, A. *Tetrahedron Lett.* **1994**, *35*, 1627. (d) Tadano, K.-i.; Isshiki, Y.; Minami, M.; Ogawa, S. *J. Org. Chem.* **1993**, *58*, 6266, and references cited therein.

(25) Aurrecoechea has recently described a related aproach using α-benzotriazolylalkenylamines: (a) Aurrecoechea, J. M.; Fernández-Acebes, A. *Tetrahedron Lett.* **1993**, *34*, 549. (b) Aurrecoechea, J. M.; López, B.; Fernández, A.; Arrieta, A.; Cossío, F. P. *J. Org. Chem.* **1997**, *62*, 1125.

(26) Fry, A. J.; Little, R. D.; Leonetti, J. *J. Org. Chem.* **1994**, *59*, 5017.

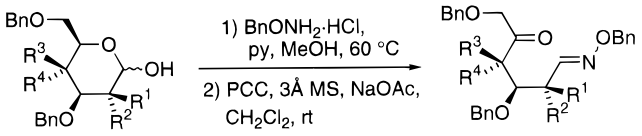
(27) Corey, E. J.; Pyne, S. G. *Tetrahedron Lett.* **1983**, 2821.

(28) (a) Shono, T.; Kise, N.; Fujimoto, T. *Tetrahedron Lett.* **1991**, *32*, 525. (b) Shono, T.; Kise, N.; Fujimoto, T.; Yamanami, A.; Nomura, R. *J. Org. Chem.* **1994**, *59*, 1730.

(29) (a) Naito, T.; Tajiri, K.; Harimoto, T.; Ninomiya, I.; Kiguchi, T. *Tetrahedron Lett.* **1994**, *35*, 2205. (b) Kiguchi, T.; Tajiri, K.; Ninomiya, I.; Naito, T. *Tetrahedron Lett.* **1995**, *36*, 253.

(30) Hanamoto, T.; Inanaga, J. *Tetrahedron Lett.* **1991**, *32*, 3555.

Scheme 10



40: $R^1 = R^3 = H$, $R^2 = R^4 = OBn$ — **17** (81%)
41: $R^1 = R^4 = OBn$, $R^2 = R^3 = H$ — **18** (88%)
42: $R^1 = R^4 = H$, $R^2 = R^3 = OBn$ — **19** (69%)

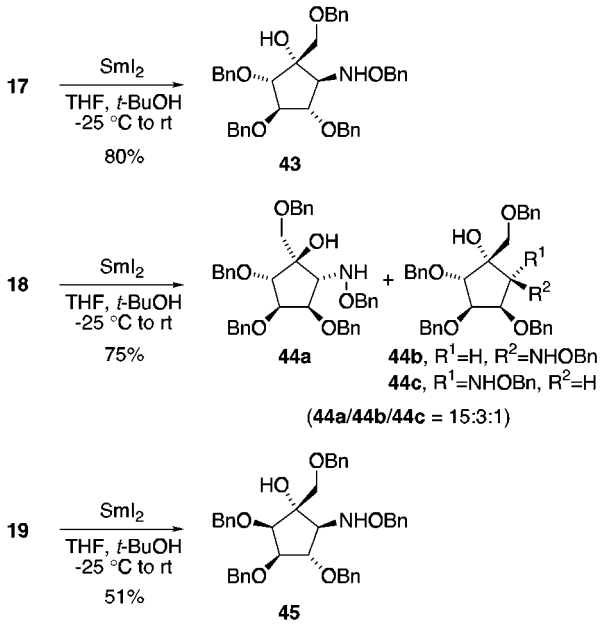
and unbranched (**H**, $n = 1$) aminocyclopentitols and to aminoinositols (**H**, $n = 2$) from precursors **E** and **G** (Scheme 1). These precursors can be easily prepared in two steps from readily available *O*-protected sugar hemiacetals by condensation with *O*-benzylhydroxylamine and subsequent oxidation of the released hydroxyl group, as discussed below.

C1. Samarium Diiodide Mediated Cyclization of Sugar-Derived Oxime Ethers with a *δ*-Carbonyl Group. The ketone/oxime ether cross-coupling was studied first. Starting from readily available sugar lactols **40**−**42**,[31] three substrates **17**−**19** were prepared by condensation with *O*-benzylhydroxylamine followed by PCC oxidation of the released hydroxyl group at C-5. These substrates differed in the configuration at C-2 (sugar numbering), the center adjacent to the oxime ether group, and at C-4, the center adjacent to the carbonyl group (Scheme 10).

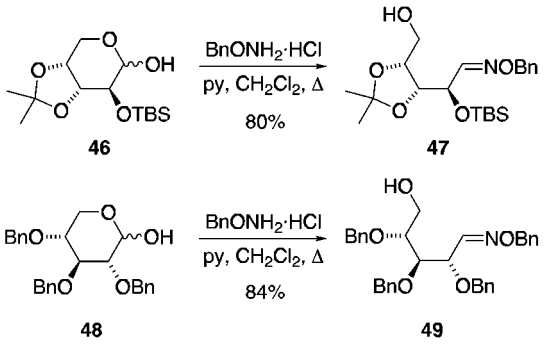
When a 0.02 M solution of ketone **17**, derived from D-glucose, in THF was added to SmI_2 in THF (2.5 mol equiv, 0.1 M) and *t*-BuOH (2.5 mol equiv) at −25 °C, the reductive coupling took place smoothly to afford the branched aminocyclopentitol **43** as a single diastereoisomer in good yield (Scheme 11).[17b] Interestingly, this coupling proceeds *in the absence of HMPA*, in contrast to the analogous intermolecular case[30] and to the corresponding coupling of hydrazones.[10b] It is also noteworthy that a single diastereoisomer is obtained out of four possible stereochemical results. A similar approach has been reported very recently using a tributyltin hydride-induced reductive coupling of the corresponding *O*-methyloxime derivative of **17**.[29b] In this case, a mixture of two diastereoisomeric aminocyclopentitols was obtained in 68% yield and 1.4:1 ratio. The minor isomer corresponds to that obtained by us using SmI_2.

Under the same conditions, ketone **18** derived from D-mannose afforded a mixture of three aminocyclopentitols **44a**−**c**[17b] (Scheme 11) in 15:3:1 ratio,[32] respectively, and in good yield. The major diastereoisomer **44a** could be isolated from this mixture in 60% yield by column chromatography. Under the same conditions, ketone **19** derived from D-galactose afforded a cyclopentylhydroxylamine **45** (Scheme 11) in moderate yield.[17b,33] It should be noted that compounds **43**−**45** can be readily converted,

Scheme 11



Scheme 12



by hydrogenolysis, into isomers of trehazolamine, the aminocyclopentitol aglycon of the trehalase inhibitor trehazoline (**2**). Thus, this sequence provides an efficient and very short entry into different enantiomerically pure analogues of this interesting aminocyclopentitol from readily available starting materials. It should be stressed that the fully functionalized cyclopentanes **43** and **44a**−**c** are obtained in just five steps from free D-glucose and D-mannose, respectively.

We have also observed that the stereochemistry of the cyclic products is independent of the geometry of the starting oxime ether.[9b] Although *syn*/*anti* mixtures of oximes have been used in all cases, a single stereochemical outcome was obtained in one instance (cyclization of **17**). In the case of **17**, the *syn*-isomer could be isolated and submited to cyclization separatedly, with the same stereochemical outcome as when a mixture enriched in the *anti*-isomer (*anti*/*syn* = 76:24) was used. In most cyclizations (see below), the major isomer shows a *trans* relationship between the hydroxyl and the *O*-benzylhydroxylamino groups, and also between the latter and the alkoxy group at C-2 (starting sugar numbering).

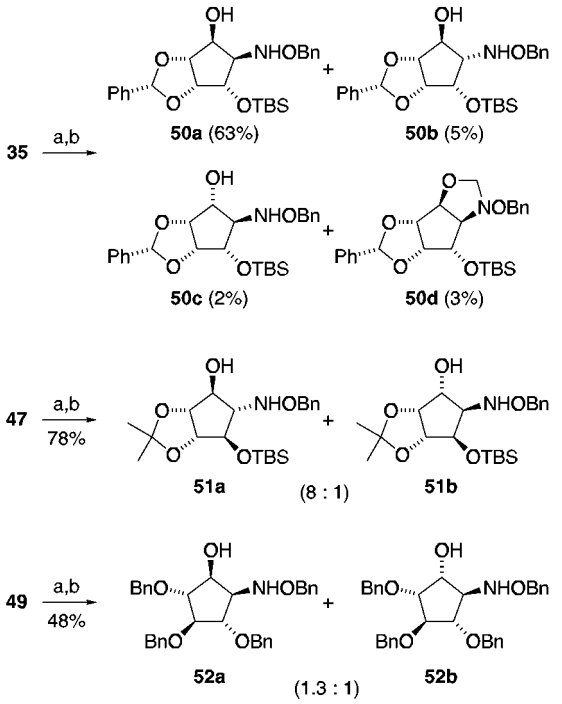
In order to explore the scope of the method we also examined the performance of aldehydes derived from sugars. For this purpose, alcohols **35** (Scheme 8), **47**, and **49** (Scheme 12) were prepared by straighforward synthetic procedures using the known intermediates **46**[24a]

(31) Lactols **40** and **41** were easily obtained in two steps from the corresponding free sugar: Decoster, E.; Lacombe, J.-M.; Strebler, J.-L.; Ferrari, B.; Pavia, A. A. *J. Carbohydr. Chem.* **1983**, *2*, 329. Lactol **42** cannot be prepared using this methodology, and it was in turn obtained from the corresponding thiophenyl glycoside (Garegg, P. J.; Hultberg, H.; Lindberg, C. *Carbohydr. Res.* **1980**, *83*, 157) by oxidative hydrolysis with NBS in aqueous acetone: Groneberg, R. D.; Miyasaki, T.; Stylianides, N. A.; Schulze, T. J.; Stahl, W.; Schreiner, E. P.; Suzuki, T.; Iwasbuchi, Y.; Smith, A. L.; Nicolaou, K. C. *J. Am. Chem. Soc.* **1993**, *115*, 7593 (for an analogous hydrolysis procedure, see: Motavia, M. S.; Marcussen, J.; Moller, B. L. *J. Carbohydr. Chem.* **1995**, *14*, 1279).

(32) Determined from the ^{1}H NMR of the crude reaction mixture.

(33) A minor cyclopentane product was also isolated in this case (see Experimental Section and the Supporting Information), but its structure could not be fully determined.

Scheme 13[a]



[a] Reagents and conditions: (a) i. $(COCl)_2$, DMSO, THF, -78 °C. ii. *i*-Pr_2NEt, -78 °C → 21 °C; (b) SmI_2 (3 equiv), *t*-BuOH (3 equiv), THF, -25 °C → 0 °C.

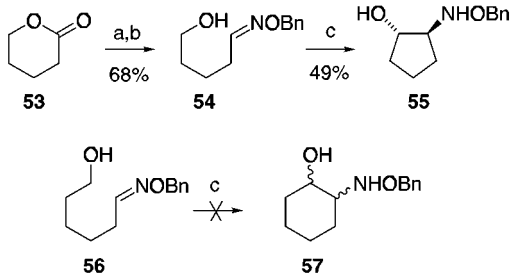
and **48**.[34] These alcohols were isolated as inseparable mixtures of *syn* and *anti* oximes.

Initially, Swern oxidation of **35** derived from D-ribose and reductive cyclization of the isolated intermediate aldehyde gave a mixture of products from which the major cyclopentane (**50a**) could be isolated in only 32% overall yield from **35** (Scheme 13). However, the overall yield was greatly improved *when the Swern oxidation and the SmI_2 cyclization were performed in a one-pot sequence*, thus avoiding the isolation of the intermediate aldehyde.[35] Under these conditions, compound **35** gave a mixture of cyclopentanes **50a**−**d**.[17b,36] The formation of compound **50d** was unexpected and probably could arise from an intermediate (methylthio)methyl ether formed with the excess of Swern reagent after cyclization. Simple treatment of compopund **50a** with formaldehyde in the presence of citric acid gave quantitatively compound **50d**, thus confirming the assigned structure.

When compound **47** derived from D-arabinose was subjected to this one-pot procedure, a nonseparable mixture of two cyclopentanes **51a**,**b**[17b] was obtained in 8:1 ratio,[32] respectively, and good overall yield (Scheme 13). Using the same procedure, the more conformationally labile precursor **49**, derived from D-xylose, produced an almost equimolar mixture of two cyclopentane diasteroisomers **52a**,**b**[17b] (Scheme 13).

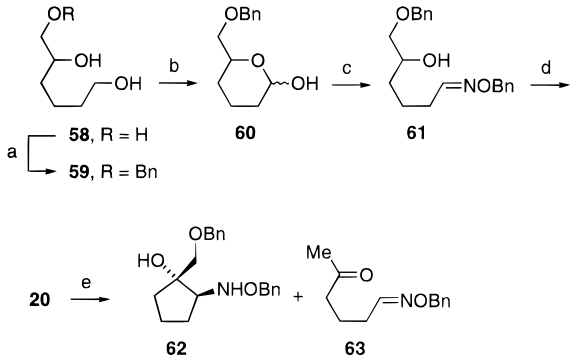
C2. Samarium Diiodide Mediated Cyclization of Simple Oxime Ethers *δ*- or *ϵ*-Functionalized with a Carbonyl Group. The above results moved us to explore also the corresponding cyclization of compounds **14**, **15**, and **20** (Figure 2) in order to extend this methodology to simple deoxygenated substrates. Compound **54**, precursor of **14**, was prepared from *δ*-valerolactone (**53**) by DIBALH reduction followed by oxime ether formation (Scheme 14). Using the previous serial oxidation−reductive cyclization conditions, compound **54** gave exclusively amino alcohol **55** in 49% yield. A 6-*exo* cyclization was also tried with aldehyde **15**. However, when compound **56**, precursor of **15**, was submitted to the same experimental conditions, a complex mixture of products resulted from which we could not isolate any carbocyclic compound (Scheme 14).

Scheme 14[a]



[a] Reagents and conditions: (a) DIBALH, toluene, -78 °C; (b) $BnONH_2$·HCl, py, MeOH, 60 °C; (c) i. $(COCl)_2$, DMSO, THF, -78 °C. ii. *i*-Pr_2NEt, -78 °C → 21 °C. iii. SmI_2 (4 equiv), *t*-BuOH (2.5 equiv), THF, -78 °C → 21 °C.

Scheme 15[a]



[a] Reagents and conditions: (a) i. $(Bu_3Sn)_2O$, toluene, 110 °C. ii. BnBr, Bu_4NBr (60%); (b) PDC, 3 Å MS, NaOAc, CH_2Cl_2 (40%); (c) $BnONH_2$·HCl, py, CH_2Cl_2 (93%); (d) PDC, 3 Å MS, NaOAc, CH_2Cl_2 (71%); (e) SmI_2 (3 equiv), *t*-BuOH (2.5 equiv), -78 °C → -40 °C (**62:** 42%, **63**: 18%).

