A Highly Efficient Pinacol Coupling Approach to Trehazolamine Starting from D-Glucose

Isabel Storch de Gracia, Hansjörg Dietrich, Sofía Bobo, and Jose Luis Chiara*

Instituto de Química Orgánica General, CSIC, Juan de la Cierva, 3, E-28006 Madrid, Spain

Received May 5, 1998

A short and very efficient synthesis of trehazolamine (**3**), the aglycon of the potent trehalase inhibitor trehazolin (**2**), has been achieved starting from D-glucose. The key transformation in this approach is a high-yielding two-step, one-pot sequence consisting of a Swern oxidation of a 1,5-diol followed by a reductive carbocyclization of the resultant 1,5-dicarbonyl compound promoted by samarium diiodide. The overall yield of **3** is 39% over nine steps from 2,3,4,6-tetra-*O*-benzyl-D-glucose (**5**). An even shorter synthesis of **30**, a diastereoisomeric analogue of **3**, is also described starting from **5**. The key transformation in this second route is a highly stereoselective ketone oxime ether reductive carbocyclization promoted also by samarium diiodide. The overall yield of **30** is 57% over four steps from **5**.

Introduction

Trehalase is an enzyme that specifically hydrolyses α,α-trehalose (**1**, Figure 1) to its two glucose units and is widely distributed in microorganisms, insects, plants, and animals. Trehalose is ubiquitously found in insects, being their principal blood sugar and used to support various energy-requiring functions, such as insect flight.[1] Trehalose and trehalase have been reported to participate also in germination of ascospores in fungi[2] and in glucose transport in mammalian kidney or intestine.[3] The development of specific and potent trehalase inhibitors is, therefore, of great interest for the control of insects and certain fungi. One such inhibitor, trehazolin (**2**), was isolated in 1991 from the culture broth of *Micromonospora* strain sp. SANK 62390[4] and from *Amycolatopsis trehalostatica*.[5] Its peculiar structure, a pseudodisaccharide consisting of an α-D-glucopyranose moiety bonded to a unique aminocyclopentitol (trehazolamine, **3**) through a cyclic isourea group, was confirmed through synthetic studies[6−9] that also allowed establishment of its absolute configuration. Trehazolin probably acts as a close mimic of the substrate α,α-trehalose (**1**) or, more likely, of the postulated glycopyranosyl cation intermediate involved in the hydrolytic step of glycosides or a transition state leading to it. By systematic chemical modifications of the sugar[10] and the aglycon,[6b,d,10d,11] a number of structure−activity relationships have been established. All previous total syntheses of **2**[6b,d,7a,c,9] followed a general retrosynthetic strategy where the molecule is assembled by linking a protected α-D-glucosyl isothiocyanate (**4**)[9,12] to free or partially protected aminocyclopentitol **3**. The reported syntheses of **3** followed long sequences (≥15 steps) starting from *myo*-inositol,[6] D-glucose,[7] D-ribonolactone,[8] or (*R*)-epichlorohydrin,[9] with only modest overall yields.[13] Ketyl radical cyclizations promoted by samarium diiodide are specially well-suited for this endeavor since they afford directly a functionalized cycloalkanol and proceed under mild conditions, usually in high yield and with a good level of stereocontrol.[14] The use of chiral polyoxygenated precursors, conveniently prepared from carbohydrates, could allow the facile preparation in this way of enantiomerically pure complex cyclitols such as **3**.[15] In 1995, we reported a short and stereose-

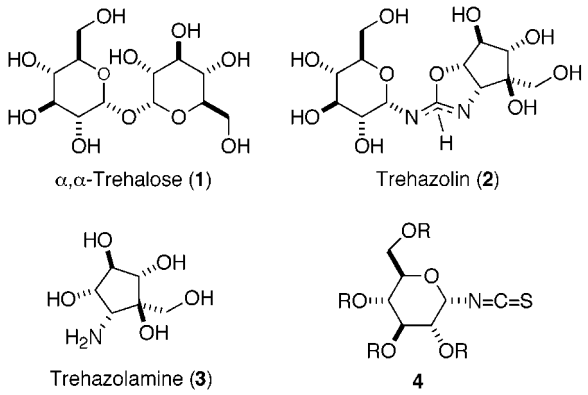

Figure 1.

* Corresponding author. Phone: +34-915622900. Fax: +34-915644853. E-mail: iqolc22@fresno.csic.es.

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(7) (a) Kobayashi, Y.; Miyazaki, H.; Shiozaki, M. *J. Am. Chem. Soc.* **1992**, *114*, 10065. (b) Kobayashi, Y.; Miyazaki, Shiozaki, M. *Tetrahedron Lett.* **1993**, *34*, 1505. (c) Kobayashi, Y.; Miyazaki, H.; Shiozaki, M. *J. Org. Chem.* **1994**, *59*, 813.

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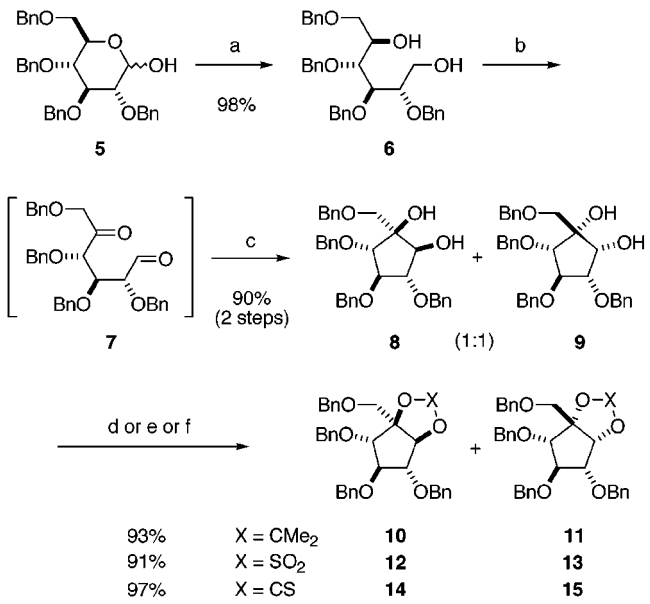
S0022-3263(98)00831-7 CCC: $15.00
Published on Web 07/30/1998

lective approach to different diastereoisomeric analogues of **3** following this approach. The key step was a highly efficient reductive carbocyclization of carbonyl-tethered oxime ethers prepared from readily available carbohydrate derivatives.[16] We now report a new, high-yielding synthesis of **3** starting from D-glucose via a very efficient pinacol coupling cyclization promoted by samarium diiodide.[17] This reducing agent has proven to be specially convenient at promoting intramolecular pinacol coupling reactions on polyoxygenated substrates under very mild conditions, in high yield, and with high diastereoselectivity.[18]

Results and Discussion

Our approach to **3** starts from hemiacetal **5** (Scheme 1), readily obtainable from D-glucose in two steps and commercially available.[19] Sodium borohydride reduction

Scheme 1[a]



[a] Reagents and conditions: (a) $NaBH_4$, $EtOH/CH_2Cl_2$ (1:1), rt; (b) (i) $(COCl)_2$, DMSO, THF, −65 °C, (ii) Et_3N, −65 °C to rt; (c) SmI_2, THF/*t*-BuOH, −50 °C to rt; (d) $(MeO)_2CMe_2$, Me_2CO, *p*-TsOH (cat.), rt; (e) (i) $SOCl_2$, Et_3N, CH_2Cl_2, 0 °C, (ii) $RuCl_3$ (cat.), $NaIO_4$, $MeCN/CCl_4/H_2O$ (1:1:1.5), rt; (f) 1,1′-thiocarbonyldiimidazole, toluene, 110 °C.

