Syntheses of Trehazolin, Trehalamine, and the Aminocyclitol Moiety of Trehazolin: Determination of Absolute Configuration of Trehazolin

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The syntheses and determination of the absolute configurations of trehazolin (1), its aglycon (trehalamine (3)), and its aminocyclitol hexaacetate moiety (5) are described. An important intermediate, optically active epoxide 16α, was obtained from an 11-step synthesis starting from D-glucose. The route has [3 + 2] cycloaddition and Sharpless epoxidation reactions as the key steps. Trehazolin and trehalamine were subsequently synthesized from 16α, utilizing 2-chloro-3-ethylbenzoxazolium tetrafluoroborate to construct aminooxazoline frameworks via the carbodiimide derivatives 30 and 27 derived from thioureas 29 and 26, respectively. The absolute configurations of the trehazolin aglycon and aminocyclitol moieties were determined to be [3a*R*-(3aα,4α,5β,6α,6aα)] and [1*R*-(1α,2β,3α,4β,5β)], respectively. Alternatively, the synthesis of trehazolin could be completed through nonprotected aminocyclitol 32, which was obtainable from deprotection of compound 5 or degradation of natural trehazolin.

Introduction

In 1991, Ando and co-workers reported the isolation of the unique natural pseudodisaccharide trehazolin (1) from a culture broth of *Micromonospora* sp. strain SANK 62390. This compound exhibited powerful inhibitory activity toward various trehalases.[1]

Trehalamine (3), which is the aglycon of trehazolin, was isolated in 1992 from both the aforementioned culture broth and one of *Amicolatopsis* sp. strain SANK 60791. It possesses weak inhibitory activity toward various α-glucosidases.[2] We anticipate that these compounds will become important candidates for therapeutic applications.

In related work, a Suntory group reported the isolation of 5-*epi*-trehazolin, named trehalostatin (2),[3] in 1991. This compound has been claimed to have similar inhibitory activity toward various trehalases. While trehalostatin has been postulated to be the same compound as trehazolin on the basis of physical data comparisons, the absolute configuration of trehazolin has not been determined. Therefore, a prerequisite of this study was to confirm the correct structure of trehazolin, including its absolute configuration.

In 1992, the Ogawa group confirmed the relative configuration of the trehazolin aminocyclitol moiety as depicted by Ando et al.[1] by synthesis of its racemic pentaacetate (4).[4]

In the same year, we reported the syntheses of trehazolin (1),[5] trehalamine (3),[5] and the aminocyclitol hexaacetate of 1 (5),[6] including the determination of their absolute configurations. Herein we describe the details of the syntheses of these compounds based on a convergent strategy starting from D-glucose and via its nonprotected aminocyclitol which was obtained from the acidic hydrolysis of compound 5 or alternatively from the degradation of trehazolin (1) (Figure 1).

Retrosynthetic Analysis

The chemical studies of trehazolin reported by Ando and co-workers in 1993[2] revealed that the hydrolysis of trehazolin (1) by 4 M hydrochloric acid at 100 °C for 24 h afforded only an aminocyclitol moiety as the degradation product. Furthermore, trehazolin hydrolysis by hydrochloric acid adjusted to pH 2.0 at 84 °C for 72 h afforded D-glucose and trehalamine (3) as the degradation products. The workers gave no indication of the absolute configuration of trehazolin.

It is envisioned that the structural resemblance between trehazolin (1) and trehalose (6) may have some bearing on the generation of trehazolin's activity toward various trehalases, and thus we hypothesize the absolute configuration of its aminocyclitol moiety to be [1*R*-(1α,2β,3α,4β,5β)] upon consideration of the relationship between the proposed relative structure of trehazolin and the absolute structure of trehalose.

In view of trehazolin's glyconic unit being D-glucose and the stereocenters of its aglycon unit being equivalent to that of D-glucose, the latter was chosen as the starting material for the construction of trehazolin. With reference to the retrosynthetic strategy outlined in Figure 2, the isoxazolin derivative [I] would be derived from D-glucose via intramolecular [3 + 2] cycloaddition. Formation of the ketone from [I] and the R^2 group would induce β-elimination simultaneously to give hydroxymethyl enone [II]. Finally the enone [II] would be transformed into an epoxide [III] in several steps, involving 1,2-reduction of the carbonyl group of enone [II] and Sharpless epoxidation of the corresponding allyl alcohol. Thus subsequent azide

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(1) Ando, O.; Satake, H.; Itoi, K.; Sato, A.; Nakajima, M.; Takahashi, S.; Haruyama, H.; Ohkuma, Y.; Kinoshita, T.; Enokita, R. *J. Antibiot.* **1991**, *44*, 1165–1168.

(2) Ando, O.; Nakajima, M.; Hamano, K.; Itoi, K.; Takahashi, S.; Takamatsu, Y.; Sato, A.; Enokita, R.; Haruyama, H.; Kinoshita, T. *J. Antibiot.* **1993**, *46*, 1116–1125.

(3) Nakayama, T.; Amachi, T.; Murao, S.; Sakai, T.; Shin, T.; Kenny, P. T.; Iwashita, T.; Zagorski, M.; Komura, H.; Nomoto, K. *J. Chem. Soc., Chem. Commun.* **1991**, 919–920.

(4) (a) Ogawa, S.; Uchida, C.; Yuming, Y. *J. Chem. Soc., Chem. Commun.* **1992**, 886–888. (b) Ogawa, S.; Uchida, C. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1939.

(5) Kobayashi, Y.; Miyazaki, H.; Shiozaki, M. *J. Am. Chem. Soc.* **1992**, *114*, 10065–10066.

(6) Kobayashi, Y.; Miyazaki, H.; Shiozaki, M. *Tetrahedron Lett.* **1993**, *34*, 1505–1506.

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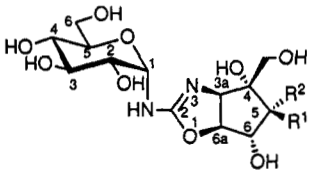
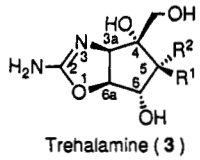
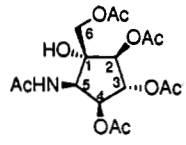


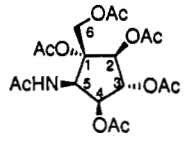
R^1 = OH, R^2 = H Trehazolin (1)
R^1 = H, R^2 = OH Trehalostatin (2)



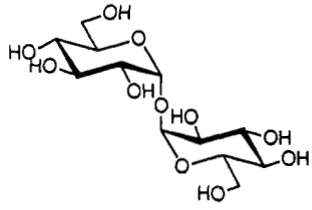
Trehalamine (3)



Aminocyclitol pentaacetate (4)



Aminocyclitol hexaacetate (5)



Trehalose (6)

Figure 1. Structures of the compounds related to trehazolin.

opening of the epoxide [III] would afford the azido alcohol [IV], the latter being the latent form of an aminocyclitol framework (Figure 2).

Synthesis of the Optically Active Key Compound (16α)

Treatment of aldehyde **7**, which was derived from D-glucose in accordance with the method developed by Bernet and Vasella,[7] with hydroxylamine hydrochloride and sodium carbonate (Na_2CO_3) afforded a separable 4:1 (*anti*:*syn*) mixture of oxime **8** (Scheme 1). Subsequently, [3 + 2] cycloaddition of the mixture of oxime **8** with 5% aqueous sodium hypochlorite and a catalytic amount of triethylamine furnished the corresponding isoxazoline **9**.[8] Isoxazoline **9** was hydrogenolyzed with Raney Ni in the presence of boric acid[9] to give the desired hydroxymethyl enone **10**.

In general, the hydrogenolysis of isoxazoline compounds with Raney Ni results in conversion to a hydroxymethyl ketone. However, in this case by virtue of the electron-withdrawing effect of the benzoyl group, β-elimination of the benzoyloxy group by the generated ketone was induced and the corresponding hydroxymethyl enone **10** was obtained.

Silylation of enone **10** with *tert*-butyldimethylsilyl chloride (TBDMSCl) and imidazole furnished the corresponding silyl ether **11**, and subsequent 1,2-reduction of **11** with sodium borohydride ($NaBH_4$) in the presence of

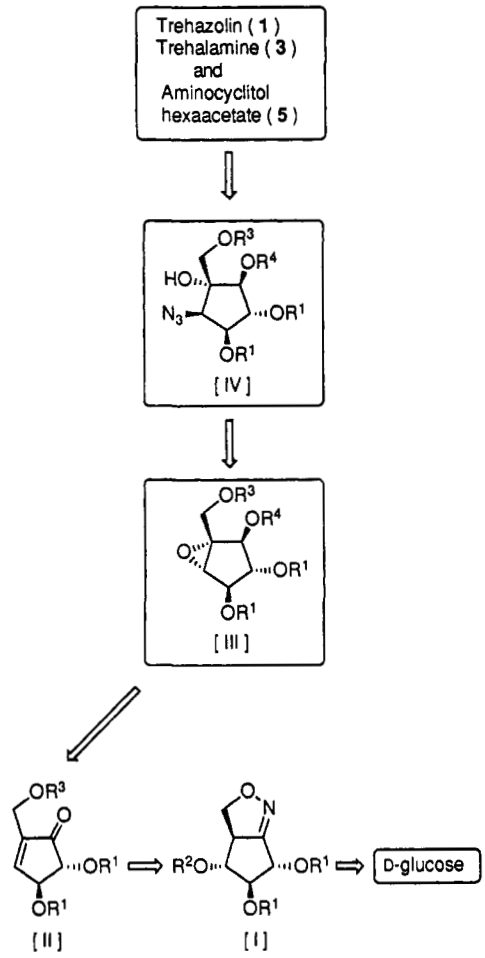


Figure 2. Retrosynthetic analysis of trehazolin (**1**) and trehalamine (**2**).

cerium(III) chloride heptahydrate ($CeCl_3 \cdot 7H_2O$)[10] to prevent double-bond reduction afforded a separable 1:2.5 (**12α**:**12β**) mixture of alcohols.

The configurations of the C-1 position of these latter two alcohols were determined by scrutiny of the ^{1}H-NMR data of the acetates **13α** and **13β**.

From the ^{1}H-NMR analyses, irradiation of the C-5 proton at 5.59 ppm in **13β** enhanced the C-3 proton's intensity at 4.50–4.46 ppm, but that the C-5 proton at 5.65 ppm in **13α** induced no nuclear Overhauser effect (NOE) on the C-3 proton at 4.77–4.69 ppm. In addition to these NOE experiments, the C-5 proton signal of **13β** was observed as a doublet of triplets which included the allyl coupling between the C-5 proton and C-2 proton and the long-range coupling between the C-5 proton and C-3 proton, but in the case of **13α**, the C-5 signal was observed as a doublet of doublets which was devoid of the latter long-range coupling. Therefore, the configuration of the C-1 position of the secondary alcohol **12β** is (*R*) and hence (*S*) for the C-1 of **12α**.

Benzylation of **12β** possessing the desired configuration with benzyl bromide (BnBr) and sodium hydride (NaH), and subsequent removal of the TBDMS group with tetra-*n*-butylammonium fluoride (TBAF), afforded the corresponding allyl alcohol **15**.