The cyclization of a 3,4,5-trideoxy-analog (**20**) of ketones **17**−**19** was investigated. This precursor was prepared from 1,2,6-hexanetriol (**58**) as shown in Scheme 15. Using our standard conditions for carbocyclization, we obtained the expected carbocycle **62** in moderate yield with minor amounts of **63** resulting from reductive elimination of the benzyloxy group (Scheme 15). Curiously enough, this side reaction was not observed in the cyclization of the corresponding sugar derivatives. The only diastereoisomers isolated in the cyclizations of these simple precursors have the hydroxyl and the *O*-benzylhydroxylamino groups in *trans* relative orientation, which is also the general tendency found for the corresponding polyhydroxylated precursors derived from sugars.

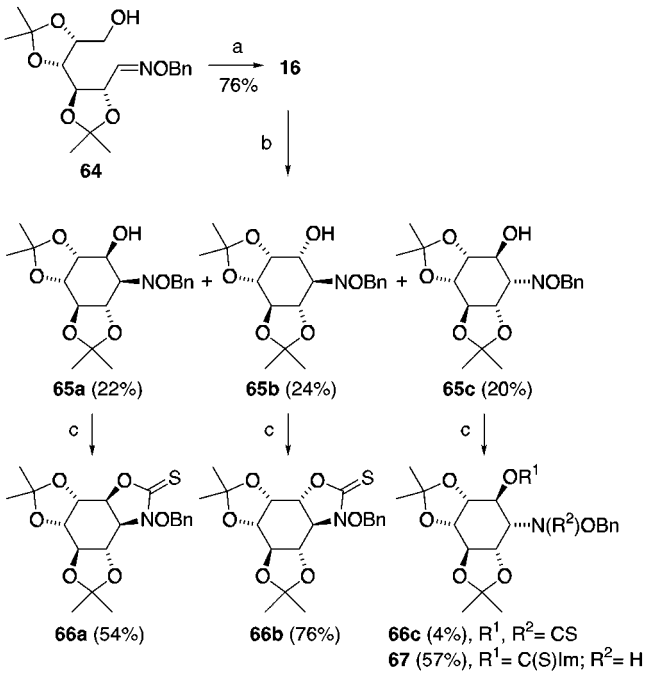
C3. Samarium Diiodide Mediated Cyclization of Sugar-Derived Oxime Ethers with an *ϵ*-Aldehyde Group. In spite of the precedent deceiving result for aldehyde **15** (Figure 2), we prepared a sugar derivative having a similar oxime ether *ϵ*-functionalized with an

(34) Tejima, S.; Ness, R. K.; Kaufman, R. L.; Fletcher, H. G. *Carbohydr. Res.* **1968**, *7*, 485.

(35) We have recently described a similar one-pot sequence consisting of a Swern oxidation and a SmI_2-induced pinacol coupling for the direct transformation of alditol-derived 1,6-diols into inositol derivatives: Chiara, J. L.; Martín-Lomas, M. *Tetrahedron Lett.* **1994**, *35*, 2969. Chiara, J. L.; Valle, N. *Tetrahedron: Asymmetry* **1995**, *6*, 1895−1898.

(36) Performing the reaction in larger scale than in our preliminary communication[13c] allowed a more complete analysis of the different products formed.

Scheme 16[a]

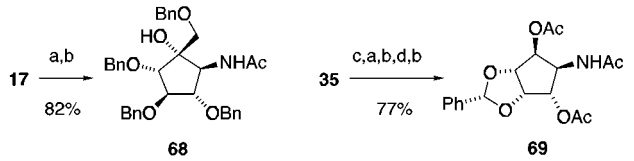


[a] Reagents and conditions: (a) Dess-Martin periodinane, CH_2Cl_2, 21 °C; (b) SmI_2 (6 equiv), THF, -50 °C → 21 °C; (c) $S=C(Im)_2$, THF, 60 °C.

aldehyde, but adding some conformational constraints in order to favor the cyclization. Our selected precursor was compound **16** (Figure 2), readily obtained from D-glucose as previously described.[37] Dess−Martin oxidation[38] of the primary hydroxyl of **64** gave the intermediate aldehyde **16** (Scheme 16). After extensive experimentation, we found conditions for a successful cyclization reaction. When a 0.02 M solution of purified **16** in THF was added to a solution of SmI_2 in THF at −45 °C, compounds **65a**−**c** were formed in good overall yield but with rather poor diastereoselection, as determined by ^{1}H NMR of the crude reaction mixture (Scheme 16). We were able to separate and purify each diastereomer. These compounds were transformed into derivatives **66a**−**c** and **67** after reaction with 1,1′-thiocarbonyldiimidazole. The analysis of their ^{1}H NMR spectra helped to confirm the assignment of the stereochemistry.[17b] This aldehyde/oxime ether cyclization is important because it opens the way for a new and exciting method for the preparation of aminoinositols in enantiomerically pure form from sugars. This result complements our previous observations on SmI_2-induced pinacol coupling for the direct transformation of an alditol-derived 1,6-diol into an inositol derivative.[13a,b]

C4. Sequential Carbonyl−Oxime Ether Cyclization and N−O Reductive Cleavage Promoted by Samarium Diiodide. As we have seen above, the cyclic *O*-benzylhydroxylamine products could further react *in situ* with excess SmI_2 by reduction of the N−O bond[19] to give the corresponding primary amine thus further enhancing the utility of this methodology. This has been demonstrated for the cyclizations of **17** and **35** (Scheme 17).[39] The N−O reductive cleavage reaction is accelerated by addition of

Scheme 17[a]



[a] Reagents and conditions: (a) (i) SmI_2 (6 equiv), THF, -25 °C. (ii) H_2O (25 equiv), -25 °C → 22 °C; (b) Ac_2O, py; (c) $(COCl)_2$, DMSO, Et_3N, -78 °C → 22 °C; (d) TBAF, THF.

water (20−25 mol equiv).[40] This one-pot two-step sequence takes place in excellent yield in the case of **17** → **68** and can be combined with a preceding Swern oxidation step allowing the direct transformation of a 5-hydroxy-oxime ether into a 2-aminocyclopentitol in a strikingly good overall yield, as exemplified for **35**. In the latter case, the sequence of Swern oxidation, reductive carbocyclization and N−O reductive cleavage produced an inseparable mixture of two products (4:1 ratio) in a remarkable 86% overall yield, which resulted from partial silyl migration to nitrogen during the reductive cleavage step.[41] Desilylation of the mixture with TBAF in THF and in situ acetylation afforded **69** as a single product in 92% yield.

Although we have not performed mechanistic studies, it seems reasonable that the samarium diiodide-promoted C=O/C=NOR cross-coupling reaction is initiated by single electron transfer to the carbonyl with generation of a ketyl radical-anion which then adds to the C=N double bond. The process is completed by reduction of the resultant intermediate aminyl radical and protonation.[42] It seems likely that cyclization does not require prior activation of the oxime ether by intramolecular chelation to the Lewis acidic Sm(III) ion in the intermediate radical, at difference with what is thought to occur in intramolecular pinacol coupling reactions promoted by samarium diiodide.[43] Thus, electronic repulsion between the oxygen of the ketyl radical-anion and the nitrogen atom of the oxime could account for the preferred *trans* relative arrangement of the hydroxyl and the hydroxylamino groups in the cyclic products. The same *trans*-selectivity has been observed for the corresponding electrochemical reaction[28b] and also for the analogous coupling with diphenylhydrazones.[10b] Additionally, if the radical cyclization step is reversible, the observation that the stereochemistry of the cyclic products is independent of the oxime isomer used could be explained. However,

(37) Marco-Contelles, J.; Pozuelo, C.; Jimeno, M. L.; Martínez, L.; Martínez-Grau, A. *J. Org. Chem.* **1992**, *57*, 2625.

(38) Dess, D. B.; Martin, J. C.; *J. Am. Chem. Soc.* **1991**, *113*, 7277, and references cited therein.

(39) To facilitate isolation, the crude reaction mixtures were treated with Ac_2O and pyridine at room temperature affording the *N*,*O*-diacetylated compounds. The tertiary hydroxyl of compound **68** is unreactive under these conditions, and when the acetylation was performed in the presence of catalytic DMAP a complex mixture of products resulted.

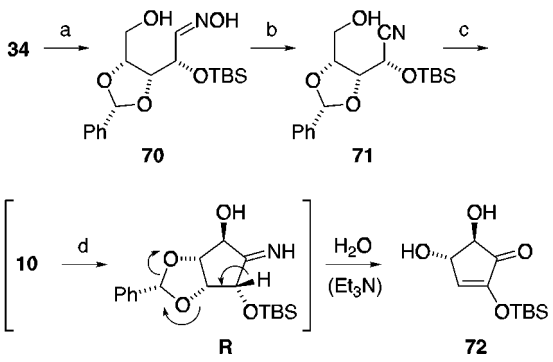
(40) For previous reports on SmI_2-promoted reactions in the presence of water, see for example: (a) Girard, P.; Namy, J. L.; Kagan , H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693. (b) Otsubo, K.; Inanaga, J.; Yamagushi, M. *Tetrahedron Lett.* **1986**, *27*, 5763. (c) Hasegawa, E.; Curran, D. P. *J. Org. Chem.* **1993**, *58*, 5008. (d) Kamoshi, Y.; Kudo, T. *Chem. Lett.* **1993**, 1495. (e) Miyoshi, N.; Takeuchi, S.; Ohgo, Y. *Chem. Lett.* **1993**, 2129. (f) Miyoshi, N.; Takeuchi, S.; Ohgo, Y. *Heterocycles* **1993**, *36*, 2383. (g) Hanessian, S.; Girard, C. *Synlett* **1994**, 861; see also ref 19a.

(41) The other minor carbocyclic products **50b**−**d** were not isolated under these conditions.

(42) Shono et al.[28b] have recently shown that oxime ethers are not electrochemically reducible under the same conditions as they are coupled to ketones, which led them to propose a similar mechanism for the corresponding electrochemical cross-coupling.

(43) (a) Molander, G. A.; Kenny, C. *J. Am. Chem. Soc.* **1989**, *111*, 8236. (b) Chiara, J. L.; Cabri, W.; Hanessian, S. *Tetrahedron Lett.* **1991**, *32*, 1125.

Scheme 18[a]



[a] Reagents and conditions: (a) $HONH_2 \cdot HCl$, py, CH_2Cl_2 (84%); (b) $(CF_3CO)_2O$, py (55%); (c) i. $(COCl)_2$, DMSO, THF, -78 °C. ii. Et_3N, -78 °C to rt; (d) SmI_2 (4 equiv), *t*-BuOH (2 equiv), THF -40 °C to rt (16% from **71**).

preferential reaction of one of the oxime isomers concomitant with a rapid isomerization under the slightly acidic reaction conditions could also account for the observed results.[44] Another general stereochemical tendency observed in our radical cyclizations of oxime ethers derived from carbohydrates with bromide, α,*β*-unsaturated ester, and carbonyl functions is the preferred *trans* disposition of the hydroxylamine group and its vicinal alkoxy group in the cyclic products. Minimization of dipolar interactions and allylic-type 1,3-strain between the oxime and the α-alkoxy group in the transition state of the cyclization could account for this tendency. A similar effect in the ketyl radical-anion moiety explains also the preferred *trans* arrangement between the hydroxyl group and its vicinal alkoxy group in the cyclic products.

D. Samarium Diiodide Mediated Cyclization of *δ*-Nitrile-Tethered Aldehydes. To conclude the present study, we decided to investigate the reductive cyclization of carbonyl compounds with nitriles promoted by samarium diiodide, a process scarcely analyzed in the literature (Scheme 18).[43a] Our one-pot oxidation and samarium diiodide cyclization protocol from alcohol **71**, *via* aldehyde **10**, gave the unexpected α,*β*-unsaturated ketone **72** in poor yield (16%). The formation of this adduct can be rationalized as shown in Scheme 18, through imine **R** by *β*-elimination with excess Et_3N from the Swern oxidation step. Of the two possible acidic protons in α-position to the imine (or the corresponding ketone formed after hydrolysis), the one close to the silyloxy group is more prone to elimination because of its antiperiplanar orientation to the vicinal benzyloxy moiety. No attempts were made to optimize this cyclization and explore other less basic reaction conditions to avoid the eliminiation.

Conclusions

A stereoselective method for the preparation of chiral 4-amino-1,2,3-cyclopentanetriols by tributyltin hydride cyclization of 5-bromo-5-deoxy-2,3-*O*-isopropylidene-D-ribose *O*-benzyl oxime ether derivatives has been achieved. The moderate yield in the cyclization is compensated for the good to excellent diastereoselectivity of the reaction and ready availability of the radical precursors. The tin-mediated radical cyclization is clearly superior to the corresponding SmI_2-mediated reaction. In the latter case, side reactions such as reductive elimination, epoxide formation, or simple dehalogenation of the substrate compete with cyclization.

A new reductive coupling reaction has been uncovered. The intramolecular coupling of an α,*β*-unsaturated ester with an oxime ether can be promoted by samarium diiodide in the presence of HMPA. The reaction proceeds with good diastereoselection, although in moderate yield, affording a branched aminocyclopentitol from a readily prepared sugar precursor.

We have also shown that the intramolecular reductive coupling of carbonyl-tethered oxime ethers can be promoted by samarium diiodide under very mild conditions, in the absence of HMPA, in good chemical yield and stereoselectivity. Moreover, the reductive coupling reaction can be performed in a one-pot sequence with a prior Swern oxidation step, allowing the direct transformation of hydroxyl-tethered oxime ethers into the corresponding aminocyclitols, a process which is specially advantageous when the cyclization involves an aldehyde. The resultant cyclic hydroxylamine ethers can be efficiently converted *in situ* to the corresponding aminocyclitols by N−O reductive cleavage promoted by excess samarium diiodide and water. These processes have been applied to highly functionalized substrates derived from carbohydrates, providing a short and selective entry to five- and six-membered amino polyols of varying regio- and stereochemistry.

Experimental Section

General. NMR sepctra were recorded at 200 MHz or 300 MHz and at 30 °C. Tetrahydrofuran (THF) was distilled under argon from sodium−benzophenone, and CH_2Cl_2 and HMPA from CaH_2. All reactions were performed under argon with anhydrous freshly distilled solvents. Samarium diiodide was prepared immediately before use by adding ICH_2CH_2I in one portion to a suspension of samarium metal powder (1.2 equiv) in THF (10 mL/mmol of ICH_2CH_2I) under argon, and stirring vigorously the resultant suspension for 1−2 h.[40a] All the cyclizations were performed in the presence of the slight excess of samarium metal used in the preparation of the reagent.

General Method for Tributyltin Hydride Mediated Carbocyclization of Bromides. Method A. To a solution of the radical precursor in toluene (0.03 M), that has been deoxygenated with argon for 1 h, a solution of tributyltin hydride (2 equiv) and AIBN (cat.) in toluene (8 M) was slowly added (*via* syringe pump) in the time indicated in each case. The flask was cooled, and the solvent was removed at reduced pressure. The residue was dissolved in Et_2O and stirred overnight with a 20% aqueous KF solution. The organic phase was separated, dried (Na_2SO_4), and concentrated. Flash chromatography gave the products.

