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DISPLACEMENT OF "PSEUDOANOMERIC" HYDROXYL GROUPS BY USING THE DIETHYL AZODICARBOXYLATE–TRIPHENYLPHOSPHINE SYSTEM

MITSUO HAYASHIDA, NOBUO SAKAIRI, AND HIROYOSHI KUZUHARA*
RIKEN (The Institute of Physical and Chemical Research), Wako-shi, Saitama 351-01 (Japan)
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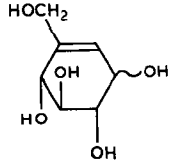
ABSTRACT

1D-(1,2,4/3)-2,3,4-Tri-*O*-benzyl-5-(trityloxymethyl)-5-cyclohexene-1,2,3,4-tetrol (**5a**) and its 1L-(1,3/2,4) isomer (**5b**) were prepared from D-glucose, and they underwent ready mutual interconversion through an S_N2 procedure employing a benzoic acid–diethyl azodicarboxylate–triphenylphosphine system and subsequent basic hydrolysis. Azido, phthalimido, and even more complex nucleophile groups could similarly also substitute the allylic hydroxyl groups of **5a** and **5b** by using the same system, with a few different results between **5a** and **5b**.

INTRODUCTION

1D-(1,2,4/3)- and 1L-(1,3/2,4)-5-(hydroxymethyl)-5-cyclohexene-1,2,3,4-tetrol† (**1**) may be regarded as α and β anomers of pseudo-D-glucopyranose, as **1**



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differs from D-glucopyranose only in possessing a C–C double bond in place of the ring-oxygen atom and its bond to C-5 of D-glucopyranose. Replacement reactions at the anomeric position of aldoses are in general greatly influenced by the inductive and mesomeric effects of the ring-oxygen atom. Replacement reactions at C-1 of such pseudosugars as **1** are quite interesting, because the electronic effects of the sp^2 carbon atom resemble those of the oxygen atom. This paper deals with

*To whom correspondence should be addressed.

†The cyclohexenetetrol derivatives described in this paper are named and numbered according to the IUPAC-IUB Recommendations for Cyclitols, detailed in *Pure Appl. Chem.*, 37 (1974) 285–297. To avoid confusion, the numbering used for the tetrols is retained for compounds **7a**, **7b**, **8a**, **8b**, **9a**, **9b**, and **16**, even though strict application of the rules would require these to be named as 4-cyclohexene-1,2,3-triols (see ref. 2).

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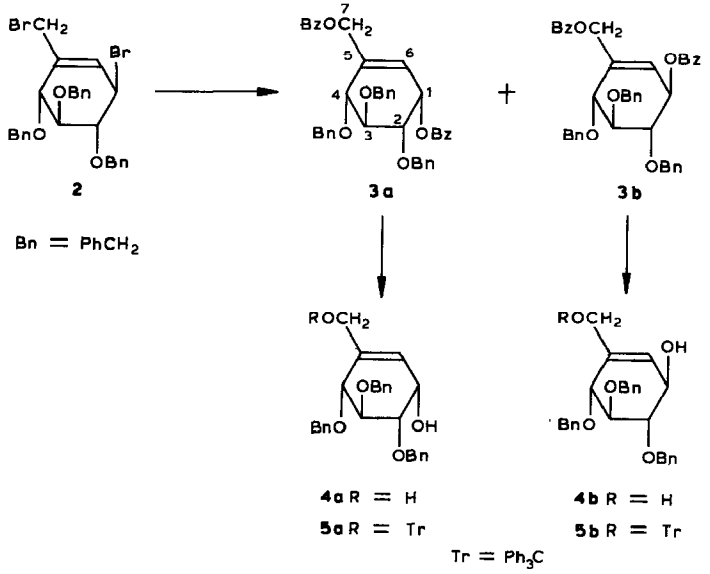
replacement of the pseudoanomeric hydroxyl groups in derivatives of **1** (**5a** and **5b**) with several nucleophiles, using the diethyl azodicarboxylate (DEAD)–triphenylphosphine (TPP) system[1].

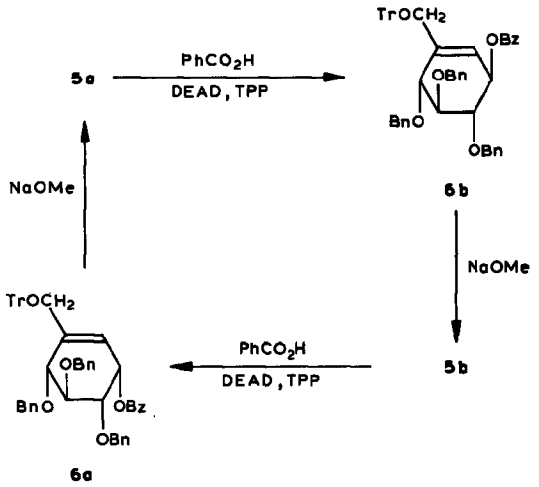


RESULTS AND DISCUSSION

The β-pseudoglycosyl halide type of *O*-benzylated compound, **2**, had been prepared from D-glucose in the course of our total synthesis[2] of Amylostatin (XG), an α-D-glucosidase inhibitor. When **2** was treated with an excess of sodium benzoate in *N,N*-dimethylformamide (DMF), 1D-(1,2,4/3)-1-*O*-benzoyl-5-(benzoyloxymethyl)-2,3,4-tri-*O*-benzyl-5-cyclohexene-1,2,3,4-tetrol (**3a**) and its 1L-(1,3/2,4) isomer (**3b**) were obtained in 36 and 34% yields, respectively. The production of these two diastereoisomers was predictable from the former observation[2] that the secondary bromide in **2** was very susceptible to epimerization under these conditions. Configurations of C-1 of such pseudosugars as **3a** and **3b** were well elucidated on the basis of the *J* value between H-1 and H-6 in their ^{1}H-n.m.r. spectra[3]. Thus, $J_{1,6}$ was 6 Hz in the spectrum of **3a**, whereas almost no coupling was observed between them in the spectrum of **3b**. Alkaline hydrolysis of **3a** and **3b** afforded the corresponding diols **4a** and **4b**, which were tritylated in the usual way to give 1D-(1,2,4/3)-2,3,4-tri-*O*-benzyl-5-(trityloxymethyl)-5-cyclohexene-1,2,3,4-tetrol (**5a**) and its 1L-(1,3/2,4) isomer (**5b**) in good yields.