Sharpless epoxidation of **15** with diisopropyl L-tartrate (L-DIPT), titanium tetraisopropoxide ($Ti(O^iPr)_4$), and

(7) Bernet, B.; Vasella, A. *Helv. Chim. Acta* **1979**, *62*, 1990–2016.
(8) (a) Lee, G. A. *Synthesis* **1982**, 508–509. (b) Kozikowski, A. P.; Stein, P. D. *J. Org. Chem.* **1984**, *49*, 2301–2309. (c) Kozikowski, A. P.; Stein, P. D. *J. Am. Chem. Soc.* **1982**, *104*, 4023–4024. (d) Tatsuta, K.; Niwata, Y.; Umezawa, K.; Toshima, K.; Nakata, M. *Tetrahedron Lett.* **1990**, *31*, 1171–1172.
(9) Curan, D. P. *J. Am. Chem. Soc.* **1983**, *105*, 5826–5833.
(10) Gemal, A. L.; Luche, J. L. *J. Am. Chem. Soc.* **1981**, *103*, 5454–5459.

Scheme 1

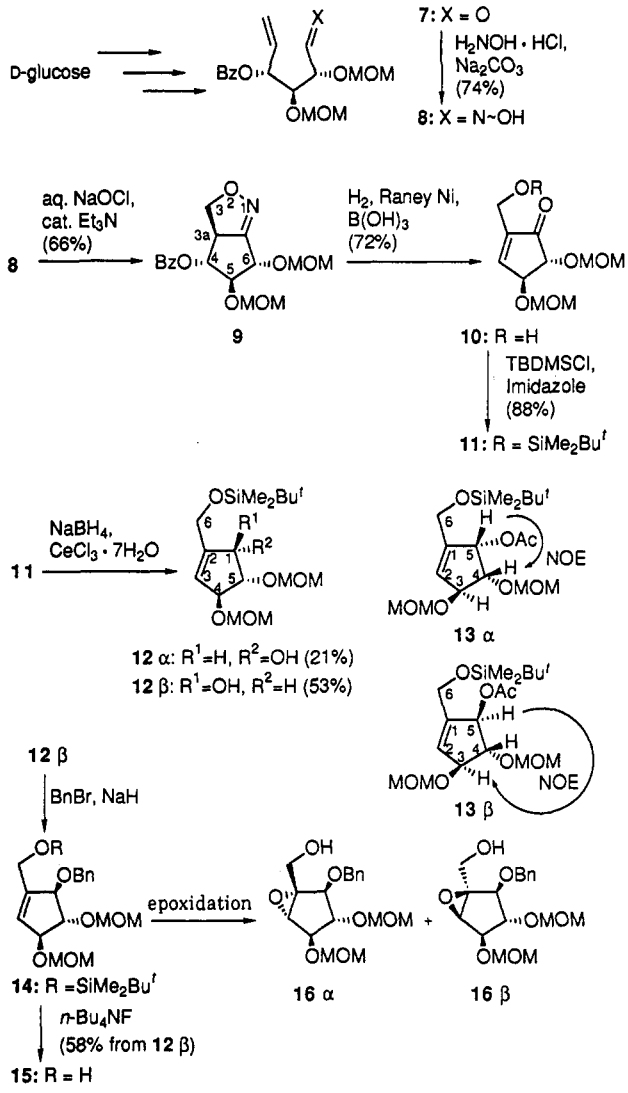


Table 1. Stereoselectivities and Yields of Epoxidation of Compound 15

entry	conditions	yield (%)	ratio (16α:16β)[a]
1	L-DIPT, $Ti(O^iPr)_4$ t-BuOOH, CH_2Cl_2, −25 °C, 5 h	94	16α only
2	D-DIPT, $Ti(O^iPr)_4$ t-BuOOH, CH_2Cl_2, −25 °C → rt 7 h	77	16β only
3	1 mol% $VO(acac)_2$, t-BuOOH CH_2Cl_2, rt, 19 h	66	1:2
4	MCPBA, CH_2Cl_2, rt, 48 h	92	1.2:1

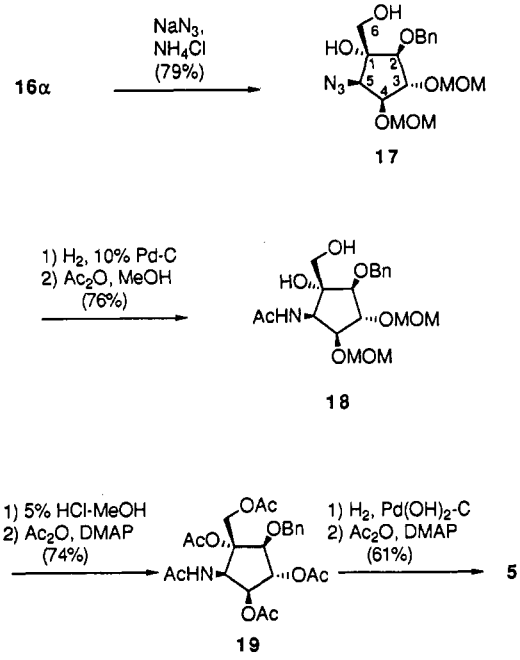
[a] The ratios were determined by ^{1}H-NMR analysis.

tert-butyl hydroperoxide (t-BuOOH)[11] furnished the desired epoxide **16α** as a single isomer. Using diisopropyl D-tartrate (D-DIPT) in place of L-DIPT, the epoxidation of **15** afforded the undesired epoxide **16β** as a single isomer (Table 1). This stereochemical outcome follows the Sharpless epoxidation rule. On the other hand, the epoxidation of **15** with MCPBA furnished an inseparable mixture of epoxides **16α** and **16β** (α:β = 1.2:1), and Sharpless epoxidation of **15** using $VO(acac)_2$[12] instead of

(11) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974–5976.

(12) (a) Sharpless, K. B.; Michaelson, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6136–6137. (b) Whitesell, J. K.; Allen, D. E. *J. Am. Chem. Soc.* **1988**, *110*, 3585–3588.

Scheme 2



L-DIPT and $Ti(O^iPr)_4$ furnished an inseparable mixture of those respective isomers (α:β = 1:2).

Synthesis of Hexaacetate 5[6]

Initially, the determination of the absolute configuration of the trehazolin aminocyclitol moiety was accomplished by the synthesis of hexaacetate **5** (Scheme 2).

Azide opening of the epoxide **16α** with sodium azide (NaN_3) and ammonium chloride (NH_4Cl)[13] produced azido diol **17** regiospecifically. Subsequent hydrogenolysis of the azido group and acetylation of the corresponding amino group with acetic anhydride in MeOH afforded acetamide **18**. After cleavage of the two methoxymethyl (MOM) groups of compound **18** with 5% methanolic hydrogen chloride, the complete acetylation of the corresponding tetrol furnished compound **19**. Finally, compound **19** was hydrogenolyzed to cleave the benzyl group and subsequent acetylation of the corresponding alcohol furnished compound **5** ($[\alpha]^{25}_D$ +6.0° (*c* 1.23, $CHCl_3$)), which was identical in all respects to the hexaacetate of the aminocyclitol ($[\alpha]^{25}_D$ +5.9° (*c* 1.08, $CHCl_3$)) obtained from natural trehazolin. The absolute configurations of the trehazolin aminocyclitol moiety and trehalamine were found to be [1*R*-(1α,2β,3α,4β,5β)] and [3a*R*-(3aα,4α,5β,6α,6aα)], respectively, as expected.

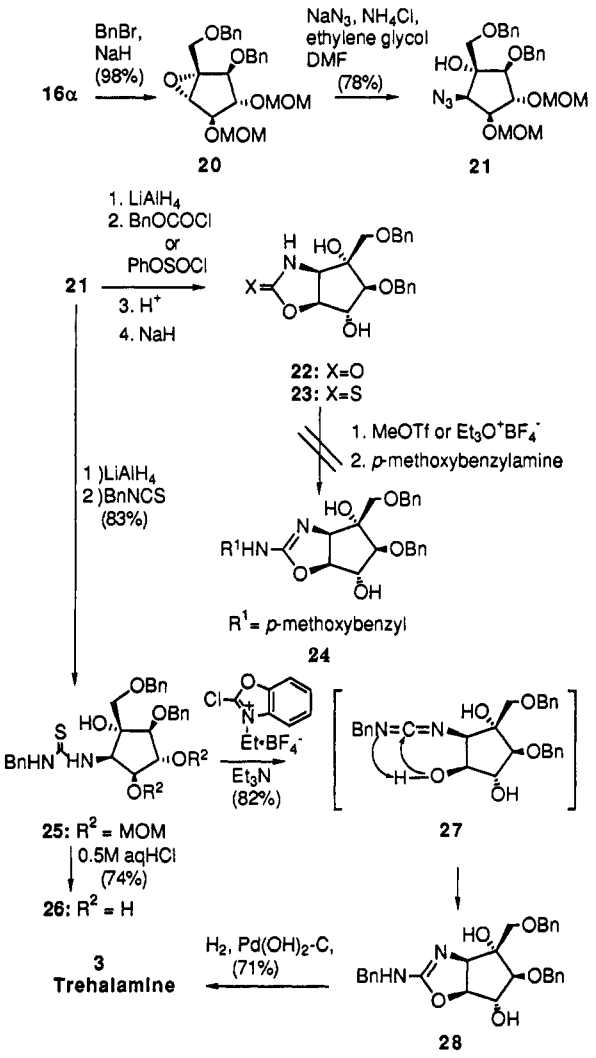
Synthesis of Trehalamine

The synthesis of trehalamine from epoxide **16α** was accomplished as follows. After benzylation of **16α** with BnBr and NaH, the corresponding benzyl ether **20** was treated with NaN_3 and NH_4Cl to afford azido alcohol **21**, regiospecifically (Scheme 3). In the next stage, the Trost method[14] was employed to construct the aminooxazoline

(13) VanderWerf, C. A.; Heisler, R. Y.; McEwen, W. E. *J. Am. Chem. Soc.* **1954**, *76*, 1231–1235.

(14) (a) Trost, B. M.; Van Vrankan, D. L. *J. Am. Chem. Soc.* **1990**, *112*, 1261–1263. (b) Trost, B. M.; Van Vrankan, D. L. *J. Am. Chem. Soc.* **1993**, *115*, 444–458. (c) Griffith, D. A.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1991**, *114*, 5863–5864. (d) Nakata, M.; Akazawa, S.; Kitamura, S.; Tatsuta, K. *Tetrahedron Lett.* **1991**, *32*, 5363–5366. (e) Simpkins, N. S.; Stokes, S.; Whittle, A. J. *Tetrahedron Lett.* **1992**, *33*, 793–796.