General Procedure for Ketone/Oxime Ether Cross-Coupling. Method B. To a solution of freshly prepared SmI_2 (0.1 M, 3 mol equiv) in THF and *t*-BuOH (5 mol equiv) at −25 °C was added dropwise a solution of the keto-oxime (0.025 M, 1 mol equiv) in THF. After stirring for 1.5 h at −25 °C, the reaction was quenched at this temperature by addition of aqueous saturated $NaHCO_3$ (20 mL/mmol of substrate) and EtOAc (20 mL/mmol of substrate). The mixture was vigorously stirred at room temperature for 0.5 h, the phases were separated, and the aqueous phase was extracted with EtOAc (3×). The combined organic extracts were washed with 10% aqueous $Na_2S_2O_3$ (1×), and brine (1×) and dried over Na_2SO_4. The solvent was removed at reduced pressure, and the residue was purified by flash column chromatography.

General Procedure for One-Pot Swern Oxidation/SmI_2 Coupling Sequence. Method C. To a solution of $(COCl)_2$ (0.5 M, 2 mol equiv) in THF at −60 °C was added dropwise a

(44) In fact, experiments perfomed by Shono et al.[28b] may suggest that the reaction of the *anti*-form of simple oximes is faster than that of the *syn*-form under electrochemical conditions.

solution of DMSO (3 M, 4 mol equiv) in THF. After stirring for 15 min at −60 °C, a solution of the 5-hydroxyoxime ether (0.15 M, 1 mol equiv) in THF was added dropwise *via* cannula. After stirring at −60 °C for 1 h, Et_3N (5 mol equiv) was added, and the reaction was stirred at −60 °C to 0 °C for 3 h. The resultant solution was diluted with THF (final substrate concentration = 0.025 M) and added dropwise via cannula to a solution of freshly prepared SmI_2 (0.1 M, 3 mol equiv) in THF and *t*-BuOH (3 mol equiv) at −25 °C. The reaction mixture was stirred at −25 °C for 1.5 h. The reaction was quenched and worked up as described in method B.

(1*R*,2*R*,3*S*,4*R*)-4-[(Benzyloxy)amino]-2,3-*O*-isopropylidene-1,2,3-cyclopentanetriol (24a). This compound has been prepared as described.[12b] Compound **24a** has been also obtained from **24d**+**25d** as follows. A mixture of **24d**+**25d** (9:1) (339 mg, 0.88 mmol) was treated with excess NaOMe in MeOH at rt for 2 h. The solvent was evaporated, the residue diluted with CH_2Cl_2, washed with brine and dried (Na_2SO_4). A compound (100 mg, 42%) was isolated after flash chromatography (hexane/EtOAc 7:3) identical to **24a**.[12b] R_f = 0.35 (hexane/EtOAc 1:1); mp 47.5−49.5 °C; $[\alpha]^{20}_D$ +9.8 (*c* 1, $CHCl_3$); IR (KBr) ν 3450, 1495, 1455 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35−7.27 (m, 5H), 5.33 (br s, 1H), 4.65 (s, 2H), 4.39 (dd, J = 5.2, 5.8 Hz, 1H), 4.35 (d, J = 5.8 Hz, 1H), 4.19 (ddd, J = 5.2, 7.6, 8.0 Hz, 1H), 3.42 (dd, J = 3.7, 4.2 Hz, 1H), 2.36 (br s, 1H), 1.81 (m, 2H), 1.35 (s, 3H), 1.16 (s, 3H); ^{13}C NMR ($CHCl_3$) δ 137.5, 128.6, 128.3, 127.9, 111.0, 82.3, 78.9, 76.7, 71.7, 63.0, 35.9, 26.9, 24.1. Anal. Calcd for $C_{15}H_{21}NO_4$: C, 64.51; H, 7.52; N, 5.01. Found: C, 64.80; H, 7.80; N, 4.99.

(1*R*,2*R*,3*S*,4*R*)4-[(Benzyloxy)amino]-1-*O*-(*tert*-butyldimetilsilyl-2,3-*O*-isopropylidene-1,2,3-cyclopentanetriol (24b). Compound **7b**[45] (783 mg, 1.65 mmol) in dry benzene (166 mL) was treated according to method A with tributyltin hydride (1.10 mL, 3.96 mmol) and AIBN (cat.) in benzene (5 mL); 6 h slow addition; 23 h at reflux. Flash chromatography (hexane/EtOAc 4:1) gave **24b** (346 mg, 53%): oil; $[\alpha]^{25}_D$ +14 (*c* 3.2, $CHCl_3$); IR (film) ν 3250, 1495 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.34−7.29 (m, 5H), 4.66 (d, J = 12 Hz, 1 H), 4.64 (d, J = 12.0 Hz, 1H), 4.32 (t, J = 5 Hz, 1H), 4.17−4.20 (m, 2H), 3.35 (m, 1H), 2.02 (ddd, J = 13.5, 7.1, 5.5 Hz, 1 H), 1.60 (m, 1H), 1.43, 1.26 (s, s, 3 H, 3 H), 0.89 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 137.5, 129.4−127.9, 110.9, 81.9, 80.0, 72.8, 76.6, 63.2, 34.78, 26.2, 24.5, 25.9. Anal. Calcd for $C_{21}H_{35}NSiO_4$: C, 64.08; H: 8.96; N, 3.55. Found: C, 61.38; H, 8.83; N, 3.12.

(1*R*,2*R*,3*S*,4*R*)1-*O*-Acetyl-4-[(benzyloxy)amino]-2,3-*O*-isopropylidene-1,2,3-cyclopentanetriol (24c). Compound **7c**[45] (540 mg, 1.35 mmol), dissolved in benzene (70 mL), was treated according to method A with tributyltin hydride (0.9 mL, 3.24 mmol, 2.4 equiv), AIBN (cat.); slow addition for 5 h, 10 h at reflux. Flash chromatography (hexane/EtOAc 3:7) gave **24c** (201 mg, 52%): mp 45−47 °C; $[\alpha]^{25}_D$ +35 (*c* 1.4, $CHCl_3$); IR (film) ν 3300, 1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.30−7.27 (m, 5H), 4.93 (ddd, J = 5.1, 6.1, 10.5 Hz, 1H), 4.58 (d, J = 12 Hz, 1H), 4.53 (d, J = 12 Hz, 1H), 4.52 (t, J = 5.4 Hz, 1H), 4.21 (d, J = 5.6 Hz, 1H), 3.33 (d, J = 5.9 Hz, 1H), 1.99 (s, 3 H), 1.98 (m, 1H), 1.77 (ddd, J = 13.6, 0.7, 6.1 Hz, 1 H), 1.35, 1.16 (s, s, 3 H, 3 H); MS (70 eV) *m*/*z* 321(M^+, 3), 306 (M^+-15, 1), 91(100). Anal. Calcd for $C_{17}H_{23}NO_5$: C, 63.53; H, 7.21; N, 4.36. Found: C, 63.40; H, 6.98; N, 4.48.

(1*R*,2*R*,3*S*,4*RS*)-1-*O*-Benzoyl-4-[(benzyloxy)amino]-2,3-*O*-isopropylidene-1,2,3-cyclopentanetriol (24d+25d). Compound **7d**[45] (700 mg, 1.52 mmol), dissolved in toluene (151 mL), was treated according to method A with tributyltin hydride (0.98 mL, 3.6 mmol, 2.4 equiv), AIBN (cat.); slow addition for 5 h 30 min, 5 h at reflux. Flash chromatography (hexane/EtOAc 7:3) gave a mixture of isomers **24d**+**25d** (339 mg, 58%; ^1H NMR analysis of the crude reaction mixture showed that the ratio **24d**/**25d** was 89:11, respectively; careful chromatography allowed us to isolate enriched fractions of **24d**+**25d** in 91:9 ratio): oil; IR (KBr) ν 3500−3200, 1725 cm^{-1}; ^1H NMR ($CDCl_3$) δ (major isomer **24d**) 8.25−8.10 (m, 2H), 7.60−7.25 (m, 7H), 5.77 (dt, J = 5.6, 9.3 Hz, 1H), 4.75 (t, J = 5.6 Hz, 1H), 4.70 (s, 2H), 4.40 (d, J = 5.6 Hz, 1H), 3.55 (q, J = 5.2 Hz, 1H), 2.26 (ddd, J = 13.3, 7, 6.4, 1H), 2.03 (dd, J = 6.4, 13 Hz, 1H), 1.41, 1.26 (s, s, 3 H, 3 H). Anal. Calcd for $C_{22}H_{25}NO_5$: C, 68.91; H, 6.57; N, 3.65. Found: C, 66.42; H, 6.16; N. 3.96.

(1*R*,2*R*,3*S*,4*RS*)-1-*O*-Benzoyl-2,3-*O*-isopropylidene-4-(methoxyamino)-1,2,3-cyclopentanetriol (24e+25e). Compound **7e**[45] (999 mg, 2.58 mmol), dissolved in toluene (130 mL), was treated according to method A with tributyltin hydride (1.67 mL, 6.21 mmol), AIBN (cat.); slow addition for 4 h; 3 h at reflux. Flash chromatography (hexane/EtOAc 7:3) gave a mixture of isomers **24e**+**25e** (556 mg, 71%); ^1H NMR analysis of the crude reaction mixture showed that the ratio **24e**/**25e** was 80:20, respectively; careful chromatography allowed us to isolate enriched fractions of **24e**+**25e** in 88:12 ratio): oil; IR (film) ν 3250, 3060, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ (major isomer **24e**) 8.01−8.00 (m, 2H), 7.99−7.98 (m, 1H), 7.38−7.33 (m, 2H), 5.24 (m, 1H), 4.79 (t, J = 5.6 Hz, 1H), 4.44 (d, J = 5.6, 1H), 3.48 (s, 3 H), 3.47 (m, 1H), 2.21 (ddd, J = 6.4, 9.8, 13.4 Hz, 1H), 1.94 (ddt, J = 0.9, 6.6, 13.4 Hz, 1H), 1.33, 1.23 (s, s, 3H, 3 H). Anal. Calcd for $C_{17}H_{23}NO_5$: C, 63.53; H, 7.21; N, 4.36. Found: C, 61.48; H, 7.33; N, 7.10.

(1*R*,2*R*,3*S*,4*R*)-4-Amino-2,3-*O*-isopropylidene-1,2,3-cyclopentanetriol (26). A 0.1 M solution of SmI_2 (4.3 mL, 4.33 mmol) in THF was added via cannula to a 0.05 M solution of **24a** (394 mg, 1.41 mmol) in THF at rt. After stirring for 2 h, the reaction mixture was filtered through a small pad of silica, rinsing with CH_2Cl_2/MeOH 4:1. The filtrate was concentrated at reduced pressure and the residue was purified by flash-chromatography (EtOH/AcOEt 1:19 to 1:9), to give **26** (193 mg, 79%) as a waxy solid. R_f = 0.16 (EtOAc/EtOH 4:1); $[\alpha]^{20}_D$ +3.7 (*c* 0.2, EtOH); IR (film) ν 3400, 1640 cm^{-1}; ^1H NMR (acetone-d_6): δ 5.04 (d, J = 5.6 Hz, 1H), 4.73 (t, J = 5.5 Hz, 1H), 4.54 (ddd, J = 4.9, 5.3, 9.0 Hz, 1H), 4.35 (m, 1H), 2,27 (ddd, J = 4.3, 4.9, 13.4 Hz, 1H), 2.21 (ddd, J = 6.6, 9.0, 13.4 Hz, 1H), 1.45 (s, 3H), 1.30 (s, 3H). ^{13}C NMR (DMSO-d_6) δ 111.4, 82.0, 80.0, 69.7, 53.5, 34.5, 26.4 , 24.7. This compound did not give correct microanalytical data.

Reaction of Oxime Ether 7a with SmI_2. To a solution of **7a**[45] (115 mg, 0.22 mmol) in THF (11 mL) and HMPA (1.3 mL, 7.3 mmol) at −40 °C was added a 0.1 M solution of SmI_2 (1.5 mL, 1.46 mmol) in THF. After stirring at −40 °C to −5 °C for 3 h, the reaction mixture was added to saturated aqueous $NaHCO_3$. The aqueous phase was extracted with EtOAc (3 × 30 mL), and the combined organic extracts were washed with 10% aqueous $Na_2S_2O_3$ and brine. The solvent was evaporated at reduced pressure, and the residue was purified by flash-chromatography (hexane/EtOAc 4:1) to give **29** (24 mg, 27%), **30** (6 mg, 7%), and **24a** (7 mg, 8%). **29**: oil; E/Z = 4:1; IR (film) ν 2995, 1495, 1450 cm^{-1}; ^1H NMR ($CDCl_3$) δ *E*-isomer: 7.54 (d, J = 7.9 Hz, 1H), 5.14 (s, 2H), 4.83 (dd, J = 6.5, 7.9 Hz, 1H), 4.01 (t, J = 6.4 Hz, 1H), 2.98 (ddd, J = 2.5, 3.9, 6.3 Hz, 1H), 2.82 (dd, J = 3.9, 5.0 Hz, 1H), 2.73 (dd, J = 2.5, 5.0 Hz, 1H), 1.52 (s, 3H), 1.38 (s, 3H); *Z*-isomer: 6.95 (d, J = 6,3 Hz, 1H), 5.12 (s, 2H), 4.80 (t, J = 6.5 Hz, 1H), 1.47 (s, 3H), 1.36 (s, 3H); ^{13}C NMR ($CDCl_3$) δ *E*-isomer: 146.4, 137.1, 128.4, 128.2, 128.0, 110.4, 77.8, 76.3, 75.2, 49.4, 45.5, 27.5, 25.1. **30**: white solid; only *E*-isomer; mp 54.5−57 °C; $[\alpha]^{20}_D$ +158 (*c* 0.2, $CHCl_3$); IR (film) ν 3450, 1380, 1270 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38−7.34 (m, 5H), 6.95 (d, J = 4.8 Hz, 1H), 5.32 (dd, J = 4.8, 6.9 Hz, 1H), 5.16 (m, 2H), 4.30 (dd, J = 4.9, 6.9 Hz, 1H), 2.93 (ddq, J = 3.2, 4.9, 9.3 Hz, 1H), 2.73 (d, J = 3.2 Hz, 1H), 2.65 (d, J = 9.3 Hz, 3H), 1.51 (s, 3H), 1.36 (s, 3H).

