Preferred Conformation of C-Glycosides. 12. Synthesis and Conformational Analysis of α,α-, α,β-, and β,β-C-Trehaloses

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A single, unified strategy for the stereocontrolled synthesis of α,α-, α,β-, and β,β-C-trehaloses (1-3) was developed. The solution conformations of C-trehaloses 1-3, as well as their permethyl derivatives, were determined on the basis of vicinal coupling constants observed in the ^{1}H NMR spectra. The preferred conformations for α,α- and β,β-C-trehaloses (1 and 3), shown in Figure 1, were predicted and experimentally proven. A diamond-lattice analysis of α,β-C-trehalose (2), shown in Figure 2, revealed the relative stability of the three staggered conformers to be **2A > 2B > 2C**, and the experimental data were found to be consistent with this trend. It was demonstrated that the inversion of the C.2 or C.2′ hydroxyl group of 2 affected its conformational preference in a predictable manner. The ^{1}H NMR spectra of α,β-C-trehalose 2 provided direct experimental evidence to illustrate that the α-C-glycosidic bond is conformationally more rigid than the β-C-glycosidic bond.

Introduction

α,α-Trehalose, α-D-glucopyranosyl 1,1′-α-D-glucopyranoside, is present in a wide variety of bacteria, fungi, plants, and insects. It has been found to play an important role in an equally diverse range of biological functions.[1] As a surfactant, trehalose prevents membrane disruption due to frost and dehydration.[2] It is also a common metabolite, and is for many winged insects the exclusive supply of energy expended during flight.[3] α,α-Trehalose 6,6′-dimycolate, implicated in the virulence of *Mycobacterium tuberculosis*, is a toxic glycolipid known to disrupt oxidative phosphorylation and respiration in mammalian mitochondria.[4] Recently, it has drawn much interest as a potent antitumor agent, especially when used as an immunostimulant in conjunction with muramyl dipeptides.[5]

Previous work from this laboratory has experimentally established that the C-glycosidic bond preferentially adopts the "exo-anomeric" conformation like its parent O-glycosidic bond does; namely, the exo-glycosidic bond exists antiperiplanar to its respective C.1–C.2 bond.[6] This conformational preference has held true for all the C-disaccharides and C-trisaccharides studied thus far and can be interpreted solely by steric considerations.

We felt that 1,1′-linked C-disaccharides such as C-trehaloses 1-3 would provide a new aspect to our conformation studies on C- and O-glycosides in that the directing effect from each glycosidic bond may interact with one another either in a cooperative or counteractive manner. In applying our previous observations and interpretations, we predicted that both α,α-C-trehalose (1) and β,β-C-trehalose (3) possess a single unique conformation (Figure 1), in which each glycosidic bond adopts the "exo-anomeric" conformation, yet is free from obvious steric destabilization.

However, in the case of α,β-C-trehalose (2), placing either glycosidic bond in an "exo-anomeric" conformation results in unavoidable 1,3-diaxial-like steric destabilization. In-

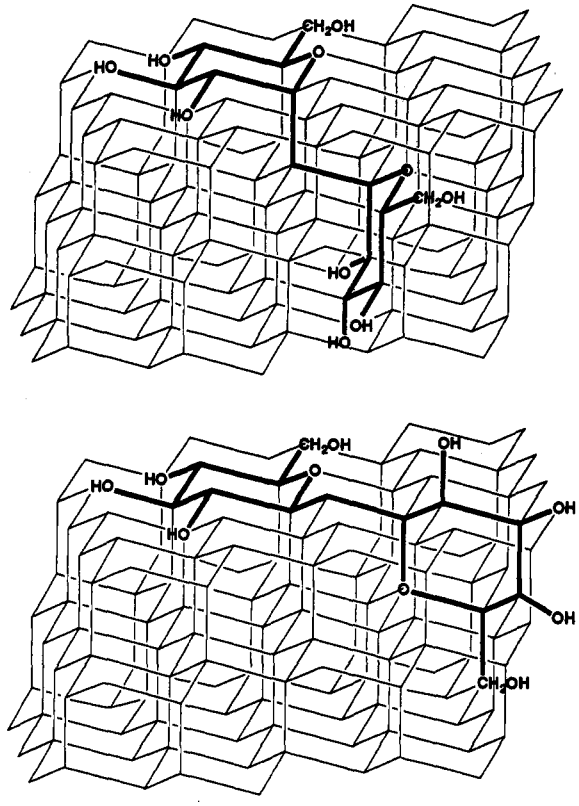

Figure 1. (Top) predicted preferred solution conformation of α,α-C-trehalose (1). (Bottom) predicted preferred solution conformation of β,β-C-trehalose (3).

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(1) For a comprehensive review on the general occurrence and biochemistry of α,α-trehalose, see: (a) Elbein, A. D. *Adv. Carbohyd. Chem. Biochem.* **1974**, *30*, 227. (b) Birch, G. G. *Adv. Carbohyd. Chem. Biochem.* **1963**, *18*, 201.

(2) Lee, C. W. B.; DasGupta, S. K.; Mattai, J.; Shipley, G. G.; Abdel-Mageed, O. H.; Makriyannis, A.; Griffin, R. G. *Biochemistry* **1989**, *28*, 5000 and references cited therein.

(3) Clegg, G. S.; Evans, D. R. *J. Exp. Biol.* **1961**, *38*, 771.

(4) For example, see: (a) Bloch, H. *J. Exp. Med.* **1950**, *91*, 197. (b) Kato, M. *Arch. Biochem. Biophys.* **1970**, *140*, 379. (c) Rastogi, N.; David, H. L. *Biochimie* **1988**, *70*, 1101. (d) Spargo, B. J.; Crowe, L. M.; Ioneda, T.; Beaman, B. L.; Crowe, J. H. *Proc. Natl. Acad. Sci. U.S.A.* **1991**, *88*, 737. (e) Azuma, I.; Sakurai, T.; Ishida, H.; Kitajima, T.; Yamazaki, M. *Carbohyd. Res.* **1991**, *212*, 47.

(5) For example, see: (a) McLaughlin, C. A.; Schwartzman, S. M.; Horner, B. L.; Jones, G. H.; Moffatt, J. G.; Nestor, J. J.; Tegg, D. *Science* **1980**, *208*, 415. (b) Retzinger, G. S.; Meredith, S. C.; Takayama, K.; Hunter, R. L.; Kézdy, F. J. *J. Biol. Chem.* **1981**, *256*, 8208. (c) Lederer, E. *J. Med. Chem.* **1980**, *23*, 819.

(6) For part 11 of this series, see: O'Leary, D. J.; Kishi, Y. *J. Org. Chem.* **1993**, *58*, 304.

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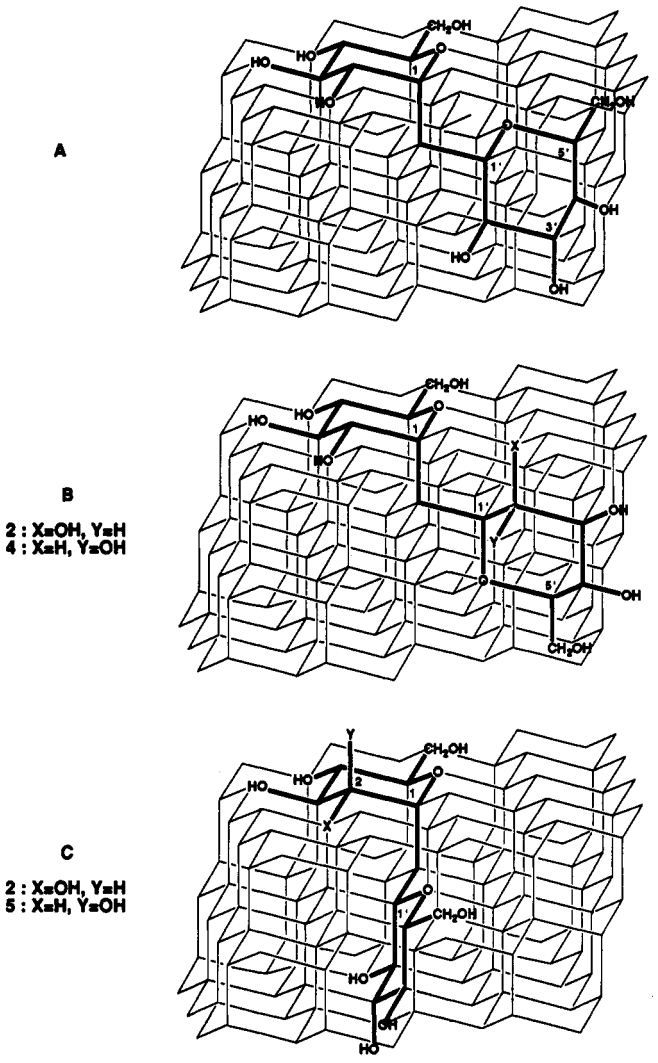