afforded D-glucitol derivative **6** quantitatively. We have shown previously[16,18c,e] that, for those carbocyclizations involving an aldehyde as pinacol partner, the yield of the cyclic product can be greatly improved if the oxidation and the reductive coupling steps are performed in a one-pot sequence avoiding the isolation of the intermediate dicarbonyl compound, which is usually rather unstable and prone to hydration. Thus, Swern oxidation of **6** in THF followed by dropwise addition of the crude reaction mixture of keto aldehyde **7** to a freshly prepared solution of SmI_2 in THF[20] containing *t*-BuOH at low temperature afforded a 1:1 mixture (determined by ^1H NMR analysis of the crude) of cyclic diols **8** and **9** in excellent yield.[21,22] Although this mixture could not be separated by column chromatography, we were able to get diol **8** pure by recrystallization from EtOAc/hexane. Both cyclic products were shown to have a cis relative stereochemistry at the two new stereocenters by their ready transformation into cyclic acetals **10** and **11**, cyclic sulfates **12** and **13**, or cyclic thionocarbonates **14** and **15** (Scheme 1), which were in each case readily separable by chromatography. The cis stereoselectivity obtained in this cyclization is in agreement with previous examples[18a−h,j−l]

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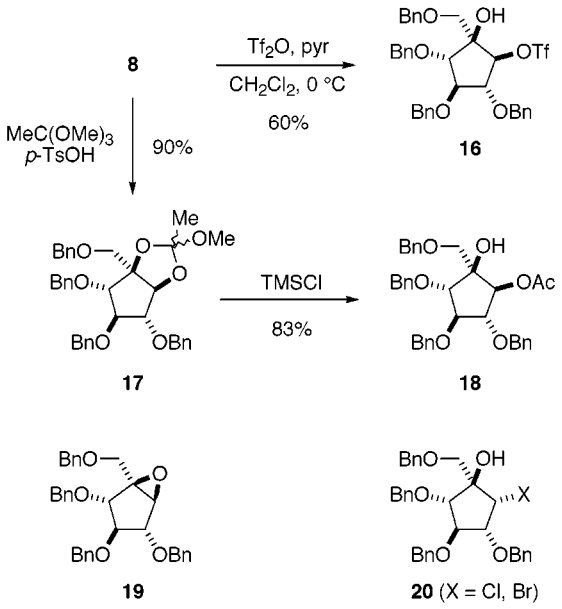
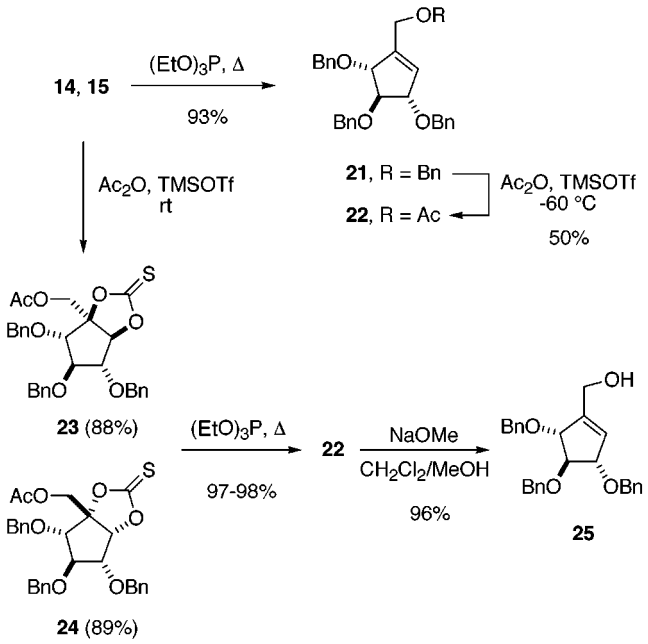
(21) This key transformation has been reported very recently and independently by us[17] and others (see also the preceding article in this issue: Boiron, A.; Zillig, P.; Faber, D.; Giese, B. *J. Org. Chem.* **1998**, *63*, 5877).[18l] The slightly different diastereoselectivity obtained in each case is probably a consequence of the different experimental procedures followed.

(22) Two very minor cyclopentanediols (**A**, 0.33%; **B**, 0.53% yield) could also be isolated by chromatography and characterized when the reaction was performed on gram scale (see Experimental Section). Neither of these compounds formed an isopropylidene acetal, showing that they are in fact the other two possible diastereoisomeric products, with trans relative stereochemistry at the new stereocenters (see Supporting Information for NOESY data).

Scheme 2



Scheme 3



of pinacol coupling reactions promoted by samarium diiodide, and it has been attributed to the chelated nature of the transition state involved.[18a,23] The complete stereochemistry of **8** and **9** was established by ^{1}H NMR and 2D NOESY studies (see the Supporting Information). Diol **8** has the correct stereochemistry of trehazolamine (**3**) at all except the stereocenter that should support the amino group. We expected to introduce this function via a nucleophilic displacement reaction. However, all attempts using cyclic sulfate **12** gave only elimination and decomposition products. The same result was obtained with monotriflate **16** (Scheme 2).[24] Steric shielding by the flanking benzyloxy and benzyloxymethyl groups probably impedes the attack of the nucleophile in the S_N2 trajectory. To circumvent these difficulties, we decided to use a reductive amination strategy. However, the different conditions tried to selectively oxidize the secondary alcohol[25] produced either keto aldehyde **7** (isolated as its cyclic monohydrated hemiacetal) or elimination and decomposition products. Since in other reported approaches[7,11b,e–g] to trehazolamine and analogues the amino group was introduced uneventfully via azide opening of an epoxide, we tried to transform diol **8** into the corresponding epoxide **19** of the same sterochemistry (Scheme 2). However, attempts to convert **8** directly into halohydrin **20** using $Me_2C(OAc)COX$ (X = Cl or Br)[26] gave monoacetate **18** and decomposition products. A similar result was obtained when Sharpless' procedure[27] was tried. Thus, treatment of cyclic ortho ester **17** (1:1 mixture of diastereoisomers) with TMSCl or AcCl produced again **18** instead of the expected chlorohydrin **20** (X = Cl).

In all these failed routes to trehazolamine, one-half of the pinacol coupling product (the "wrong" diastereoisomer **9**) was being discarded. A route where both diastereoisomeric diols, **8** and **9**, could be carried through to **3** was evidently highly desirable. With this objective, the mixture of cyclic thionocarbonates **14** and **15** was converted into the common elimination product **21** in very good yield by heating with triethyl phosphite[28] (Scheme 3). At this point we were prepared to install the requisite 1,2-amino alcohol functionality in a stepwise manner through stereoselective epoxidation of the double bond followed by regioselective epoxide opening with a nitrogen nucleophile. However, epoxidation of **21** with *m*-CPBA furnished an inseparable mixture of epoxides (ratio 1.6:1, determined by ^{1}H NMR analysis of the crude).[29] To overwhelm the modest diastereofacial preference exhibited by **21**, a reagent-control strategy, Sharpless epoxidation,[30] was in order. But prior to oxidation, a selective deprotection of the primary hydroxyl group of **21** was needed. This could be achieved via an acetolysis–methanolysis sequence. Treatment of **21** with TMSOTf in Ac_2O[31] at low temperature afforded monoacetate **22** in modest yield due to its instability under the reaction conditions. Other conditions tried did not improve this result.[32] However, the yield of monoacetate was doubled when the acetolysis was performed on the cyclic thionocarbonates **14** and **15** (Scheme 3). The monoacetates **23** and **24** obtained in this way were heated with triethyl phosphite,[28] giving **22** in excellent yield. Methanolysis of **22** under basic conditions afforded the allylic alcohol **25**. Sharpless epoxidation of **25** with diisopropyl L-tartrate, titanium tetraisopropoxide, and *tert*-butyl hydroperoxide yielded the desired epoxide **26** in very high yield (Scheme 4).[29,33] Using diisopropyl D-tartrate furnished the other epoxide **28** as a single diastereoisomer.[29]