Reaction of Oxime Ether 7d with SmI_2. Compound **7d**[45] (98 mg, 0.21 mmol) was treated with SmI_2 following the procedure described for **7a**. Flash chromatography (hexane/EtOAc 4:1) afforded **24d** (34 mg, 42%) and **31** (21 mg, 37%). **31**: colorless oil; E/Z = 9:1; R_f = 0.42 (hexane/EtOAc 4:1); ^1H NMR ($CDCl_3$) δ (*E*-isomer) 7.38−7.35 (m, 5H), 7.33 (d, J = 3.6 Hz, 1H), 5.72 (ddd, J = 6.3, 10.5, 16.7 Hz, 1H), 5.40 (dd, J = 1.5, 16.7 Hz, 1H), 5.29 (dd, J = 1.5, 10.5 Hz, 1H), 5.10 (s, 2H), 4.72 (m, 2H), 1.54 (s, 3H), 1.42 (s, 3H); ^{13}C NMR ($CDCl_3$) δ (*E*-isomer) 148.7, 137.9, 133.0, 129.1, 128.9, 128.6, 119.8, 110.6, 79.8, 76.8, 76.6, 28.6, 26.1. Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.93; H, 7.34; N, 5.36. Found: C, 68.83; H, 7.49; N, 5.64.

3,4-*O*-Benzylidene-2-*O*-(*tert*-butyldimethylsilyl)-D-ribose *O*-Benzyl Oxime Ether (35). To a solution of 3,4-*O*-

(45) See the Supporting Information.

benzylidene-2-*O*-(*tert*-butyldimethylsilyl)-*δ*-D-ribonolactone **33**[23] (1.4 g, 4.0 mmol), in toluene (50 mL) at −78 °C, was added a 1 M solution of DIBALH in cyclohexane (8.0 mL, 8.0 mmol) dropwise. The reaction mxture was stirred at this temperature for 1 h, MeOH (35 mL) was added dropwise, and the mixture was allowed to warm to rt. After stirring for 3 h, the resultant suspension was filtered through Celite, and the filter was washed with MeOH (3 × 50 mL). The filtrate was concentrated at reduced pressure, and the residue was purified by flash-chromatography (hexane/EtOAc 3:1), to give **34** [(1.4 g, 98%); ^{1}H NMR ($CDCl_3$) δ 7.61−7.36 (m, 5H), 5.81 (s, 1H), 5.16 (dd, J = 3.4, 6.3 Hz, 1H), 4.45 (dd, J = 2.9, 7.9 Hz, 1H), 4.38 (m, 1H), 3.90 (dd, J = 2.9, 13.2 Hz, 1H), 3.78 (m, 2H), 2.75 (d, J = 3.7 Hz, 1H), 0.92 (s, 9H), 0.15 (s, 6H)]. This compound (1.35 g, 3.83 mmol) was treated with *O*-benzylhydroxylamine hydrochloride following the procedure applied for **7a**. Flash-chromatography (hexane/EtOAc 4:1) afforded **35** (1.42 g, 81%) as a white semisolid, inseparable 85:15 mixture of *E*/*Z* isomers, respectively. R_f = 0.21 (hexane/EtOAc 4:1); IR (film) ν 3460, 1460, 1255, 1090 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.52−7.29 (m, 11H), 6.78 (d, J = 5.1 Hz, 1H, *Z*-isomer), 5.82 (s, 1H), 5.09 (s, 2H), 4.65 (t, J = 7.0 Hz, 1H), 4.41−4.24 (m, 2H), 3.87−3.79 (m, 2H), 2.42 (t, J = 6.9 Hz, 1H), 0.87 (s, 9H), 0.08 (s, 3H), 0.01 (s, 3H). Anal. Calcd for $C_{25}H_{35}NO_5Si$: C, 65.60; H, 7.72; N, 3.06. Found: C, 65.24; H, 7.92; N, 3.05.

3,4-*O*-Benzylidene-5-bromo-2-*O*-(*tert*-butyldimethylsilyl)-5-deoxy-D-ribose Oxime Ether (8). To a solution of **35** (769 mg, 1.68 mmol) and Ph_3P (1.76 g, 6.72 mmol) in pyridine (20 mL) at 0 °C was added CBr_4 (1.11 g, 3.36 mmol). The solution was warmed to rt and then heated at reflux for 17 h. After cooling to rt, MeOH (15 mL) was added, and the solvent was removed at reduced pressure. Flash-chromatography of the residue (hexane/EtOAc 19:1) afforded **8** (422 mg, 48%) as a colorless oil, inseparable 85:15 mixture of *E*/*Z* isomers. R_f = 0.27 (hexane/EtOAc 19:1); IR (film) ν 1465, 1255, 1090, 1020 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ (*E*-isomer) 7.55−7.30 (m, 10H), 7.52 (d, J = 7.0 Hz, 1H), 5.88 (s, 1H), 5.11 (s, 2H), 4.62−4.52 (m, 2H), 4.31 (t, J = 6.5 Hz, 1H), 3.75 (dd, J = 3.0, 11.0 Hz, 1H), 3.56 (m, 1H), 0.89 (s, 9H), 0.06 (s, 3H), 0.01 (s, 3H); ^{13}C NMR ($CDCl_3$) δ (*E*-isomer) 149.5, 137.4, 136.4, 129.5, 128.4, 128.3, 128.2, 128.0, 126.9, 103.8, 79.8, 78.7, 76.2, 69.2, 31.5, 25.7, 18.5, −4.0, −4.1. Anal. Calcd for $C_{25}H_{34}BrNO_4Si$: C, 57.67; H, 6.60; N, 2.69. Found: C, 57.98; H, 6.90; N, 2.65.

Cyclization of Oxime Ether 8. With Bu_3SnH. Compound **8** (365 mg, 0.71 mmol) in toluene (35 mL) was treated according to method A with tributyltin hydride (0.46 mL, 1.70 mmol) and AIBN (cat.) in benzene (2 mL); 3 h slow addition; 3 h at reflux. Flash-chromatography (hexane/EtOAc 100:0 to 85:15) afforded **36a** (159 mg, 51%) and **36b** (89 mg, 29%). **With SmI_2.** Compound **8** (53 mg, 0.10 mmol) in THF (5 mL) was treated with SmI_2 as indicated for **7a**. Flash-chromatography (hexane/EtOAc 9:1) afforded unreacted **8** (19 mg) and **36a** (18 mg, 40%, 61% based on recovered **8**). The ^{1}H NMR of the crude showed also the presence of traces of **36b**. **36a**: Colorless oil; R_f = 0.29 (hexane/EtOAc 85:15); $[\alpha]^{20}_D$ + 92 (*c* 4.0, $CHCl_3$); IR (KBr) ν 3400, 1460, 1400, 1250, 1140 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.56−7.27 (m, 10H), 5.90 (br s, 1H), 5.70 (s, 1H), 4.69 (s, 2H), 4.58 (t, J = 5.8 Hz, 1H), 4.40 (t, J = 5.7 Hz, 1H), 3.90 (dd, J = 5.4 and 9.4 Hz, 1H), 3.53 (ddd, J = 6.3, 9.4, 11.5 Hz, 1H), 2.10 (dd, J = 6.3, 14.0 Hz, 1H), 1.65 (ddd, J = 5.6, 11.5, 14.0 Hz, 1H), 0.91 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 137.6, 136.8, 129.3, 128.3, 128.2, 127.8, 127.0, 104.2, 79.1, 77.7, 76.8, 73.5, 63.9, 31.1, 25.6, 16.2, −4.5, −4.8. Anal. Calcd for $C_{25}H_{34}NO_4Si$: C, 67.98; H, 8.00; N, 3.17. Found: C, 67.69; H, 7.99; N, 3.42. **36b**: R_f = 0.19 (hexane/EtOAc 85:15); $[\alpha]^{20}_D$ −108 (*c* 1.5, $CHCl_3$); IR (film) ν 3400, 1460, 1400, 1250, 1220 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.61−7.28 (m, 10H), 5.78 (s, 1H), 4.67 (s, 2H), 4.68−4.39 (m, 4H), 2.04 (dd, J = 5.7, 14.2 Hz, 1H), 1.85 (m, 1H), 0.90 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 140.7, 136.7, 129.4, 128.5, 128.2, 127.5, 127.0, 126.9, 104.7, 80.0, 79.0, 78.1, 76.7, 65.2, 31.7, 25.8, 16.2, −4.6.

Reduction of 36a with SmI_2. A solution of **36a** (116 mg, 0.26 mmol) in THF (5 mL) was added to a 0.1 M solution of SmI_2 (7.9 mL, 0.79 mmol) in THF at rt. Water (0.10 mL, 5.26 mmol) was added, and the mixture was stirred for 3.5 h. Ac_2O (2 mL) and pyridine (4 mL) were added at rt, and the mixture was stirred for 15 h. The reaction mixture was diluted with EtOAc (25 mL) and washed with aqueous saturated $NaHCO_3$. The aqueous phase was extracted with EtOAc (3 × 50 mL), and the combined organic extracts were washed with 10% aqueous $Na_2S_2O_3$, and brine. The solvent was removed at reduced pressure and the crude was purified by flash-chromatography (hexane/EtOAc 1:4) affording **37** (77 mg, 78%) as a white solid, 5:1 mixture of regioisomers (see text). R_f = 0.12 (hexane/EtOAc 2:3); IR (KBr) ν 3500, 1655, 1580, 1470 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ (major product) 7.57−7.37 (m, 5H), 5.71 (s, 1H), 5.47 (brd, J = 5.0 Hz, 1H), 4.60 (t, J = 5.8 Hz, 1H), 4.41 (t, J = 5.1 Hz, 1H), 4.12−4.05 (m, 2H), 2.24 (dd, J = 6.1, 14.0 Hz, 1H), 1.97 (s, 3H), 1.78 (ddd, J = 5.5, 11.5, 14.0 Hz, 1H), 0.91 (s, 9H), 0.11 (s, 6H); (minor product) 5.74 (s, 1H), 2.10 (s, 3H), 0.91 (s, 9H), 0.14 (s, 6H); ^{13}C NMR ($CDCl_3$) δ (major product) 170.3, 136.5, 129.4, 128.2, 127.0, 104.1, 78.3, 77.5, 76.3, 54.4, 32.2, 25.7, 18.2, −4.5, −4.8; (minor product) 128.4, 126.7, 79.3, 77.3, 76.7, 56.2, 30.9, 23.7. Anal. Calcd for $C_{20}H_{31}NO_4Si$: C, 63.63; H, 8.29; N, 3.70. Found: C, 63.84; H, 8.48; N, 3.72.

(1*R*,2*R*,3*S*,4*R*)-4-*N*-Acetyl-3-*O*-acetyl-1,2-*O*-benzylidene-1,2,3-cyclopentanetriol (38). To a solution of **37** (62 mg, 0.16 mmol) in THF (5 mL) was added a 1.0 M solution of tetrabutylammonium fluoride (0.49 mL, 0.49 mmol) in THF at rt. After stirring for 2 h, Ac_2O (2 mL) and pyridine (4 mL) were added. The reaction mixture was stirred at rt for 5 h, and the solvent was removed at reduced pressure. The residue was suspended in EtOAc (30 mL) and water (25 mL). The phases were separated, and the aqueous phase was extracted with EtOAc (3 × 25 mL). The combined organic extracts were dried over Na_2SO_4 and evaporated at reduced pressure. Flash-chromatography (EtOAc) of the residue afforded **38** (40 mg, 81%) as a white solid. R_f = 0.25 (EtOAc); mp 188−190 °C; $[\alpha]^{22}_D$ +30 (*c* 1.3, $CHCl_3$); IR (KBr) ν 3450, 1735, 1645, 1560 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.54−7.40 (m, 5H), 5.74 (m, 1H), 5.70 (s, 1H), 4.84 (ddd, J = 5.5, 9.4, 11.6 Hz, 1H), 4.69−4.56 (m, 3H), 2.53 (dd, J = 6.9, 14.3 Hz, 1H), 2.11 (s, 3H), 1.97 (s, 3H), 1.61 (ddd, J = 5.5, 11.6, 14.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 172.1, 170.9, 136.1, 130.3, 128.9, 127.5, 105.1, 78.1, 77.3, 76.9, 51.8, 34.1, 23.9, 21.3. Anal. Calcd for $C_{16}H_{18}NO_5$: C, 62.03; H, 6.29; N, 4.59. Found: C, 62.97; H, 6.25; N, 4.58.

Synthesis of Oxime Ether 9. To a solution of $(COCl)_2$ (0.60 mL, 6.21 mmol) in CH_2Cl_2 (12 mL) at −60 °C was added dropwise DMSO (0.88 mL, 12.42 mmol). After stirring for 15 min at −60 °C, a solution of **35** (945 mg, 2.07 mmol) in dry CH_2Cl_2 (15 mL) was added dropwise. After stirring at −60 °C for 45 min, Et_3N (4,3 mL, 31.05 mmol) was added dropwise and the reaction stirred at −60 to 0 °C for 3 h. The reaction mixture was diluted with CH_2Cl_2 (30 mL) and washed with aqueous saturated NH_4Cl. The aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL), and the combined organic layers were dried over Na_2SO_4 and concentrated at reduced pressure, affording the corresponding crude aldehyde **11**. To a stirred solution of crude **11** in toluene (20 mL) at room temperature was added $Ph_3P{=}CHCO_2Et$ (1.80 g, 5.17 mmol). After stirring at 25 °C for 16 h the mixture was heated at 70 °C for 5 h until the reaction was complete. After cooling, the toluene was removed at reduced pressure, and the residue was purified by flash column chromatography (hexane/EtOAc 9:1) to afford **9** (798 mg, 73%) as a colorless oil, mixture of two isomers. A fraction of pure major isomer (*E* oxime ether/*E* C=C) was obtained followed by mixed fractions of both isomers (*E* oxime ether/*E* C=C and *Z* oxime ether/*E* C=C). Major isomer (*E* oxime ether/*E* C=C): R_f = 0.28 (hexane/EtOAc 9:1); IR (film): 1725, 1660 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.49 (m, 2H), 7.40−7.27 (m, 9H), 7.06 (dd, J = 15.6, 5.2 Hz, 1H), 6.12 (dd, J = 15.6, 1.6 Hz, 1H), 5.06 (s, 2H), 4.89 (ddd, J = 1.6, 1.7, 5.2 Hz, 1H), 4.33 (m, 2H), 4.19 (q, J = 7.1 Hz, 2H), 1.28 (t, J = 7.1 Hz, 3H), 0.86 (s, 9H), 0.03 (s, 3H), 0.00 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.8, 149.8, 142.2, 137.5, 136.2, 129.5, 128.3, 128.2, 127.8, 127.0, 123.5, 104.0, 80.5, 77.2, 76.1, 69.6, 60.4, 25.8, 17.9, 14.2, −3.8, −5.1; $[\alpha]^{25}_D$ −33.9 (*c* 1.3, $CHCl_3$). Anal. Calcd for $C_{29}H_{39}NO_6Si$: C, 66.12; N, 2.66; H, 7.67. Found: C, 66.36; N, 2.70; H, 7.64.