Figure 2.

spection of the three staggered conformers **2A–C**[7] on a diamond lattice (Figure 2) illustrates the situation: **2A** has both glycosidic bonds in the "exo-anomeric" position but the C.1–O.1 and the C.1′–O.1′ bonds in a 1,3-diaxial-like position; **2B** (X = OH, Y = H) has the C.1′–C.α bond in an "exo-anomeric" position but the C.1–C.α and the C.2′–O.2′ bonds in a 1,3-diaxial-like position; **2C** (X = OH, Y = H) has the C.1–C.α bond in an "exo-anomeric" position but the C.1′–C.α and C.2–O.2 bonds in a 1,3-diaxial-like position. On the basis of the data obtained in the previous work in this series,[8] coupled with the values known in the literature,[9] we can estimate, at least qualitatively, the

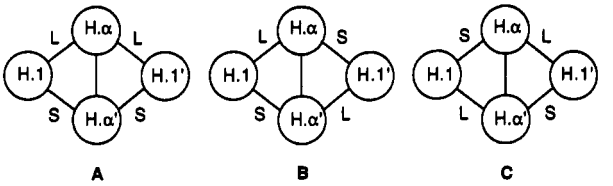


Figure 3. Expected patterns of ^{1}H NMR coupling constants for staggered conformations **A-C**. L and S represent large (typically ca. 10 Hz) and small (typically ca. 3 Hz) spin coupling constants.

relative stability of these conformers. Assuming the energy of the axial *C*-"exo-anomeric" stabilization to be ca. 1.2 kcal/mol, the equatorial *C*-"exo-anomeric" stabilization to be ca. 0.6 kcal/mol, and the 1,3-diaxial-like destabilizations found in **2A–2C** to be ca. 1.9 kcal/mol, the order of relative stability is **2A** > **2B** (ca. +0.6 kcal/mol) > **2C** (ca. +1.2 kcal/mol).

On the basis of diamond lattice analysis of 1,4-*C*-disaccharides, we previously predicted, and experimentally proved, that the strategic removal or inversion of a hydroxyl group proximal to the aglyconic bond created a staggered conformation free from unfavorable 1,3-diaxial-like interactions, consequently affecting the conformational balance of a given system.[10] This approach has been extended to α,β-*C*-trehalose **2**. The steric destabilization in the conformers **2B** and **2C** can be removed by inverting the stereochemistry of the C.2 or C.2′ hydroxyl group, respectively. Thus, the staggered conformer **B** for the C.2′ epimer **4** (X = H, Y = OH) no longer suffers from 1,3-diaxial-like interactions, whereas the staggered conformer **C** for the C.2 epimer **5** (X = H, Y = OH) is free from 1,3-diaxial-like steric destabilization. Applying the same assumptions to compounds **4** and **5** as before, the relative stability is roughly estimated to be **4B** > **4A** (ca. +1.3 kcal/mol) > **4C** (ca. +2.5 kcal/mol) and **5C** > **5A** (ca. +0.7 kcal/mol) > **5B** (ca. +1.3 kcal/mol), respectively.

Experimentally, the spin coupling constants observed for the bridging methylene protons should provide support for these predictions. The spin coupling system of **2** is expected to follow pattern **A**, probably with some distortion on the equatorial *C*-glycosidic side to avoid the 1,3-diaxial-like steric destabilization. Likewise, the spectrum of **4** is expected to follow the pattern **B** and the spectrum of **5** to follow the pattern **C** (Figure 3).

In this paper, we report the synthesis of the 1,1′-linked *C*-disaccharides **1–5** by a unified synthetic strategy and their preferred solution conformations. In connection with this work, it should be noted that when this study was undertaken, none of the *C*-trehaloses were known, but the synthesis and conformational analysis of β,β-*C*-trehalose (**3**) were recently reported by Martin.[11]

Results and Discussion

Synthetic Plan. A single, unified strategy to synthesize the *C*-disaccharides **1–5** has been developed (Scheme 1). The precedents for the key steps in this plan come largely from our previous work in related areas.[6,10] These include (1) inversion of the C.2′ stereocenter, e.g., **b** → **a**, (2) transformation of an epoxy alcohol into a tetrahydropyran, e.g., **c** → **b**, (3) selective protection of a 1,2-diol, e.g., **d** → **c**, (4) stereoselective osmylation, e.g., **e** → **d**, (5) selective

(7) Nine staggered conformers exist for **2**. Inspection on a diamond lattice shows that the conformers other than **A–C** possess two or more 1,3-diaxial-like steric destabilizations.

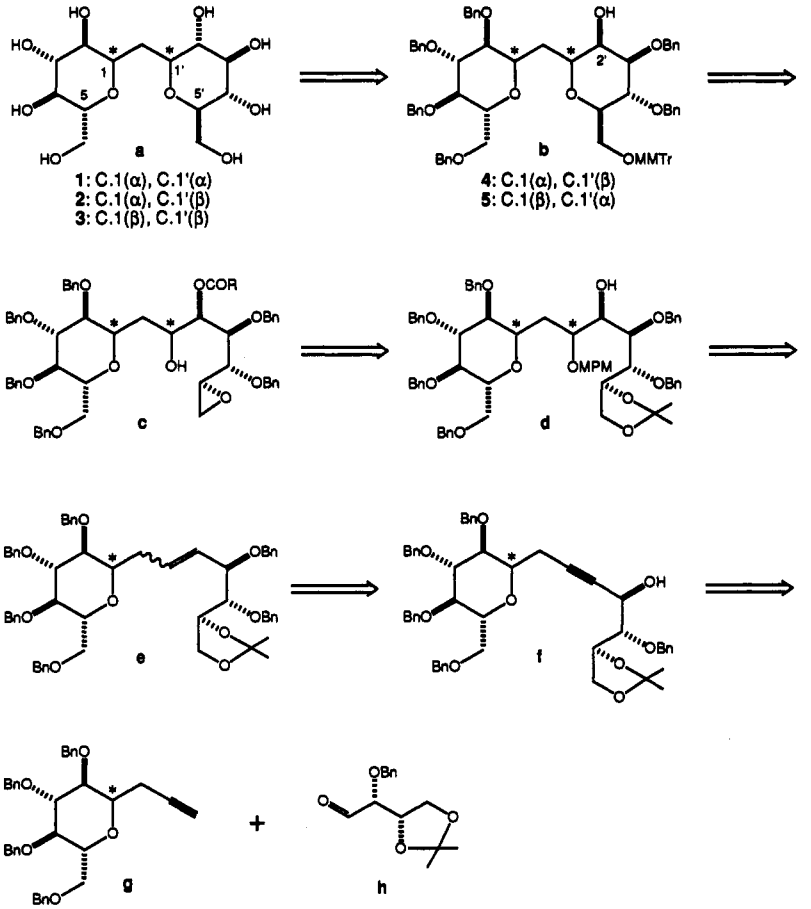
(8) On the basis of our previous work (Goekjian, P. G.; Wu, T.-C.; Kishi, Y. *J. Org. Chem.* **1991**, *56*, 6412), we estimated the axial and equatorial *C*-exo-anomeric stabilization to be roughly 1.2 and 0.6 kcal/mol, respectively. Recently, Houk performed theoretical calculations on related systems to suggest 1.8 and 2.2 kcal/mol for the axial and equatorial *C*-exo-anomeric stabilization (Houk, K. N.; Eksterowicz, J. E.; Wu, Y.-D.; Fuglesang, C. D.; Mitchell, D. B. *J. Am. Chem. Soc.* **1993**, *115*, 4170). It is also interesting to note that the stereoelectronic stabilization in the *O*-series has been estimated to be 1.4–1.5 kcal/mol (for example, see: Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon Press: Oxford, 1983).

(9) The 1,3-diaxial destabilization both for OMe/CH_2R and OH/OH groups is estimated to be 1.9 kcal/mol (Tavernier, D.; DePessemier, F.; Anteunis, M. *Bull. Soc. Chim. Belg.* **1975**, *84*, 333. Allinger, N. L.; Graham, J. C.; Dewhurst, B. B. *J. Org. Chem.* **1974**, *39*, 2615 and references cited therein.