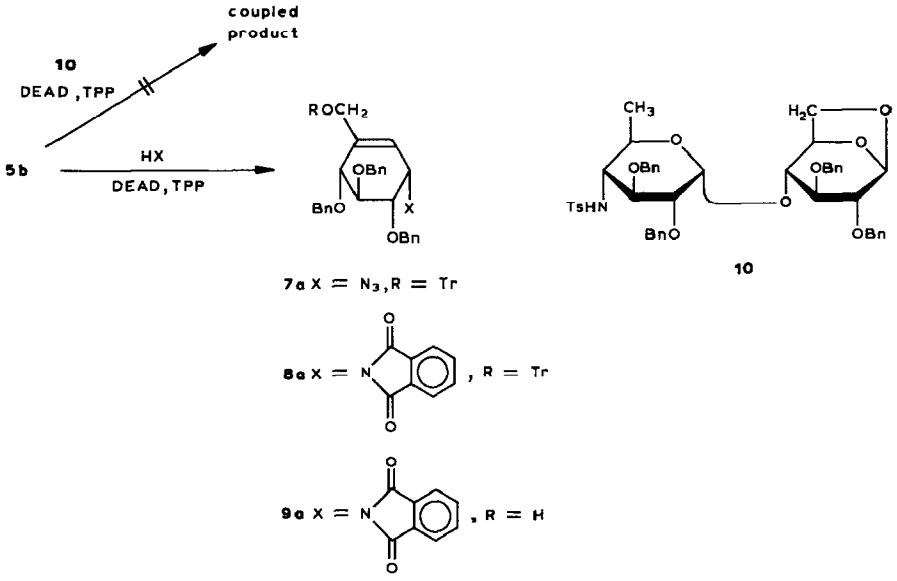
Replacement of the pseudoanomeric hydroxyl groups in **5a** and **5b** with several nucleophiles was attempted, employing Mitsunobu's procedure[1]. First, **5a** was treated with benzoic acid in the presence of diethyl azodicarboxylate (DEAD) and triphenylphosphine (TPP), giving 1L-(1,3/2,4)-1-*O*-benzoyl-2,3,4-tri-*O*-benzyl-

5-trityloxymethyl)-5-cyclohexene-1,2,3,4-tetrol (**6b**) in 70% yield. Removal of the benzoyl group from **6b** under basic conditions gave **5b**. In the same way, **5b** was readily converted into the 1D-(1,2,4/3) isomer (**6a**) of **6b**, which gave **5a** on basic treatment. These replacement reactions at the pseudoanomeric position proceeded with complete inversion of the configuration, showing sharp contrast to the



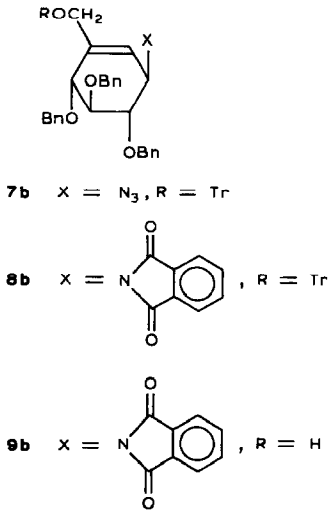
epimerization observed during the conversion of **2** into **3a** and **3b**. Such an S_N2 type of replacement of the labile hydroxyl groups at an allylic position has been regarded as one of the most useful characteristics of the Mitsunobu reaction[1]. In this way, ready mutual interconversion between **5a** and **5b** was attained.

Next, introduction of amine precursors into pseudosugar derivatives was attempted. Paulsen[4] reported the reaction, with hydrazoic acid, DEAD, and TPP, of an analog of **5b** benzoylated at O-7. Employing a modification of this procedure, **5b** was treated with the same combination of reagents, to give 1D-(1,2,4/3)-1-azido-2,3,4-tri-*O*-benzyl-5-(trityloxymethyl)-5-cyclohexene-2,3,4-triol (**7a**) in 72% yield. Efficient cooling below $-10°$ was essential for this conversion. When phthalimide was employed as the reagent, instead of hydrazoic acid, the conversion of **5b** into the phthalimido derivative **8a** proceeded satisfactorily in oxolane solution at room temperature. For structural elucidation, the trityl group of **8a** was removed, to give 1D-(1,2,4/3)-2,3,4-tri-*O*-benzyl-5-(hydroxymethyl)-1-phthalimido-5-cyclohexene-2,3,4-triol (**9a**). It was quite interesting that the bulky phthalimido group could be introduced into the position *cis* to the vicinal benzyloxy group. The success of this phthalimido replacement prompted us to examine the reaction of **5b** with a bulky *N*-*p*-toluenesulfonylated, amino sugar derivative, such as **10** [derived from an intermediate[5] for the Amylostatin (XG) synthesis]. However, this attempt failed, and no coupled product was obtained. The 1D-(1,2,4/3) isomer (**5a**) of **5b** also underwent substitution with azido and phthalimido groups under the same reaction