Minor isomer (*Z* oxime ether/*E* C=C): R_f = 0.26 (hexane/

EtOAc 9:1); ^{1}H NMR ($CDCl_3$) δ (aromatic protons not included): 7.14 (dd, J = 6.3, 15.7 Hz, 1H), 6.71 (d, J = 6.5 Hz, 1H), 6.11 (dd, J = 1.4, 15.7 Hz, 1H), 5.82 (s, 1H), 5.10 (s, 2H), 4.79 (ddd, J = 1.3, 1.4, 6.3 Hz, 1H), 4.33 (m, 2H); 4.20 (q, J = 7.1 Hz, 2H), 1.28 (t, J = 7.1 Hz, 3H), 0.86 (s, 9H), 0.01 (s, 3H), −0.02 (s, 3H).

Cyclization of Oxime Ether 9. A solution of compound **9** (83 mg, 0.16 mmol) in THF (8 mL) was added dropwise via cannula to a 0.1 M solution of SmI_2 (4.8 mL, 0.48 mmol) in THF and HMPA (0.42 mL, 2.4 mmol) at room temperature. The SmI_2 was consumed immediately after finishing the addition. The reaction mixture was worked up as described in method B. Flash chromatography (hexane/EtOAc 4:1) of the crude afforded **39** as a colorless oil (43 mg, 52%). $[\alpha]^{25}_D$ −25.9 (*c* 2.4, $CHCl_3$); ^{1}H NMR (acetone-d_6) δ 7.50−7.28 (m, 10H), 6.22 (d, J = 2.9 Hz, 1H), 5.70 (s, 1H), 4.68 (m, 2H), 4.66 (dd, J = 5.5, 5.9 Hz, 1H), 4.53 (dd, J = 5.4, 5.9 Hz, 1H), 4.20 (dd, J = 5.4, 9.3 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H), 2.96 (ddd, J = 2.9, 9.3, 11.7 Hz, 1H), 2.58 (, J = 4.5, 16.8 Hz, 1H), 2.50 (dd, J = 9.9, 16.8 Hz, 1H), 1.24 (t, J = 7.1 Hz, 3H), 0.90 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 173.1, 137.9, 136.9, 129.2, 128.4, 128.3, 128.1, 127.7, 127.0, 126.6, 103.9, 78.4, 78.0,76.5 71.3, 67.3, 60.2, 35.4, 31.2, 25.8, 18.2, 14.1, −4.6, −4.9. Anal. Calcd for $C_{29}H_{41}NO_6Si$: C, 66.03; H, 7.78; N, 2.66. Found: C, 65.88; H, 8.01; N, 2.58.

Synthesis of Oxime Ether 17. A suspension of 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (**40**)[31] (990 mg, 1.83 mmol) and *O*-benzylhydroxylamine hydrochloride (352 mg, 2.20 mmol) in MeOH (12 mL) and pyridine (1 mL) was heated at 60 °C for 8 h. The solvent was removed at reduced pressure, and the residue was purified by flash column chromatography (hexane/EtOAc 3:1) to afford 1.13 g (96%) of a mixture of oximes (E/Z = 3.3:1, by ^{1}H NMR), as a colorless oil. A solution of this mixture (980 mg, 1.52 mmol) in CH_2Cl_2 (4 mL) was added to a suspension of PCC (1.29 g, 6.00 mmol), NaOAc (70 mg, 0.81 mmol), and 3 Å MS (1 g) in CH_2Cl_2 (10 mL) at room temperature. After stirring for 2 h at room temperature, the mixture was diluted with Et_2O (200 mL), and the resultant suspension was filtered through a short column of silica, eluting thoroughly with Et_2O. The filtrate was concentrated at reduced pressure, and the crude was purified by flash column chromatography (hexane/EtOAc 6:1) to afford **17** (820 mg, 84%), as a colorless oil. ^{1}H NMR ($CDCl_3$) δ *E* isomer: 7.54 (d, J = 7.8 Hz, 1 H), 7.4−7.1 (m, 25 H), 5.13 (s, 2 H), 4.73−4.21 (series of m, 13 H), 4.18 (d, J = 3.3 Hz), 4.07 (dd, J = 6.7, 3.3 Hz); *Z* isomer: 7.4−7.1 (m, 25 H), 6.92 (d, J = 6.6 Hz), 5.07 (s, 2 H), 5.04 (dd, J = 6.6, 2.0 Hz), 4.54−4.19 (series of m, 13H), 4.14 (d, J = 7.1 Hz), 4.06 (Ψt, J = 4.6 Hz); ^{13}C NMR ($CDCl_3$) δ (aromatic carbons not included) *E* isomer: 207.7, 148.5, 82.7, 80.5, 76.3, 76.0, 74.5, 74.4, 74.0, 73.2, 71.6; *Z* isomer: 206.5, 150.7, 81.7, 79.7, 76.4, 74.3, 74.2, 73.7, 73.2, 72.6, 71.1. Anal. Calcd for $C_{41}H_{43}NO_6$: C, 76.49; H, 6.42; N, 2.18. Found: C, 76.30; H, 6.25; N, 1.98.

Synthesis of Oxime Ether 18. Following the same procedure as for **17**, compound **18** was obtained from 2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranose (**41**)[31] in 88% overall yield as a colorless oil. ^{1}H NMR ($CDCl_3$) (aromatic protons not included) (E/Z = 3:1) δ 7.39 (d, J = 8.1 Hz, 1 H, *E* isomer), 6.81 (d, J = 7.3 Hz, 1 H, *Z* isomer), 5.14 (s, 2 H, *E* isomer), 5.13 (s, 1H, *Z* isomer), 5.05 (dd, J = 7.3, 6.4 Hz, 1 H, *Z* isomer), 4.55−4.17 (series of multiplets), 4.10 (dd, J = 7.6, 3.3 Hz, *E* isomer); ^{13}C NMR ($CDCl_3$) δ (aromatic carbons not included) *E* isomer: 208.1, 148.4, 83.7, 80.3, 76.1, 75.7, 74.4, 74.2, 73.2, 70.6; *Z* isomer: 207.4, 149.7, 83.1, 80.1, 76.3, 74.1, 71.6, 70.3. Anal. Calcd for $C_{41}H_{43}NO_6$: C, 76.49; H, 6.42; N, 2.18. Found: C, 76.21; H, 6.32; N, 2.22.

2,3,4,6-Tetra-*O*-benzyl-β-D-galactopyranose (42). To a solution of phenyl 2,3,4,6-tetra-*O*-benzyl-1-thio-β-D-galactopyranoside[31] (584 mg, 0.92 mmol) in acetone (20 mL) at −15 °C were added H_2O (18 μL, 1.02 mmol) and NBS (210 mg, 1.11 mmol). After stirring at −15 °C for 1 h, the reaction mixture was partioned between CH_2Cl_2 (100 mL) and aqueous saturated $NaHCO_3$ (30 mL). The organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2 (2 × 30 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated at reduced pressure. Flash chromatography of the residue (hexane/EtOAc 1:1) afforded **42** (400 mg, 80%) as a colorless oil. R_f = 0.31 (hexane/EtOAc 1:1); ^{1}H NMR ($CDCl_3$) δ 7.32 (m, 20 H), 5.26 (d, J = 3,5 Hz, 1H), 4.95−4.53 (m, 6H), 4.42 (m, 2H), 4.15 (brt, J = 6.6 Hz, 1H), 4.02 (dd, J = 3.5, 9.5 Hz, 1H), 3.93 (m, 2H), 3.89 (dd, J = 2.7, 9.7 Hz, 1H), 3.74 (dd, J = 7.4, 9.7 Hz, 1H), 3.56 (dd, J = 5.3, 9.7 Hz, 1H).

Synthesis of Oxime Ether 19. Following the same procedure as for **17**, compound **19** was obtained from **42** in 69% overall yield as a colorless oil, 3:1 mixture of *E*/*Z*-oximes, respectively. R_f = 0.35 (hexane/EtOAc 4:1); ^{1}H NMR ($CDCl_3$) δ *E*-isomer: 7.53 (d, J = 7.9 Hz, 1H), 7.37−7.24 (m, 25H), 5.11 (s, 2H), 4.62−4.12 (m, 13H); *Z*-isomer: 6.94 (d, J = 6.5 Hz, 1H), 5.10 (s, 2H), 5.01 (dd, J = 5.0 y 6.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ (aromatic carbons not included) *E*-isomer: 206.8, 149.0, 81.8, 81.3, 76.7, 76.1, 74.3, 74.1, 73.2, 73.1, 71.3; *Z*-isomer: 151.1, 80.8, 80.4, 76.4, 74.5, 74.4, 72.9, 72.3, 71.7. Anal. Calcd for $C_{41}H_{41}NO_6$: C, 76.49; H, 6.42; N, 2.18. Found: C, 76.46; H, 6.48; N, 2.34.

Cyclization of Oxime Ether 17. Following method B, oxime **17** (640 mg, 0.99 mmol) gave aminocyclitol **43** (520 mg, 81%): R_f = 0.26 (hexane/EtOAc 2:1); $[\alpha]^{20}_D$ +20.6 (*c* 1.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.40−7.22 (m, 25H), 6.03 (d, J = 6.0 Hz, 1H), 4.77−4.38 (m, 10H), 4.13 (dd, J = 6.3, 7.5 Hz, 1H), 3.86 (d, J = 7.5 Hz, 1H), 3.76 (t,, J = 6.2 Hz, 1H), 3.59 (d, J = 10.2 Hz, 1H), 3.46 (t, J = 6.1 Hz, 1H), 3.45 (d, J = 10.2 Hz, 1H), 2.89 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 138.0 (2C), 137.8, 137.7, 128.4, 128.3, 128.0, 127.9 (2C), 127.7, 127.5, 86.9, 82.3, 82.1, 77.7, 76.1, 73.7, 73.2, 72.4 (2C), 71.7, 71.2. Anal. Calcd for $C_{41}H_{43}NO_6$: C, 76.25; H, 6.71; N, 2.17. Found: C, 76.17; H, 6.83; N, 2.23.

Cyclization of Oxime Ether 18. Following method B, oxime **18** (256 mg, 0.40 mmol) gave aminocyclitol **44a** (154 mg, 60%) and an inseparable 3:1 mixture of **44b** and **44c** (38 mg, 15%). **44a**: R_f = 0.50 (hexane/EtOAc 1:1); $[\alpha]^{20}_D$ −32.0 (*c* 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.40−7.22 (m, 25H), 6.43 (d, J = 7.5 Hz, 1H), 4.74 (m, 2H), 4.71−4.47 (m, 8H), 4.17 (dd, J = 0.8, 8.4 Hz, 1H), 4.11 (dd, J = 6.3, 8.4 Hz, 1H), 4.02 (br s, 1H), 3.85 (dd, J = 4.3, 6.3 Hz, 1H), 3.73 (d, J = 9.5 Hz, 1H), 3.70 (d, J = 9.5 Hz, 1H), 3.64 (ddd, J = 0.8, 4.3, 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 138.6, 138.3 (2C), 137.7, 137.5, 128.6, 128.4, 128.2, 128.1, 127.9, 127.8, 127.6, 127.4, 88.1, 80.3, 79.6, 76.1, 76.0, 73.7, 73.1, 72.3, 72.1, 71.5, 69.8. Anal. Calcd for $C_{41}H_{43}NO_6$: C, 76.25; H, 6.71; N, 2.17. Found: C, 76.41; H, 6.68; N, 2.19. **44b** (as an inseparable mixture with **44c**): R_f = 0.60 (hexano/AcOEt 1:1); ^{1}H NMR (acetone-d_6) δ 7.41−7.22 (m, 25H), 6.41 (d, J = 10.5 Hz, 1H), 4.91−4.48 (m, 10H), 4.25 (dd, J = 3.7, 4.6 Hz, 1H), 4.19 (d, J = 8.8 Hz, 1H), 3.97 (dd, J = 3.7, 8.8 Hz, 1H), 3.61 (d, J = 9.2 Hz, 1H), 3.60 (br s, 1H), 3.57 (dd, 4.6, 10.5 Hz, 1H), 3.48 (d, J = 9.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 138.7, 138.3, 138.1, 137.9, 128.4, 128.3, 127.7, 127.6, 127.5 (2C), 84.0, 83.7, 75.8, 75.4, 74.4, 73.9, 73.6, 73.4, 72.4, 69.3. **44c** (as an inseparable mixture with **44b**): R_f = 0.60 (hexane/EtOAc 1:1) ^{1}H NMR (acetone-d_6) δ 7.41−7.22 (m, 25H), 6.39 (d, J = 8.9 Hz, 1H), 4.91−4.48 (m, 10H), 4.11 (d, J = 7.1 Hz, 1H), 4.05 (dd, J = 6.3, 7.1 Hz, 1H), 3.78 (dd, J = 5.1, 6.3 Hz, 1H), 3.73 (s, 1H), 3.65 (dd, J = 5,1, 8.9 Hz, 1H), 3.62 (d, J= 9.1 Hz, 1H), 3.55 (d, J= 9.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 128.6, 128.1, 128.0, 127.9, 127.8, 82.5, 81.4, 79.7, 76.6, 76.2, 74.0, 73.5, 72.0, 71.3, 66.2.

Cyclization of Oxime Ether 19. Following method B, oxime **19** (112 mg, 0.17 mmol) gave aminocyclitol **45** (57 mg, 51%) and a minor compound (28 mg, structure not determined), as colorless oils. **45**: R_f = 0.21 (hexane/EtOAc 4:1); $[\alpha]^{20}_D$ +21.6 (*c* 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$): see Table 2; ^{13}C NMR ($CDCl_3$) δ 138.7, 138.6, 138.4, 137.9, 137.8, 128.5, 128.4, 128.2, 128.1, 127.9, 127.8, 127.5, 127.4 (2C), 127.3, 87.1, 85.5, 82.2, 80.4, 75.7, 73.8, 73.6, 72.3 , 72.0, 71.5, 69.8. Anal. Calcd for $C_{41}H_{43}NO_6$: C, 76.25; H, 6.71; N, 2.17. Found: C, 75.98; H, 7.00; N, 2.46. Minor compound: R_f = 0.19 (hexane/EtOAc 4:1); ^{1}H NMR ($CDCl_3$) δ 7.30−7.05 (m, 25H), 4.71−4.44 (4 m, 8H), 4.51 (dd, J = 5.2, 5.6 Hz, 1H), 4.21 (t, J = 5.1 Hz, 1H), 3.93 (d, J = 5.0 Hz, 1H), 3.89 (d, J = 5.6 Hz, 1H), 3.85 (d, J = 9.6 Hz, 1H), 3.73 (d, J = 9.6 Hz, 1H), 3.38 (s, 1H); ^{13}C NMR

($CDCl_3$) δ 138.5, 138.2, 137.7, 137.5, 128.4, 128.3, 128.2, 128.0, 127.8, 127.6, 127.5, 87.9, 84.3, 83.0, 81.7, 81.4, 73.6, 73.3, 72.4, 71.8, 69.8.