(23) Molander, G. A.; Kenny, C. *J. Am. Chem. Soc.* **1989**, *111*, 8236.
(24) We used different conditions: NaN_3 or LiN_3 in DMF at room temperature to 125 °C, n-Bu_4NN_3 in DMF or toluene at room temperature to 125 °C.
(25) PCC produced an elimination product, Swern gave decomposition, Dess–Martin periodinane produced keto aldehyde **8**, and n-Bu_2SnO/Br_2 afforded only starting material.
(26) (a) Greenberg, S.; Moffatt, J. G. *J. Am. Chem. Soc.* **1973**, *95*, 4016. (b) Robins, M. J.; Hansske, F.; Low, N. H.; Park, J. I. *Tetrahedron Lett.* **1984**, *25*, 367.
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(28) Corey, E. J.; Winter, R. A. E. *J. Am. Chem. Soc.* **1963**, *85*, 2677.
(29) A similar result was obtained by Shiozaki et al.[7c] for the epoxidation of a closely related cyclopentene derivative.
(30) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974. For a recent review, see: Johnson, R. A.; Sharpless, K. B. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH Publishers: New York 1993; pp 103–158.
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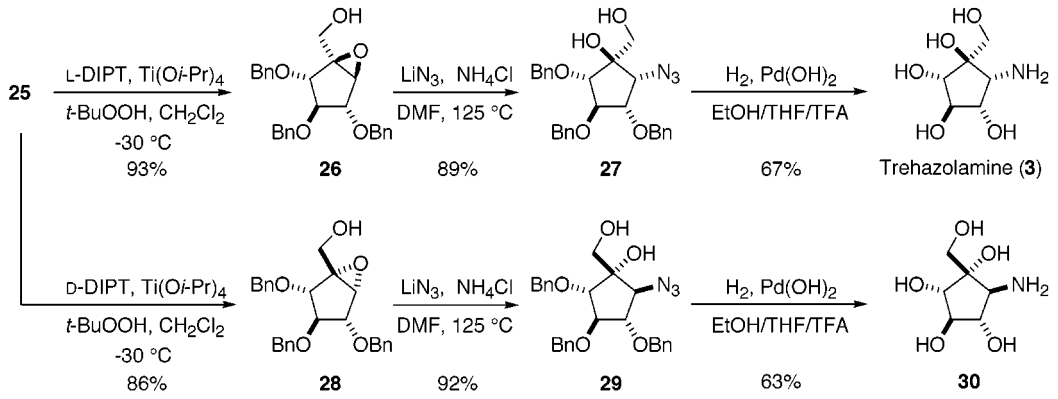
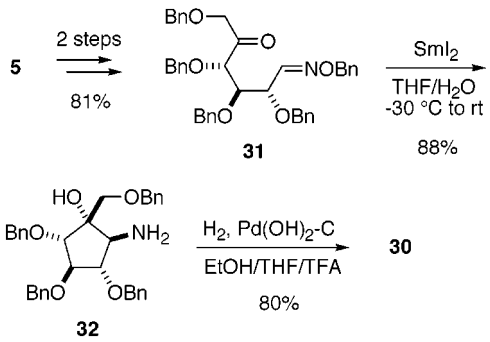
Scheme 4



Scheme 5



These stereochemical results are in agreement with Sharpless' empirical rule.[30] Opening of **26** with LiN_3/NH_4Cl[34] in DMF yielded azide **27** regioselectively and in high yield. Hydrogenolysis of **27** gave finally trehazolamine (**3**), whose physical and spectroscopic data were identical to those described for natural[5b] and synthetic[6a,7c] **3**. An analogous sequence produced trehazolamine diastereoisomer **30** from epoxide **28**. The described approach produces trehazolamine (**3**) in nine steps in an exceedingly good 39% overall yield from readily available D-glucose derivative **5**. The preparation of trehazolin (**1**) from aminocyclitol **3** has been already described in the literature.[6c,d,9]

A shorter, more direct route to **30** was also developed from D-glucose (Scheme 5). Reductive carbocyclization of readily available[15] keto oxime ether **31** using an excess of samarium diiodide, under conditions previously described by us,[16] took place with subsequent N−O reductive cleavage, affording directly the aminocyclopentitol **32** in an excellent overall yield. Hydrogenolysis of **32** afforded finally **30**. This route produced the unnatural trehazolamine analogue **30** in only four steps from **5** (six steps from D-glucose) and 57% overall yield.

Conclusion

The described synthesis of **3** and **30** demonstrate the general effectiveness of ketyl radical cyclizations promoted by samarium diiodide for the efficient preparation of densely functionalized cyclitols under very mild conditions and using readily available carbohydrate derivatives as starting materials. The one-pot sequence of Swern oxidation and reductive carbocyclization has proved to be very advantageous when the coupling involves an aldehyde, giving higher overall yields than the alternative two-step process.

Experimental Section

General. NMR sepctra were recorded at 200, 300, or 400 MHz (^{1}H frequency) and at 30 °C. Tetrahydrofuran (THF) was distilled under argon from sodium−benzophenone, and CH_2Cl_2 was distilled 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.[20] The reductive carbocyclizations were performed in the presence of the slight excess of samarium metal used in the preparation of the reagent.

2,3,4,6-Tetra-*O*-benzyl-D-glucitol (6). To a solution of 2,3,4,6-tetra-*O*-benzyl-D-glucopiranose[19] (5.84 g, 10.84 mmol) in EtOH/CH_2Cl_2 1:1 (59 mL) at room temperature was added $NaBH_4$ (1.64 g, 43.21 mmol). After completion of the reaction, 2 M HCl (30 mL) was slowly added, the phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (2 × 40 mL). The combined organic extracts were dried (Na_2SO_4) and the solvent was evaporated at reduced pressure. The residue was purified by flash chromatography (EtOAc/hexane 1:3), affording **6** (5.74 g, 98%) as a colorless oil. R_f = 0.37 (EtOAc/hexane 1:2); $[\alpha]^{22}_D$ +9.9 (*c* 1.5, $CHCl_3$);^{1}H NMR ($CDCl_3$) δ 7.41−7.27 (m, 20H), 4.79 (d, 1H, J = 11.3 Hz), 4.79 (d, 1H, J = 11.6 Hz), 4.71 (d, 1H, J = 11.3 Hz), 4.68 (d, 1H, J = 11.6 Hz), 4.67 (d, 1H, J = 11.3 Hz), 4.62 (d, 1H, J = 11.9 Hz), 4.60 (d, 1H, J = 11.3 Hz), 4.55 (d, 1H, J = 11.9 Hz), 4.13−4.06 (m, 1H), 3.96 (dd, 1H, J = 6.2, 3.6 Hz), 3.91−3.75 (m, 3H), 3.71−3.61 (m, 3H), 3.04 (d, 1H, J = 5.2 Hz), 2.25 (t, 1H, J = 6.3 Hz); ^{13}C NMR ($CDCl_3$) δ 142.2, 142.0, 141.8, 141.6, 132.4-l31.5 (20 C), 83.3, 82.9, 81.4, 81.2, 80.8, 80.2, 78.2, 74.9, 74.5, 65.6.