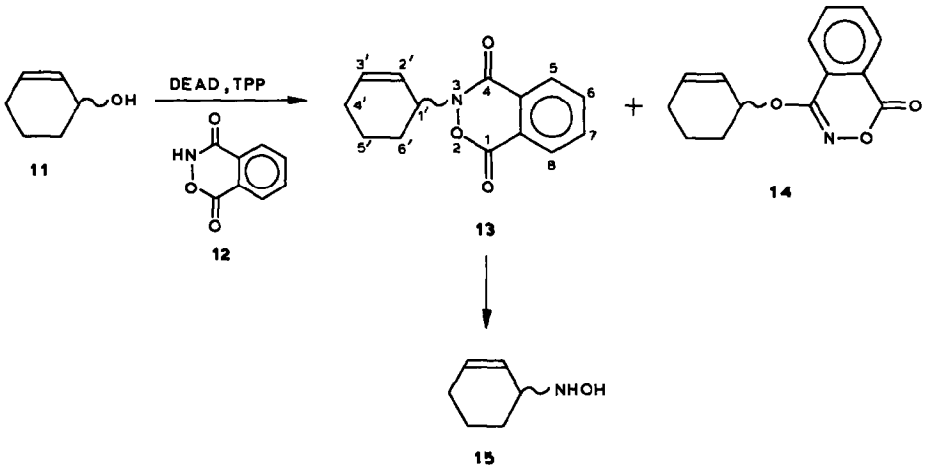


conditions as those employed for the reaction of **5b**, giving the 1L-(1,3/2,4) isomers, **7b** and **8b**, respectively. Again, **8b** was converted into the *O*-detritylated compound **9b** for structural elucidation.

The successful reaction between **5a** (and **5b**) and phthalimide also led to an extension of the reaction using a variant of the reagent, namely, *N,O*-phthaloylhydroxylamine[6] (**12**), as introduction of a hydroxylamine group into the pseudosugar molecule was interesting from both the chemical and biological viewpoints. 2-Cyclohexenol (**11**) was first chosen as a model substrate in place of **5a** and **5b**. Treatment of **11** with **12**, DEAD, and TPP in oxolane gave two products, in 40 and

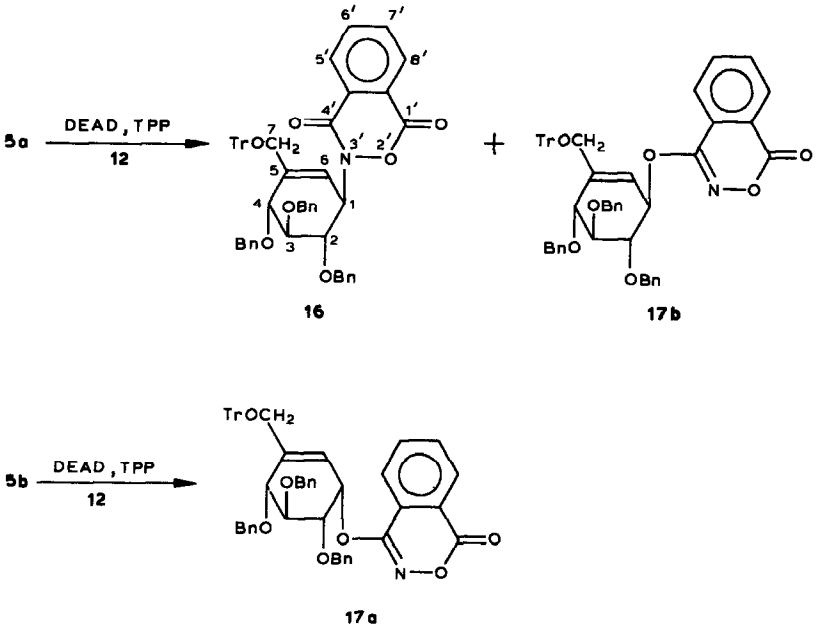


35% yields, respectively. Results of the elemental analyses showed that both compounds had the same elemental composition, $C_{14}H_{13}NO_3$. The i.r. spectrum of the compound obtained in the higher yield revealed two carbonyl absorptions, at 1750 (O–C=O) and 1645 (N–C=O) cm^{-1}, whereas that of the other compound showed only one carbonyl absorption, at 1740 cm^{-1} (O–C=O). Furthermore, in their ^{1}H-n.m.r. spectra, the former compound revealed, in the magnetic field lower than 8 p.p.m., two signals assignable to the aromatic protons in the position *ortho* to the carbonyl groups, whereas the latter revealed only one such signal. On the basis of these data, the structures of the two products were elucidated to be 3-(2-cyclohexenyl)-4-hydro-1,4-dioxo-1*H*-2,3-benzoxazine (**13**) and 4-(2-cyclohexenyloxy)-1-oxo-1*H*-2,3-benzoxazine (**14**), respectively. For confirmation of its structure, **13** was treated with hydrazine hydrate, giving *N*-(2-cyclohexenyl)hydroxylamine (**15**) as



crystals. When **5a** was treated with **12**, DEAD, and TPP in oxolane, two compounds, showing spectral patterns similar to those of **13** and **14**, were obtained, and these were elucidated as being 1L-(1,3/2,4)-2,3,4-tri-*O*-benzyl-1-(1,4-dioxo-4-hydro-1*H*-2,3-benzoxazin-3-yl)-5-(trityloxymethyl)-5-cyclohexene-2,3,4-triol (**16**) and 1L-(1,3/2,4)-2,3,4-tri-*O*-benzyl-1-*O*-(1-oxo-1*H*-2,3-benzoxazin-4-yl)-5-(trityloxymethyl)-5-cyclohexene-1,2,3,4-tetrol (**17b**), respectively. In contrast, the same treatment of **5b** gave only one compound, which was elucidated as being **17a**, the diastereoisomer of **17b**, on the basis of the results of elemental analyses and spectral data. The isomer of **16** was not produced from the attempted reaction of **5b**.

These pseudo-*N*-glycosyl derivatives are potential synthons for biologically active pseudo-oligosaccharides.