Synthesis of *O*-(*tert*-Butyldimethylsilyl)-3,4-*O*-isopropylidene-D-arabinose *O*-Benzyl Oxime Ether (47). A solution of 3,4-*O*-isopropylidene-2-*O*-(*tert*-butyldimethylsilyl)-D-arabinose (**46**)[24a] (1.52 g, 5.00 mmol) was treated with *O*-benzylhydroxylamine hydrochloride as described for **35**, to give **47** (1.70 g, 80%) as a colorless oil, 9:1 mixture of *E* and *Z* oximes. R_f = 0.32 (hexane/EtOAc 2:1); IR (film) ν 3475, 1470, 1460 cm^{-1}; ^1H NMR ($CDCl_3$) δ (aromatic protons not included) *E*-isomer: 7.47 (d, J = 6.6 Hz, 1H), 5.08 (s, 2H), 4.43 (t, J = 6.5 Hz, 1H), 4.23 (m, 2H), 3.75−3.69 (m, 2H), 2.39 (d, J = 6.5 Hz, 1H), 1.42 (s, 3H), 1.34 (s, 3H), 0.87 (s, 9H), 0.06 (s, 3H), 0.03 (s, 3H); *Z*-isomer: 6.79 (d, J = 7.1 Hz, 1H), 5.10 (s, 2H), 4.77 (dd, I= 2.0, 7.6 Hz, 1H). Anal. Calcd for $C_{21}H_{35}NO_5Si$: C, 61.56; H, 8.63; N, 3.42. Found: C, 61.81; H, 8.60; N, 3.17.

2,3,4-Tetra-*O*-benzyl-D-xylose *O*-Benzyl Oxime Ether (49). To a solution of **48**[34] (895 mg, 2.13 mmol) in CH_2Cl_2 (20 mL) *O*-benzylhydroylamine hydrochloride (849 mg, 5.32 mmol) and pyridine (0.52 mL, 6.39 mmol). After heating the reaction mixture at reflux for 15 h, it was partitioned between CH_2Cl_2 (35 mL) and aqueous saturated $NaHCO_3$. Usual extractive workup and flash-chromatography (hexane/EtOAc 4:1) of the resultant residue afforded **49** (940 mg, 84%) as a colorless oil, 3:1 mixture of *E* and *Z* oximes. R_f = 0.26 (hexane/EtOAc 2:1); IR (film) ν 3450, 1500, 1455 cm^{-1}; ^1H NMR ($CDCl_3$) δ *E*-isomer: 7.48 (d, J = 7.7 Hz, 1H), 7.39−7.25 (m, 20H), 5.12 (s, 2H), 4.70−4.32 (m, 9H), 4.24 (dd, J = 5.1, 7.7 Hz, 1H), 3.78−3.60 (m, 3H), 1.91 (brt, J = 6.4 Hz, 1H). Anal. Calcd for $C_{33}H_{35}NO_5$: C, 75.40; H, 6.71; N, 2.67. Found: C, 75.70; H, 6.92; N, 2.71.

Cyclization of Oxime Ether 35. Following method C, oxime **35** (515 mg, 1.12 mmol) gave aminocyclitols **50a** (325 mg, 63%), **50b** (26 mg, 5%), **50c** (10 mg, 2%), and **50d** (22 mg, 4%). **50a**: R_f = 0.34 (hexane/EtOAc 7:3); $[\alpha]^{20}_D$ −77.2 (*c* 2.4, $CHCl_3$); ^1H NMR (acetone-d_6) δ 7.61−7.34 (m, 10H), 6.22 (br s, 1H), 5.76 (s, 1H), 4.72 (s, 2H), 4.57 (dd, J = 5.3, 6.1 Hz, 1H), 4.44 (d, J = 6.1 Hz, 1H), 4.03 (d, J = 4.3 Hz, 1H), 3.98 (dd, J = 5.3, 9.9 Hz, 1H), 3.64 (dd, J = 4.3, 9.9 Hz, 1H), 0.89 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 137.1, 136.3, 129.5, 128.7, 128.6, 128.3, 126.9, 104.8, 82.7, 76.8, 76.4, 72.4, 70.3, 66.6, 25.8, 18.1, −4.5, −4.9. Anal. Calcd for $C_{25}H_{35}NO_5Si$: C, 65.62; H, 7.71; N, 3.06. Found: C, 65.64; H, 7.59; N, 2.99. **50b**: R_f = 0.21 (hexane/EtOAc 7:3); $[\alpha]^{20}_D$ −52.2 (*c* 1.3, $CHCl_3$); ^1H NMR (acetone-d_6) δ 7.66−7.28 (m, 10H), 6.25 (d, J = 7.0 Hz, 1H), 5.73 (s, 1H), 4.75 (m, 2H), 4.60 (ddd, J = 0.8, 5.0, 6.9 Hz, 1H), 4.49 (dd, J = 5.0, 5.6 Hz, 1H), 4.43 (ddd, J = 1.0, 1.8, 6.9 Hz, 1H), 4.22 (d, J = 3.8 Hz, 1H), 4.17 (ddd, J = 1.8, 3.8, 4.2 Hz, 1H), 3.47 (ddd, J = 1.0, 4.2, 5.6 Hz, 1H), 0.87 (s, 9H), 0.15 (s, 3H), 0.02 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 137.8, 136.1, 129.3, 128.4, 128.0, 127.8, 127.4, 106.8, 85.0, 79.2, 77.0, 76.3, 70.7, 70.5, 25.9, 18.4, −4.4, −5.4. **50c**: R_f = 0.18 (hexane/EtOAc 7:3); $[\alpha]^{20}_D$ −39.7 (*c* 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.53−7.29 (m, 10H), 5.84 (s, 1H), 4.78 (m, 2H), 4.54 (dd, J = 5.7, 5.9 Hz, 1H), 4.48 (dd, J = 4.9, 5.9 Hz, 1H), 3.99 (dd, J = 4.9, 9.9 Hz, 1H), 3.93 (dd, J = 5.7, 9.8 Hz, 1H), 3.20 (t, J = 9.9 Hz, 1H), 2.30 (d, J = 9.7 Hz, 1H), 0.92 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 137.7, 136.1, 129.6, 128.4, 128.2, 127.6, 126.9, 104.7, 78.5, 77.2, 76.7, 69.3, 66.6, 66.4, 25.8, 18.3, −4.6, −4.8. **50d**: R_f = 0.34 (hexane/EtOAc 4:1); $[\alpha]^{20}_D$ −66.3 (*c* 1.2, $CHCl_3$); IR (film) ν 1495, 1405, 1255, 1210; ^1H NMR (C_6D_6) δ 7.52−7.31 (m, 10H), 5.57 (s, 1H), 4.86 (d, J = 8.9 Hz, 1H), 4.76 (d, J = 5.5 Hz, 1H), 4.72 (s, 2H), 4.56 (d, J = 5.2 Hz, 1H), 4.53 (dd, J = 5.5, 8.5 Hz, 1H), 4.44 (d, J =, 8.9 Hz, 1H), 4.26 (dd, J = 4.4, 5.2 Hz, 1H), 3.67 (dd, J = 4.4, 8.5 Hz, 1H), 0.94 (s, 9H), 0.16 (s, 3H), 0.11 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 137.3, 136.6, 129.4, 128.9, 128.6, 128.3, 128.0, 127.8, 126.9, 105.5, 90.1, 82.5, 82.2, 81.6, 77.7, 75.3, 74.6, 25.8, 18.3, −4.6, −4.9. Anal. Calcd for $C_{26}H_{35}NO_5Si$: C, 66.49; H, 7.53; N, 2.98. Found: C, 66.61; H, 7.80; N, 3.06.

Cyclization of Oxime Ether 47. Following method C, oxime **47** (109 mg, 0.27 mmol) gave an inseparable mixture of aminocyclitols **51a** and **51b** (85 mg, 78%, **51a**/**51b** = 8:1). Colorless oil; R_f = 0.32 (hexane/EtOAc 2:1). Anal. Calcd for $C_{21}H_{35}NO_5Si$: C, 61.58; H, 8.61; N, 3.42. Found: C, 61.87; H, 8.78; N, 3.46. **51a**:^1H NMR ($CDCl_3$) δ 7.38−7.31 (m, 5H), 5.65 (br s, 1H), 4.72 (m, 2H), 4.42 (ddd, J = 0.9, 2.5, 7.0 Hz, 1H), 4.32 (ddd, J = 0.9, 2.8, 7.0 Hz, 1H), 4.07 (dd, J = 2.8, 5.5 Hz, 1H), 3.96 (ddd, J = 0.9, 2.5, 5.8 Hz, 1H), 3.13 (dt, J = 0.9, 1.0, 5.5 Hz, 1H), 2.40 (s, 1H), 1.39 (s, 3H), 1.26 (s, 3H), 0.88 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 37.7, 128.5, 128.4, 128.0, 111.4, 84.9, 84.6, 76.9, 76.5, 76.3, 73.2, 26.3, 25.7, 24.0, 17.9, −4.8, −5.1. **51b**: ^1H NMR ($CDCl_3$) δ 7.38−7.31 (m, 5H), 5.65 (br s, 1H), 4.73 (s, 2H), 4.54 (dd, J = 5.6, 5.8 Hz, 1H), 4.29 (d, J = 5.8 Hz, 1H), 4.06 (d, J = 3.9 Hz, 1H), 3.75 (dd, J = 5.6, 9.6 Hz, 1H), 3.37 (dd, J = 3.9, 9.6 Hz, 1H), 2.41 (s, 1H), 1.44 (s, 3H), 1.28 (s, 3H), 0.86 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 128.2, 127.7, 111.4, 82.9, 76.2, 72.3, 71.6, 67.3, 26.0, −5.3.

Cyclization of Oxime Ether 49. Following method C, oxime **49** (63 mg, 0.12 mmol) gave aminocyclitols **52a** (17 mg, 27%) and **52b** (13 mg, 21%). **52a**: colorless oil; R_f = 0.30 (hexane/EtOAc 2:1); $[\alpha]^{20}_D$ −7.1 (*c* 2.1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.40−7.28 (m, 20H), 5.85 (brs 1H), 4.77−4.50 (m, 8H), 4.08 (m, 1H), 3.95 (ddd, J = 0.6, 4.6, 5.9 Hz, 1H), 3.82 (dd, J = 5.9, 8.0 Hz, 1H), 3.81 (dd, J = 3.5, 4.6 Hz, 1H), 3.51 (dd, J = 5.7, 8.0 Hz, 1H), 2.70 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 138.2 (2C), 138.1, 137.3, 128.6, 128.5, 128.4, 128.3, 128.2, 127.9, 127.7, 127.6, 87.3, 86.7, 81.9, 76.5, 72.2, 72.0, 71.8, 65.1. Anal. Calcd for $C_{33}H_{35}NO_5$: C, 75.40; H, 6.71; N, 2.66. Found: C, 75.10; H, 6.71; N, 2.86. **52b**: white solid; mp 73−75 °C; R_f = 0.20 (hexane/EtOAc 2:1); $[\alpha]^{20}_D$ −6.0 (*c* 0.7, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.33−7.10 (m, 20H), 5.40 (br s, 1H), 4.57 (m, 3H), 4.38 (m, 2H), 4.23 (t, J = 5.6 Hz, 1H), 4.10 (t, J = 5.4 Hz, 1H), 3.96 (t, J = 5.5 Hz, 1H), 3.82 (t, J = 5.3 Hz, 1H), 3.52 (t, J = 5.4 Hz, 1H), 2.35 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 138.4, 138.2, 137.7, 128.7, 128.5, 128.4, 128.1, 128.0, 127.9, 127.7, 127.6, 85.7, 82.1, 81.4, 76.7, 72.2, 72.0, 70.8, 70.2. Anal. Calcd for $C_{33}H_{35}NO_5$: C, 75.40; H, 6.71; N, 2.66. Found: C, 75.53; H, 6.44; N, 2.67.

Cyclization of 54. DMSO (0.057 mL, 0.80 mmol) was added dropwise to a stirred solution of oxalyl chloride (0.035 mL, 0.40 mmol) in dry THF (1 mL) at −78 °C. The solution was stirred for 5 min and oxime **54**[45] (0.033 g, 0.16 mmol) in dry THF (1 mL) was added dropwise. The reaction mixture was stirred at −78 °C for 1 h 50 min, Et_3N (0.225 mL, 1.60 mmol) was added, and the reaction mixture was stirred from −78 °C to −50 °C for 2.5 h. Dry THF (5 mL) was added to this mixture, and the crude aldehyde **14** was added dropwise over 30 min *via* cannula to a stirred solution of SmI_2 in THF (0.1 M in THF, 7 mL, 0.70 mmol) and *t*-BuOH (0.040 mL, 0.42 mmol) at −70 °C under argon. The reaction mixture was stirred from −70 °C to −55 °C for 1 h, and at rt for 45 min before being partioned between EtAOc (20 mL) and aqueous saturated $NaHCO_3$ (15 mL). The reaction was worked up as described in method B and the residue was purified by flash column chromatography (hexane/EtAOc 4:1 to 3:2) affording **55** (16 mg, 49% yield) as a pale yellow oil. R_f = 0.28 (hexane/EtOAc 3:2); IR (film) ν 3350, 3030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.36 (m, 5 H), 4.73 (s, 2 H), 4.08 (br q, J = 6 Hz, 1H), 3.35 (dt, J = 7, 6 Hz, 1H), 1.22−2.04 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 138.0, 128.9, 128.8, 128.7, 128.5, 78.1, 77.0, 69.3, 33.2, 27.7, 21.4. Anal. Calcd for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.78; H, 8.17; N, 6.68.

1-*O*-Benzyl-1,2,6-hexanetriol (59). A mixture of 1,2,6-hexanetriol (500 mg, 3.73 mmol) in toluene (10 mL) and dibutyltin oxide (700 mg, 2.80 mmol) was heated at reflux in a Dean−Stark apparatus for 6 h. Benzyl bromide (1.8 mL, 15.1 mmol) and tetrabutylammonium bromide (840 mg, 2.61 mmol) were added and the solution was heated at reflux for 5 h. The reaction mixture was diluted with CH_2Cl_2 (30 mL) and poured into aqueous 15% $NaHCO_3$. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 25 mL). The combined organic extracts were washed with brine and dried over Na_2SO_4. The solvent was removed at reduced pressure and the residue was purified by flash-chromatography (EtOAc) affording **59** (504 mg, 60%) as a colorless oil. R_f = 0.31 (EtOAc); IR (film) ν 3400(br), 1125, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.32 (m, 5H), 4.55 (s, 2H), 3.82 (m, 1H), 3.63 (m, 3H), 3.50 (dd, J = 3.2, 9.4 Hz, 1H), 3.33 (dd, J = 7.9, 9.4 Hz, 1H), 2.58 (br s, 1H), 1.84−1.38 (m, 6H).