Cyclization of Compound 6 through a One-Pot Swern Oxidation−SmI_2 Reductive Coupling Process. Synthesis of [1*S*-(1α,2α,3*β*,4α,5*β*)]-3,4,5-tris(benzyloxy)-1-(benzyloxymethyl)-1,2-cyclopentanediol (8) and [1*R*-(1α,2α,3α,4*β*,5α)]-3,4,5-tris(benzyloxy)-1-(benzyloxymethyl)-1,2-cyclopentanediol (9). To a solution of $(COCl)_2$ (1.9 mL, 21.84 mmol) in THF (39 mL) at −65 °C was added dropwise a solution of DMSO (3.4 mL, 43.67 mmol) in THF (39 mL). After stirring for 15 min at −65 °C, a solution of **6** (3.95 g, 7.28 mmol) in THF (15 mL + 6 mL rinse) was added dropwise. After stirring at −65 °C for 45 min, Et_3N (10.2 mL, 72.79 mmol) was added dropwise and the reaction was stirred from −65 °C to room temperature for 1 h. The reaction mixture was diluted with THF (47 mL) and added dropwise to a freshly prepared 0.1 M solution of SmI_2 in THF (218 mL, 21.84 mmol) and *t*-BuOH (1.66 mL, 18.20 mmol) at −50 °C. After stirring at −50 °C for 3 h, the reaction was allowed to slowly attain room temperature overnight. Aqueous saturated $NaHCO_3$

(33) Traces (≤1%) of the other epoxide could be observed in the ^{1}H NMR of the crude reaction mixture.

(34) VanderWerf, C. A.; Heisler, R. Y.; McEwen, W. E. *J. Am. Chem. Soc.* **1954**, *76*, 1231.

(200 mL) was added to the reaction mixture and, after stirring for 30 min, the aqueous phase was extracted with EtOAc (4 × 150 mL). The combined organic extracts were washed with 10% aqueous $Na_2S_2O_3$ and dried over Na_2SO_4. The mixture was filtered and solvent was removed at reduced pressure. The crude was purified by flash chromatography (EtOAc/hexane 1:5), affording an inseparable 1:1 mixture of cis diols **8** and **9** (3.54 g, 90%), and the trans diols **A** (13 mg, 0.33%) and **B** (21 mg, 0.53%). A pure sample of **8** was obtained by fractional crystallization from EtOAc/hexane. **8**: white solid. $R_f = 0.18$ (EtOAc/hexane 1:3); mp 101−103 °C; $[\alpha]^{22}_D$ +1.85 (*c* 1.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.37−7.24 (m, 20H), 4.77 (d, 1H, *J* = 11.8 Hz), 4.63 (d, 1H, 11.8 Hz), 4.58−4.56 (m, 6H), 4.02 (t, 1H, *J* = 5.3 Hz), 3.97 (td, 1H, *J* = 5.8, 0.8 Hz), 3.88 (d, 1H, *J* = 4.5 Hz), 3.83 (td, 1H, *J* = 4.8, 0.7 Hz), 3.81 (d, 1H, *J* = 9.6 Hz), 3.66 (d, 1H, *J* = 9.6 Hz), 3.20 (s, 1H), 2.70 (d, 1H, *J* = 4.9 Hz); ^{13}C NMR ($CDCl_3$) δ 138.3, 138.1, 137.9, 137.5, 128.4−127.5 (20 C), 87.0, 85.8, 85.3, 78.5, 77.1, 73.8, 72.4, 72.0, 71.8, 71.7. Anal. Calcd for $C_{34}H_{36}O_6$: C, 75.53; H, 6.71. Found: C, 75.81; H, 6.80. **9** (as a mixture with **8**): $R_f = 0.18$ (EtOAc/hexane 1:3); ^{1}H NMR ($CDCl_3$) δ 7.39−7.24 (m, 20H), 4.73−4.47 (m, 8H), 4.14 (dd, 1H, *J* = 5.7, 4.8 Hz), 4.09 (t, 1H, *J* = 6.4 Hz), 3.90 (d, 1H, *J* = 6.0 Hz), 3.86 (dd, 1H, *J* = 6.0, 4.6 Hz), 3.47 (d, 1H, *J* = 9.4 Hz), 3.41 (d, 1H, *J* = 9.5 Hz), 3.11 (s, 1H), 2.94 (d, 1H, *J* = 7.4 Hz); ^{13}C NMR ($CDCl_3$) δ 138.2, 138.0, 137.9, 137.7, 128.5−126.9 (20C), 87.6, 81.6, 81.2, 77.3, 73.5, 73.1, 72.7, 72.2, 71.4, 70.5. **A**: $R_f = 0.28$ (EtOAc/hexane 1:3); ^{1}H NMR ($CDCl_3$) δ 7.37−7.23 (m, 20H), 4.67 (d, 1H, *J* = 11.6 Hz), 4.62−4.54 (m, 6H), 4.53 (d, 1H, *J* = 11.8 Hz), 4.15 (t, 1H, *J* = 4.9 Hz), 4.07 (dd, 1H, *J* = 5.2, 4.1 Hz), 4.01 (td, 1H, *J* = 5.1, 1.1 Hz), 3.95 (d, 1H, *J* = 9.6 Hz), 3.81 (dd, 1H, *J* = 4.1, 1.1 Hz), 3.80 (d, 1H, *J* = 9.6 Hz), 2.95 (s, 1H), 2.80 (d, 1H, *J* = 5.1 Hz); ^{13}C NMR ($CDCl_3$) δ 138.1, 138.0, 137.81, 137.76, 128.5−127.7 (20 C), 88.0, 87.6, 83.2, 80.4, 75.9, 73.8, 72.6, 72.3, 71.9, 70.4. **B**: $R_f = 0.17$ (EtOAc/hexane 1:3); ^{1}H NMR ($CDCl_3$) δ 7.40−7.24 (m, 20H), 4.81−4.43 (m, 8H), 4.10−4.05 (m, 2H), 3.91 (d, 1H, *J* = 7.1 Hz), 3.75 (t, 1H, *J* = 6.6 Hz), 3.57 (d, 1H, *J* = 9.8 Hz), 3.49 (d, 1H, *J* = 9.8 Hz), 3.04 (d, 1H, *J* = 5.6 Hz), 2.99 (s, 1H).