Scheme 3



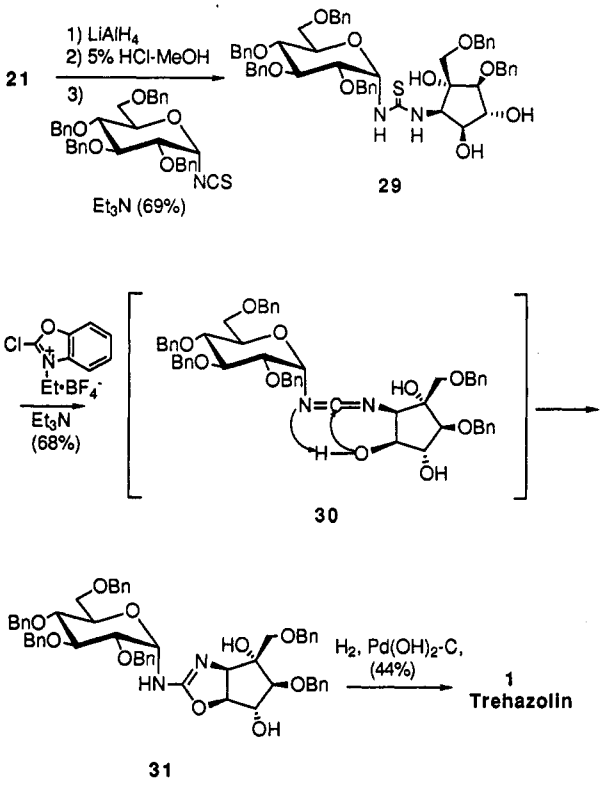
skeleton of trehalamine. After treatment of oxazolidinone **22** or oxazolidinethione **23** with MeOTf or $Et_3O^+BF_4^-$, which were derived from **21** in four steps, *p*-methoxybenzylamine was added to the reaction mixture; however, compound **24** was not obtained. This indicated that the Trost methodology was unsuitable in this example.

Next, we applied Mukaiyama's method,[15] in which cyclization occurred between the unstable carbodiimide intermediate and the adjacent *cis*-hydroxy group, to construct the aminooxazoline.

Reduction of compound **21** with lithium aluminum hydride ($LiAlH_4$) and subsequent treatment of the corresponding amino alcohol with benzyl isothiocyanate furnished the thiourea derivative **25**. Compound **25** was hydrolyzed to cleave the two MOM groups and thus the corresponding triol **26** was produced. Treatment of **26** with 2-chloro-3-ethylbenzoxazolium tetrafluoroborate and triethylamine afforded the corresponding aminooxazoline compound **28**. Finally, compound **28** was hydrogenolyzed to cleave three benzyl groups and to give trehazolin aglycon **3** ($[\alpha]^{25}_D$ +14.4°·(*c* 0.32, H_2O)), which was identical in all respects to natural trehalamine ($[\alpha]^{25}_D$ +13.5° (*c* 0.74, H_2O)).

(15) (a) Shibanuma, T.; Shiono, M.; Mukaiyama, T. *Chem. Lett.* **1977**, 575–576. (b) Review: Mukaiyama, T. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 707–721. (c) Takeda, T.; Mukaiyama, T. *Chem. Lett.* **1980**, 163–166.

Scheme 4



Synthesis of Trehazolin

Following the procedure for the synthesis of trehalamine, the synthesis of trehazolin was also accomplished (Scheme 4). After reduction of **21** with $LiAlH_4$ and subsequent cleavage of the two MOM groups with 5% methanolic hydrogen chloride, coupling between the corresponding amino triol hydrochloride and 2,3,4,6-tetra-*O*-benzyl-1-deoxy-α-D-glucopyranosyl isothiocyanate[16] in the presence of triethylamine afforded the α-D-glucopyranosyl thiourea derivative **29**. However, after formation of the thiourea, acidic hydrolysis of the corresponding derivatives to remove the two MOM groups gave rise to an anomeric mixture (α:β = 1:1) of compound **29**.

Treatment of compound **29** with the aforementioned cyclization furnished the aminooxazoline derivative **31**, and finally, compound **31** was hydrogenolyzed to cleave the benzyl groups and generate trehazolin (**1**). Synthesized trehazolin ($[\alpha]^{30}_D$ +112.7° (*c* 0.59, H_2O)) was identical to natural trehazolin ($[\alpha]^{25}_D$ +99.5° (*c* 0.44, H_2O)) in all respects including biological activities (Figure 3).

Synthesis of Trehazolin through Its Nonprotected Aminocyclitol Moiety[17]

Finally, the synthesis of trehazolin from a nonprotected aminocyclitol moiety derived from compound **5** or natural trehazolin was also attained. The purpose of this synthetic approach is important from the point of view of synthesizing various derivatives possessing the trehalamine moiety (Scheme 5).

Hydrolysis of compound **5**, followed by purification using an ion-exchange resin (Amberite CG-50, ammonium type),

(16) Camarasa, M. J.; F-Resa, P.; Garcialopez, M. T.; G delas Heras, F.; M-Castrillon, P. P.; Felix, A. S. *Synthesis* **1984**, 509–510.

(17) The Ogawa group recently independently reported the synthesis of trehazolin via its aminocyclitol. Ogawa, S.; Uchida, C. *Chem. Lett.* **1993**, 173–176.

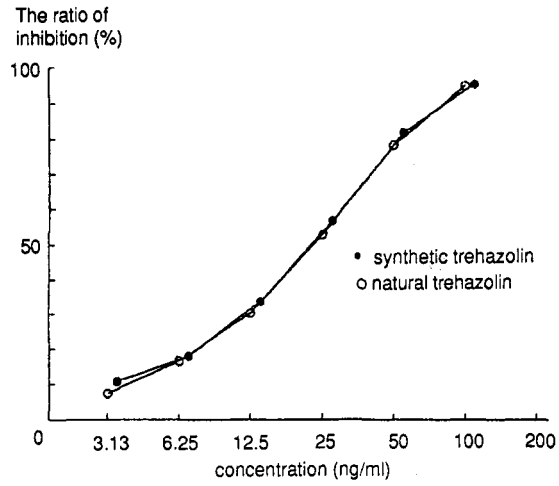
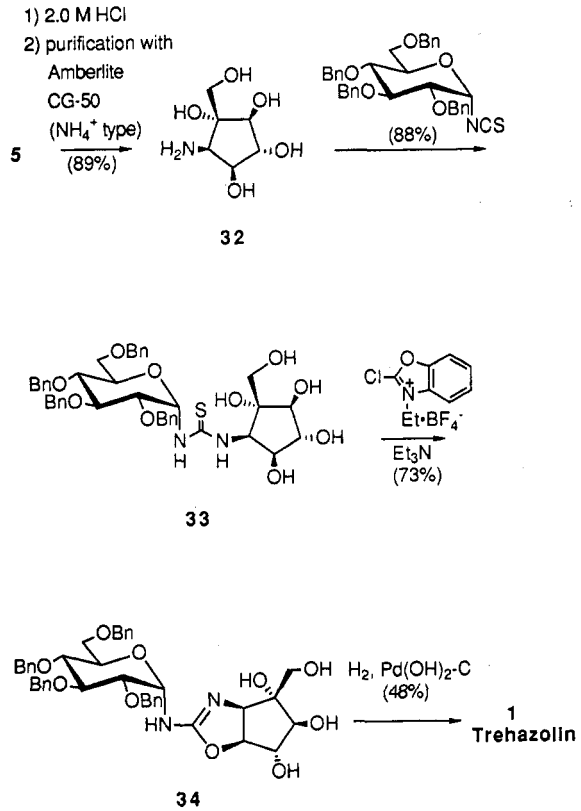


Figure 3. Inhibitory activity toward porcine trehalase of the synthetic trehazolin compared to that of natural trehazolin.

Scheme 5



afforded the corresponding aminocyclitol **32** ($[\alpha]^{25}_D$ +1.7° (*c* 0.41, H_2O)), which was identical in all respects including the circular dichroism (CD) spectral data to the aminocyclitol ($[\alpha]^{25}_D$ +4.5° (*c* 1.1, H_2O)) derived from natural trehazolin (Figure 4).

Treatment of **32** with 2,3,4,6-tetra-*O*-benzyl-1-deoxy-α-D-glucopyranosyl isothiocyanate furnished the thiourea derivative **33**. Subsequent treatment of **33** with 2-chloro-3-ethylbenzoxazolium tetrafluoroborate and triethylamine gave aminooxazoline **34** as a single stereoisomer via the carbodiimide intermediate **35**. The possibility of the formation of bicyclo[3.4.0] framework **36** derived from the cyclization between the primary hydroxy group at C-6 position of the aminocyclitol moiety and the carbodiimide group of compound **35** was suspected, but only compound **34**, possessing the bicyclo[3.3.0] system, was obtained (Figure 5).

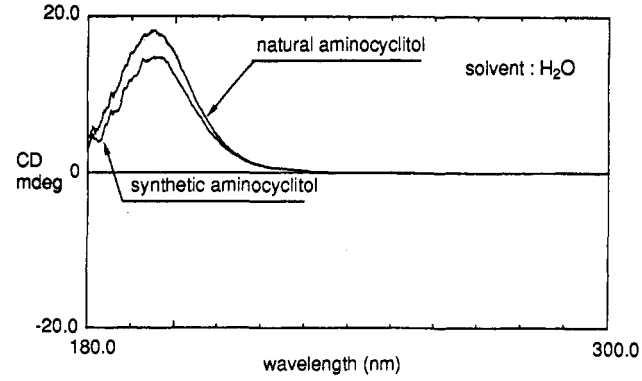


Figure 4. CD spectrum of natural aminocyclitol obtained from trehazolin in comparison to the synthesized one.

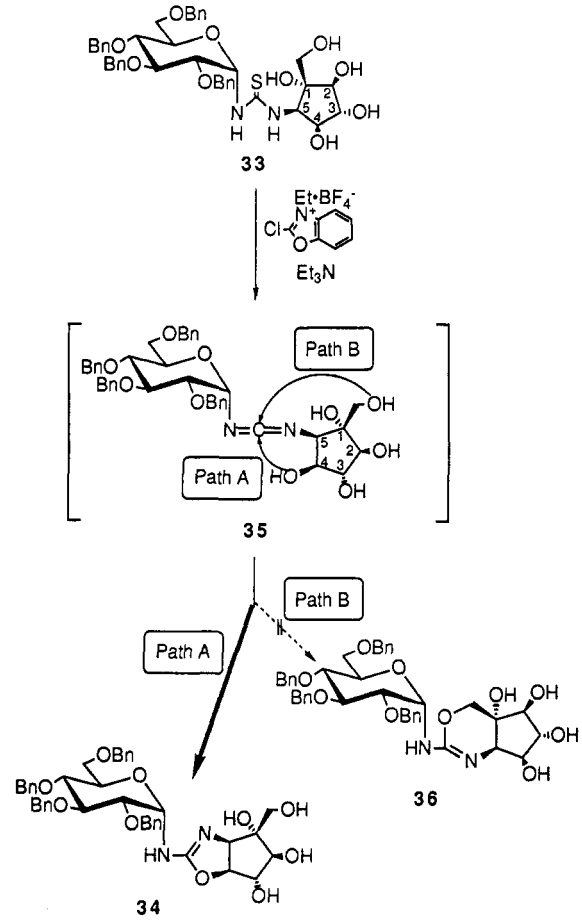


Figure 5.

Finally, hydrogenolysis using $Pd(OH)_2$ on carbon as a catalyst to cleave four benzyl groups afforded trehazolin (1) ($[\alpha]^{24}_D$ +119.2° (*c* 1.03, H_2O)), which was again identical in terms of physical and spectroscopic data to that of natural trehazolin. This result reveals the possibility of syntheses of various derivatives from the aminocyclitol, which is the degradation product of trehazolin.