6-*O*-Benzyl-5,6-dihydroxyhexanal *O*-Benzyl Oxime Ether (61). To a suspension of PDC (843 mg, 2.24 mmol), NaOAc (63 mg, 0.75 mmol), and 3 Å MS (350 mg) in CH_2Cl_2 (10 mL) was added at rt a solution of **59** (335 mg, 1.49 mmol) in CH_2Cl_2 (5 mL). The mixture was stirred at rt for 5 h, Et_2O (20 mL) was added, and the suspension was filtered through a small pad of silica eluting with Et_2O. The filtrate was concentrated a reduced pressure and the residue was purified by flash-chromatography (hexane/EtOAc 3:1) affording **60** [(130 mg, 40%); IR (film) ν 3430, 1725, 1455 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.73 (m, 1H), 7.32 (m, 5H), 4.65 (m, 2H), 4.00 (m, 1H), 3.79 (br s, 1H, OH), 2.59−1.37 (m, 6H)]. A solution of this compound (120 mg, 0.54 mmol) in MeOH (10 mL) was treated with *O*-benzylhydroxylamine hydrochloride (173 mg, 1.08 mmol) and pyridine (0.13 mL, 1.62 mmol) as described for **17**. Flash-chromatography (hexane/EtOAc 7:3) afforded **61** (166 mg, 93%) as a colorless oil, 56:44 mixture of *E* and *Z* oximes, respectively. R_f = 0.31 (hexane/EtOAc 7:3); IR (film): 3450, 1500, 1220 cm^{-1}; ^1H NMR ($CDCl_3$) δ (*E*-isomer) 7.45 (t, J = 6.3 Hz, 1H), 7.39 (m, 10H), 5.07 (s, 2H), 4.58 (s, 2H), 3.81 (m, 1H), 3.48 (dd, J = 3.9, 10.8 Hz, 1H), 3.34 (m, 1H), 2.38 (d, J = 3.9 Hz, 1H), 2.22 (q, J = 6.9 Hz, 2H), 1.78−1.40 (m, 4H); (*Z*-isomer) 7.37 (m, 10H), 6.71 (t, J = 5.2 Hz, 1H), 5.12 (s, 2H), 4.59 (s, 2H), 3.85 (m, 1H, 1H), 3.33 (dd, J = 8.0, 9.1 Hz, 1H), 2.49−2.38 (m, 3H), 1.78−1.40 (m, 4H). Anal. Calcd for $C_{20}H_{25}NO_3$: C, 73.35; H, 7.71; N, 4.28. Found: C, 73.61; H, 7.47; N, 3.99.

1-(Benzyloxy)-6-[(benzyloxy)imino]-2-hexanone (20). To a suspension of PDC (82 mg, 0.38 mmol), NaOAc (11 mg, 0.13 mmol), and 3 Å MS (100 mg) in CH_2Cl_2 (8 mL) was added a solution of **61** (82 mg, 0.25 mmol) in CH_2Cl_2 (5 mL). After stirring at rt for 8 h, Et_2O (15 mL) was added, and the suspension was filtered through a small pad of silica eluting with Et_2O thoroughly. The filtrate was concentrated at reduced pressure, and the residue was purified by flash-chromatography (hexane/EtOAc 7:3) affording **20** (58 mg, 71%) as a colorless oil, 56:44 mixture of *E* and *Z* isomers. R_f = 0.37 (hexane/EtOAc 3:7); IR (film) ν 1750, 1495, 1370, 1210 cm^{-1}; ^1H NMR ($CDCl_3$) δ (*E*-isomer) 7.40 (t, J = 6.0 Hz, 1H), 7.31 (m, 10H), 5.03 (s, 2H), 4.58 (s, 2H), 4.00 (m, 2H), 2.48 (dt, J = 3.6, 7.3 Hz, 2H), 2.37 (dt, J = 5.5, 7.6 Hz, 1H), 2.19 (m, 1H), 1.78 (dq, J = 3.0, 7.1 Hz, 2H); *Z*-isomer: 6.65 (t, J = 5.6 Hz, 1H), 5.08 (s, 2H), 4.56 (s, 2H). Anal. Calcd for $C_{20}H_{23}NO_3$: C, 73.80; H, 7.14; N, 4.31. Found: C, 74.06; H, 6.95; N, 4.19.

Reaction of 20 with SmI_2. Oxime **20** (0.109 g, 0.33 mmol) in dry THF (10 mL) was added dropwise over 25 min to a stirred solution of SmI_2 in THF (0.1 M in THF, 10 mL, 1.0 mmol) and *t*-BuOH (0.080 mL, 0.83 mmol) at −78 °C under argon. The reaction mixture was stirred for 3.5 h from −78 to −30 °C and then filtered through a short silica gel column eluting with EtOAc/hexane (1:1). The eluate was concentrated under reduced pressure. The crude product (0.12 g) was purified by flash column chromatography. Elution with hexane/EtOAc (4:1) gave **62** (0.046 g, 42%) and **63** (0.013 g, 18%, as a 1:2 mixture of *E*/*Z* isomers). **62**: Colorless oil; R_f = 0.38 (hexane/EtOAc 7:3); IR (film) ν 3450, 3040 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.52−2.20 (m, 6 H), 2.67 (br s, 1 H), 3.46 (m, 1 H), 3.53 (d, J = 9.4 Hz, 1 H), 3.64 (d, J = 9.4 Hz, 1 H), 4.55 (s, 2 H), 4.66 (s, 2 H), 5.76 (br s, 1 H), 7.34 (br s, 10 H); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ 138.5, 138.1, 128.9, 128.8, 128.7, 128.5, 128.2, 82.5, 76.7, 74.0, 69.8, 35.8, 29.1, 21.5; MS (70 eV *m*/*z* 328 (M^++H, 2), 91 (100), 77 (4), 65 (5). Anal. Calcd for $C_{20}H_{25}NO_3$: C, 73.37; H, 7.70; N, 4.28. Found: C, 73.60; H, 7.65; N, 4.28. **63**: Colorless oil; R_f = 0.46 (hexane/EtOAc 7:3); IR (film) ν 2920, 1720 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.42 (t, J = 6.0 Hz, 0.5 H, *E*), 7.34 (m, 5 H + 2.5 H, *Z* and *E*), 6.67 (t, J = 5.5 Hz, 1 H,*Z*), 5.10 (s, 2 H, *Z*), 5.05 (s, 1 H *E*), 2.15−2.49 (m, 4 H + 2H, *Z* and *E*), 2.11 (s, 3 H+ 1.5 H, *Z* and *E*), 1.72 (m, 2 H + 1H, *Z* and *E*); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ 207.8, 207.7, 151.3, 150.2, 137.7, 137.5, 128.3, 128.1, 128.0, 127.7, 127.5, 127.4, 127.2, 126.7, 75.6, 75.3, 42.5, 42.1, 29.5, 28.5, 29.7, 29.7, 20.1, 19.9. Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 71.39; H, 7.58; N, 6.12.

Synthesis and Reaction of Aldehyde 16 with SmI_2. To a suspension of Dess−Martin periodinane[38] (1.00 g, 2.36 mmol) in CH_2Cl_2 (6 mL) was added a solution of **64**[37] (664 mg, 1.82 mmol) in CH_2Cl_2 (1.2 mL) at rt. After stirring vigorously for 2 h, Et_2O (10 mL) was added and the mixture was poured into 10 mL of saturated aqueous $NaHCO_3$ containing 2.3 g of Na_2SO_3. The mixture was stirred for 5 min, Et_2O was added (20 mL), phases were separated, and the aqueous phase was extracted with Et_2O (3 × 30 mL). The combined organic extracts were washed with 10 mL of aqueous saturated $NaHCO_3$ and 10 mL of water and dried ($MgSO_4$). The solvent was removed at reduced pressure, and the residue was purified by flash-chromatography (hexane/EtOAc 5:1) affording **16** [(487 mg, 76%) as a colorless oil, 3:1 mixture of *E* and *Z* isomers. ^1H NMR (200 MHz, $CDCl_3$) δ 9.63 (d, J = 2.1 Hz, 1H, *E*-isomer), 9.56 (d, J = 3.5 Hz, 1H, *Z*-isomer), 7.41 (d, J = 6.4 Hz, 1H, *E*-isomer), 6.88 (d, J = 4.6 Hz, 1H, *Z*-isomer)]. To a solution of **16** (75.1 mg, 0.21 mmol) in THF (10.5 mL) at −45 °C was added dropwise a 0.1M THF solution of SmI_2 (6.0 mL, 0.60 mmol), and the reaction was stirred at −45 °C to rt for 6 h. The reaction mixture was worked up as described in method B. The residue was purified by flash-chromatography (hexane/EtOAc 5:1 to 3:2) affording, in order of elution, **65a** (16.8 mg, 22%), **65b** (18.4 mg, 24%), and **65c** (15.3 mg, 20%). **65a**: colorless oil; R_f = 0.36 (hexane/EtOAc 7:3); $[\alpha]^{25}_D$ +7.1 (*c* 0.2, $CHCl_3$); ^1H NMR (acetone-d_6) δ 7.42−7.29 (m, 5H), 6.40 (d, J =1.9 Hz, 1H), 4.74 (s, 2H), 4.35 (dd, J =3,9, 5.6 Hz, 1H), 4.31 (m, J =4.2, 3.9, 3.4 Hz, 1H), 4.24 (dd, J =8.3, 5.6 Hz, 1H), 4.04 (d, J =3.4 Hz, 1H), 3.69 (dd, J =9.9, 8.3 Hz, 1H), 3.57 (t, J =10.0, 9.9 Hz, 1H), 3.37 (dd, J =10.0, 4.2 Hz, 1H), 1.28 (s, 3H), 1.31 (s, 3H), 1.34 (s, 3H), 1.43 (s, 3H); ^{13}C NMR ($CDCl_3$) δ: 137.0, 128.7, 128.6, 128.3, 111.9, 109.5, 80.8, 78.7, 76.7, 71.9, 68.1, 61.8, 28.1 , 26.9, 26.9, 25.7. Anal. Calcd for $C_{19}H_{27}NO_6$: C, 62.45; H, 7.45; N, 3.83. Found: C, 62.25; H, 7.40; N, 3.64. **65b**: Colorless oil; R_f = 0.24 (hexane/EtOAc 7:3); $[\alpha]^{25}_D$ −3.7 (*c* 1.3, $CHCl_3$); IR (KBr) ν 3450, 1495, 1455, 1220 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.37−7.35 (m, 5H), 5.94 (br s, 1H), 4.73 (s, 2H), 4.41 (dd, J =6.7, 3.9 Hz, 1H), 4.27 (t, J = 8.0, 6.7 Hz, 1H), 4.07 (dd, J = 10.0, 8.0 Hz, 1H), 4.03 (t, J = 3.9, 3.8, 3.0 Hz, 1H), 3.51 (t, J = 10.4, 10.0 Hz, 1H), 3.31(dd, J = 10.4, 3.8 Hz, 1H), 2.55 (dd, J = 3.0 Hz, 1H), 1.55 (s, 3H), 1.44 (s, 3H), 1.43 (s, 3H), 1.38(s, 3H); ^{13}C NMR ($CDCl_3$) δ 138.1, 129.5, 129.3, 129.0, 113.1, 111.3, 79.3, 78.1, 77.5, 77.3, 74.6, 71.4, 64.9, 27.9, 25.6. Anal. Calcd for $C_{19}H_{27}NO_6$: C, 62.45; H, 7.45; N, 3.83. Found: C, 62.41; H, 7.30; N, 3.82. **65c**: White solid; R_f = 0.16 (hexane/EtOAc 7:3); mp 102−104 °C; $[\alpha]^{25}_D$ +35.6 (*c* 1.4, $CHCl_3$); IR (KBr) ν 3450, 1450, 1375, 1290 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.37−7.30 (m, 5H), 6.10 (br s, 1H), 4.76 (m, 2H), 4.31 (dd, J = 7.5, 7.2 Hz, 1H), 4.21 (dd, J = 8.8 Hz, 7.5 Hz, 1H), 4.15 (dd, J = 10.8, 7.2 Hz, 1H), 3.90 (dd, J = 8.8, 5.5 Hz, 1H), 3.68 (dd, J = 10.8, 7.0 Hz, 1H), 3.40 (dd, J = 7.0, 5.5 Hz, 1H), 2.40 (brs , 1H), 1.51 (s, 3H), 1.42 (s, 3H), 1.40 (s, 3H), 1.33 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 137.2, 129.4, 128.7, 128.0, 112.9, 110.5, 78.1, 76.8, 76.7, 75.9, 74.8, 73.3, 60.2, 27.3, 27.0, 26.5, 24.5. Anal. Calcd for $C_{19}H_{27}NO_6$: C, 62.45; H, 7.45; N, 3.83. Found: C, 62.77; H, 7.28; N, 3.51.

Reaction of 65a with Thiocarbonyl Diimidazole. A solution of **65a** (51 mg, 0.14 mmol) and 1,1′-thiocarbonyldiimidazole (99 mg, 0.56 mmol) in THF (14 mL) was heated at reflux for 21 h. The solvent was removed at reduced pressure, and the residue was purified by flash-chromatography (hexane/EtOAc 4:1) affording **66a** (31 mg, 54%) as a white solid. R_f = 0.29 (hexane/EtOAc 4:1); mp 213−215 °C; $[\alpha]^{25}_D$ +7.1 (*c* 0.2, $CHCl_3$); IR (KBr) ν 1475, 1460, 1390, 1375 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.56−7.39 (m, 5H), 5.23 (m, 2H), 4.79 (dd, J = 9.4, 5.7 Hz, 1H), 4.47 (dd, J = 7.5, 5.8 Hz, 1H), 4.33 (dd, J = 7.7, 7.6 Hz, 1H), 4.06 (dd, J = 9.4, 7.9 Hz, 1H), 3.53 (dd, J = 10.6, 7.8 Hz, 1H), 3.44 (dd, J = 10.6, 7.9 Hz, 1H), 1.50 (s, 3H), 1.45 (s, 3H), 1.34 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 191.9, 133.9, 129.6, 129.0, 128.4, 113.3, 110.7, 81.2, 77.4, 76.6, 76.5, 75.4, 75.1, 60.5, 30.6, 26.9, 26.7, 24.4. Anal. Calcd for $C_{20}H_{25}NO_6S$: C, 58.95; H, 6.18; N, 3.44; S, 7.87. Found: C, 58.60; H, 6.28; N, 3.25; S, 7.57.

Reaction of 65b with Thiocarbonyl Diimidazole. A solution of **65b** (42 mg, 0.12 mmol) and 1,1′-thiocarbonyldiimidazole (85 mg, 0.48 mmol) in THF (10 mL) was heated at reflux for 26 h. The solvent was removed at reduced pressure, and the residue was purified by flash-chromatography (hexane/EtOAc 3:1) affording **66b** (36 mg, 76%) as a white solid. R_f = 0.30 (hexane/EtOAc 7:3); mp 222−224 °C; $[\alpha]^{25}_D$ −50.1 (*c* 0.6, $CHCl_3$); IR (KBr) ν 1460, 1420, 1375, 1320 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.60−7.30 (m, 5H), 5.15 (m, 2H), 4.71 (dd, *J* = 4.8, 3.0 Hz, 1H), 4.36 (dd, *J* =8.6, 4.8 Hz, 1H), 4.17 (dd, *J* = 12.2, 3.0 Hz, 1H), 4.05 (dd, *J* = 12.2, 9.5 Hz, 1H), 3.58 (t, *J* = 9.0, 8.6 Hz, 1H), 3.36 (t, *J* = 9.5, 9.0 Hz, 1H), 1.51 (s, 3H), 1.42 (s, 3H), 1.40 (s, 3H), 1.33 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 192.5, 135.0, 130.5, 129.4, 128.9, 114.1, 113.6, 83.0, 78.4, 78.3, 76.5, 76.1, 72.0, 64.2, 29.1, 27.2, 27.1, 26.1. Anal. Calcd for $C_{20}H_{25}NO_6S$: C, 58.95; H, 6.18; N, 3.44; S, 7.87. Found: C, 58.90; H, 6.07; N, 3.375; S, 7.78.