(10) Wang, Y.; Babirad, S. A.; Kishi, Y. *J. Org. Chem.* **1992**, *57*, 468.

(11) (a) Martin, O. R.; Lai, W. *J. Org. Chem.* **1990**, *55*, 5188. (b) Martin, O. R.; Lai, W. *J. Org. Chem.* **1993**, *58*, 176.

Scheme 1



reduction of an acetylenic alcohol to a *cis*- or *trans*-olefin, e.g., **f** → **e**, and (6) coupling of an acetylene with an aldehyde, e.g., **g** + **h** → **f**. In turn, **g** and **h** are readily available from inexpensive D-glucose and L-xylose, respectively.

Synthesis. The Ni(II)/Cr(II)-mediated coupling[12] was found to be most effective for the carbon–carbon bond formation required for the present study. The acetylenic iodide **6**, obtained from *C*-allyl *O*-tetrabenzyl-α-D-glucopyranoside,[13] was coupled with the aldehyde derived from threitol **7**, prepared from L-xylose,[14] furnishing a 4:1 mixture of acetylenic alcohols (Scheme 2). The C.3′ stereochemistry of major diastereomer **8** was established by a chemical correlation of compound **9** with an authentic sample.[15] The minor, undesired C.3′ diastereomer was recycled into the desired alcohol **8** *via* an oxidation–reduction sequence; the reduction was best achieved with L-Selectride, yielding a 7:1 mixture with **8** being the major product. Acetylenic alcohol **8** was subjected to hydrogenation in the presence of Lindlar catalyst, followed by benzylation, to give the *cis*-allylic benzyl ether **9**. Osmylation of **9** yielded the *erythro*-diol **10** as the sole product. On the basis of the empirical rule developed in this laboratory,[16] the major product was tentatively assigned as the desired diastereomer, which was ultimately proven by the spectroscopic characterization of α,α-*C*-trehalose (**1**) (*vide supra*).

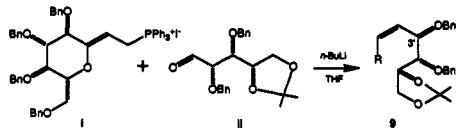
As discussed in a previous paper,[10] in order to prevent tetrahydrofuran formation during the acid-catalyzed epoxide opening (cf. **12** → **13**), it was necessary to protect the O.2′ alcohol with an electron-withdrawing group, which necessitated a method to functionalize selectively the C.2′ or C.1′ alcohol. After having examined several possible methods, we found the regioselective (*p*-methoxyphenyl)methyl (MPM) ether protection at O.1′ *via* cyclic 1,2-dibutylstannylene formation, followed by CsF/MPM-Cl/$(n\text{-Bu})_4$NI,[17] to be most satisfactory. Under these conditions, the O.1′ hydroxyl of **10** was protected exclusively with an MPM group. The regioselectivity of this process appeared to be quite general for all the 1,2-diols studied regardless of stereochemistry; *threo*-diol **16** (Scheme 3, *vide supra*) exhibited the poorest ratio of O.1′:

(12) (a) Jin, H.; Uenishi, J.; Christ, W. J.; Kishi, Y. *J. Am. Chem. Soc.* **1986**, *108*, 5644. (b) Takai, K.; Tagashira, M.; Kuroda, T.; Oshima, K.; Utimoto, K.; Nozaki, H. *J. Am. Chem. Soc.* **1986**, *108*, 6048.

(13) Acetylenic iodide **4** was prepared in 88% overall yield from *C*-allyl *O*-tetrabenzyl-α-D-glucopyranoside as follows: (i) O_3, MeOH:CH_2Cl_2 (2:1), −78 °C, then Me_2S, (ii) $(MeO)_2P(O)CHN_2$, KO-*t*-Bu, THF, −78 °C, (iii) I_2, morpholine, benzene, 50 °C.

(14) Aldehyde **5** was prepared in 85% overall yield from the *O*-2,3;4,5-diisopropylidene derivative of 1-deoxy-1-iodo-L-xylitol as follows: (i) activated Zn, 95% aqueous *i*-PrOH, reflux; (ii) BnBr, NaH, imidazole, TBAI, THF/DMF (4:1); (iii) O_3, MeOH/CH_2Cl_2 (2:1), −78 °C, then $NaBH_4$, 0 °C; (iv) Dess–Martin periodinane, $NaHCO_3$, 4-Å molecular sieves, CH_2Cl_2. A reaction similar to step i was recently reported: Fürstner, A. *Tetrahedron Lett.* **1990**, *31*, 3735.

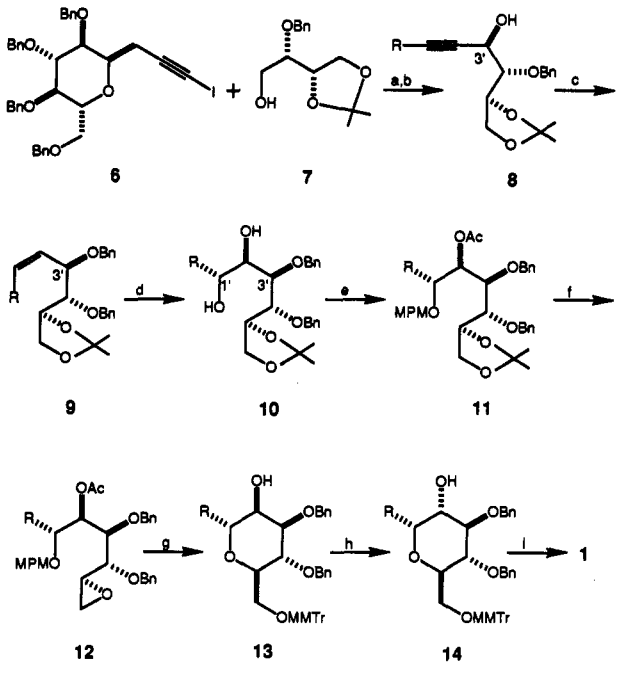
(15) Compound **9** was also synthesized by using the Wittig reaction depicted, in which the C.3′ stereochemistry was already fixed.



(16) (a) Cha, J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron Lett.* **1983**, *24*, 3943. (b) Christ, W. J.; Cha, J. K.; Kishi, Y. *Tetrahedron Lett.* **1983**, *24*, 3947. (c) Cha, J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron* **1984**, *40*, 2247.

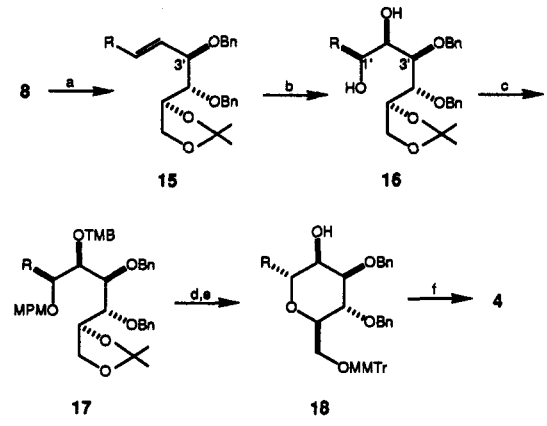
(17) Nagashima, N.; Ohno, M. *Chem. Lett.* **1987**, 141.

Scheme 2[a]



[a] Reagents and conditions: (a) (i) Dess–Martin periodinane, $NaHCO_3$, 3-Å molecular sieves, CH_2Cl_2, (ii) 0.02% $NiCl_2$ in $CrCl_2$, THF/DMF (4:1); (b) for the minor isomer only, (i) Dess–Martin periodinane, CH_2Cl_2, 3-Å molecular sieves, (ii) L-Selectride, THF; (c) (i) Pd–Pb on $CaCO_3$, H_2, MeOH, (ii) BnBr, NaH, imidazole, TBAI, THF/DMF (4:1); (d) OsO_4, THF/pyridine (4:1); (e) (i) Bu_2SnO, toluene, (ii) CsF, MPM–Cl, TBAI, DMF, (iii) Ac_2O, DMAP, pyridine; (f) (i) 80% AcOH, (ii) *p*-TsCl, pyridine, (iii) NaH, imidazole, THF; (g) (i) DDQ, CH_2Cl_2, pH 7 phosphate buffer, (ii) *p*-TsOH·H_2O, CH_2Cl_2, (iii) MMTrCl, pyridine, (iv) K_2CO_3, MeOH; (h) (i) Swern oxidation, (ii) BH_3, THF; (i) (i) AcOH/H_2O/THF (4:1:1), (ii) $Pd(OH)_2$ on C, H_2, MeOH.