EXPERIMENTAL

General methods. — Melting points were determined with a Yamato micro melting-point apparatus, and are uncorrected. Optical rotations were determined with a Perkin–Elmer Model 241MC polarimeter. I.r. spectra were recorded with a Shimadzu IR-27 spectrometer, for potassium bromide disks or, for thin films, on KRS (thallium bromide-iodide). ^{1}H-N.m.r. spectra were recorded at 400 MHz with a JEOL JNM-GX 400 spectrometer, using tetramethylsilane as the internal standard, for solutions in chloroform-*d*. Chromatography was performed in a column of silica gel Merck (70–230 mesh; E. Merck, Darmstadt, Germany). Thin-layer chromatography was conducted on precoated plates (layer thickness, 0.25 mm; E. Merck, Darmstadt, Germany) of silica gel $60F_{254}$. Preparative thin-layer chromatography was performed with precoated plates (layer thickness 2 mm; E. Merck, Darmstadt, Germany) of silica gel $60F_{254}$. Solvent extracts were dried with anhydrous sodium sulfate unless otherwise specified; and solutions were evaporated under diminished pressure.

1D-(1,2,4/3)-1-O-Benzoyl-5-(benzoyloxymethyl)-2,3,4-tri-O-benzyl-5-cyclohexene-1,2,3,4-tetrol (**3a**) *and 1L-(1,3/2,4)-1-O-benzoyl-5-(benzoyloxymethyl)-2,3,4-tri-O-benzyl-5-cyclohexene-1,2,3,4-tetrol* (**3b**). — A mixture of 1D-(1,3/2,6)-1,2,3-tri-*O*-benzyl-6-bromo-4-(bromomethyl)-4-cyclohexene-1,2,3-triol[2] (**2**; 15 g, 16 mmol) and sodium benzoate (8.1 g, 56 mmol) in *N,N*-dimethylformamide (300 mL) was heated for 3 h at 90–100°. The mixture was cooled, diluted with water (200 mL), and extracted with ethyl ether; the extracts were combined, washed with

brine, dried, and evaporated. The residual syrup was agitated in dichloromethane–2-propanol, giving **3b** (3.25 g, 31%) as crystals. After removal of **3b** by filtration, the mother liquor was evaporated, and the residue chromatographed with 99:1 (v/v) benzene–ethyl acetate as the eluant, to give **3a** (3.8 g, 36%) and additional **3b** (0.36 g, 3%). Compound **3a**: $[\alpha]_D^{20}$ +39.5° (*c* 0.41, chloroform); ν_{max}^{film} 1720 cm^{-1} (C=O); δ_H 3.82 (dd, 1 H, *J* 9.5 and 3.7 Hz, H-2), 4.24–4.31 (m, 2 H, H-3,4), 4.62–5.05 (m, 8 H, H-7a,7b, 3 PhCH_2), 5.93 (dd, 1 H, *J* 6 and 3.7 Hz, H-1), and 6.03 (dd, 1 H, *J* 6 and 2 Hz, H-6).

Anal. Calc. for $C_{42}H_{38}O_7$: C, 77.05; H, 5.85. Found: C, 77.14; H, 5.82.

Compound **3b**: m.p. 129–130°, $[\alpha]_D^{19}$ −152° (*c* 0.52, chloroform); ν_{max}^{KBr} 1720 cm^{-1} (C=O); δ_H 3.96–4.04 (m, 2 H, H-2,3), 4.46 (broad d, 1 H, *J* 7 Hz, H-4), 4.7–5.05 (m, 8 H, H-7a,7b, 3 PhCH_2), 5.80 (s, 1 H, H-6), and 5.85 (broad d, 1 H, *J* 7 Hz, H-1).

Anal. Calc. for $C_{42}H_{38}O_7$: C, 77.05; H, 5.85. Found: C, 77.10; H, 5.82.

1D-(1,2,4/3)-2,3,4-Tri-O-benzyl-5-(hydroxymethyl)-5-cyclohexene-1,2,3,4-tetrol (**4a**). — Methanolic sodium methoxide (28%, 0.5 mL) was added to a solution of **3a** (4.6 g, 7 mmol) in methanol (50 mL); the mixture was stirred overnight at room temperature and evaporated. Water (20 mL) was added to the residue, and the mixture was extracted with dichloromethane. The extracts were combined, washed successively with M aqueous hydrochloric acid, saturated aqueous sodium hydrogencarbonate, and brine, dried, and evaporated. The residue was chromatographed with 99:1 (v/v) chloroform–methanol as the eluant, to give **4a** (2.45 g, 78%) as an amorphous solid; $[\alpha]_D^{24}$ −10.6° (*c* 1.15, chloroform); ν_{max}^{KBr} 3350 cm^{-1} (OH); δ_H 1.81 (t, 1 H, *J* 6.1 Hz, primary O*H*), 2.62 (d, 1 H, *J* 3.7 Hz, sec. O*H*), 3.60 (dd, 1 H, *J* 9.3 and 4.1 Hz, H-2), 4.08 (dd, 1 H, *J* 9.3 and 6.8 Hz, H-3), 4.11 (d, 2 H, *J* 6.1 Hz, H-7a,7b), 4.15 (broad d, 1 H, *J* 6.8 Hz, H-4), 4.29 (m, 1 H, H-1), 4.65–4.94 (m, 6 H, 3 PhCH_2), and 5.85 (d, 1 H, *J* 3.4 Hz, H-6).

Anal. Calc. for $C_{28}H_{30}O_5$: C, 75.31; H, 6.77. Found: C, 74.88; H, 6.76.

1L-(1,3/2,4)-2,3,4-Tri-O-benzyl-5-(hydroxymethyl)-5-cyclohexene-1,2,3,4-tetrol (**4b**). — Methanolic sodium methoxide (28%, 0.5 mL) was added to a suspension of **3b** (3.27 g, 5 mmol) in methanol (50 mL); the mixture was stirred overnight at room temperature, and treated as described for the preparation of **4a**. The powdery prouct was recrystallized from 2-propanol–isopropyl ether, to give crystalline **4b** (1.84 g, 82%); m.p. 110–111°, $[\alpha]_D^{18}$ −69° (*c* 1.2, chloroform); ν_{max}^{KBr} 3350 cm^{-1} (OH); δ_H 1.93 (t, 1 H, *J* 6.3 Hz, primary O*H*), 2.17 (d, 1 H, *J* 4.4 Hz, sec. O*H*), 3.56 (dd, 1 H, *J* 10.0 and 7.3 Hz, H-2), 3.85 (dd, 1 H, *J* 10.0 and 7.3 Hz, H-3), 4.07 (d, 2 H, *J* 6.3 Hz, H-7a,7b), 4.30–4.36 (m, 2 H, H-1,4), 4.70–4.99 (m, 6 H, 3 PhCH_2), and 5.66 (s, 1 H, H-6).