Reaction of 65c with Thiocarbonyl Diimidazole. A solution of **65c** (41 mg, 0.11 mmol) and 1,1′-thiocarbonyldiimidazole (78 mg, 0.44 mmol) in THF (10 mL) was heated at reflux for 24 h. The solvent was removed at reduced pressure, and the residue was purified by flash-chromatography (hexane/EtOAc 4:1) affording **66c** (2 mg, 4%) as a white solid, and **67** (30 mg, 57%) as a light yellow oil. **66c**: R_f = 0.44 (hexane/EtOAc 7:3); mp 213−215 °C; $[\alpha]^{25}_D$ −4.5 (*c* 0.1, $CHCl_3$); IR (KBr) ν 1375, 1320, 1270, 1235 1160 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.56−7.31 (m, 5H), 5.18 (m, 2H), 4.71−4.48 (m, 3H), 4.09 (dt, *J* = 9.6, 8.7 Hz, 1H), 3.85−3.75 (m, 2H), 3.78 (s, 3H), 1.59 (s, 3H), 1.58 (s, 3H), 1.56 (s, 3H), 1.37 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 195.3, 135.1, 130.5, 129.3, 128.9, 115.1, 113.6, 79.7, 79.1, 79.0, 75.5, 75.3, 71.6, 61.6, 27.2, 27.1, 26.9, 24.0. Anal. Calcd for $C_{20}H_{25}NO_6S$: C, 58.95; H, 6.18; N, 3.44; S, 7.87. Found: C, 58.77; H, 6.32; N, 3.38; S, 7.63. **67**: R_f = 0.27 (hexane/EtOAc 1:1); $[\alpha]^{25}_D$ −4.5 (*c* 0.1, $CHCl_3$); IR (KBr) ν 1375, 1320, 1270, 1235 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.56−7.31 (m, 5H), 5.18 (m, 2H), 4.58 (m, 3H), 4.09 (dt, *J* = 9.6, 8.7 Hz, 1H), 3,78 (s, 3H), 1.59 (s, 3H), 1.58 (s, 3H), 1.56 (s, 3H), 1.37 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 195.3, 135.1, 130.5, 129.3, 128.9, 115.1, 113.6, 79.7, 79.1, 79.0, 75.5, 75.3, 71.6, 61.6, 27.2, 27.1, 26.9, 24.0. Anal. Calcd for $C_{23}H_{29}N_3O_6S$: C, 58.09; H, 6.15; N, 8.84; S, 6.74. Found: C, 57.87; H, 6.04; N, 8.65; S, 6.55.

Compound 68. To a 0.1 M solution of SmI_2 (6 mL, 0.60 mmol) in THF at −25 °C was added dropwise a solution of **17** (66 mg, 0.10 mmol) in THF (2 mL). After stirring at −25 °C for 1, water (50 μL, 2.8 mmol) was added and the reaction mixture was stirred at −25 °C to rt for 2 h. Pyridine (1 mL) and Ac_2O (1 mL) were added and the mixture was stirred at rt for 15 h. The reaction mixture was worked up as described in method B, and the product was purified by flash-chromatography (hexane/EtOAc 1:1) affording **68** (49 mg, 82%) as a white solid. R_f = 0.24 (hexane/EtOAc 2:1); mp 143.5−144.5 °C; $[\alpha]^{20}_D$ +2.7 (*c* 1.1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.33 (m, 20H), 5.99 (d, *J* = 7.9 Hz, 1H), 4.71 (s, 2H), 4.69 (s, 2H), 4.62 (s, 2H), 4.40 (m, 2H), 4.31 (dd, *J* = 7.0, 7.9 Hz, 1H), 4.12 (t, *J* = 6.6 Hz, 1H), 3.99 (d, *J* = 6.8 Hz, 1H), 3.71 (dd, *J* = 6.5, 7.0 Hz, 1H), 3.48 (s, 1H), 3.45 (d, *J* = 10.2 Hz, 1H), 3.28 (d, *J* =10.2 Hz, 1H), 1.75 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 170.3, 138.3, 138.1, 137.7, 137.1, 128.6, 128.4, 128.3, 128.1, 128.0, 127.9, 127.8, 127.7, 86.3, 83.4, 80.7, 76.0, 73.6, 73.0, 72.5, 72.1, 71.7, 60.8, 23.0. Anal. Calcd for $C_{36}H_{39}NO_6$: C, 74.33; H, 6.76; N, 2.41. Found: C, 74.61; H, 7.01; N, 2.44.

Compound 69. To a solution of $(COCl)_2$ (51 μL, 0.58 mmol) in THF (1 mL) at −60 °C was added DMSO (82 μL, 1.16 mmol) dropwise. After stirring at −60 °C for 15 min, a solution of **35** (135 mg, 0.29 mmol) in THF (2 mL) was added. The reaction mixture was stirred for 1 h at −60 °C, Et_3N was added (0.2 mL, 1.45 mmol), the cooling bath was removed, and the reaction mixture was stirred at rt for 4 h. After diluting with THF (5 mL), the mixture was added dropwise via cannula to a 0.1 M solution of SmI_2 (17.5 mL, 1.75 mmol) in THF at −25 °C. The reaction was stirred for 1 h at −25 °C, water (50 μL, 5.40 mmol) was added, the cooling bath was removed, and the mixture was stirred at rt for 2 h. Pyridine (1 mL) and Ac_2O (1 mL) were added and the mixture was stirred at rt for 15 h. The reaction mixture was worked up as described in method B, and the crude was purified by flash-chromatography (hexane/EtOAc 1:2 to 1:4) affording 108 mg (86%) of a 5.4:1 mixture of silyl-migrated products. R_f = 0.52 (hexane/EtOAc 1:4); IR (film) ν 3320, 1760, 1750, 1655, 1560, 1380, 1230; ^1H NMR ($CDCl_3$) δ (major product) 7.58−7.37 (m, 5H), 5.76 (s, 1H), 5.52 (d, *J* = 8.8 Hz, 1H), 5.06 (d, *J* = 5.0 Hz, 1H), 4.80 (ddd, *J* = 5.0, 9.0, 10.3 Hz, 1H), 4.47 (dd, *J* = 4.9, 6.1 Hz, 1H), 4.39 (d, *J* = 6.1 Hz, 1H), 4.05 (dd, *J* = 4.9, 10.5 Hz, 1H), 2.10 (s, 3H), 2.00 (s, 3H), 0.91 (s, 9H), 0.13 (s, 6H); (minor product) 5.81 (s, 1H), 5.01 (d, *J* = 5.0 Hz, 1H), 4.50 (dd, *J* = 4.8, 6.4 Hz, 1H), 4.15 (dd, *J* = 4.8, 10.2 Hz, 1H), 2.08 (s, 3H), 0.94 (s, 9H), 0.14 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 169.6, 169.2, 135.6, 129.6, 128.3, 127.0, 105.4, 81.1, 77.6, 75.4, 73.6, 53.6, 25.6, 23.3, 20.9, 18.1, −4.5, −4.9; EM (70 eV) *m*/*z*: 379 (11), 378 (45), 273 (18), 272 (97), 188 (11), 170 (27), 158 (25), 129 (39), 116 (24), 105 (32), 96 (23), 75 (56), 73 (66), 59 (19), 43 (100). Anal. Calcd for $C_{22}H_{33}NO_6Si$: C, 60.66; H, 7.64; N, 3.22. Found: C, 60.42; H, 7.38; N, 3.09.

A portion of this mixture (16.0 mg) was dissolved in THF (1 mL), and it was treated with a 0.1 M solution of TBAF (0.12 mL, 0.12 mmol) in THF at rt. After stirring the mixture for 3 h, pyridine (0.2 mL) and Ac_2O (0.1 mL) were added, and the mixture was stirred for 16 h. The solvent was removed at reduced pressure, and the residue was purified by flash-chromatography (EtOAc), affording **69** (12 mg, 90%) as a white foam. R_f: 0.33 (EtOAc); mp 65−67 °C; $[\alpha]^{20}_D$ −63.0 (*c* 1.0, EtOH); IR (KBr) ν 3300, 1750, 1660, 1550; ^1H NMR ($CDCl_3$) δ 7.55−7.40 (m, 5H), 5.83 (d, *J* = 8.2 Hz, 1H), 5.75 (s, 1H), 5.19 (d, *J* = 4.6 Hz, 1H), 5.11 (dd, *J* = 4.8, 10.8 Hz, 1H), 5.02 (ddd, *J* = 4.6, 8.2, 10.8 Hz, 1H), 4.77 (dd, *J* = 4.8, 6.1 Hz, 1H), 4.49 (d, *J* = 6.1 Hz, 1H), 2.13 (s, 3H), 2.12 (s, 3H), 1.99 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 171.5, 169.9, 169.1, 134.9, 130.0, 128.5, 127.0, 105.8, 81.1, 75.7, 74.7, 73.1, 51.8, 23.2, 20.8; EM (70 eV) *m*/*z*: 362 (2), 257 (10), 214 (12), 155 (12), 148 (11), 139 (20), 115 (15), 105 (22), 101 838), 91 (13), 84 (17), 77 (12), 59 (15), 43 (100). Anal. Calcd for $C_{18}H_{21}NO_7 \cdot H_2O$: C, 56.68; H, 6.08; N, 3.67. Found: C, 56.80; H, 5.64; N, 3.70.

Compound 70. To a solution of **34** (550 mg, 1.56 mmol) in pyridine (10 mL) was added hydroxylamine hydrochloride (326 mg, 4.69 mmol), and the mixure was stirred at rt for 4 h. The reaction mixture was diluted with Et_2O (25 mL), and the solution was washed with brine and dried ($MgSO_4$). The solvent was removed at reduced pressure, and the residue was purified by flash-chromatography (hexane/EtOAc 3:1) affording **70** (480 mg, 84%) as a colorless oil, 4:1 mixture of *E* and *Z* oximes, respectively. R_f = 0.16 (hexane/EtOAc 7:3); IR (film) ν 3350, 1465, 1415, 1260 cm^{-1}; ^1H NMR ($CDCl_3$) δ (*E*-isomer) 8.71 (br s, 1H), 7.47 (m, 1H), 7.45−7.36 (m, 5H), 5.82 (s, 1H), 4.67 (t, *J* = 7.1 Hz, 1H), 4.36 (m, 2H), 3.87 (brd, 2H), 2.71 (brt, 1H), 0.90 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H); (*Z*-isomer) 8.22 (br s, 1H), 6.82 (d, *J* = 6.2 Hz, 1H). Anal. Calcd for $C_{18}H_{29}NO_5Si$: C, 58.81; H, 7.97; N, 3.81. Found: C, 59.03; H, 7.77; N, 3.79.

Compound 71. To a solution of **70** (445 mg, 1.22 mmol) in CH_2Cl_2 (15 mL) were added pyridine (0.60 mL, 7.32 mmol) and trifluoroacetic anhydride (0.52 mL, 6.1 mmol) at rt. After stirring for 5h at rt, the reaction mixture was diluted with CH_2Cl_2, and the solution was washed with brine and dried ($MgSO_4$). The solvent was removed at reduced pressure, and the residue was purified by flash-chromatography (hexane/EtOAc 4:1) affording **71** (233 mg, 55%) as a colorless oil. R_f = 0.28 (hexane/EtOAc 9:1); $[\alpha]^{20}_D$ 29.3 (*c* 2.6 , $CHCl_3$); IR (film) ν 3450, 2340, 1455, 1410 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.53−7.39 (m, 5H) 5.87 (s, 1H), 4.82 (m, 1H), 4.37 (m, 2H), 3.93 (m, 2H), 2.12 (t, *J* = 6.0 Hz, 1H), 0.93 (s, 9H), 0.28 (s, 3H), 0.20 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 135.8, 129.7, 128.5, 126.5, 118.4, 103.6, 78.5, 77.7, 62.0, 60.1, 25.5, 18.0, −4.9, −5.2. Anal. Calcd for $C_{18}H_{27}NO_4Si$: C, 61.85; H, 7.80; N, 4.01. Found: C, 62.04; H, 8.01; N, 3.96.

Cyclization of 71 through Oxidation−SmI_2 Reductive Coupling Sequence. To a solution of $(COCl)_2$ (35 μL, 0.40 mmol) in THF (1.5 mL) at −60 °C was added DMSO (57 μL, 0.80 mmol) dropwise. After stirring the mixture at −60 °C for 10 min, a solution of **71** (56 mg, 0.16 mmol) in THF (3 mL) was added dropwise. The reaction mixture was stirred at −60 °C for 1 h, Et_3N (0.34 mL, 2.40 mmol) was added, and the mixture was slowly warmed to rt for 5 h. The reaction mixture

was diluted with THF (3 mL), *t*-BuOH (31 μL, 0.32 mmol) was added, and the resultant solution was added to a 0.1 M solution of SmI_2 in THF (6.5 mL, 0.65 mmol) at −40 °C. The reaction mixture was stirred at −40 °C to −20 °C for 15 h. The reaction was worked up as described in method B, and the product was purified by flash-chromatography (hexane/EtOAc 9:1 to 1:3) affording **72** (6 mg, 16%) as a pale fellow oil. R_f = 0.15 (hexane/EtOAc 1:1); $[\alpha]^{20}_D$ −16.1 (*c*, 0.5, $CHCl_3$); IR (film) ν 3375, 1730, 1630, 1465, 1335 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.39 (d, J = 2.5 Hz, 1H), 4.69 (t, J = 2.2 Hz, 1H), 4.12 (d, J = 2.0 Hz, 1H), 3.00 (br s, 2H), 0.96 (s, 9H), 0.24 (s, 3H), 0.22 (s, 3H); ^{13}C NMR (acetone-d_6) δ 206.5, 135.1, 122.6, 80.7, 73.7, 25.8, 19.2, −3.7, −4.1.

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Supporting Information Available: Experimental procedures and characterization data for compounds **7b**−**e**, **23**, **54**, and **56**, and tables of ^1H NMR and 2D NOESY cross-peak intensities for the carbocyclic products **39**, **43**, **44a**−**c**, **45**, **50a**−**d**, **51a**,**b**, **52a**,**b**, **65a**−**c** (8 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering instructions.

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