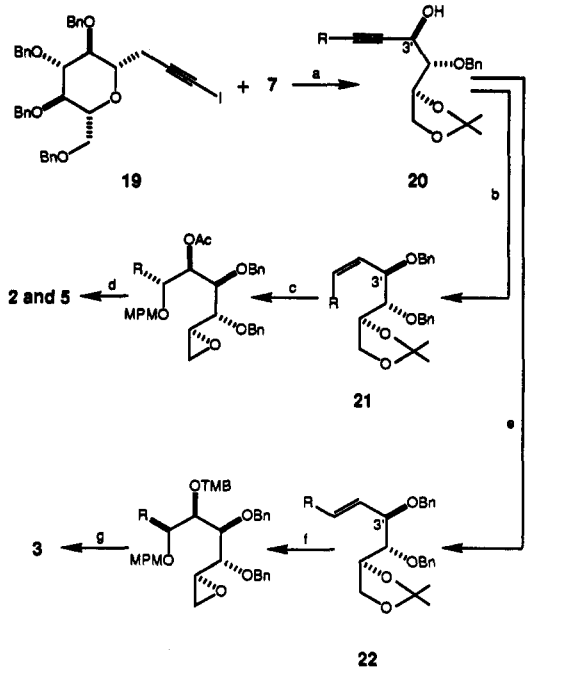
Scheme 3[a]



[a] Reagents and conditions: (a) (i) Red-Al, Et_2O, (ii) BnBr, NaH, imidazole, TBAI, THF/DMF (4:1); (b) OsO_4, THF/pyridine (4:1); (c) (i) Bu_2SnO, toluene, (ii) CsF, MPM-Br, DMF, (iii) 3,4,5-trimethoxybenzoyl 2,4,6-trichlorobenzoate, DMAP, toluene; (d) (i) 80% AcOH, (ii) *p*-TsCl, pyridine, (iii) NaH, imidazole, THF, (iv) DDQ, CH_2Cl_2, pH 7 phosphate buffer, (v) *p*-TsOH·H_2O, CH_2Cl_2, (vi) MMTrCl, pyridine; (e) DIBAL-H, CH_2Cl_2; (f) (i) AcOH/H_2O/THF (4:1:1), (ii) $Pd(OH)_2$ on C, H_2, MeOH.

O.2′ protection (3.5:1), but protection of the *erythro*- and *threo*-diols derived from the C.1 β-series (Scheme 4, *vide supra*) yielded the O.1′ MPM products exclusively and in a 16:1 ratio, respectively. One explanation for the high selectivity observed could be a combination of inductive effects of the C.3′–O bond adjacent to the C.2′–O–Sn bond

Scheme 4[a]



[a] Reagents and conditions: (a) (i) Dess–Martin periodinane, $NaHCO_3$, 3-Å molecular sieves, CH_2Cl_2, (ii) 0.02% $NiCl_2$ in $CrCl_2$, THF/DMF (4:1), (iii) Dess–Martin periodinane, 3-Å molecular sieves, CH_2Cl_2, (iv) $LiBH_4$, $TbCl_3$·$6H_2O$, MeOH/THF (10:1); (b) (i) Pd-Pb on $CaCO_3$, H_2, MeOH, (ii) BnBr, NaH, imidazole, TBAI, THF/DMF (4:1); (c) (i) OsO_4, *N,N′*-diisopropylethylenediamine, CH_2Cl_2, (ii) Bu_2SnO, toluene, (iii) CsF, MPM-Br, DMF, (iv) Ac_2O, DMAP, pyridine, (v) 80% AcOH, (vi) *p*-TsCl, Et_3N, CH_2Cl_2, (vii) NaH, imidazole, THF; (d) (i) DDQ, CH_2Cl_2, pH 7 phosphate buffer, (ii) *p*-TsOH·H_2O, CH_2Cl_2, (iii) MMTrCl, pyridine, (iv) K_2CO_3, MeOH, (v) Swern oxidation, (vi) BH_3, THF, (vii) AcOH/H_2O/THF (4:1:1), (viii) $Pd(OH)_2$ on C, H_2, MeOH; (e) (i) Red-Al, Et_2O, (ii) for the minor isomer only, Dess–Martin periodinane, 3-Å molecular sieves, CH_2Cl_2, (iii) $LiBH_4$, $TbCl_3$·$6H_2O$, MeOH/THF (10:1), (iv) BnBr, NaH, imidazole, TBAI, 4:1 THF/DMF (4:1); (f) (i) OsO_4, THF/pyridine (4:1), (ii) Bu_2SnO, toluene, (iii) CsF, MPM-Br, DMF, (iv) 3,4,5-trimethoxybenzoyl 2,4,6-trichlorobenzoate, DMAP, toluene, (v) 75% AcOH, (vi) *p*-TsCl, pyridine, (vii) NaH, imidazole, THF; (g) (i) DDQ, CH_2Cl_2, pH 7 phosphate buffer, (ii) *p*-TsOH·H_2O, CH_2Cl_2, (iii) MMTrCl, pyridine, (iv) DIBAL-H, CH_2Cl_2, (v) Swern oxidation, (vi) $(iBu)_3Al$, CH_2Cl_2, (vii) AcOH/H_2O/THF (4:1:1), (viii) $Pd(OH)_2$ on C, H_2, MeOH.

and steric effects, i.e., greater accessibility of the electrophile to O.1′.

The O.1′-protected alcohol thus obtained was acetylated to yield **11**. The ^1H NMR spectrum **11** confirmed the regiochemistry assignment of the selective mono-MPM protection; upon acetylation, the C.2′ proton exhibited a 1.95 ppm downfield shift. **11** was then converted in three steps into the epoxide **12**. Deprotection of the MPM group, followed by acid-catalyzed epoxide opening and (*p*-methoxyphenyl)diphenylmethyl (MMTr) protection of the primary alcohol, exclusively furnished tetrahydropyran **13**. Removal of its O.2′ acetate, Swern oxidation, and reduction with borane–THF (5:1 stereoselectivity) furnished the partially protected α,α-*C*-trehalose **14**. The remaining protecting groups were removed in two steps to yield α,α-*C*-trehalose (**1**). The ^1H and ^{13}C NMR spectra clearly showed **1** to possess the expected C_2 symmetry, which confirmed the tentative assignment of stereochemistry for osmylation product **10**.

Conversion of **8** to the *trans*-allylic benzyl ether **15** was effected by sodium bis(methoxyethoxy)aluminum hydride (Red-Al),[18] followed by benzylation (Scheme 3). Osmy-

lation of 15 yielded a mixture of the expected *threo*-diols in a 12:1 stereoselectivity. Once again, the major product was assigned as the desired *threo*-diol 16 on the basis of the empirical rule.

Previous work from this laboratory suggested that for the 1,2-*threo*-series, an electron-rich ester such as 3,4,5-trimethoxybenzoate (TMB) would be required to prevent 1,2-acyl migration and subsequent tetrahydrofuran formation during the acid-catalyzed ring opening of epoxide.[10] Thus, 16 was regioselectively protected at O.1′ as the MPM ether and then subjected to the Yamaguchi mixed-anhydride method[19] to prepare the TMB ester 17. This product was converted into an epoxide and subjected to O.1′ deprotection and acid-catalyzed cyclization followed by MMTr protection of O.6′ and deprotection at O.2′ to give exclusively the desired tetrahydropyran 18. Complete deprotection of 18 yielded 4, the C.2′ epimer of α,β-*C*-trehalose.

For the synthesis of 2, 3, and 5, the acetylenic iodide 19, obtained from *C*-allyl *O*-tetrabenzyl-β-D-glucopyranoside,[20] was coupled with the aldehyde derived from 7 to give a 1:1 ratio of acetylenic alcohols (Scheme 4). This mixture was oxidized and reduced to enrich the ratio in favor of the desired alcohol 20; $LiBH_4/TbCl_3$ in MeOH was found to give the best stereoselectivity (ca. 6:1) for this case. The stereochemical assignment of 20 was established by a chemical correlation with an authentic sample.[21] Following the same sequence of reactions as the α-series, 20 was transformed to the final 1,1′-linked *C*-disaccharides; the *cis*-allylic ether 21 furnished α,β-*C*-trehalose (2) and its C.2′ epimer 5, whereas the *trans*-allylic ether 22 gave β,β-*C*-trehalose (3).[22] These transformations were accomplished virtually in the same efficiency as observed in the α-series. It should be noted that the minor C.3′ diastereomer was removed at a later stage in each synthetic sequence for practical reasons; the 1,2-diol derived from *cis*-alkene 21 could be isolated as a single diastereomer, whereas the *trans*-allylic alcohols preceding 22 were chromatographically separable (see Experimental Section for details).