Conclusion

Syntheses of the trehazolin aminocyclitol hexaacetate (**5**), trehalamine (**3**), and trehazolin (**1**) enabled determination of their absolute configurations. The synthesis of trehazolin (**1**) was accomplished from compound **16α** via **30** or the nonprotected aminocyclitol moiety **32**. Compound **32** in turn could be derived from acidic hydrolysis

of either compound 5 or natural trehazolin. This strategy should be applicable to the syntheses of various derivatives possessing the trehalamine moiety.

Experimental Section

General Method. Melting points are uncorrected. ^{1}H-NMR spectra (270 MHz) were recorded using tetramethylsilane as an internal reference. Elemental analyses were performed by the Institute of Science and Technology, Inc.. Analytical chromatography was performed on Merck Art 5715 silica gel 60-F_{245} plates. Flash chromatography was performed on Merck Art 9385 silica gel 60 (230–400 mesh). THF was distilled from $LiAlH_4$ and used immediately thereafter. Et_2O was dried by being passed through ICN Alumina N-Super I. CH_2Cl_2 was dried by being passed through ICN Alumina B-Super I. DMF and pyridine were dried by storage over 4A molecular sieves. MeCN was dried by storage over 3A molecular sieves. All other commercial reagents were used directly as received.

[3a*R*-(3aα,4α,5β,6α)]-4-(Benzoyloxy)-5,6-bis(methoxymethoxy)-3a,4,5,6-tetrahydro-3*H*-cyclopent[*c*]isoxazole (9). (i) To a solution of 7 (5.36 g, 19.3 mmol) in Et_2O (100 mL) was added a solution of hydroxylamine hydrochloride (13.4 g, 193 mmol) in water (53.5 mL) dropwise with stirring at rt, and then a solution of Na_2CO_3 (20.4 g, 193 mmol) in water (40 mL) was added dropwise to this mixture. After being stirred at rt for 8 h, the resulting mixture was extracted twice with Et_2O and the combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with benzene–EtOAc (3:1) gave 3.77 g (57%) of the *anti* isomer of 8 and 1.19 g (18%) of the *syn* isomer of 8 as colorless oil, respectively. ***anti* isomer of 8**: IR (film) 3391, 2952, 2897, 1725, 1602 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.15–8.05 (2H, m), 7.65–7.54 (1H, m), 7.51–7.40 (3H, m), 7.36 (1H, s), 6.21–5.90 (1H, m), 5.82 (1H, t, J = 5.6 Hz), 5.44 (1H, d, J = 17.2 Hz), 5.34 (1H, d, J = 10.6 Hz), 4.85 (1H, d, J = 6.6 Hz), 4.77 (1H, d, J = 6.6 Hz), 4.73 (1H, d, J = 6.6 Hz), 4.66 (1H, d, J = 6.6 Hz), 4.45 (1H, dd, J = 7.6, 5.6 Hz), 3.99 (1H, t, J = 5.6 Hz), 3.42 (3H, s), 3.41 (3H, s); MS m/z 353 (M^+), 322 (M^+ – OMe); R_f = 0.38 (benzene:EtOAc = 3:1). Anal. Calcd for $C_{17}H_{23}NO_7$: C, 57.78; H, 6.56; N, 3.96. Found: C, 57.56; H, 6.41; N, 3.83. ***syn* isomer of 8**: IR (film) 3374, 3090, 2952, 2896, 1724, 1602 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.08 (2H, d, J = 7.9 Hz), 7.73 (1H, br s), 7.65–7.35 (3H, m), 6.92 (1H, d, J = 5.9 Hz), 6.12–5.95 (1H, m), 5.82 (1H, t, J = 5.9 Hz), 5.49 (1H, d, J = 15.8 Hz), 5.37 (1H, d, J = 10.6 Hz), 5.12 (1H, dd, J = 5.9, 3.0 Hz), 4.87–4.60 (4H, m), 4.21 (1H, dd, J = 5.9, 3.0 Hz), 3.46 (3H, s), 3.35 (3H, s); MS m/z 353 (M^+), 322 (M^+ – OMe); R_f = 0.26 (benzene:EtOAc = 3:1). Anal. Calcd for $C_{17}H_{23}NO_7$: C, 57.78; H, 6.56; N, 3.96. Found: C, 57.58; H, 6.41; N, 3.96.

(ii) To a solution of a geometrical isomer mixture of the above-obtained 8 (4.72 g, 13.3 mmol) and triethylamine (0.19 mL, 1.36 mmol) in CH_2Cl_2 (240 mL) was added dropwise aqueous 5% sodium hypochlorite (75 mL) with stirring at 0 °C. After being stirred at 0 °C for 40 min, the resulting mixture was extracted twice with CH_2Cl_2. The combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with hexane–EtOAc (3:1) gave 3.00 g (66%) of 9 as a white crystal: $[\alpha]^{25.5}_D$ –96.0° (*c* 1.05, $CHCl_3$); mp 66–67 °C (recrystallized from hexane–EtOAc); IR (KBr) 1728 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.04 (2H, d, J = 7.3 Hz), 7.61 (1H, t, J = 7.3 Hz), 7.47 (2H, t, J = 7.3 Hz), 4.90–4.64 (8H, m), 4.43 (1H, dd, J = 11.0, 9.2 Hz), 3.91 (1H, dt, J = 11.0, 9.2 Hz), 3.45 (3H, s), 3.40 (3H, s); MS m/z 351 (M^+); R_f = 0.43 (hexane:EtOAc = 3:1). Anal. Calcd for $C_{17}H_{21}NO_7$: C, 58.11; H, 6.02; N, 3.99. Found: C, 58.13; H, 6.07; N, 3.85.

(4*S*-*trans*)-2-(Hydroxymethyl)-4,5-bis(methoxymethoxy)-2-cyclopenten-1-one (10). To a solution of 9 (5.00 g, 14.2 mmol) in MeOH (150 mL) containing 1,4-dioxane (50 mL) and water (30 mL) were added boric acid (4.4 g, 71 mmol) and Raney nickel (5 mL after refluxing in acetone for 3.5 h) at 0 °C, and this mixture was hydrogenolyzed with vigorous stirring at 25 °C. After 5 h, the resulting mixture was filtered through Celite and concentrated to give a residue, which was diluted with CH_2Cl_2 and washed with saturated aqueous $NaHCO_3$. The aqueous layer was extracted twice with CH_2Cl_2. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with benzene–EtOAc (1:2) gave 2.36 g (72%) of enone 10 as a pale yellow oil: $[\alpha]^{25}_D$ +91.6° (*c* 1.13, $CHCl_3$); IR (neat) 3460, 1725 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.32 (1H, q, J = 1.8 Hz), 4.98 (1H, d, J = 6.7 Hz), 4.88 (1H, d, J = 6.7 Hz), 4.85 (1H, d, J = 6.7 Hz), 4.80 (1H, d, J = 6.7 Hz), 4.69 (1H, quintet, J = 1.8 Hz), 4.43–4.36 (2H, m), 4.29 (1H, d, J = 1.8 Hz), 3.47 (3H, s), 3.45 (3H, s), 2.12 (1H, t, J = 5.9 Hz); MS m/z 232 (M^+), 170 (M^+ – MeO × 2); R_f = 0.45 (benzene:EtOAc = 1:2). Anal. Calcd for $C_{10}H_{16}O_6$: C, 51.72; H, 6.94. Found: C, 51.50; H, 7.02.

(4*S*-*trans*)-2-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-4,5-bis(methoxymethoxy)-2-cyclopenten-1-one (11). To a solution of 10 (2.15 g, 9.3 mmol) in DMF (45 mL) were added TBDMSCl (2.08 g, 14.0 mmol) and imidazole (0.96 g, 14.1 mmol) with stirring at 0 °C. After 10 min, the reaction mixture was warmed to 25 °C and stirred for 16 h. To this mixture was added MeOH (0.68 mL) with stirred at 0 °C. After 30 min, the reaction mixture was diluted with EtOAc and washed with brine. The aqueous layer was extracted twice with EtOAc. The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with hexane–EtOAc (4:1) gave 2.82 g (88%) of 11 as a colorless oil: $[\alpha]^{25.5}_D$ +65.4° (*c* 1.12, $CHCl_3$); IR (neat) 1724 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.28 (1H, q, J = 2.1 Hz), 4.96 (1H, d, J = 5.9 Hz), 4.86 (1H, d, J = 5.9 Hz), 4.82 (1H, d, J = 5.9 Hz), 4.78 (1H, d, J = 5.9 Hz), 4.64 (1H, quintet, J = 2.1 Hz), 4.36 (2H, q, J = 2.1 Hz), 4.26 (1H, d, J = 2.1 Hz), 3.46 (3H, s), 3.42 (3H, s), 0.90 (9H, s), 0.07 (6H, s); MS m/z 346 (M^+), 315 (M^+ – MeO); R_f = 0.85 (hexane:EtOAc = 1:1). Anal. Calcd for $C_{16}H_{30}O_6Si$: C, 55.46; H, 8.73. Found: C, 55.32; H, 8.66.

[1*S*-(1α,4β,5α)]-2-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-4,5-bis(methoxymethoxy)-2-cyclopenten-1-ol (12α) and [1*R*-(1α,4α,5β)]-2-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-4,5-bis(methoxymethoxy)-2-cyclopenten-1-ol (12β). To a solution of 11 (2.67 g, 7.7 mmol) in MeOH (55 mL) was added $CeCl_3 \cdot 7H_2O$ (4.5 g, 12.1 mmol) with stirring at 0 °C. After 30 min, $NaBH_4$ (0.45 g, 11.9 mmol) was added to this mixture at 25 °C, and the resulting mixture was stirred for 2 h. AcOH–MeOH solution (10% (v/v), 6 mL) was added with stirring at 0 °C. After 15 min, the reaction mixture was diluted with EtOAc and washed with saturated aqueous $NaHCO_3$. The aqueous layer was extracted twice with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with benzene–EtOAc (3:1) gave 1.41 g (53%) of (1*R*)-12 (12β) and 0.56 g (21%) of (1*S*)-12 (12α) as colorless oils, respectively: **(1*R*)-12 (12β)**: $[\alpha]^{25}_D$ –26.6° (*c* 1.66, $CHCl_3$); IR (neat) 3460, 1650 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.73 (1H, m), 4.80 (2H, s), 4.79 (1H, d, J = 7.3 Hz), 4.71 (1H, d, J = 7.3 Hz), 4.50–4.41 (2H, m), 4.41–4.22 (2H, m), 3.88 (1H, t, J = 5.1 Hz), 3.47 (3H, s), 3.46 (1H, d, J = 4.6 Hz), 3.39 (3H, s), 0.92 (9H, s), 0.09 (6H, s); MS m/z 331 (M^+ + 1 – H_2O); R_f = 0.49 (benzene:EtOAc = 3:1). Anal. Calcd for $C_{16}H_{32}O_6Si$: C, 55.14; H, 9.26. Found: C, 54.94; H, 9.10. **(1*S*)-12 (12α)**: $[\alpha]^{25.5}_D$ +52.8° (*c* 1.21, $CHCl_3$); IR (neat) 3450 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.89–5.80 (1H, m), 4.82 (1H, d, J = 6.3 Hz), 4.78 (1H, d, J = 6.3 Hz), 4.77 (1H, d, J = 6.3 Hz), 4.72 (1H, d, J = 6.3 Hz), 4.73–4.66 (1H, m), 4.62 (1H, t, J = 4.7 Hz), 4.42–4.22 (2H, m), 4.07 (1H, dd, J = 4.7, 6.1 Hz), 3.45 (3H, s), 3.39 (3H, s), 2.66 (1H, d, J = 4.7 Hz), 0.92 (9H, s), 0.08 (6H, s); MS m/z 331 (M^+ + 1 – H_2O); R_f = 0.40 (benzene:EtOAc = 3:1). Anal. Calcd for $C_{16}H_{32}O_6Si$: C, 55.14; H, 9.26. Found: C, 54.99; H, 9.30.