Anal. Calc. for $C_{28}H_{30}O_5$: C, 75.31; H, 6.77. Found: C, 75.05; H, 6.69.

1D-(1,2,4/3)-2,3,4-Tri-O-benzyl-5-(trityloxymethyl)-5-cyclohexene-1,2,3,4-tetrol (**5a**). — Chlorotriphenylmethane (1.84 g, 6.6 mmol) was added to a solution of **4a** (2.45 g, 5.5 mmol) in pyridine (15 mL); the resulting solution was kept for 3 days at room temperature, diluted with water (20 mL), and extracted with ethyl

ether. The extracts were combined, washed with brine, dried (anhydrous potassium carbonate), and evaporated; the residual, syrupy product was chromatographed with 99:1 (v/v) benzene–ethyl acetate as the eluant, to give amorphous, powdery **5a** (3.4 g, 89%); $[\alpha]_D^{25}$ −8.9° (*c* 0.96, chloroform); ν_{max}^{KBr} 3400 cm^{-1} (OH); δ_H 2.55 (d, 1 H, *J* 3.2 Hz, sec. O*H*), 3.56 (dd, 1 H, *J* 9.5 and 4.0 Hz, H-2), 3.67 (d, 1 H, *J* 13.2 Hz, H-7a), 3.83 (d, 1 H, *J* 13.2 Hz, H-7b), 4.03 (dd, 1 H, *J* 9.5 and 7.1 Hz, H-3), 4.10 (d, 1 H, *J* 7.1 Hz, H-4), 4.31 (m, 1 H, H-1), 4.46–4.90 (m, 6 H, 3 PhCH_2), and 6.02 (d, 1 H, *J* 5 Hz, H-6).

Anal. Calc. for $C_{47}H_{44}O_5$: C, 81.95; H, 6.44. Found: C, 82.14; H, 6.51.

1L-(1,3/2,4)-2,3,4-Tri-O-benzyl-5-(trityloxymethyl)-5-cyclohexene-1,2,3,4-tetrol (**5b**). — A solution of **4b** (2.23 g, 6 mmol) in pyridine (10 mL) was treated with chlorotriphenylmethane (1.67 g, 6 mmol) as described in the preparation of **5a**, to give amorphous, powdery **5b** (3.0 g, 87%); $[\alpha]_D^{25}$ −51° (*c* 1.1, chloroform); ν_{max}^{KBr} 3450 cm^{-1} (OH); δ_H 2.08 (d, 1 H, *J* 4.4 Hz, sec. O*H*), 3.56 (dd, 1 H, *J* 10.0 and 7.6 Hz, H-2), 3.68 (d, 1 H, *J* 12.9 Hz, H-7a), 3.78 (d, 1 H, *J* 12.9 Hz, H-7b), 3.81 (dd, 1 H, *J* 10.0 and 7.1 Hz, H-3), 4.39–4.31 (m, 2 H, H-1,4), 4.47–5.00 (m, 6 H, 3 PhCH_2), and 5.85 (s, 1 H, H-6).

Anal. Calc. for $C_{47}H_{44}O_5$: C, 81.95; H, 6.44. Found: C, 81.65; H, 6.49.

1L-(1,3/2,4)-1-O-Benzoyl-2,3,4-tri-O-benzyl-5-(trityloxymethyl)-5-cyclohexene-1,2,3,4-tetrol (**6b**), *and its alkaline treatment.* — Diethyl azodicarboxylate (1.4 mL) was added dropwise at −10° to a mixture of **5a** (1.38 g, 2 mmol), benzoic acid (490 mg, 4 mmol), triphenylphosphine (2.1 g, 8 mmol), and molecular sieves 3A (1 g) in oxolane (20 mL); the mixture was stirred for 30 min at −10° and then for 1 h at room temperature, and filtered. The filtrate was evaporated, and the residue was chromatographed, with benzene as the eluant, to give amorphous, powdery **6b** (1.12 g, 70%); $[\alpha]_D^{26}$ −80° (*c* 1.1, chloroform); ν_{max}^{KBr} 1720 cm^{-1} (C=O); δ_H 3.72 (d, 1 H, *J* 13.1 Hz, H-7a), 3.83 (d, 1 H, *J* 13.1 Hz, H-7b), 3.90–3.92 (m, 2 H, H-2,3), 4.35 (m, 1 H, H-4), 4.55–4.98 (m, 6 H, 3 PhCH_2), 5.75 (s, 1 H, H-6), and 5.84 (m, 1 H, H-1).

Anal. Calc. for $C_{54}H_{48}O_6$: C, 81.79; H, 6.10. Found: C, 81.59; H, 6.17.

Treatment of **6b** (120 mg, 0.15 mmol) in methanol (2 mL) with methanolic sodium methoxide (28%, 0.1 mL) and, subsequently, the usual work-up, gave **5b** (95 mg, 92%), identical with the specimen obtained by tritylation of **4b**.