Conformational Analysis. In previous ^1H NMR studies of *C*-glycosides, analysis of the vicinal coupling constants around each pyranose ring affirmed its expected chair conformation, whereas analysis of the coupling constants across the interannular methylene bridge provided the information concerning the conformational preference about each exocyclic bond. While the coupling constants of the *C*-trehaloses 1–3 do demonstrate that all rings are in the chair conformer (Table 1), the C_2 symmetry of 1 and 3 prevents a straightforward determination of the coupling constants about the *C*-glycosidic bonds. Both 1 and 3 possess two pairs of chemically equivalent but magnetically nonequivalent protons (H.1 and H.1′; H.α and H.α′), giving rise to an AA′XX′ spin system. This higher-order spin system complicates our original approach, but two pieces of evidence confirm that both α,α-*C*-trehalose (1) and β,β-*C*-trehalose (3) preferentially adopt the single conformation as predicted. First, the O.2′-acetate of 14, an unsymmetrically protected derivative of 1, yields coupling constants which do not suffer from the higher-order splittings and clearly shows a preference for the double "exo-anomeric" conformation ($J_{1,\alpha}$ = 11.45 Hz, $J_{1,\alpha'}$ = 3.5, $J_{1',\alpha}$ = 3.5, and $J_{1',\alpha'}$ = 11.4). The analogously protected derivative of 3 gives unambiguous vicinal coupling constants supporting its predicted conformation ($J_{1,\alpha}$ = 11.05 Hz, $J_{1,\alpha'}$ = 2.0, $J_{1',\alpha}$ = 2.0, and $J_{1',\alpha'}$ = 10.85). Previous work from this laboratory has established that protecting groups have a minimal effect on the overall conformation of *C*-glycosides.[8] Second, the vicinal and geminal coupling constants obtained from these unsymmetrized substances, along with the chemical shifts measured from 1 and 3, were used in an NMR simulation program (PANIC from Bruker Magnetics). This produced a higher-order splitting pattern for the methylene protons and was found to be superimposable on the spectrum observed for the unprotected *C*-disaccharides (see Figure 4).

Unlike its C_2-symmetric stereoisomers, the bridging methylene protons of α,β-*C*-trehalose (2) do not suffer from virtual coupling effects, and its vicinal coupling constants have been measured directly. The coupling constants across the axial *C*-glycosidic bond ($J_{1,\alpha}$ = 9.7 Hz and $J_{1,\alpha'}$ = 4.0; D_2O) indicate a preference of its adopting the ideal "exo-anomeric" conformation, whereas the coupling constants across the equatorial *C*-glycosidic bond ($J_{1',\alpha}$ = 7.1 Hz and $J_{1',\alpha'}$ = 3.7; D_2O) suggest that it adopts either a conformer somewhat distorted from the "exo-anomeric" position or a mixture of staggered conformers.

Previous work from this laboratory has suggested that the axial *C*-glycosidic bond is conformationally more rigid than the equatorial *C*-glycosidic bond.[8] The experimental

Table 1.[a] Selected ^1H NMR Data for *C*-Disaccharides 1–3

	chemical shift[b] (coupling constants in Hz)		
proton	1[c]	2	3[c]
C.1	4.02[d]	4.13 (ddd, 4.0, 5.9, 9.6)	3.43[d]
C.2	3.61 (dd, 6.1, 9.8)	3.57 (dd, 5.9, 9.8)	3.07 (dd, 9.2, 9.6)
C.3	3.47 (dd, 8.8, 9.8)	3.47 (dd, 8.9, 9.8)	3.22 (dd, 9.0, 9.6)
C.4	3.20 (dd, 8.8, 9.8)	3.21 (dd, 8.9, 9.4)	3.33 (t, 9.0)
C.5	3.36 (ddd, 2.2, 5.6, 9.8)	3.51 (buried)	3.25 (ddd, 2.0, 5.8, 9.0)
C.6	3.54 (dd, 5.9, 12.45)	3.56 (buried)	3.54 (dd, 5.8, 12.3)
C.6	3.69 (dd, 2.2, 12.45)	3.69 (dd, 2.2, 12.0)	3.75 (dd, 2.0, 12.3)
C.α	1.83[d]	1.75 (ddd, 7.1, 9.7, 15.4)	1.77[d]
C.α′		2.06 (ddd, 3.7, 4.0, 15.4)	
C.1′		3.32 (ddd, 3.7, 7.1, 9.7)	
C.2′		3.14 (dd, 8.9, 9.7)	
C.3′		3.29 (t, 8.9)	
C.4′		3.22 (buried)	
C.5′		3.52 (buried)	
C.6′		3.56 (buried)	
C.6′		3.72 (dd, 1.9, 12.3)	

[a] All spectra were recorded on a Bruker AM-500 (500 MHz) spectrometer. [b] The chemical shifts are relative to the signal of HOD at 295 K (4.63 ppm). [c] Due to the C_2 symmetry of these compounds, protons at C.1–C.α are equivalent to protons at C.1′–C.α′. [d] Measurements of the coupling constants for protons at C.1 and C.α of compounds 1 and 3 were complicated by higher-order effects.

(18) Denmark, S. E.; Jones, T. K. *J. Org. Chem.* **1982**, *47*, 4595.
(19) Inanaga, J.; Hirata, K.; Saeki, H.; Katsuki, T.; Yamaguchi, M. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1989.
(20) Acetylenic iodide 19 was prepared in 86% overall yield from *C*-allyl *O*-tetrabenzyl-β-D-glucopyranoside as follows: (i) O_3, $MeOH/CH_2Cl_2$ (1:1), −78 °C, then Ph_3P, (ii) $(MeO)_2P(O)CHN_2$, KO-*t*-Bu, THF, −78 °C, (iii) I_2, morpholine, benzene, 50 °C.
(21) The *cis*-allylic benzyl ether derived from compound 20 was also synthesized by a Wittig reaction, cf. ref 15.
(22) The spectroscopic data of this substance correlates well with the data reported by Martin.[11b]

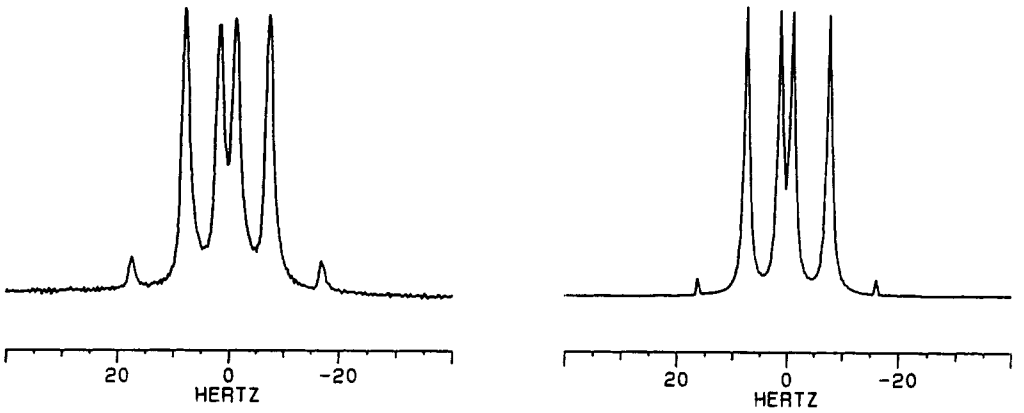


Figure 4. Actual ^{1}H NMR signal of the bridging methylene protons of 1, taken at 500 MHz (left), and simulated NMR signal (right).