[3*S*-(3α,4β,5α)]-5-Acetoxy-1-[[(*tert*-butyldimethylsilyl)oxy]methyl]-3,4-bis(methoxymethoxy)-1-cyclopentene (13β). To a solution of 12β (96 mg, 0.27 mmol) in pyridine (1 mL) was added acetic anhydride (0.1 mL) with stirring at rt. After 16 h, EtOH (1 mL) was added to the reaction mixture with stirring at rt. After 30 min, this reaction mixture was diluted with EtOAc and washed with brine. The aqueous layer was extracted twice with EtOAc. The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with benzene–EtOAc (8:1) gave 96 mg (92%) of 13β as a colorless oil: $[\alpha]^{25}_D$ –16.7° (*c* 1.04, $CHCl_3$); IR (film) 2954, 2932, 2891, 2858, 1742 cm^{-1}; ^{1}H

NMR ($CDCl_3$) δ 5.94–5.88 (1H, m), 5.59 (1H, dt, J = 3.6, 0.9 Hz), 4.78 (1H, d, J = 6.6 Hz), 4.76 (1H, d, J = 6.6 Hz), 4.73 (1H, d, J = 6.6 Hz), 4.72 (1H, d, J = 6.6 Hz), 4.50–4.46 (1H, m), 4.19 (1H, br d, J = 15.1 Hz), 4.18 (1H, t, J = 3.6 Hz), 4.10 (1H, br d, J = 15.1 Hz), 3.40 (3H, s), 3.37 (3H, s), 2.08 (3H, s), 0.90 (9H, s), 0.06 (6H, s); MS m/z 329 ($M^+ - CH_2OCH_3$), 303, 271, 267, 229, 225, 197; R_f = 0.46 (benzene:EtOAc = 8:1). Anal. Calcd for $C_{18}H_{34}O_7Si$: C, 55.36; H, 8.78. Found: C, 55.12; H, 8.64.

[3*S*-(3α,4β,5β)]-5-Acetoxy-1-[[(*tert*-butyldimethylsilyl)oxy]methyl]-3,4-bis(methoxymethoxy)-1-cyclopentene (13α). To a solution of **12α** (95 mg, 0.27 mmol) in pyridine (1 mL) was added acetic anhydride (0.1 mL) with stirring at rt. After 16 h, EtOH (1 mL) was added to the reaction mixture with stirring at rt. After 30 min, this reaction mixture was diluted with EtOAc and washed with brine. The aqueous layer was extracted twice with EtOAc. The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with benzene–EtOAc (8:1) gave 97 mg (94%) of **13α** as a colorless oil: $[\alpha]^{25}_D$ +102.3° (*c* 0.92, $CHCl_3$); IR (film) 2955, 2931, 2893, 2858, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.04–5.98 (1H, m), 5.65 (1H, dd, J = 5.6, 1.0 Hz), 4.80 (1H, d, J = 6.6 Hz), 4.77–4.69 (1H, m), 4.72 (1H, d, J = 6.6 Hz), 4.69 (1H, d, J = 6.6 Hz), 4.64 (1H, d, J = 6.6 Hz), 4.22–4.15 (2H, m), 4.14 (1H, dd, J = 5.6, 4.9 Hz), 3.40 (3H, s), 3.38 (3H, s), 2.08 (3H, s), 0.90 (9H, s), 0.06 (6H, s); MS m/z 390 (M^+), 359, 329, 303, 271, 269; R_f = 0.35 (benzene:EtOAc = 8:1). Anal. Calcd for $C_{18}H_{34}O_7Si$: C, 55.36; H, 8.78. Found: C, 55.23; H, 8.84.

[3*S*-(3α,4β,5α)]-5-(Benzyloxy)-1-(hydroxymethyl)-3,4-bis(methoxymethoxy)-1-cyclopentene (15). To a solution of **12β** (1.41 g, 4.0 mmol) in DMF (28 mL) were added NaH (0.27 g, 6.0 mmol, 55% in oil dispersion) and benzyl bromide (1.0 mL, 8.4 mmol) with stirring at 0 °C. After 1 h, MeOH (0.37 mL) was added to the reaction mixture with stirring at 0 °C. After 30 min, this reaction mixture was diluted with EtOAc and washed with brine. The aqueous layer was extracted twice with EtOAc. The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with hexane–EtOAc (5:1) gave 1.33 g (75%) of **14** as a colorless oil. To a solution of **14** (1.33 g, 3.0 mmol) in THF (26 mL) was added TBAF (1 M THF solution, 3.64 mL) with stirring at 0 °C. After 1 h, water was added to this reaction mixture with stirring at 0 °C. After 30 min, this reaction mixture was diluted with EtOAc and washed with brine. The aqueous layer was extracted twice with EtOAc. The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with hexane–EtOAc (1:1) gave 765 mg (58% from **12β**) of **15** as a colorless oil: $[\alpha]^{25.5}_D$ +29.6° (*c* 1.28, $CHCl_3$); IR (neat) 3470 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40–7.25 (5H, m), 5.84 (1H, br s), 4.85 (1H, d, J = 6.3 Hz), 4.78 (1H, d, J = 11.6 Hz), 4.77 (1H, d, J = 6.3 Hz), 4.75 (1H, d, J = 6.3 Hz), 4.72 (1H, d, J = 6.3 Hz), 4.62 (1H, d, J = 11.6 Hz), 4.47–4.40 (2H, m), 4.31 (1H, t, J = 4.2 Hz), 4.31–4.15 (2H, m), 3.44 (3H, s), 3.40 (3H, s), 1.95 (1H, br s); MS m/z 307 ($M^+ + 1 - H_2O$); R_f = 0.38 (hexane:EtOAc = 1:1). Anal. Calcd for $C_{17}H_{24}O_6$: C, 62.95; H, 7.46. Found: C, 62.87; H, 7.53.

[1*R*-(1α,2α,3β,4α,5α)]-2-(Benzyloxy)-1-(hydroxymethyl)-3,4-bis(methoxymethoxy)-6-oxabicyclo[3.1.0]hexane (16α). A solution of titanium tetraisopropoxide (0.33 mL, 1.3 mmol) and diisopropyl L-tartrate (0.28 mL, 1.3 mmol) in CH_2Cl_2 (15 mL) was stirred at −25 °C under N_2 for 20 min. To this mixture was added a solution of **15** (294 mg, 0.91 mmol) in CH_2Cl_2 (26 mL). After 20 min, *t*-BuOOH (3 M toluene solution, 0.6 mL) was added to this reaction mixture, maintaining the temperature at −25 °C and a nitrogen atmosphere. After 5 h, this reaction mixture was diluted with Et_2O, and 10% NaOH–brine was added to the mixture with stirring at 25 °C. After 15 min, this reaction mixture was extracted twice with Et_2O. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with hexane–EtOAc (1:2) gave 289 mg (94%) of **16α** as a colorless oil: $[\alpha]^{25.5}_D$ +45.6° (*c* 1.06, $CHCl_3$); IR (neat) 3460 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.42–7.27 (5H, m), 4.77 (1H, d, J = 11.8 Hz), 4.76 (1H, d, J = 6.6 Hz), 4.73 (1H, d, J = 6.6 Hz), 4.67 (1H, d, J = 6.6 Hz), 4.58 (1H, d, J = 11.8 Hz), 4.56 (1H, d, J = 6.6 Hz), 4.16 (1H, s), 4.12 (1H, s), 4.11 (1H, dd, J = 12.5, 6.6 Hz), 3.96 (1H, s), 3.90 (1H, dd, J = 12.5, 6.6 Hz), 3.67 (1H, s), 3.41 (3H, s), 3.37 (3H, s), 1.90 (1H, t, J = 6.6 Hz, OH); MS m/z 340 (M^+), 308, 295; R_f = 0.36 (hexane:EtOAc = 1:2). Anal. Calcd for $C_{17}H_{24}O_7$: C, 59.99; H, 7.11. Found: C, 60.00; H, 7.33.

[1*S*-(1α,2β,3α,4β,5α)]-2-(Benzyloxy)-1-(hydroxymethyl)-3,4-bis(methoxymethoxy)-6-oxabicyclo[3.1.0]hexane (16β). Using the above procedure but addition of D-tartrate in lieu of L-tartrate, **15** was converted to **16β** in 77% yield. However, after addition of *t*-BuOOH, the temperature was elevated to rt and maintained for 7 h. **Physical data of 16β**: $[\alpha]^{23}_D$ +16.5° (*c* 0.65, $CHCl_3$); mp 88–89 °C (recrystallized from Et_2O–hexane); IR (KBr) 3269, 3093, 3069, 3052, 3030, 3001 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.45–7.25 (5H, m), 4.82 (1H, d, J = 6.7 Hz), 4.79 (1H, d, J = 12.5 Hz), 4.78 (1H, d, J = 6.7 Hz), 4.77 (1H, d, J = 6.7 Hz), 4.71 (1H, d, J = 6.7 Hz), 4.69 (1H, d, J = 12.5 Hz), 4.04 (1H, t, J = 5.8 Hz), 4.01 (1H, d, J = 5.8 Hz), 3.95–3.85 (2H, m including dd at δ 3.91, J = 12.5, 4.2 Hz), 3.81 (1H, dd, J = 12.5, 8.3 Hz), 3.67 (1H, d, J = 2.1 Hz), 3.45 (3H, s), 3.39 (3H, s), 1.76 (1H, dd, J = 8.3, 4.2 Hz, OH); MS m/z 341 ($M^+ + 1$), 295, 277, 246, 215, 171, 127, 110; R_f = 0.36 (hexane:EtOAc = 1:2). Anal. Calcd for $C_{17}H_{24}O_7$: C, 59.99; H, 7.11. Found: C, 59.96; H, 7.03.