Synthesis of Acetals 10 and 11. To a solution of **8** and **9** (10 mg, 0.018 mmol) in acetone (0.5 mL) and 2,2-dimethoxypropane (0.5 mL) was added a catalytic amount of PPTS. The mixture was stirred at room temperature for 3 h. After adding Et_3N (250 μL), the solvent was removed at reduced pressure and the residue was purified by flash chromatography (EtOAc/hexane 1:8) to afford **10** (4.5 mg, 43%) and **11** (5.2 mg, 50%). **10**: $R_f = 0.53$ (EtOAc/hexane 1:2); ^{1}H NMR ($CDCl_3$) δ 7.37−7.25 (m, 20H), 4.81−4.52 (m, 9H), 4.11 (dd, 1H, *J* = 9.7, 6.6 Hz), 4.02 (dd, 1H, *J* = 9.4, 0.8 Hz), 3.94 (ddd, 1H, *J* = 6.6, 2.5, 0.8 Hz), 3.73 (s, 2H), 1.48 (s, 3H), 1.40 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 138.6, 138.2, 138.1, 138.0, 128.3−127.1 (20 C), 113.1, 88.2, 87.5, 86.6, 85.1, 83.5, 73.7, 72.9, 72.7, 71.7, 69.7, 28.4, 26.8. **11**: $R_f = 0.45$ (EtOAc/hexane 1:2); ^{1}H NMR ($CDCl_3$) δ 7.37−7.17 (m, 20H), 4.84−4.41 (m, 8H), 4.36 (dd, 1H, *J* = 4.2 Hz), 4.30 (dd, 1H, *J* = 9.0, 7.8 Hz), 3.69 (d, 1H, *J* = 7.8 Hz), 3.66 (dd, 1H, *J* = 9.0, 4.2 Hz), 3.47 (d, 1H, *J* = 9.4 Hz), 3.42 (d, 1H, *J* = 9.4 Hz), 1.38 (s, 3H), 1.26 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 138.7, 138.6, 138.2, 137.7, 128.4−127.4 (20 C), 112.2, 86.4, 84.3, 80.2, 79.7, 78.8, 73.6, 73.1, 72.8, 72.3, 72.0, 26.8, 26.7.

Synthesis of Cyclic Sulfates 12 and 13. To a solution of **8** (33 mg, 0.06 mmol) in CH_2Cl_2 (0.5 mL) at 0 °C were added Et_3N (34 μL, 0.24 mmol) and $SOCl_2$ (7 μL, 0.09 mmol) at 0 °C. After stirring at 0 °C for 20 min, the reaction was diluted with Et_2O and extracted twice with water. The combined organic phases were dried over $MgSO_4$ and filtered, and the solvent was removed at reduced pressure. The residue was dissolved in $CCl_4/CH_3CN/H_2O$ 1:1:1.5 (0.7 mL) and cooled to 0 °C. $NaIO_4$ (26 mg, 0.12 mmol) and a catalytic amount of $RuCl_3 \cdot H_2O$ were added, and the solution was stirred vigorously for 30 min at 0 °C. The reaction was diluted with Et_2O, and the organic layer was washed with brine, concentrated, and filtered through silica. The solvent was removed at reduced pressure to afford **12** (33 mg, 91%). Following the same procedure for the mixture of diols **8** and **9**, both sulfates **12** and **13** were obtained in similar yields and could be easily separated by flash chromatography (EtOAc/hexane 1:10). **12**: colorless oil; $R_f =$ 0.46 (EtOAc/hexane 1:3); ^{1}H NMR ($CDCl_3$) δ 7.38−7.25 (m, 20H), 5.09 (d, 1H, *J* = 4.7 Hz), 4.75−4.56 (m, 8H), 4.37 (d, 1H, *J* = 9.4 Hz), 4.23 (dd, 1H, *J* = 8.2, 4.7 Hz), 3.97 (dd, 1H, *J* = 9.4, 8.2 Hz), 3.81 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 137.7, 136.9, 136.8, 136.7, 128.5−127.6 (20 C), 91.4, 85.9, 84.7, 82.6, 82.0, 73.9, 73.8, 73.2, 72.5, 67.6; **13**: colorless oil; $R_f = 0.35$ (EtOAc/hexane 1:3); ^{1}H NMR ($CDCl_3$) δ 7.40−7.29 (m, 18H), 7.20−7.16 (m, 2H), 4.89 (d, 1H, *J* = 4.8 Hz), 4.85 (d, 1H, *J* = 11.5 Hz), 4.75 (d, 1H, *J* = 11.5 Hz), 4.73−4.55 (m, 4H), 4.42 (t, 1H, *J* = 9.0 Hz), 4.42 (d, 1H, *J* = 11.7 Hz), 4.33 (d, 1H, *J* = 11.7 Hz), 3.94 (d, 1H, *J* = 8.8 Hz), 3.79 (dd, 1H, *J* = 9.3, 4.8 Hz), 3.67 (d, 1H, *J* = 9.4 Hz), 3.49 (d, 1H, *J* = 9.4 Hz); ^{13}C NMR ($CDCl_3$) δ 138.0, 137.4, 136.9, 136.5, 128.6−127.8 (20 C), 88.0, 84.4, 81.2, 78.0, 77.9, 73.9 (2C), 73.5, 72.6, 68.8.

Synthesis of Cyclic Thionocarbonates 14 and 15. A solution of the 1:1 mixture of **8** and **9** (612 mg, 1.13 mmol) and 1,1′-thiocarbonyldiimidazole (303 mg, 1.70 mmol) in toluene (7.2 mL) was heated at reflux for 4 h. After removal of the solvent at reduced pressure, the crude product was purified by flash column chromatography (EtOAc/hexane 1:6), to afford **14** (296 mg, 45%) and **15** (342 mg, 52%). **14**: colorless oil. $R_f = 0.45$ (EtOAc/hexane 1:4); $[\alpha]^{22}_D$ −3.1 (*c* 1.0, $CHCl_3$); IR (film) 2880, 1455, 1320, 1100, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.39−7.27 (m, 20H), 5.08 (d, 1H, *J* = 4.5 Hz), 4.78−4.56 (m, 8H), 4.20 (d, 1H, *J* = 8.4 Hz), 4.09 (dd, 1H, *J* = 7.6, 4.5 Hz), 3.95 (t, 1H, *J* = 8.4 Hz), 3.86 (d, 1H, *J* = 11.7 Hz), 3.76 (d, 1H, *J* = 11.7 Hz); ^{13}C NMR ($CDCl_3$) δ 190.4, 137.6, 136.9, 136.7 (2 C), 128.5−127.6 (20 C), 93.9, 87.5, 85.1, 83.6, 82.8, 73.8 (2 C), 73.0, 72.4, 67.7. Anal. Calcd for $C_{35}H_{34}O_6S$: C, 72.14; H, 5.88. Found: C, 72.54; H, 6.01. **15**: white solid. $R_f = 0.28$ (EtOAc/hexane 1:4); mp 79−81 °C; $[\alpha]^{22}_D$ +46.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.38−7.26 (m, 18H), 7.22−7.19 (m, 2H), 4.91 (d, 1H, *J* = 5.4 Hz), 4.82 (d, 1H, *J* = 11.5 Hz), 4.76 (d, 1H, *J* = 11.7 Hz), 4.72 (d, 1H, *J* = 12.0 Hz), 4.71 (d, 1H, *J* = 11.5 Hz), 4.65 (d, 1H, *J* = 12.0 Hz), 4.55 (d, 1H, *J* = 11.7 Hz), 4.45 (d, 1H, *J* = 11.8 Hz), 4.38 (d, 1H, *J* = 11.8 Hz), 4.21 (t, 1H, *J* = 8.8 Hz), 3.86 (d, 1H, *J* = 8.7 Hz), 3.79 (dd, 1H, *J* = 8.8, 8.7 Hz), 3.55 (d, 1H, *J* = 10.1 Hz), 3.43 (d, 1H, *J* = 10.1 Hz); ^{13}C NMR ($CDCl_3$) δ 190.6, 137.9, 137.3, 137.0, 136.6, 128.6−127.7 (20 C), 91.2, 84.5, 81.9, 79.1, 78.3, 73.7, 73.6, 73.3, 72.3, 68.4. Anal. Calcd for $C_{35}H_{34}O_6S$: C, 72.14; H, 5.88. Found: C, 72.20; H, 5.93.