1D-(1,2,4/3)-1-O-Benzoyl-2,3,4-tri-O-benzyl-5-(trityloxymethyl)-5-cyclohexene-1,2,3,4-tetrol (**6a**), *and its alkaline treatment.* — A solution of **5b** (180 mg, 0.26 mmol) was treated with benzoic acid (100 mg, 0.8 mmol), triphenylphosphine (560 mg, 2.1 mmol), and diethyl azodicarboxylate (0.35 mL) in the presence of molecular sieves 3A (100 mg), as described in the conversion of **5a** into **6b**, to give syrupy **6a** (130 mg, 63%); $[\alpha]_D^{22}$ +49° (*c* 1.4, chloroform); ν_{max}^{film} 1720 cm^{-1} (C=O); δ_H 3.73 (dd, 1 H, *J* 6.8 and 3.9 Hz, H-2), 3.77 (d, 1 H, *J* 13.4 Hz, H-7a), 3.87 (d, 1 H, *J* 13.4 Hz, H-7b), 4.15–4.19 (m, 2 H, H-3,4), 4.54–5.01 (m, 6 H, 3 PhCH_2), 5.91 (dd, 1 H, *J* 5.6 and 3.9 Hz, H-1), and 6.03 (d, 1 H, *J* 5.6 Hz, H-6).

Anal. Calc. for $C_{54}H_{48}O_6$: C, 81.79; H, 6.10. Found: C, 82.24; H, 6.22.

Compound **6a** was treated with base as described in the conversion of **6b** into **5b**, to give **5a**.

*1D-(1,2,4/3)-1-Azido-2,3,4-tri-*O*-benzyl-5-(trityloxymethyl)-5-cyclohexane-2,3,4-triol* (**7a**). — A benzene solution of hydrazoic acid (10%, 30 mL)[7] was added to a mixture of **5b** (1.1 g, 1.6 mmol) and triphenylphosphine (1.68 g, 6.4 mmol) in toluene (30 mL), and the whole mixture was thoroughly cooled; diethyl azodicarboxylate (1 mL) was added dropwise to the mixture, with stirring, below −10°, and kept thereat for 30 min and for an additional 2 h at room temperature. The precipitate was filtered off, and the filtrate was evaporated; the residue was chromatographed, with benzene as the eluant, to give syrupy **7a** (820 mg, 72%); $[\alpha]_D^{24}$ +49.8° (*c* 1.16, chloroform); ν_{max}^{film} 2100 cm^{-1} (N_3); δ_H 3.64 (dd, 1 H, *J* 9.8 and 4.9 Hz, H-2), 3.65 (d, 1 H, *J* 14.0 Hz, H-7a), 3.85 (d, 1 H, *J* 14.0 Hz, H-7b), 4.01 (dd, 1 H, *J* 9.8 and 7.3 Hz, H-3), 4.07 (d, 1 H, *J* 7.3 Hz, H-4), 4.16 (dd, 1 H, *J* 4.9 and 5.5 Hz, H-1), 4.45–4.98 (m, 6 H, 3 PhCH_2), and 5.90 (dd, 1 H, *J* 5.5 and <1 Hz, H-6).

Anal. Calc. for $C_{47}H_{43}N_3O_4$: C, 79.07; H, 6.08; N, 5.89. Found: C, 79.30; H, 6.10; N, 5.59.

*1L-(1,3/2,4)-1-Azido-2,3,4-tri-*O*-benzyl-5-(trityloxymethyl)-5-cyclohexene-2,3,4-triol* (**7b**). — Compound **5a** (206 mg, 0.3 mmol) in toluene (3 mL) was treated with a benzene solution of hydrazoic acid (10%, 7.5 mL), triphenylphosphine (320 mg, 1.2 mmol), and diethylazodicarboxylate (0.2 mL), as described in the preparation of **7a**, to give syrupy **7b** (180 mg, 84%); $[\alpha]_D^{23}$ −39.0° (*c* 1.51, chloroform); ν_{max}^{film} 2100 cm^{-1} (N_3); δ_H 3.65 (m, 2 H, H-2,7a), 3.80 (m, 2 H, H-3,7b), 4.17 (broad d, 1 H, *J* 8.5, H-1), 4.27 (d, 1 H, *J* 7.81, H-4), 4.48–4.95 (m, 6 H, 3 PhCH_2), and 5.75 (s, 1 H, H-6).

Anal. Calc. for $C_{47}H_{43}N_3O_4$: C, 79.07; H, 6.08; N, 5.89. Found: C, 79.32; H, 6.14; N, 5.64.

*1D-(1,2,4/3)-2,3,4-Tri-*O*-benzyl-5-(hydroxymethyl)-1-phthalimido-5-cyclohexene-2,3,4-triol* (**9a**) via *its 7-*O*-trityl derivative* (**8a**). — Diethyl diazodicarboxylate (0.1 mL, 0.58 mmol) was added at 0° to a solution of **5b** (100 mg, 0.145 mmol), phthalimide (32 mg, 0.22 mmol), and triphenylphosphine (150 mg, 0.58 mmol) in oxolane (2 mL); the mixture was stirred for 1 h at room temperature, evaporated, and chromatographed with 99:1 (v/v) benzene–ethyl acetate, to give crude **8a** (72 mg). This was dissolved in 1:1 (v/v) dichloromethane–methanol containing *p*-toluenesulfonic acid (10 mg), and the solution stirred overnight at room temperature, evaporated, and extracted with chloroform (10 mL); the extract was washed successively with saturated aqueous sodium hydrogencarbonate and brine, dried, and evaporated. The residue was purified by preparative t.l.c. with 9:1 (v/v) benzene–ethyl ether, to give amorphous, powdery **9a** (35 mg, 41%); $[\alpha]_D^{26}$ +176° (*c* 0.84, chloroform); ν_{max}^{film} 3450 (OH) and 1710 cm^{-1} (C=O); δ_H 1.64 (broad s, 1 H, O*H*), 3.89 (dd, 1 H, *J* 10.01 and 6.6 Hz, H-2), 4.13 (m, 2 H, H-7a,7b), 4.29 (d, 1 H, *J* 7.08 Hz, H-4), 4.55 (dd, 1 H, *J* 10.01 and 7.08 Hz, H-3), 4.58–4.96 (m, 6 H, 3 PhCH_2), 5.28 (broad t, 1 H, *J* 5.1 Hz, H-1), and 5.65 (broad d, 1 H, *J* 5.1 Hz, H-6).