[1*R*-(1α,2β,3α,4β,5β)]-5-Azido-2-(benzyloxy)-1-(hydroxymethyl)-3,4-bis(methoxymethoxy)-1-cyclopentanol (17). To a solution of **16α** (289 mg, 0.85 mmol) in DMF (14.5 mL) were added sodium azide (664 mg, 10.2 mmol) and ammonium chloride (551 mg, 10.3 mmol) with stirring at rt, and this mixture was warmed to 125 °C and stirred for 72 h. After completion of the reaction, this reaction mixture was diluted with EtOAc and washed with brine. The aqueous layer was extracted twice with EtOAc. The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with hexane–EtOAc (1:2) gave 256 mg (79%) of **17** as a pale yellow oil: $[\alpha]^{24}_D$ −19.3° (*c* 1.02, $CHCl_3$); IR (neat) 3400, 2100 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.45–7.27 (5H, m), 4.80 (1H, d, J = 6.3 Hz), 4.77 (1H, d, J = 6.3 Hz), 4.77 (1H, d, J = 10.5 Hz), 4.72 (1H, d, J = 6.3 Hz), 4.68 (1H, d, J = 6.3 Hz), 4.60 (1H, d, J = 10.5 Hz), 4.18 (1H, dd, J = 5.3, 4.2 Hz), 4.13 (1H, t, J = 4.2 Hz), 3.97 (1H, dd, J = 11.6, 5.0 Hz), 3.95 (1H, d, J = 6.3 Hz), 3.83 (1H, d, J = 4.2 Hz), 3.81 (1H, dd, J = 11.6, 8.4 Hz), 3.52 (1H, br s, OH), 3.43 (3H, s), 3.41 (3H, s), 2.39 (1H, s, OH); MS m/z 324 ($M^+ + 1 - N_2$), 310, 292; R_f = 0.54 (hexane:EtOAc = 1:2). Anal. Calcd for $C_{17}H_{25}N_3O_7$: C, 53.26; H, 6.57; N, 10.96. Found: C, 53.03; H, 6.75; N, 10.75.

[1*R*-(1α,2β,3α,4β,5β)]-5-Acetamido-2-(benzyloxy)-1-(hydroxymethyl)-3,4-bis(methoxymethoxy)-1-cyclopentanol (18). To a solution of **17** (226 mg, 0.59 mmol) in MeOH (22 mL) was added 10% Pd on carbon (45 mg) with stirring at rt, and the mixture was hydrogenolyzed at rt. After 2 h, this reaction mixture was filtered. To this filterate was added acetic anhydride (0.28 mL, 3.0 mmol), and the mixture was stirred at rt for 5 h. After completion of the reaction, the reaction mixture was concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with CH_2Cl_2–MeOH (18:1) gave 236 mg (76%) of **18** as a white crystal: $[\alpha]^{25}_D$ +53.1° (*c* 1.07, $CHCl_3$); mp 74–75 °C (recrystallized from hexane–EtOAc); IR (KBr) 3433, 3296, 3206, 3076, 1653 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.45–7.25 (5H, m), 6.25 (1H, d, J = 6.6 Hz), 4.80 (1H, d, J = 6.6 Hz), 4.74 (1H, d, J = 6.6 Hz), 4.73 (1H, d, J = 6.6 Hz), 4.71 (1H, d, J = 11.9 Hz), 4.67 (1H, d, J = 6.6 Hz), 4.59 (1H, d, J = 11.9 Hz), 4.42 (1H, dd, J = 6.6, 4.2 Hz), 4.27 (1H, t, J = 6.6 Hz), 4.16 (1H, t, J = 4.2 Hz), 3.89 (1H, s, OH), 3.81 (1H, dd, J = 11.6, 5.3 Hz), 3.80 (1H, d, J = 4.2 Hz), 3.57 (1H, dd, J = 11.6, 8.4 Hz), 3.43 (3H, s), 3.40 (3H, s), 2.05 (3H, s), 1.71 (1H, br s, OH); MS m/z 400 ($M^+ + 1$); R_f = 0.43 (CH_2Cl_2:MeOH = 18:1). Anal. Calcd for $C_{19}H_{29}NO_7$: C, 57.12; H, 7.32; N, 3.51. Found: C, 57.27; H, 7.29; N, 3.53.

[1*R*-(1α,2β,3α,4β,5β)]-5-Acetamido-1,3,4-triacetoxy-1-(acetoxymethyl)-2-(benzyloxy)cyclopentane (19). To a solution of **18** (50 mg, 0.124 mmol) in MeOH (0.74 mL) was added 10% hydrogen chloride in MeOH (0.74 mL) with stirring at rt. After 5 min, this mixture was warmed to 50 °C and stirred for 20 min. After completion of the reaction, the reaction mixture was concentrated *in vacuo* to give a residue, which was dried under the reducing pressure for 3 h. To a solution of this residue in pyridine (2.0 mL) were added acetic anhydride (0.5 mL) and DMAP (1.5 mg) with stirring at rt. After 24 h, EtOH (2 mL) was added to the reaction mixture at rt. After being stirred for 30

min, this reaction mixture was concentrated *in vacuo* to give a mixture, which was diluted with EtOAc and washed with 1 M hydrochloric acid. The aqueous layer was extracted twice with EtOAc, and the combined organic layer was washed with saturated aqueous $NaHCO_3$ and brine. The organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with benzene–MeCN (2:1) gave 44 mg (74%) of **19** as a pale yellow oil: $[\alpha]^{25}_D$ +20.2° (*c* 1.69, $CHCl_3$); IR (film) 1747, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.50–7.28 (5H, m), 6.00 (1H, d, J = 11.2 Hz), 5.46 (1H, dd, J = 6.9, 4.6 Hz), 5.22 (1H, d, J = 4.6 Hz), 5.09 (1H, ddd, J = 11.2, 6.9, 1.6 Hz), 4.87 (1H, d, J = 11.9 Hz), 4.77 (1H, d, J = 12.5 Hz), 4.70 (1H, d, J = 12.5 Hz), 4.65 (1H, d, J = 11.9 Hz), 4.47 (1H, br s), 2.07 (3H, s), 2.05 (3H × 2, s), 2.04 (3H, s), 1.91 (3H, s); MS m/z 480 (M^+ + 1), 437, 420; R_f = 0.27 (benzene:MeCN = 2:1); high resolution mass, calcd for $C_{23}H_{30}O_{10}N$ 480.1870, found 480.1865 (M^+ + 1).

[1*R*-(1α,2β,3α,4β,5β)]-5-Acetamido-1,2,3,4-tetraacetoxy-1-(acetoxymethyl)cyclopentane (5). A mixture of **19** (70 mg, 0.145 mmol) and 20% $Pd(OH)_2$ on carbon (410 mg) in EtOH (7.0 mL) was hydrogenolyzed at rt. After 1 h, the reaction mixture was filtered and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with benzene–acetonitrile (1:1) gave 48 mg (83%) of the corresponding alcohol as a colorless oil. To a solution of this alcohol in pyridine (2.4 mL) were added acetic anhydride (0.24 mL) and DMAP (5.0 mg), and this mixture was stirred at rt for 5 h. After completion of the reaction, to this reaction mixture was added EtOH (1 mL), and the mixture was stirred for 30 min and concentrated *in vacuo* to give a residue, which was diluted with EtOAc and washed with 1 M hydrochloric acid. The aqueous layer was extracted twice with EtOAc and the combined organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with benzene–MeCN (3:2) gave 38 mg (61% from **19**) of **5** as a white crystal: $[\alpha]^{25.5}_D$ +6.0° (*c* 1.23, $CHCl_3$); mp 129–130 °C (recrystallized from hexane–EtOAc); IR (KBr) 3367, 1744, 1726, 1695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.86 (1H, d, J = 8.5 Hz), 5.81 (1H, d, J = 4.9 Hz), 5.38 (1H, dd, J = 8.5, 4.9 Hz), 5.33 (1H, t, J = 8.5 Hz), 5.24 (1H, t, J = 4.9 Hz), 4.63 (1H, d, J = 11.9 Hz), 4.56 (1H, d, J = 11.9 Hz), 2.14 (3H, s), 2.13 (3H, s), 2.09 (3H, s), 2.08 (3H, s), 2.07 (3H, s), 2.02 (3H, s); MS m/z 432 (M^+ + 1); R_f = 0.30 (benzene:MeCN = 3:2). Anal. Calcd for $C_{18}H_{25}NO_{11}$: C, 50.12; H, 5.84; N, 3.25. Found: C, 50.34; H, 6.02; N, 3.33.

[1*R*-(1α,2α,3β,4α,5α)]-2-(Benzyloxy)-1-[(benzyloxy)methyl]-3,4-bis(methoxymethoxy)-6-oxabicyclo[3.1.0]hexane (20). To a solution of **16α** (647 mg, 1.9 mmol) in DMF (19.4 mL) were added NaH (169 mg, 2.9 mmol, 55% in oil dispersion) and benzyl bromide (0.34 mL, 2.9 mmol) with stirring at 0 °C. After 5 min, this mixture was warmed to rt and stirred for 2 h. After completion of the reaction, EtOH (0.2 mL) was added to the reaction mixture with stirring at 0 °C. After 30 min, the reaction mixture was diluted with EtOAc and washed with brine. The aqueous layer was extracted twice with EtOAc. The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with hexane–EtOAc (2:1) gave 801 mg (98%) of **20** as a colorless oil: $[\alpha]^{25}_D$ +26.9° (*c* 1.21, $CHCl_3$); IR (film) 3032 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40–7.20 (10H, m), 4.75 (1H, d, J = 6.9 Hz), 4.71 (1H, d, J = 6.9 Hz), 4.74 (1H, d, J = 12.5 Hz), 4.66 (1H, d, J = 12.5 Hz), 4.63 (1H, d, J = 12.5 Hz), 4.62 (1H, d, J = 6.6 Hz), 4.55 (1H, d, J = 12.5 Hz), 4.50 (1H, d, J = 6.6 Hz), 4.33 (1H, d, J = 11.9 Hz), 4.13 (1H, s), 4.11 (1H, s), 4.00 (1H, s), 3.60 (1H, s), 3.53 (1H, d, J = 11.9 Hz), 3.39 (3H, s), 3.33 (3H, s); MS m/z 398 (M^+ + 1 − OMe); R_f = 0.73 (hexane:EtOAc = 1:1). Anal. Calcd for $C_{24}H_{30}O_7$: C, 66.95; H, 7.02. Found: C, 66.67; H, 7.18.

[1*R*-(1α,2β,3α,4β,5β)]-5-Azido-2-(benzyloxy)-1-[(benzyloxy)methyl]-3,4-bis(methoxymethoxy)-1-cyclopentanol (21). To a solution of **20** (500 mg, 1.16 mmol) in DMF (25 mL) and ethylene glycol (5 mL) were added sodium azide (910 mg, 14 mmol) and ammonium chloride (750 mg, 14 mmol) with stirring at rt, and this mixture was warmed to 125 °C and stirred for 48 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed with brine. The aqueous layer was extracted twice with EtOAc. The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with benzene–MeCN (10:1) gave 430 mg (78%) of **21** as a pale yellow oil: $[\alpha]^{24}_D$ +11.0° (*c* 1.36, $CHCl_3$); IR (film) 3445, 3089, 3065, 3032, 2107 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.45–7.25 (10H, m), 4.78 (1H, d, J = 6.6 Hz), 4.77 (1H, d, J = 6.6 Hz), 4.74 (1H, d, J = 6.6 Hz), 4.71 (1H, d, J = 10.9 Hz), 4.68 (1H, d, J = 6.6 Hz), 4.63 (1H, d, J = 10.9 Hz), 4.56 (1H, d, J = 10.9 Hz), 4.55 (1H, d, J = 10.9 Hz), 4.33 (1H, dd, J = 7.3, 4.6 Hz), 4.19 (1H, dd, J = 7.3, 4.0 Hz), 3.87 (1H, d, J = 9.8 Hz and 1H, dd, J = 4.6, 1.3 Hz), 3.72 (1H, dd, J = 4.0, 1.3 Hz), 3.64 (1H, d, J = 9.8 Hz), 3.45 (3H, s), 3.39 (3H, s), 3.03 (1H, s, OH); MS m/z 444 (M^+ + 1 − N_2), 400, 354, 322, 292; R_f = 0.26 (benzene:EtOAc = 5:1). Anal. Calcd for $C_{24}H_{31}N_3O_7$: C, 60.88; H, 6.60; N, 8.87. Found: C, 61.18; H, 6.60; N, 8.64.