Table 2. Selected ^{1}H NMR (500 MHz) Coupling Constants (Hz) for Compounds 2, 4, and 5 at Room Temperature

compd/solvent	J(H.1–H.α)	J(H.1–H.α')	J(H.1′–H.α)	J(H.1′–H.α')
2				
pyridine-d_5	10.2	3.2	5.5	3.2
methanol-d_4	9.8	3.6	6.0	3.6
DMSO-d_6	9.4	3.7	6.5	3.7
D_2O	9.7	4.0	7.1	3.7
permethyl 2				
benzene-d_6	9.3	4.7	6.3	3.6
chloroform-d	9.4	5.1	7.0	3.2
acetone-d_6	8.6	5.2	6.9	3.7
pyridine-d_5	9.0	5.3	6.5	3.9
methanol-d_4	9.2	5.0	7.0	3.3
DMSO-d_6	8.4	5.3	7.2	3.3
4				
pyridine-d_5	10.8	4.0	5.8	8.0
methanol-d_4				
DMSO-d_6	10.6	4.3	5.5	8.5
D_2O				
permethyl 4				
benzene-d_6	10.6	4.9	6.0	7.8
chloroform-d				
acetone-d_6	10.4	5.1	6.1	7.7
pyridine-d_5	10.6	4.9	5.9	8.0
methanol-d_4				
DMSO-d_6	9.9	4.9	6.0	7.3
5				
pyridine-d_5	8.1	5.5	7.0	3.3
methanol-d_4	7.8	6.2	6.8	3.1
DMSO-d_6	7.2	7.0	7.2	2.8
D_2O	7.7	7.0	7.7	3.1
permethyl 5				
benzene-d_6				
chloroform-d	7.1	7.9	7.1	3.6
acetone-d_6	6.8	7.2	6.8	3.8
pyridine-d_5	6.7	6.9	6.7	3.9
methanol-d_4	7.0	7.2	7.0	3.6
DMSO-d_6	6.8	7.1	6.8	3.7

evidence presented here proves this to be indeed the case. It is worthwhile to note that α,β-*C*-trehalose (**2**) provided for the first time an opportunity to compare directly the conformational rigidity of the axial *C*-glycosidic bond with that of the equatorial *C*-glycosidic bond.

The ^{1}H NMR spectra of **2** have been measured in four different solvents: pyridine-d_5, methanol-d_4, deuterium oxide, and dimethyl sulfoxide-d_6 (Table 2). In addition to these solvent systems (except for D_2O), the ^{1}H NMR spectra of the permethyl ethers of **2** have also been taken in benzene-d_6, chloroform-d, and acetone-d_6.

Overall, the solution polarity has little influence on the conformational preference of the 1,1′-*C*-disaccharides in both free and protected forms. α,β-*C*-Trehalose (**2**) shows some sensitivity to solvent effects with respect to its overall conformation; the data suggest a slight weakening in the preference of the α-glycosidic bond for the "exo-anomeric" conformation with increasing solvent polarity.[23] Comparison of **2** with its permethyl ether also shows modest differences in conformational preference.

The solvent effects on *C*-trehaloses **1** and **3** and their permethyl ethers were also examined. As before, the C_2 symmetry of these compounds did not allow for the straightforward determination of the vicinal coupling constants across the methylene bridge, but comparison with the computer-simulated spectra indicates very little deviation from their expected conformation.

Conformational Analysis of C.2 and C.2′ Epimers of α,β-*C*-Trehalose. The ^{1}H NMR data of **4** and **5** and their permethyl derivatives in various solvents are summarized in Table 2. Again, neither solvent polarity nor protecting groups were major factors in determining overall conformational behaviors.

The spin coupling constants observed for the bridging methylene protons (for example, $J_{1,\alpha} = 10.6$ Hz, $J_{1,\alpha'} = 4.3$, $J_{1',\alpha} = 5.5$, $J_{1',\alpha'} = 8.5$; DMSO-d_6) demonstrate that the C.2′ epimer **4** exists in a conformation close to that depicted in **4B**. The data observed for **5** (for example, $J_{1,\alpha} = 7.2$ Hz, $J_{1,\alpha'} = 7.0$, $J_{1',\alpha} = 7.2$, and $J_{1',\alpha'} = 2.8$; DMSO-d_6) suggest that the equatorial *C*-glycosidic bond exists in a conformation close to the "exo-anomeric" orientation, whereas its axial *C*-glycosidic bond deviates significantly from the ideal "exo-anomeric" conformation. The fact that $J_{1,\alpha}$ and $J_{1,\alpha'}$ do not exhibit a clear "small–large" spin coupling pattern as predicted for conformation **5C** (Figure 3) might be explained by a smaller difference in the conformational energies between **5A** and **5C** than the one roughly estimated. Still, these observations are qualitatively consistent with the prediction that the relative stability of **2**, **4**, and **5** to be **A** > **B** > **C**, **B** > **A** > **C**, and **C** > **A** > **B** (Figure 2), respectively. This change in the conformational balance is effected by the strategic inversion of the C.2 and C.2′ hydroxyl groups in **2**.

Conclusions

A single, efficient strategy was able to provide the three diastereomeric *C*-trehaloses **1**–**3**, as well as the C.2 and C.2′ epimers **4** and **5** of α,β-*C*-trehalose.

α,α-*C*-Trehalose (**1**) and β,β-*C*-trehalose (**3**) were predicted, and experimentally proven, to have a single conformer in which both *C*-glycosidic bonds adopt an "exo-

(23) For the weakening of anomeric effects in water, see: Lemieux, R. U.; Pavia, A. A.; Martin, J. C.; Watanabe, K. A. *Can. J. Chem.* **1969**, *47*, 4427.

anomeric" conformation. The conformational behavior of α,β-*C*-trehalose (**2**) indicates a strong preference for the axial-*C*-glycosidic bond preferentially to adopt the "exo-anomeric" conformation. On the other hand, the equatorial *C*-glycosidic bond deviates significantly from the ideal "exo-anomeric" conformation, indicating that the axial-*C*-glycosidic bond is conformationally more rigid than the equatorial-*C*-glycosidic bond. It was also demonstrated that the inversion of the C.2 or C.2′ hydroxyl group in α,β-*C*-trehalose (**2**) affected its conformational preference in a predictable manner. Taking into account the conformational behavior found in the 1,4-*C*-disaccharides and *C*-trisaccharides, i.e., the *C*-glycosidic bond is conformationally more rigid than the *C*-aglyconic bond,[10] we now see an interesting trend in conformational rigidity: axial *C*-glycosidic bond > equatorial *C*-glycosidic bond > *C*-aglyconic bond.

Experimental Section

General Experimental Procedures. For the general experimental procedures, see Part 6 of this series. Only selected spectral data are presented. ^1H and ^{13}C NMR spectra are included in the supplementary material to demonstrate the purity of each compound.

Acetylenic Alcohol 8. A stirred solution of the primary threitol **7** (460 mg, 1.86 mmol) in dry CH_2Cl_2 (6.4 mL) was treated with 3-Å powdered molecular sieves (700 mg), $NaHCO_3$ (530 mg), and Dess–Martin periodinane (1.18 g, 2.78 mmol). After 90 min of stirring, the reaction mixture was diluted with Et_2O (20 mL) and passed through Celite. Aqueous workup (Et_2O) gave the crude aldehyde, which was combined with acetylenic iodide **6** (1.92 g, 2.79 mmol) and dried first by azeotropic removal of water with toluene and then in vacuo. A stirred solution of acetylenic iodide and aldehyde in 4:1 THF/DMF (18 mL) was then treated with $CrCl_2$ containing 0.02% $NiCl_2$ (780 mg, 6.35 mmol) in a glovebox with a nitrogen atmosphere. The reaction mixture was stirred at room temperature for 12 h and quenched with saturated NH_4Cl. Aqueous workup (EtOAc) and silica gel chromatography (flash silica, 12%–30% EtOAc/hexanes) yielded acetylenic alcohol **8** and its C.3′ epimer as clear, colorless oils [*threo*: 864 mg, 1.06 mmol, 57% yield; *erythro*: 219 mg, 0.27 mmol, 15% yield]. ***threo*-Diastereomer 8.** IR (neat): 3437 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.35 (3H, s), 1.41 (3H, s), 2.60–2.72 (2H, m), 2.71 (1H, d, J = 6.3 Hz), 3.47 (1H, dd, J = 4.8, 5.9 Hz), 3.81 (1H, t, J = 7.7 Hz), 4.00 (1H, dd, J = 6.25, 8.45 Hz), 4.22 (1H, dt, J = 9.6, 4.8 Hz), 4.29 (1H, q, J = 6.6 Hz), 4.36 (1H, m). ^{13}C NMR ($CDCl_3$): δ 17.05, 25.59, 26.45, 109.15. HRMS (FAB, NaI): calcd for $C_{51}H_{56}O_9$ (M + Na) 835.3822; found 835.3851. $[\alpha]_D$: +37.5° (*c* 1.32, $CHCl_3$). ***erythro*-Diastereomer.** IR (neat): 3450 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.37 (3H, s), 1.41 (3H, s), 2.58–2.70 (2H, m), 3.08 (1H, d, J = 7.3 Hz), 3.40 (1H, dd, J = 4.7, 5.3 Hz), 3.78 (1H, dd, J = 7.6, 8.5 Hz), 3.98 (1H, dd, J = 6.75, 8.5 Hz), 4.21 (1H, dt, J = 9.1, 5.6 Hz). ^{13}C NMR ($CDCl_3$): δ 17.08, 25.71, 26.28, 109.40. HRMS (FAB, NaI): calcd for $C_{51}H_{56}O_9$ (M + Na) 835.3822; found 835.3829. $[\alpha]_D$: +42.5° (*c* 0.49, $CHCl_3$).