Anal. Calc. for $C_{36}H_{33}NO_6$: C, 75.11; H, 5.78; N, 2.43. Found: C, 74.71; H, 5.83; N, 2.38.

1,6-Anhydro-2,3,2',3'-tetra-O-benzyl-4',6'-dideoxy-4'-(p-toluenesulfonamido)-β-maltose (**10**). — *p*-Toluenesulfonyl chloride (60 mg, 0.3 mmol) was added at 0° to a solution of 4'-amino-1,6-anhydro-2,3,2',3'-tetra-*O*-benzyl-4',6'-dideoxy-β-maltose[5] (100 mg, 0.15 mmol) in dichloromethane (3 mL)–triethylamine (0.5 mL); the mixture was stirred overnight at room temperature, diluted with ethyl ether (30 mL), and washed successively with water and brine, dried (magnesium sulfate), and evaporated; the residue was chromatographed with 13:3 (v/v) benzene–ethyl acetate as the eluant, to give syrupy **10** (100 mg, 81%); $[\alpha]_D^{26}$ +14.3° (*c* 1.00, chloroform); ν_{max}^{film} 1320 and 1155 cm^{-1} (SO_2NH); δ_H 1.17 (d, 3 H, *J* 6.35 Hz, CH_3), 2.25 (s, 3 H, $C_6H_4CH_3$), 3.23 (m, 2 H, H-4', N*H*), 3.37 (s, 1 H, H-4), 3.46 (dd, 1 H, *J* 9.2 and 3.42 Hz, H-2'), 3.52 (s, 1 H, H-2), 3.58 (t, 1 H, *J* 9.2 Hz, H-3'), 3.65 (s, 1 H, H-3), 3.70 (dd, 1 H, *J* 7.08 and 5.86 Hz, H-6a), 3.89 (m, 1 H, H-5'), 4.00 (d, 1 H, *J* 7.08 Hz, H-6b), 4.31–4.63 (m, 9 H, 4 PhCH_2, H-5), 4.81 (d, 1 H, *J* 3.42 Hz, H-1'), and 5.57 (s, 1 H, H-1).

Anal. Calc. for $C_{47}H_{51}NO_{10}S$: C, 68.68; H, 6.25; N, 1.70; S, 3.90. Found: C, 68.81; H, 6.30; N, 1.57; S, 3.93.

1L-(1,3/2,4)-2,3,4-Tri-O-benzyl-5-(hydroxymethyl)-1-phthalimido-5-cyclohexene-2,3,4-triol (**9b**) via *its 7-O-trityl derivative* (**8b**). — Compound **5a** (100 mg, 145 μmol) was treated as in the conversion of **5b** into **8a**, to give crude **8b** (90 mg). Subsequent removal of the trityl group of **8b**, and purification of the product, were also conducted as described for **8a**, to give syrupy **9b** (40 mg, 48%); $[\alpha]_D^{26}$ −191° (*c* 1.38, chloroform); ν_{max}^{film} 3450 (OH) and 1710 cm^{-1} (C=O); δ_H 1.77 (broad s, 1 H, O*H*), 3.99 (dd, 1 H, *J* 10.26 and 8.3 Hz, H-2), 4.11 (m, 2 H, H-7a,7b), 4.27 (dd, 1 H, *J* 10.26 and 7.81 Hz, H-3), 4.54 (broad s, 1 H, *J* 7.81 Hz, H-4), 4.46–5.09 (m, 7 H, 3 PhCH_2, H-1), and 5.41 (s, 1 H, H-6).

Anal. Calc. for $C_{36}H_{33}NO_6$: C, 75.11; H, 5.78; N, 2.43. Found: C, 74.67; H, 5.81; N, 2.32.

3-(2-Cyclohexenyl)-4-hydro-1,4-dioxo-1H-2,3-benzoxazine (**13**) *and 4-(2-cyclohexenyloxy)-1-oxo-1H-2,3-benzoxazine* (**14**). — Diethyl azodicarboxylate (13.2 mL, 80 mmol) was added dropwise at 0° to a solution of 2-cyclohexenol (3.93 g, 40 mmol), **12** (7.17 g, 44 mmol), and triphenylphosphine (21 g, 80 mmol) in oxolane (100 mL); the mixture was stirred overnight at room temperature, and evaporated. The residual syrup was chromatographed with 199:1 (v/v) benzene–ethyl acetate, to give **13** (3.9 g, 40%) and **14** (3.4 g, 35%); both compounds were recrystallized from isopropyl ether–hexane. Compound **13**: m.p. 104–105.5°; ν_{max}^{KBr} 1750 (O–C=O) and 1645 cm^{-1} (N–C=O); δ_H [1.75 (m, 1 H), 1.94 (m, 1 H), 2.06 (m, 3 H), and 2.17 (m, 1 H) (H-4'a,4'b,5'a,5'b,6'a,6'b)], 5.55 (m, 1 H, H-1'), 5.66 (dd, 1 H, *J* 10.1 and 2.2 Hz, H-2'), 6.05 (m, 1 H, H-3'), 7.84 (dt, 1 H, H-7), 7.93 (dt, 1 H, H-6), 8.25 (dd, 1 H, H-5), and 8.31 (dd, 1 H, H-8).

Anal. Calc. for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39; N, 5.76. Found: C, 68.98; H, 5.39; N, 5.82.

Compound **14**: m.p. 96.5–98°; ν_{max}^{KBr} 1740 cm^{-1} (O–C=O); δ_H [1.73 (m, 1 H), 1.87 (m, 1 H), 2.04 (m, 2 H), 2.10 (m, 1 H), and 2.16 (m, 1 H) (H-4'a,4'b,5'a,5'b,6'a,6'b)], [5.47 (m, 1 H), 6.00 (m, 1 H), and 6.06 (m, 1 H) (H-1',2',3')], 7.84 (dt, 1 H, H-7), 7.90 (dd, 1 H, H-5), 7.93 (dt, 1 H, H-6), and 8.32 (dd, 1 H, H-8).