***N*-Benzyl-*N'*-[[1*R*-(1α,2β,3α,4β,5β)]-2-(benzyloxy)-1-[(benzyloxy)methyl]-1-hydroxy-3,4-bis(methoxymethoxy)-1-cyclopent-5-yl]thiourea (25).** A solution of **21** (204 mg, 0.43 mmol) in Et_2O (6.0 mL) was added dropwise to a suspension of $LiAlH_4$ (65.3 mg, 1.72 mmol) in Et_2O (12.0 mL) with stirring at 0 °C under N_2. After 4 h, this reaction mixture was diluted with Et_2O, and saturated aqueous Na_2SO_4 was added to the mixture at 0 °C. After being stirred at rt for 1 h, this mixture was extracted twice with Et_2O. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with CH_2Cl_2–MeOH (15:1) gave 166 mg (86%) of the corresponding amine as a colorless oil: R_f = 0.36 (CH_2Cl_2:MeOH = 15:1). To a solution of 166 mg of the amine in THF (7.0 mL) was added benzyl isothiocyanate (0.07 mL, 0.47 mmol) with stirring at rt. After 3 h, this reaction mixture was diluted with EtOAc and washed with brine. The aqueous layer was extracted twice with EtOAc. The combined organic layer was dried over $MgSO_4$ and concentrated in vacuo to give a crude product, which was chromatographed on silica gel. Elution with benzene–EtOAc (4:1) gave 179 mg (97%, 83% from **21**) of **25** as a colorless oil: $[\alpha]^{24}_D$ +9.5° (*c* 1.18, $CHCl_3$); IR (film) 3336, 3088, 3063, 3031, 1547 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.50–7.25 (15H, m), 7.18 (1H, br s), 6.81 (1H, br s), 4.80–4.57 (8H, m), 4.53 (1H, d, J = 10.4 Hz), 4.48 (1H, d, J = 10.4 Hz), 4.35–4.09 (2H, m), 4.03 (1H, dull d, J = 4.0 Hz), 3.87 (2H, dull d, 5.3 Hz), 3.72 (1H, d, J = 9.9 Hz), 3.68 (1H, br s, OH), 3.37 (3H, s), 3.32 (3H, s); MS m/z 596 (M^+), 565 (M^+ − OMe); R_f = 0.5 (benzene:EtOAc = 3:1). Anal. Calcd for $C_{32}H_{40}N_2O_7S$: C, 64.41; H, 6.76; N, 4.69; S, 5.37. Found: C, 64.18; H, 6.67; N, 4.68; S, 5.22.

***N*-Benzyl-*N'*-[[1*R*-(1α,2β,3α,4β,5β)]-2-(benzyloxy)-1-[(benzyloxy)methyl]-1,3,4-trihydroxycyclopent-5-yl]thiourea (26).** To a solution of **25** (82 mg, 0.14 mmol) in 1,4-dioxane (2.5 mL) was added 0.5 M hydrochloric acid (2.5 mL) with stirring at rt, this reaction mixture was then warmed to 60 °C and stirred for 24 h. After the reaction was complete, the reaction mixture was diluted with EtOAc and washed with saturated aqueous $NaHCO_3$. The aqueous layer was extracted twice with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with benzene–EtOAc (1:1) gave 52 mg (74%) of **26** as a white foamy glass: $[\alpha]^{24}_D$ +54.5° (*c* 1.11, $CHCl_3$); IR (KBr) 3331, 3088, 3063, 3031, 1545 cm^{-1}; ^1H NMR ($CD_3OD/CDCl_3$ = 2/1) δ 7.45–7.20 (15H, m), 4.82 (4H, s), 4.78 (2H, s), 4.70 (1H, br s), 4.55–4.40 (2H, m), 4.03 (1H, dd, J = 7.3, 1.9 Hz), 4.02 (1H, s), 3.78 (1H, d, J = 7.3 Hz), 3.73 (1H, d, J = 9.7 Hz), 3.51 (1H, d, J = 9.7 Hz); MS m/z 492, 402, 383, 360; R_f = 0.19 (benzene:EtOAc = 2:1). Anal. Calcd for $C_{28}H_{32}N_2O_5S$: C, 66.12; H, 6.34; N, 5.51; S, 6.30. Found: C, 66.14; H, 6.47; N, 5.73; S, 6.12.

[3a*R*-(3aα,4α,5β,6α,6aα)]-2-(Benzylamino)-5-(benzyloxy)-4-[(benzyloxy)methyl]-3a,5,6,6a-tetrahydro-4*H*-cyclopentoxazole-4,6-diol (28). To a solution of 2-chloro-3-ethylbenzoxazolium tetrafluoroborate (32 mg, 0.12 mmol) in MeCN (2.5 mL) was added a solution of **26** (50 mg, 0.1 mmol) in MeCN (1 mL) with stirring at 0 °C under N_2. After being stirred for 1 h, Et_3N (0.033 mL, 0.24 mmol) was added to this mixture while maintaining the temperature at 0 °C under N_2. After 3 h, this reaction mixture was diluted with EtOAc and washed with saturated aqueous $NaHCO_3$. The aqueous layer was extracted twice with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a

crude product, which was chromatographed on silica gel. Elution with CH_2Cl_2–MeOH (12:1) gave 41 mg (82%) of **28** as a pale yellow foamy glass: $[\alpha]^{24}_D$ −7.0° (*c* 1.12, $CHCl_3$); IR ($CHCl_3$) 3450, 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40–7.10 (15H, m), 5.00 (1H, dd, *J* = 8.0, 1.4 Hz), 4.65 (1H, d, *J* = 11.8 Hz), 4.61 (1H, d, *J* = 11.8 Hz), 4.54 (1H, d, *J* = 11.8 Hz), 4.48 (1H, d, *J* = 8.0 Hz), 4.44 (1H, d, *J* = 11.8 Hz), 4.30 (1H, s), 4.26 (1H, d, *J* = 14.5 Hz), 4.19 (1H, d, *J* = 14.5 Hz), 3.94 (1H, d, *J* = 9.9 Hz), 3.77 (1H, d, *J* = 1.4 Hz), 3.76 (1H, d, *J* = 9.9 Hz), 3.45 (3H, br s, NH, OH × 2); MS *m/z* 474 (M^+); R_f = 0.27 (CH_2Cl_2:MeOH = 12:1); high resolution mass, calcd for $C_{28}H_{30}N_2O_5$ 474.2154, found 474.2162 (M^+).

[3a*R*-(3aα,4α,5β,6α,6aα)]-2-Amino-4-(hydroxymethyl)-3a,5,6,6a-tetrahydro-4*H*-cyclopentoxazole-4,5,6-triol (Trehalamine) (3). A mixture of **28** (11 mg, 0.024 mmol) and 20% $Pd(OH)_2$ on carbon (170 mg) in MeOH (2.5 mL) was hydrogenolyzed at 60 °C for 30 min. After completion of the reaction, this reaction mixture was filtered and concentrated *in vacuo* to give a crude product, which was chromatographed on Amberlite CG-50 (NH_4^+ type). Elution with 0.5 M aqueous NH_3 gave 3.5 mg (71%) of **3** as a white solid: $[\alpha]^{24}_D$ +14.4° (*c* 0.32, H_2O); IR (KBr) 3332, 1715, 1678 cm^{-1}; ^1H NMR (D_2O/external TMS) δ 4.80 (1H, ddd, *J* = 8.8, 2.5, <1.0 Hz), 4.16 (1H, d, *J* = 8.8 Hz), 4.02 (1H, dd, *J* = 3.9, 2.5 Hz), 3.77 (1H, dt, *J* = 3.9, <1.0 Hz), 3.63 (1H, d, *J* = 9.8 Hz), 3.53 (1H, d, *J* = 9.8 Hz); FAB-MS, positive *m/z* 205 $(M + H)^+$, negative *m/z* 203 $(M - H)^-$; R_f = 0.58 (MeCN:H_2O:AcOH = 13:5:2); high resolution mass, calcd for $C_7H_{13}N_2O_5$ 205.0824, found 205.0822 $(M + H)^+$.

***N*-(2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl)-*N'*-[[1*R*-(1α,2β,3α,4β,5β)]-2-(benzyloxy)-1-[(benzyloxy)methyl]-1,3,4-trihydroxycyclopent-5-yl]thiourea (29).** A solution of **21** (51 mg, 0.11 mmol) in Et_2O (3.0 mL) was added dropwise to a suspension of $LiAlH_4$ (18 mg, 0.44 mmol) in Et_2O (2.6 mL) with stirring at 0 °C under N_2. After 4 h, this reaction mixture was diluted with Et_2O, and saturated aqueous Na_2SO_4 was added to the mixture at 0 °C. After being stirred at rt for 1 h, the mixture was extracted twice with Et_2O. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with CH_2Cl_2–MeOH (15:1) gave 44 mg (91%) of the corresponding amine as a colorless oil: R_f = 0.36 (CH_2Cl_2:MeOH = 15:1). To a solution of this amine (44 mg) in MeOH (0.7 mL) was added 10% hydrogen chloride in methanol (0.7 mL) with stirring at 0 °C, and after 5 min, this mixture was warmed to 50 °C and stirred for 5 h. After completion of the reaction, this reaction mixture was concentrated *in vacuo* to give a residue, which was dried under reduced pressure for 3 h. Then, to a solution of this residue in THF (2.2 mL) were added a solution of 2,3,4,6-tetra-*O*-benzyl-1-deoxy-α-D-glucopyranosyl isothiocyanate (58 mg, 0.1 mmol) in THF (2.2 mL) and Et_3N (0.0205 mL, 0.15 mmol) with stirring at 0 °C. After being stirred for 5 min at 0 °C, this mixture was warmed to rt and stirred for 18 h. After completion of the reaction, this reaction mixture was diluted with EtOAc and washed with brine. The aqueous layer was extracted twice with EtOAc. The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with benzene–EtOAc (5:2) gave 70 mg (69% from **21**) of **29** as a colorless foamy glass: $[\alpha]^{24}_D$ +109.1° (*c* 1.01, $CHCl_3$); IR (KBr) 3289, 3063, 3030, 1535 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.76 (1H, br d, *J* = 6.4 Hz, NH), 7.40–7.10 (30H, m), 6.68 (1H, br s, NH), 5.59 (1H, br s, OH), 5.06 (1H, br s), 4.89 (1H, d, *J* = 10.6 Hz), 4.82 (1H, d, *J* = 10.6 Hz), 4.80 (1H, d, *J* = 10.6 Hz), 4.78 (1H, d, *J* = 10.6 Hz), 4.70 (1H, t, *J* = 6.4 Hz), 4.66 (1H, d, *J* = 10.6 Hz), 4.65 (1H, d, *J* = 10.6 Hz), 4.60 (1H, d, *J* = 10.6 Hz), 4.48 (1H, d, *J* = 10.6 Hz), 4.41 (2H, s), 4.34 (1H, d, *J* = 10.6 Hz), 4.21 (1H, d, *J* = 10.6 Hz), 4.06 (1H, dd, *J* = 7.5, 2.8 Hz), 4.00 (1H, d, *J* = 6.4 Hz), 3.90 (1H, d, *J* = 7.5 Hz), 3.80–3.60 (6H, m), 3.54 (1H, d, *J* = 9.4 Hz), 3.41 (1H, d, *J* = 10.3 Hz), 2.13 (2H, br s, OH × 2); FAB-MS, positive *m/z* 941 $(M + H)^+$, negative *m/z* 939 $(M - H)^-$; R_f = 0.32 (benzene: EtOAc = 5:2); high resolution mass, calcd for $C_{55}H_{61}N_2O_{10}S$ 941.4047, found 941.4070 $(M + H)^+$.