***cis*-Alkene 9.** A stirred solution of acetylenic alcohol **8** (154 mg, 0.189 mmol) in MeOH (10 mL) was hydrogenated over Lindlar catalyst (10% Pd–Pb on $CaCO_3$, 36 mg) under 1 atm of H_2 at room temperature for 12 h. The reaction mixture was passed through Celite, concentrated, and purified by silica gel chromatography (flash silica, 25%–40% EtOAc/hexanes) to yield the corresponding *cis*-allylic alcohol as a colorless oil (137.3 mg, 0.169 mmol, 89% yield). A stirred solution of the dry allylic alcohol in 4:1 THF/DMF (2 mL) at 0 °C under N_2 was treated with NaH (30 mg of a 60% dispersion in oil, 0.75 mmol) and imidazole (1.5 mg, 0.02 mmol). The reaction was stirred at room temperature for 15 min and then treated with benzyl bromide (50 μL, 0.41 mmol) and tetrabutylammonium iodide (TBAI) (7.4 mg, 0.02 mmol), stirred for 6 h, and quenched with saturated NH_4Cl. Aqueous workup (Et_2O) and silica gel chromatography (flash silica, 12%–25% EtOAc/hexanes) yielded *cis*-alkene **9** as a colorless oil (133.7 mg, 0.148 mmol, 88% yield). IR (neat): 2868 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.31 (3H, s), 1.35 (3H, s), 2.48 (1H, dddd, J = 2.05, 4.1, 6.45, 16.4 Hz), 2.58 (1H, dddd, J = 1.5, 7.05, 11.1, 16.4 Hz), 3.47 (1H, t, J = 5.3 Hz), 3.57 (1H, ddd, J = 2.05, 3.8, 9.7 Hz), 3.88 (1H, dd, J = 6.2, 8.2 Hz), 4.15 (1H, m), 4.26 (1H, ddd, J = 5.3, 6.2, 8.9 Hz), 4.38 (1H, ddd, J = 0.9, 5.8, 9.4 Hz), 5.52 (ddt, J = 9.4, 11.1, 1.75 Hz), 5.80 (ddt, J = 1.0, 11.1, 7.0 Hz). ^{13}C NMR ($CDCl_3$): δ 24.08, 25.80, 26.53, 108.83, 131.71, 138.62. HRMS (FAB, NaI): calcd for $C_{58}H_{64}O_9$ (M + Na) 927.4448; found 927.4454. $[\alpha]_D$: +25.8 (*c* 1.02, $CHCl_3$).

***erythro*-Diol 10.** A stirred solution of *cis*-alkene **9** (121.4 mg, 0.134 mmol) in 4:1 THF/pyridine (1.75 mL) was treated at −35 °C with OsO_4 (0.42 mL of a 0.39 M solution in toluene). After being stirred for 2 days, the reaction mixture was diluted with MeOH (50 mL), saturated with H_2S gas for 3 min and then stirred for 30 min. The black suspension was purged with N_2 and then passed through Celite and purified by silica gel chromatography (flash silica, 20%–40% EtOAc/hexanes) to yield as a white crystalline solid *erythro*-diol **10** (115.2 mg, 0.123 mmol, 91% yield). IR (neat): 3484 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.37 (3H, s), 1.44 (3H, s), 1.85 (1H, ddd, J = 4.1, 9.1, 15.25 Hz), 2.19 (1H, ddd, J = 1.8, 10.3, 15.25 Hz), 3.18 (1H, br d, J = 4.4 Hz), 3.74 (1H, dd, J = 3.2, 6.45 Hz), 3.84 (1H, dt, J = 7.5, 5.3 Hz), 4.52 (1H, dt, J = 8.5, 6.3 Hz). ^{13}C NMR ($CDCl_3$): δ 25.67, 26.54, 28.68, 109.26. HRMS (FAB, NaI): calcd for $C_{58}H_{66}O_{11}$ (M + Na) 961.4503; found 961.4501. $[\alpha]_D$: +16° (*c* 1.76, $CHCl_3$).

Acetate 11. A stirred solution of the diol **10** (52.45 mg, 55.9 μmol) and dibutyltin oxide (20.85 mg, 83.8 μmol) in toluene (2 mL) was refluxed using a Dean-Stark apparatus for 2 h. The solvent was evaporated leaving the crude dibutylstannylene, which was combined with CsF (17 mg, 112 μmol) and dried in vacuo for 2 h. The reaction flask was charged with dry DMF (1.5 mL) and stirred under N_2 at room temperature for 10 min. The reaction was treated with MPM-Cl (23 μL, 168 μmol) and TBAI (4.1 mg, 12 μmol), stirred for 36 h, and then diluted with Et_2O and quenched with H_2O. Aqueous workup (Et_2O) and preparative TLC (0.5 mm, 25% EtOAc/hexanes) yielded the desired mono-MPM alcohol as a colorless oil (58.55 mg, 55.3 μmol, 99% yield). A stirred solution of the alcohol in pyridine (1 mL) and acetic anhydride (1 mL) was treated with 4-(dimethylamino)pyridine (DMAP) (1.5 mg) and stirred for 30 min. Solvent removal followed by silica gel chromatography (flash silica, 25% EtOAc/hexanes) yielded the acetate **11** as a colorless oil (57.8 mg, 52.5 μmol, 95% yield). IR (neat): 1741 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.37 (3H, s), 1.44 (3H, s), 2.02 (1H, m), 2.03 (3H, s), 2.10 (1H, m), 3.36 (1H, dd, J = 2.6, 9.7 Hz), 3.46 (1H, dd , J = 3.9, 9.7 Hz), 3.62 (1H, t, J = 8.7 Hz), 3.81 (3H, s), 3.98 (br d, J = 10.4 Hz), 4.27 (1H, q, J = 7.8 Hz), 5.58 (1H, dd, J = 3.0, 8.2 Hz). ^{13}C NMR ($CDCl_3$): δ 21.07, 25.57, 26.05, 26.52, 55.19, 109.16, 113.71, 159.20, 169.80. HRMS (FAB, NaI): calcd for $C_{68}H_{76}O_{13}$ (M + Na) 1123.5186; found 1123.5216. $[\alpha]_D$: +23.4° (*c* 1.59, $CHCl_3$).

Epoxide 12. Acetate **11** (127 mg, 0.115 mmol) was stirred in 80% aqueous AcOH (20 mL) at room temperature for 12 h. Solvent removal followed by silica gel chromatography (30%–75% EtOAc/ hexanes) yielded the corresponding diol as a colorless oil (117.2 mg, 0.109 mmol, 95% yield). A stirred solution of the diol in pyridine (4 mL) was treated with *p*-TsCl (82 mg, 0.42 mmol). After 9 h, the reaction was quenched with saturated $NaHCO_3$. Aqueous workup (Et_2O) gave the crude primary tosylate, which was quickly passed through a short silica gel column (50% EtOAc/hexanes), followed by azeotropic removal of water with toluene. A stirred solution of the primary tosylate in THF (11 mL) was treated at 0 °C under N_2 with NaH (50 mg of a 60% dispersion in mineral oil, 12.5 mmol) and imidazole (3 mg, 0.04 mmol), followed by quenching with H_2O at −30 °C after 20 min. Aqueous workup (Et_2O) and silica gel chromatography (12%–30% EtOAc/hexanes) yielded the epoxide **12** as a colorless oil (75.6 mg, 71.8 μmol, 66% yield). IR (neat): 1740 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.85 (6H, s), 1.98–2.12 (2H, m), 2.45 (1H, br d, J = 4.1 Hz), 2.60 (1H, br d, J = 4.1 Hz), 3.16 (2H, br), 3.39 (1H, br d, J = 10.5 Hz), 3.63 (1H, t, J = 8.2 Hz), 3.71 (1H, t, J = 9.1 Hz), 3.79 (3H, s), 4.00 (1H, m), 5.45 (br d, J = 7.6 Hz). ^{13}C NMR ($CDCl_3$): δ 21.00, 26.25, 43.00, 53.17, 55.20, 113.62, 159.09, 169.69. HRMS (FAB, NaI): calcd for $C_{65}H_{70}O_{12}$ (M + Na) 1065.4765; found 1065.4790. $[\alpha]_D$: +16.5° (*c* 1.18, $CHCl_3$).