[3*S*-(3α,4*β*,5α)]-3,4,5-Tris(benzyloxy)-1-(benzyloxymethyl)-1-cyclopentene (21). A solution of **14** (280 mg, 0.48 mmol) in $(EtO)_3P$ (5 mL) was heated at 155 °C for 2 h. The solvent was removed at reduced pressure and the residue was purified by flash column chromatography (EtOAc/hexane 1:10) to afford **21** (226 mg, 93%) as a colorless oil. Following this procedure, compound **15** afforded **21** in similar yield: $R_f = 0.50$ (EtOAc/hexane 1:3); $[\alpha]^{22}_D$ +37.5 (*c* 1.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.42−7.31 (m, 20H), 5.98−5.97 (m, 1H), 4.73 (d, 1H, *J* = 11.7 Hz), 4.71 (d, 1H, *J* = 9.4 Hz), 4.67 (d, 1H, *J* = 9.1 Hz), 4.66 (d, 1H, *J* = 11.8 Hz), 4.64 (d, 1H, *J* = 9.5 Hz), 4.62 (d, 1H, *J* = 11.8 Hz), 4.61 (d, 1H, *J* = 11.8 Hz), 4.24 (d, 1H, *J* = 11.8 Hz), 4.54−4.53 (m, 1H), 4.30 (t, 1H, *J* = 3.8 Hz), 4.19−4.18 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 143.2, 138.4, 138.3, 138.1, 138.0, 128.3−127.2 (21 C), 91.4, 85.5, 85.2, 72.6, 71.9, 71.6, 70.8, 66.5. Anal. Calcd for $C_{34}H_{34}O_4$: C, 80.60; H, 6.76. Found: C, 80.74; H, 6.94.

Synthesis of Thionocarbonate 23 by Acetolysis of 14. To a solution of **14** (30 mg, 0.05 mmol) in acetic anhydride (0.5 mL) was added TMSOTf (27 μL, 0.15 mmol). After stirring for 17 h at room temperature, the mixture was diluted with CH_2Cl_2 (2 mL), and aqueous saturated $NaHCO_3$ (2 mL) was cautiously added. After stirring for 30 min, the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL), and the combined organic phases were dried over Na_2SO_4 and concentrated at reduced pressure. The residue was purified by flash column chromatography (CH_2Cl_2/hexane 1:1), affording unreacted **14** (12 mg) and **23** (17 mg, 58%; 88% based on recovered **14**). **23** crystallized from ether/hexane as a white solid: $R_f = 0.52$ (EtOAc/hexane 1:3); mp 72−73 °C; $[\alpha]^{22}_D$ +4.89 (*c* 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.39−7.28 (m, 15H), 4.96 (d, 1H, *J* = 4.1 Hz), 4.78−4.60 (m, 6H), 4.59 (d, 1H, *J* = 13.2 Hz), 4.36 (d, 1H,

J = 13.2 Hz), 4.25 (d, 1H, J = 7.5 Hz), 4.11 (dd, 1H, J = 7.0, 4.1 Hz), 3.98 (dd, 1H, J = 7.5, 7.0 Hz), 2.11 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 189.6, 169.8, 137.2, 136.5, 136.3, 128.5−127.7 (15 C), 93.0, 87.7, 84.7, 83.4, 82.4, 73.7, 72.9, 72.4, 62.2, 20.4. Anal. Calcd for $C_{30}H_{30}O_7S$: C, 67.40; H, 5.66. Found: C, 67.65; H, 5.71.

Synthesis of Thionocarbonate 24 by Acetolysis of 15. Following the same procedure as for **23**, compound **24** was obtained from **15** in 61% yield (89% based on recovered **15**) as a white solid: R_f = 0.24 (EtOAc/hexane 1:3); mp 158−160 °C; $[\alpha]^{22}_D$ +47.0 (*c* 0.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.36−7.29 (m, 15H), 4.89 (d, 1H, J = 5.6 Hz), 4.81 (d, 1H, J = 11.5 Hz), 4.78 (d, 1H, J = 11.7 Hz), 4.73 (m, 2H), 4.69 (d, 1H, J = 11.5 Hz), 4.54 (d, 1H, J = 11.7 Hz), 4.30 (d, 1H, J = 12.4 Hz), 4.22 (d, 1H, J = 8.3 Hz), 4.04 (d, 1H, J = 12.4 Hz), 3.82 (dd, 1H, J = 8.3, 5.6 Hz), 3.73 (d, 1H, J = 8.3 Hz), 2.03 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 190.0, 169.3, 137.4, 136.64, 136.57, 128.3−127.2 (15 C), 90.7, 84.0, 81.0, 78.5, 78.2, 73.0, 72.9, 71.9, 62.5, 19.9. Anal. Calcd for $C_{30}H_{30}O_7S$: C, 67.40; H, 5.66. Found: C, 67.02; H, 5.66.

[3*S*-(3α,4*β*,5α)]-1-(Acetoxymethyl)-3,4,5-tris(benzyloxy)-1-cyclopentene (22). From 23. A solution of **23** (168 mg, 0.32 mmol) in $(EtO)_3P$ (3.2 mL) was heated at 155 °C for 3 h. The solvent was removed at reduced pressure and the residue was purified by flash column chromatography (EtOAc/hexane 1:10) to afford **22** (140 mg, 97%) as a colorless oil.

From 24. A solution of **24** (406 mg, 0.76 mmol) in $(EtO)_3P$ (7.7 mL) was heated at 155 °C for 2 h. The solvent was removed at reduced pressure and the residue was purified by flash column chromatography (EtOAc/hexane 1:10) to afford **22** (342 mg, 98%) as a colorless oil.

By Acetolysis of 21. To a solution of **21** (20 mg, 0.04 mmol) in Ac_2O (1 mL) at −60 °C was added TMSOTf (8 μL, 0.04 mmol). After stirring at −60 °C for 1 h, the reaction mixture was diluted with CH_2Cl_2 (15 mL) and aqueous saturated $NaHCO_3$ was carefully added. The aqueous layer was extracted with CH_2Cl_2 (2 × 30 mL), and the combined organic extracts were dried over Na_2SO_4, filtered, and evaporated. The residue was coevaporated with toluene and purified by flash chromatography (EtOAc/hexane 1:10) to afford unreacted **21** (3 mg) and **22** (9 mg, 50%; 58% based on recovered **21**) as a colorless oil: **22**: R_f = 0.31 (EtOAc/hexane 1:4); $[\alpha]^{22}_D$ +44.0 (*c* 1.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.37−7.29 (m, 15H), 5.90 (m, 1H), 4.75−4.55 (m, 8H), 4.75−4.45 (m, 2H), 4.26 (t, 1H, J = 3.8 Hz), 2.04 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 170.5, 141.0, 138.2 (2 C), 138.1, 128.4−127.7 (16 C), 91.3, 85.4, 85.3, 72.0, 71.6, 71.0, 60.5, 20.8.