1-[[[3a*R*-(3aα,4α,5β,6α,6aα)]-5-(Benzyloxy)-4-[(benzyloxy)-methyl]-3a,5,6,6a-tetrahydro-4,6-dihydroxy-4*H*-cyclopentoxazol-2-yl]amino]-1-deoxy-2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (31). To a solution of 2-chloro-3-ethylbenzoxazolium tetrafluoroborate (27 mg, 0.1 mmol) in MeCN (2.7 mL) was added a solution of **29** (54 mg, 0.06 mmol) in MeCN (1 mL) with stirring at 0 °C under N_2. After being stirred for 1 h, Et_3N (0.026 mL, 0.19 mmol) was added to this mixture, maintaining the temperature at 0 °C. After 1 h, this reaction mixture was diluted with EtOAc and washed with saturated aqueous $NaHCO_3$. The aqueous layer was extracted twice with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with benzene–EtOAc (1:1) gave 35 mg (68%) of **31** as a colorless oil: $[\alpha]^{24}_D$ +44.2° (*c* 1.01, $CHCl_3$); IR (film) 3419, 3088, 3063, 3031, 1672 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40–7.00 (30H, m), 5.32 (1H, d, *J* = 5.3 Hz), 4.97 (1H, dd, *J* = 8.6 Hz), 4.86 (1H, d, *J* = 11.3 Hz), 4.74 (1H × 2, d, *J* = 11.3 Hz), 4.62 (1H, d, *J* = 11.3 Hz), 4.56 (1H, d, *J* = 11.3 Hz), 4.54 (1H, d, *J* = 12.6 Hz), 4.52 (1H, d, *J* = 12.6 Hz), 4.50 (1H, d, *J* = 8.6 Hz), 4.43 (1H, d, *J* = 11.3 Hz), 4.40 (1H, d, *J* = 12.6 Hz), 4.37 (1H, d, *J* = 12.6 Hz), 4.28 (1H, s), 4.04 (2H, s), 4.00 (1H, d, *J* = 9.9 Hz), 3.78 (1H, d, *J* = 9.9 Hz), 3.72 (1H, s), 3.70–3.57 (4H, m), 3.54 (1H, br d, *J* = 11.0 Hz), 3.43 (1H, br d, *J* = 11.0 Hz), 3.35–2.40 (3H, br s, OH × 2, NH); FAB-MS, positive *m/z* 907 $(M + H)^+$, negative *m/z* 905 $(M - H)^-$; R_f = 0.37 (benzene: EtOAc = 1:1); high resolution mass, calcd for $C_{55}H_{59}N_2O_{10}$ 907.4170, found 907.4193 $(M + H)^+$.

[1*R*-(1α,2β,3α,4β,5β)]-5-Amino-1-(hydroxymethyl)-1,2,3,4-cyclopentanetetrol (32). A suspension of **5** (12 mg, 0.028 mmol) in 2M hydrochloric acid (0.5 mL) was stirred at 80 °C for 2 h. After completion of the reaction, this reaction mixture was concentrated *in vacuo* to give a crude product, which was chromatographed on Amberlite CG-50 (NH_4^+ type). Elution with 0.5 M aqueous NH_3 gave 5 mg (89%) of **32** as a pale yellow powder: $[\alpha]^{25}_D$ +1.7° (*c* 0.41, H_2O); IR (KBr) 3354 cm^{-1}; ^1H NMR (D_2O/external TMS) δ 3.88 (1H, dd, *J* = 6.8, 5.9 Hz), 3.78 (1H, t, *J* = 5.9 Hz), 3.60 (1H, d, *J* = 11.7 Hz and 1H, d, *J* = 5.9 Hz), 3.54 (1H, d, *J* = 11.7 Hz), 3.05 (1H, d, *J* = 6.8 Hz); FAB-MS, positive *m/z* 180 $(M + H)^+$, negative *m/z* 178 $(M - H)^-$, R_f = 0.36 (MeCN:H_2O:AcOH = 13:5:2); high resolution mass, calcd for $C_6H_{14}NO_5$ 180.0872, found 180.0874 $(M + H)^+$.

***N'*-(2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl)-*N*-[[1*R*-(1α,2β,3α,4β,5β)]-1-(hydroxymethyl)-1,2,3,4-tetrahydroxycyclopent-5-yl]thiourea (33).** To a solution of **32** (23 mg, 0.13 mmol) in water (0.23 mL) was added a solution of 2,3,4,6-tetra-*O*-benzyl-1-deoxy-α-D-glucopyranosyl isothiocyanate (84 mg, 0.14 mmol) in THF (0.23 mL) with stirring at rt. After 48 h, this reaction mixture was concentrated *in vacuo* to give a residue, which was dried under reduced pressure and chromatographed on silica gel. Elution with CH_2Cl_2–MeOH (10:1) gave 86 mg (88%) of **33** as a white foamy glass: $[\alpha]^{25}_D$ +146.7° (*c* 0.48, $CHCl_3$); IR (KBr) 3312, 3088, 3063, 3031, 1536 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.74 (1H, br s), 7.55–7.00 (20H, m), 6.75 (1H, br s), 5.45 (1H, br s), 5.18 (1H, br s), 5.00–4.25 (8H, m), 4.20–3.20 (12H, m), 1.70 (4H, br s including H_2O); FAB-MS, positive *m/z* 761 $(M + H)^+$, negative *m/z* 759 $(M - H)^-$; R_f = 0.37 (CH_2Cl_2:MeOH = 10:1). Anal. Calcd for $C_{41}H_{48}N_2SO_{10}$: C, 64.72; H, 6.36; N, 3.68; S, 4.21. Found: C, 64.50; H, 6.49; N, 3.53; S, 4.11.

1-Deoxy-1-[[[3a*R*-(3aα,4α,5β,6α,6aα)]-4-(hydroxymethyl)-3a,5,6,6a-tetrahydro-4,5,6-trihydroxy-4*H*-cyclopentoxazol-2-yl]amino]-2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (34). To a solution of 2-chloro-3-ethylbenzoxazolium tetrafluoroborate (42 mg, 0.16 mmol) in MeCN (3.4 mL) was added a solution of **33** (68 mg, 0.09 mmol) in MeCN (1 mL) with stirring at 0 °C under N_2. After being stirred for 1 h, Et_3N (0.045 mL, 0.32 mmol) was added to this mixture, maintaining the temperature at 0 °C. After 1 h, this reaction mixture was diluted with EtOAc and washed with saturated aqueous $NaHCO_3$. The aqueous layer was extracted twice with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude product, which was chromatographed on silica gel. Elution with CH_2Cl_2–MeOH (10:1) gave 47 mg (73%) of **34** as a white foamy glass: $[\alpha]^{26}_D$ +60° (*c* 0.61, $CHCl_3$); IR (KBr) 3389, 3088, 3063, 3031, 1668 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.45–7.05 (20H, m), 5.31 (1H, d, *J* = 5.3 Hz), 4.91 (1H, d, *J* = 11.2 Hz), 4.80 (1H, d, *J* = 7.9Hz), 4.78 (1H, d, *J* = 11.2 Hz), 4.76 (1H, d, *J* = 11.2 Hz), 4.60 (1H, d, *J* = 11.8 Hz), 4.55 (1H, d, *J* = 11.8 Hz), 4.46 (1H, d, *J* = 11.2 Hz), 4.44 (1H, d, *J* = 11.2 Hz), 4.40 (1H, d, *J* = 11.2 Hz), 4.31 (1H, d, *J* = 7.9 Hz), 4.05–3.60

(13H, m), 3.53 (1H, dd, J = 9.9, 5.9 Hz), 3.41 (1H, t, J = 9.2 Hz); FAB-MS, positive m/z 727 $(M + H)^+$, negative m/z 725 $(M - H)^-$; R_f = 0.36 (CH_2Cl_2:MeOH = 10:1); high resolution mass, calcd for $C_{41}H_{47}N_2O_{10}$ 727.3219, found m/z 727.3219 $(M + H)^+$.

1-Deoxy-1-[[[3a*R*-(3aα,4α,5β,6α,6aα)]-4-(hydroxymethyl)-3a,5,6,6a-tetrahydro-4,5,6-trihydroxy-4*H*-cyclopentoxazol-2-yl]amino]-α-D-glucopyranose (Trehazolin) (1). (**a**) To a solution of **31** (33 mg, 0.04 mmol) in MeOH (6.7 mL) was added 20% $Pd(OH)_2$ on carbon (1.0g) at rt, and the mixture was hydrogenolyzed at 60 °C for 30 min. After completion of the reaction, this reaction mixture was filtered and concentrated *in vacuo* to give a crude product, which was chromatographed on Amberlite CG-50 (NH_4^+ type/H^+ type = 3:2, 5 mL). Elution with 0.5 M aqueous NH_3 gave 5.9 mg (44%) of 1 as a white powder: $[\alpha]^{30}_D$ +112.7° (c 0.59, H_2O). (**b**) The same treatment of **34** (43 mg, 0.06 mmol) as mentioned above in procedure (**a**) gave 10.3 mg (48%) of 1: $[\alpha]^{25}_D$ +119.2° (c 1.03, H_2O); IR (KBr) 3375, 1664 cm^{-1}; ^1H NMR (D_2O/external TMS) δ 5.14 (1H, d, J = 5.5 Hz), 4.74 (1H, dd, J = 8.8, 2.3 Hz), 4.15 (1H, d, J = 8.8 Hz), 4.00 (1H, dd, J = 5.0, 2.3 Hz), 3.75 (1H, d, J = 5.0 Hz), 3.68–3.42 (6H, m), 3.37 (1H, ddd, J = 10.1, 5.4, 2.3 Hz), 3.21 (1H, dd, J = 9.8, 8.8 Hz); FAB-MS, positive m/z 367 $(M + H)^+$, negative m/z 365 $(M - H)^-$; R_f = 0.32 (MeCN:H_2O:AcOH = 13:5:2); high resolution mass, calcd for $C_{13}H_{23}N_2O_{10}$ 367.1353, found m/z 367.1353 $(M + H)^+$.

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