Anal. Calc. for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39; N, 5.76. Found: C, 69.13; H, 5.38; N, 5.74.

N-(2-Cyclohexenyl)hydroxylamine (**15**). — Hydrazine hydrate (0.5 mL) in methanol (2 mL) was added at 0° to a solution of **13** (2.43 g, 10 mmol) in dichloromethane (20 mL), and the mixture was stirred for 2 h at room temperature. The resulting precipitate was filtered off, and washed with dichloromethane; the filtrate and washings were combined, successively washed with 5M aqueous sodium hydroxide and water, dried, and evaporated. The residue was agitated in isopropyl ether–hexane causing it to crystallize, and giving **15** (0.93 g, 82%); m.p. 97–98.5°; ν_{max}^{KBr} 3250 cm^{-1} (NHOH); δ_H [1.54–1.84 (m, 5 H) and 2.01 (m, 2 H) (H-4a,4b,5a,5b,6a,6b) and O*H*], 3.52 (m, 1 H, H-1), 5.68 (m, 1 H, H-2), and 5.89 (m, 1 H, H-3).

Anal. Calc. for $C_6H_{11}NO$: C, 63.69; H, 9.80; N, 12.38. Found: C, 63.19; H, 9.71; N, 12.40.

1L-(1,3/2,4)-2,3,4-Tri-O-benzyl-1-(1,4-dioxo-4-hydro-1H-2,3-benzoxazin-3-yl)-5-(trityloxymethyl)-5-cyclohexene-2,3,4-triol (**16**) *and 1L-(1,3/2,4)-2,3,4-tri-O-benzyl-1-O-(1-oxo-1H-2,3-benzoxazin-4-yl)-5-(trityloxymethyl)-5-cyclohexene-1,2,3,4-tetrol* (**17b**). — Diethyl azodicarboxylate (0.14 mL, 0.8 mmol) was added at 0° to a solution of **5a** (140 mg, 0.2 mmol), **12** (65 mg, 0.4 mmol), and triphenylphosphine (210 mg, 0.8 mmol) in oxolane (3 mL); the mixture was stirred for 2 h at room temperature, and evaporated. The residue was chromatographed, with 99:1 (v/v) benzene–ethyl acetate as the eluant, and roughly separated fractions were purified by p.l.c. with 199:1 (v/v) benzene–ethyl acetate, to give **16** (48 mg, 28%) and **17b** (55 mg, 33%). Compound **16**: $[\alpha]_D^{25}$ −82° (*c* 1.37, chloroform); ν_{max}^{film} 1755 (O–C=O) and 1655 cm^{-1} (N–C=O); δ_H 3.62 (d, 1 H, *J* 13.4 Hz, H-7a), 3.82 (d, 1 H, *J* 13.4 Hz, H-7b), 3.98 (dd, 1 H, *J* 10.26 and 8.06 Hz, H-2), 4.18 (dd, 1 H, *J* 10.26 and 7.81 Hz, H-3), 4.38 (broad d, 1 H, *J* 7.81 Hz, H-4), 4.53–5.06 (m, 6 H, 3 PhCH_2), 5.69 (broad d, 1 H, H-1), 5.79 (s, 1 H, H-6), 7.83 (m, 1 H, H-7'), 7.91 (m, 1 H, H-6'), 8.10 (m, 1 H, H-5'), and 8.25 (m, 1 H, H-8').

Anal. Calc. for $C_{55}H_{47}NO_7 \cdot 1.5\ H_2O$: C, 76.72; H, 5.85; N, 1.62. Found: C, 76.78; H, 5.89; N, 1.91.

Compound **17b**: $[\alpha]_D^{25}$ −92° (*c* 0.496, chloroform); ν_{max}^{KBr} 1745 cm^{-1} (O–C=O); δ_H 3.73 (d, 1 H, *J* 13.4 Hz, H-7a), 3.85 (d, 1 H, *J* 13.4 Hz, H-7b), 3.90 (dd, 1 H, *J* 10.3 and 7.8 Hz, H-2), 4.01 (dd, 1 H, *J* 10.3 and 7.8 Hz, H-3), 4.36 (broad d, 1 H, *J* 7.8 Hz, H-4), 4.56–4.97 (m, 6 H, 3 PhCH_2), 5.74 (broad d, 1 H, 7.8 Hz, H-1), 5.97 (s, 1 H, H-6), 7.70 (m, 1 H, H-5'), 7.86 (m, 2 H, H-6',7'), and 8.32 (m, 1 H, H-8').

Anal. Calc. for $C_{55}H_{47}NO_7 \cdot 1.5\ H_2O$: C, 76.72; H, 5.85, N, 1.62. Found: C, 76.70; H, 5.81; N, 1.67.

1D-(1,2,4/3)-2,3,4-Tri-O-benzyl-1-O-(1-oxo-1H-2,3-benzoxazin-4-yl)-5-(trityloxymethyl)-5-cyclohexene-1,2,3,4-tetrol (**17a**). — Compound **5b** (140 mg, 0.2 mmol) was treated as in the coupling reaction between **5a** and **12**, to give syrupy **17a** (97 mg, 58%); $[\alpha]_D^{20}$ +47° (*c* 0.87, chloroform); ν_{max}^{film} 1740 cm^{-1} (O–C=O); δ_H 3.79 (m, 2 H, H-2,7a), 3.86 (d, 1 H, *J* 13.4 Hz, H-7b), 4.25 (m, 2 H, H-3,4), 4.56–5.50 (m, 6 H, 3 PhCH_2), 5.74 (dd, 1 H, *J* 5.5 and 3.67 Hz, H-1), 6.16 (broad d, 1 H, *J* 5.5 Hz, H-6), 7.82–7.88 (m, 3 H, H-5′,6′,7′), and 8.29 (m, 1 H, H-8′).

Anal. Calc. for $C_{55}H_{47}NO_7$: C, 79.21; H, 5.68; N, 1.68. Found: C, 78.77; H, 5.80; N, 1.48.

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