[3*S*-(3α,4*β*,5α)]-3,4,5-Tris(benzyloxy)-1-(hydroxymethyl)-1-cyclopentene (25). A solution of **22** (27 mg, 0.06 mmol) in CH_2Cl_2/MeOH 1:1 (2 mL) was treated with a few drops of a freshly prepared solution of NaOMe in MeOH. After stirring for 1 h at room temperature, Amberlite IR-120 (H^+ type) was added and the reaction mixture was stirred for 10 min. The mixture was filtered, the solvent was evaporated at reduced pressure, and the residue was purified by flash column chromatography (EtOAc/hexane 1:3) to afford **25** (24 mg, 96%) as a white solid: R_f = 0.14 (EtOAc/hexane 1:3); mp 78−80 °C; $[\alpha]^{22}_D$ +46.5 (*c* 1.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.36−7.28 (m, 15H), 5.87 (m, 1H), 4.70 (d, 1H, J = 11.6 Hz), 4.69 (d, 1H, J = 11.8 Hz), 4.63 (d, 1H, J = 11.7 Hz), 4.63 (d, 1H, J = 11.7 Hz), 4.59 (d, 1H, J = 11.7 Hz), 4.56 (d, 1H, J = 11.7 Hz), 4.50 (m, 2H), 4.28 (dd, 1H, J = 14.1, 4.6 Hz), 4.25 (t, 1H, J = 3.8 Hz), 4.19 (dd, 1H, J = 14.1, 7.1 Hz), 1.92 (dd, 1H, J = 7.1, 4.6 Hz); ^{13}C NMR ($CDCl_3$) δ 145.1, 138.3, 138.1 (2 C), 128.4−127.8 (15 C), 126.2, 91.6, 86.0, 85.5, 72.0, 71.8, 71.0, 60.3. Anal. Calcd for $C_{27}H_{28}O_4$: C, 77.86; H, 6.78. Found: C, 78.13; H, 6.85.

[1*R*-(1α,2α,3*β*,4α,5α)]-2,3,4-Tris(benzyloxy)-1-(hydroxymethyl)-6-oxabicyclo[3.1.0]hexane (26). To a solution of diisopropyl L-tartrate (235 mg, 1.0 mmol) in CH_2Cl_2 (11 mL) at −30 °C was added $Ti(O^iPr)_4$ (295 μL, 1.0 mmol). After stirring for 20 min at −30 °C, a solution of **25** (287 mg, 0.69 mmol) in CH_2Cl_2 (19 mL) was added dropwise. After 20 min, *t*-BuOOH (5.5 M in decane, 251 μL, 1.38 mmol) was added and the stirring continued at −30 °C for 20 h. The reaction mixture was diluted with Et_2O (20 mL) and a solution of NaOH (3 g) in brine (30 mL) was added. After stirring for 15 min, the aqueous phase was extracted with Et_2O (2 × 20 mL), and the combined organic phases were washed with brine. The aqueous brine layer was extracted with EtOAc (2 × 20 mL), and the combined organic phases were dried over $MgSO_4$ and concentrated at reduced pressure. The residue was purified by flash column chromatography (EtOAc/hexane 1:3) affording epoxide **26** (278 mg, 93%). **26** crystallized from Et_2O as a white solid: R_f = 0.20 (EtOAc/hexane 1:2); mp 73−74 °C; $[\alpha]^{22}_D$ +25.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.37−7.27 (m, 15H), 4.57 (d, 1H, J = 12.0 Hz), 4.55 (s, 2H), 4.46 (d, 1H, J = 12.0 Hz), 4.44 (d, 1H, J = 12.3 Hz), 4.37 (d, 1H, J = 12.3 Hz), 4.08 (dd, 1H, J = 12.7, 7.0 Hz), 3.99 (t, 1H, J = 1.2 Hz), 3.96 (d, 1H, J = 1.1 Hz), 3.95 (m, 1H), 3.87 (dd, 1H, J = 12.7, 6.2 Hz), 3.63 (s, 1H), 1.85 (t, 1H, J = 6.7 Hz); ^{13}C NMR ($CDCl_3$) δ 137.6 (3C), 128.4−127.8 (15 C), 89.7, 82.3, 82.0, 72.0 (2 C), 71.6, 68.4, 61.8, 59.5. Anal. Calcd for $C_{27}H_{28}O_5$: C, 74.98; H, 6.52. Found: C, 74.86; H, 6.44.

[1*S*-(1α,2*β*,3α,4*β*,5α)]-2,3,4-Tris(benzyloxy)-1-(hydroxymethyl)-6-oxabicyclo[3.1.0]hexane (28). Following the same procedure as for **26** but using diisopropyl D-tartrate, epoxide **28** was obtained from **25** in 86% yield as a white solid. R_f = 0.23 (EtOAc/hexane 1:1); mp 141−143 °C; $[\alpha]^{22}_D$ +41.3 (*c* 0.5, $CHCl_3$); ^{1}H NMR (C_6D_6) δ 7.32−7.24 (m, 5H), 7.21−7.07 (m, 10H), 4.70 (d, 1H, J = 11.8 Hz), 4.68 (d, 1H, J = 12.0 Hz), 4.56 (d, 1H, J = 12.0 Hz), 4.53 (d, 1H, J = 11.8 Hz), 4.52 (d, 1H, J = 12.0 Hz), 4.37 (d, 1H, J = 12.0 Hz), 4.18 (t, 1H, J = 5.8 Hz), 3.89 (d, 1H, J = 5.8 Hz), 3.62 (dd, 1H, J = 5.8, 1.3 Hz), 3.58 (m, 2H), 3.23 (d, 1H, J = 1.3 Hz); ^{13}C NMR ($CDCl_3$) δ 138.2, 138.0, 137.8, 128.5−127.7 (15 C), 84.0, 81.5, 80.7, 72.5, 72.0, 71.3, 64.3, 59.3, 56.7. Anal. Calcd for $C_{27}H_{28}O_5$: C, 74.98; H, 6.52. Found: C, 74.58; H, 6.52.

[1*R*-(1α,2*β*,3α,4*β*,5*β*)]-5-Azido-2,3,4-tris(benzyloxy)-1-(hydroxymethyl)-1-cyclopentanol (27). To a solution of **26** (50 mg, 0.11 mmol) in DMF (2 mL) were added lithium azide (68 mg, 1.39 mmol) and NH_4Cl (74 mg, 1.39 mmol), and this mixture was stirred at 100 °C for 5 days. After disappearance of **26** (TLC toluene/acetone 8:1), DMF was evaporated at reduced pressure. The residue was dissolved in EtOAc (10 mL) and washed with water (3 mL), and the aqueous phase was extracted twice with EtOAc. The combined organic phases were dried over Na_2SO_4 and filtered, and the solvent was removed at reduced pressure. The residue was purified by flash column chromatography (EtOAc/hexane 1:3), affording azide **27** (48 mg, 89%) as a colorless oil: R_f = 0.23 (acetone/toluene 1:8); $[\alpha]^{22}_D$ −12.0 (*c* 0.6, $CHCl_3$); IR (KBr) 3440, 2100, 1080 cm^{-1}; ^{1}H NMR (C_6D_6) δ 7.30−7.03 (m, 15H), 4.49 (d, 2H, J = 11.7 Hz), 4.42 (d, 1H, J = 11.2 Hz), 4.39 (d, 1H, J = 11.5 Hz), 4.36 (d, 1H, J = 11.8 Hz), 4.26 (d, 1H, J = 11.7 Hz), 4.09 (t, 1H, J = 5.2 Hz), 3.98 (t, 1H, J = 5.5 Hz), 3.92 (d, 1H, J = 11.7 Hz), 3.84 (d, 1H, J = 5.8 Hz), 3.83 (d, 1H, J = 11.7 Hz), 3.58 (dd, 1H, J = 5.6, 0.6 Hz), 3.20 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 137.7, 137.5, 137.4, 128.7−127.6 (15 C), 88.8, 87.0, 81.0, 80.1, 72.8 (2 C), 72.1, 66.1, 63.2.

[1*S*-(1α,2α,3*β*,4α,5*β*)]-5-Azido-2,3,4-tris(benzyloxy)-1-(hydroxymethyl)-1-cyclopentanol (29). To a solution of **28** (24 mg, 0.055 mmol) in DMF (1 mL) were added lithium azide (33 mg, 0.66 mmol) and NH_4Cl (36 mg, 0.66 mmol), and this mixture was stirred at 125 °C overnight. DMF was evaporated at reduced pressure and the residue was dissolved in EtOAc (10 mL) and washed with water (3 mL), and the aqueous phase was extracted twice with EtOAc. The combined organic phases were dried over Na_2SO_4 and filtered, and the solvent was removed at reduced pressure. The residue was purified by flash column chromatography (EtOAc/hexane 1:3) affording azide **29** (24 mg, 92%) as a white solid: R_f = 0.38 (EtOAc/hexane 1:1); mp 55−57 °C; $[\alpha]^{22}_D$ +48.7 (*c* 0.5, $CHCl_3$); IR ($CHCl_3$) 3540, 2120, 1070, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.40−7.25 (m, 15H), 4.71 (d, 1H, J = 11.7 Hz), 4.71 (d, 1H, J = 11.8 Hz), 4.63 (d, 1H, J = 11.7 Hz), 4.60 (d, 1H, J = 11.8 Hz), 4.60 (d, 1H, J = 11.7 Hz), 4.54 (d, 1H, J = 11.7 Hz), 3.98 (dd, 1H, J = 5.6, 4.2 Hz), 3.94 (d, 1H, J = 7.4 Hz), 3.86 (d, 1H, J = 4.2 Hz), 3.74 (dd, 1H, J = 12.0, 5.4 Hz), 3.73 (ddd, 1H, J = 7.4, 5.6, 0.7 Hz), 3.50 (ddd, 1H, J = 12.0, 8.0, 0.7 Hz), 3.27 (s, 1H), 2.06 (dd, 1H, J = 8.0, 5.4 Hz); ^{13}C NMR ($CDCl_3$) δ 137.7, 137.5,

137.4, 128.7−127.6 (15 C), 88.8, 87.0, 81.0, 80.1, 72.8 (2 C), 72.1, 66.1, 63.2.

[1*R*-(1α,2*β*,3α,4*β*,5*β*)]-5-Amino-1-(hydroxymethyl)-1,2,3,4-cyclopentanetetrol (Trehazolamine) (3). To a solution of **27** (38 mg, 0.08 mmol) in EtOH/THF 3:1 (4 mL) were added TFA (31 μL, 0.40 mmol) and 25% $Pd(OH)_2$ on charcoal (135 mg). This mixture was stirred under H_2 (2 atm) at room temperature overnight. The reaction mixture was filtered through Celite and the filter was washed with MeOH (4 × 50 mL) and water (50 mL). The solvent was removed at reduced pressure and the residue was purified by column chromatography on Amberlite CG-50 (NH_4^+ type). Elution with 0.5 M aqueous NH_3 afforded **3** (10 mg, 67%) as a white solid after freeze-drying: R_f = 0.53 (CH_3CN/AcOH/H_2O 6:1:3); $[\alpha]^{22}_D$ +2.0 (*c* 0.6, H_2O); ^{1}H NMR (D_2O) δ 4.06 (dd, 1H, *J* = 6.8, 5.7 Hz), 3.95 (dd, 1H, *J* = 6.6, 5.7 Hz), 3.78 (d, 1H, *J* = 6.6 Hz), 3.78 (d, 1H, *J* = 11.9 Hz), 3.72 (d, 1H, *J* = 11.9 Hz), 3.25 (d, 1H, *J* = 6.8 Hz); ^{13}C NMR (D_2O) δ 82.2, 81.9, 79.7, 73.7, 61.9, 58.5.

[1*S*-(1α,2α,3*β*,4α,5*β*)]-1-Amino-3,4,5-tris(benxyloxy)-1-(benzyloxymethyl)-1-cyclopentanol (32). To a freshly prepared 0.1 M solution of SmI_2 in THF (31 mL, 3.13 mmol) and *t*-BuOH (250 μL, 2.61 mmol) at −30 °C was added dropwise a solution of **31**[16] (336 mg, 0.52 mmol) in THF (21 mL). After stirring for 1 h at −30 °C, the cooling bath was removed, the reaction mixture was allowed to attain room temperature. Water (282 μL, 15.66 mmol) was added and stirring continued for 1 h. The reaction mixture was diluted with EtOAc (50 mL) and aqueous saturated $NaHCO_3$ (100 mL) was added. The phases were separated, and the aqueous phase was extracted with EtOAc (3 × 50 mL). The combined organic extracts were washed with brine and dried over Na_2SO_4. The mixture was filtered and the solvent was removed at reduced pressure. The crude was purified by flash chromatography (CH_2Cl_2/MeOH 60:1), affording **32** (250 mg, 88%). Amino alcohol **32** was recrystallized from *i*-PrOH as a white solid: R_f = 0.55 (CH_2Cl_2 /MeOH 10:1); mp 105 °C; $[\alpha]^{22}_D$ +3.6 (*c* 0.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.36−7.27 (m, 20H), 4.72 (s, 2H), 4.69 (d, 1H, 11.6 Hz), 4.62 (d, 1H, 11.6 Hz), 4.61 (s, 2H), 4.52 (s, 2H), 4.02 (dd, 1H, *J* = 6.1, 5.8 Hz), 3.94 (d, 1H, *J* = 5.8 Hz), 3.55 (dd, 1H, *J* = 7.9, 6.1 Hz), 3.54 (d, 1H, *J* = 9.8 Hz), 3.47 (d, 1H, *J* = 9.8 Hz), 3.27 (d, 1H, *J* = 7.9 Hz), 3.00 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 138.4, 138.2, 137.8, 137.7, 128.3−127.6 (20 C), 86.5 (2C), 81.8, 77.1, 73.6, 73.2, 72.4, 72.3, 71.9, 63.1.

[1*S*-(1α,2α,3*β*,4α,5*β*)]-5-Amino-1-(hydroxymethyl)-1,2,3,4-cyclopentanetetrol (30). Following the same procedure as for **3**, its diastereoisomer **30** was obtained from **29** or **32** in 63% and 80% yield, respectively, as a white solid: R_f = 0.37 (CH_3CN/AcOH/H_2O 6:1:3); mp 121−123 °C; $[\alpha]^{22}_D$ +2.3 (*c* 1.2, H_2O); ^{1}H NMR (D_2O) δ 3.81 (dd, 1H, *J* = 8.6, 8.4 Hz), 3.66 (d, 1H, *J* = 8.6 Hz), 3.63 (s, 2H), 3.53 (dd, 1H, *J* = 8.5, 8.4 Hz), 3.06 (d, 1H, *J* = 8.5 Hz); ^{13}C NMR (D_2O) δ 79.8, 79.3, 77.3, 75.6, 64.7, 64.4.

Acknowledgment. This work was supported by grants PB-93-0127-C02-01 and PB-96-0833 from DGES, Ministerio de Educación y Cultura of Spain.

Supporting Information Available: Experimental procedures and characterization data for compounds **16**−**18**, and ^{1}H NOE data for compounds **12**, **13**, and *trans*-diols **A** and **B** (3 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 information.

JO980831B