***C*-Disaccharide 13.** A stirred solution of epoxide **12** (75.6 mg, 71.8 μmol) in CH_2Cl_2 (7 mL) and pH 7 phosphate buffer (0.2

mL) was treated at 0 °C with DDQ (49 mg, 215 μmol). The reaction mixture was stirred for 2 h and then quenched with saturated $NaHCO_3$. Aqueous workup (CH_2Cl_2) and silica gel chromatography (flash silica, 20%–50% EtOAc/hexanes) yielded the corresponding epoxy alcohol. A stirred solution of the epoxy alcohol in CH_2Cl_2 (25 mL) was treated with p-TsOH·H_2O (10 mg, 52.6 μmol). The reaction mixture was stirred for 50 min and then quenched with saturated $NaHCO_3$. Aqueous workup (CH_2Cl_2) and silica gel chromatography (flash silica, 20%–50% EtOAc/hexanes) yielded the corresponding tetrahydropyran as a colorless oil (59.2 mg, 64.1 μmol, 89% yield). A stirred solution of the tetrahydropyran in pyridine (2 mL) was treated at 50 °C with MMTrCl (60 mg, 0.192 mmol). The reaction mixture was stirred for 6 h, concentrated, and purified by silica gel chromatography (flash silica, 12%–30% THF/hexanes) to yield the corresponding MMTr ether as a yellow oil (68.8 mg, 57.6 μmol, 90% yield). The purified product was then treated with K_2CO_3 (50 mg, 0.362 mmol) in MeOH (10 mL) at room temperature for 3 h. The reaction mixture was concentrated, passed through silica gel, and then concentrated again and subjected to silica gel chromatography (flash silica, 20%–40% EtOAc/hexanes) to yield the desired C-disaccharide **13** as a colorless oil (63.0 mg, 54.6 μmol, 95% yield). IR (neat): 3437 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.86 (1H, ddd, J = 2.9, 11.45, 15.0 Hz), 2.10 (1H, ddd, J = 1.75, 10.85, 15.0 Hz), 2.56 (1H, d, J = 4.7 Hz), 3.37 (1H, dd, J = 5.85, 9.7 Hz), 3.48 (1H, dd, J = 3.5, 9.7 Hz), 3.61 (1H, m), 3.75 (3H, s), 4.15 (1H, dt, J = 11.15, 6.2 Hz). ^{13}C NMR ($CDCl_3$): δ 23.66, 55.09, 113.02, 144.47, 158.41. HRMS (FAB, NaI): calcd for $C_{75}H_{76}O_{11}$ (M + Na) 1175.5285; found 1175.5294. [α]$_D$: +30° (c 1.28, $CHCl_3$).

α,α-*C*-Trehalose Derivative 14. The C-disaccharide **13** (63.0 mg, 54.6 μmol) was oxidized to the ketone by the usual Swern procedure. A stirred solution of the crude ketone in THF (4 mL) was treated at 0 °C under N_2 with BH_3 (0.7 mL of a 0.9 M THF solution). The reaction mixture was stirred for 10 min and then quenched with saturated NH_4Cl. Aqueous workup (Et_2O) and silica gel chromatography (flash silica, 16%–30% EtOAc/hexanes) yielded α,α-C-trehalose derivative **14** and its C.2′ epimer C-disaccharide **13** as colorless oils [**14**: 46.7 mg, 40.5 μmol, 74% yield; **13**: 9.65 mg, 8.4 μmol, 15% yield]. **14**. IR (neat): 3435 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.99–2.11 (2H, m), 2.77 (1H, d, J = 4.45 Hz), 3.36 (1H, dd, J = 5.3, 9.7 Hz), 3.49 (1H, dd, J = 4.4, 9.7 Hz), 3.74 (3H, s), 3.86 (1H, q, J = 5.0 Hz), 4.13 (1H, dt, J = 8.6, 4.4 Hz). ^{13}C NMR ($CDCl_3$): δ 21.41, 55.11, 113.04, 144.47, 144.49, 158.46. HRMS (FAB, NaI): calcd for $C_{75}H_{76}O_{11}$ (M + Na) 1175.5285; found 1175.5273. [α]$_D$: +36° (c 1.24, $CHCl_3$).

α,α-*C*-Trehalose (1). The α,α-C-trehalose derivative **14** (46.7 mg, 40.5 μmol) was stirred in 4:1:1 AcOH/H_2O/THF (6 mL) at 50 °C for 8 h and then subjected to silica gel chromatography (20%–50% EtOAc/hexanes). A stirred solution of the resultant diol (35.7 mg, 40.5 μmol) in MeOH (5 mL) was hydrogenated over Pearlman's catalyst (10% $Pd(OH)_2$ on C, 40 mg) under 1 atm of H_2 for 4 h. The reaction mixture was passed through Celite and then filter paper (Whatman #42) to yield α,α-C-trehalose (**1**) dihydrate as a white solid (15.2 mg), mp (MeOH) 225 °C dec. ^1H NMR (D_2O): δ 1.83 (1H, m), 3.20 (1H, dd, J = 8.8, 9.8 Hz), 3.36 (1H, ddd, J = 2.2, 5.6, 9.8 Hz), 3.47 (1H, dd, J = 8.8, 9.8 Hz), 3.54 (1H, dd, J = 5.9, 12.45 Hz), 3.61 (1H, dd, J = 6.1, 9.8 Hz), 3.69 (1H, dd, J = 2.2, 12.45 Hz), 4.02 (1H, m). ^{13}C NMR (9:1 D_2O/CD_3OD): δ 18.53, 62.16, 71.36, 71.72, 72.02, 73.77, 74.24. HRMS (FAB, NaI): calcd for $C_{13}H_{24}O_{10}$ (M + H) 341.1448; found 341.1460. [α]$_D$: +81.8° (c 1.59, H_2O).

***trans*-Alkene 15.** A stirred solution of acetylenic alcohol **8** (196.5 mg, 0.242 mmol) in Et_2O (35 mL) was treated at 0 °C under argon with Red-Al (1.75 mL of a 3.4 M solution in toluene). The reaction mixture was stirred for 90 min and then quenched by dropwise addition of MeOH, followed by treatment with crushed Glauber's salt (Na_2SO_4·$10H_2O$, 4 g) for 2 h. Silica gel chromatography (flash silica, 25%–40% EtOAc/hexanes) yielded the corresponding *trans*-allylic alcohol as a colorless oil (120.3 mg, 0.148 mmol, 61% yield). Benzylation of the *trans*-allylic alcohol was performed according to an earlier procedure (cf. *cis*-alkene **9**) to yield the *trans*-alkene **15** as a white solid (117.7 mg, 0.130 mmol, 88% yield), mp (hexanes/EtOAc) 97–100 °C. IR (neat): 2869 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.34 (3H, s), 1.38 (3H, s), 2.43–2.56 (2H, m), 3.38 (1H, dd, J = 4.8, 6.4 Hz), 3.60 (1H, t, J = 7.9 Hz), 3.86 (1H, br dd, J = 4.8, 7.5 Hz), 4.10 (1H, dt, J = 9.7, 5.3 Hz), 5.57 (1H, dd, J = 7.5, 15.6 Hz), 5.72 (1H, dt, J = 15.6, 6.7 Hz). ^{13}C NMR ($CDCl_3$): δ 25.79, 26.60, 28.25, 108.72, 128.83, 131.20. HRMS (FAB, NaI): calcd for $C_{58}H_{64}O_9$ (M + Na) 927.4448; found 927.4459. [α]$_D$: +17.8° (c 1.18, $CHCl_3$).

***threo*-Diol 16.** A stirred solution of *trans*-alkene **15** (117.7 mg, 0.130 mmol) in 4:1 THF/pyridine (1.75 mL) was treated at −78 °C with OsO_4 (400 μL of a 0.39 M solution in toluene). The reaction mixture was stirred for 24 h and then worked up according to an earlier procedure (cf. *erythro*-diol **10**). Silica gel chromatography (flash silica, 20%–30% EtOAc/hexanes) yielded *threo*-diol **16** as a colorless oil (106.9 mg, 0.114 mmol, 88% yield). IR (neat): 3512 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.34 (3H, s), 1.41 (3H, s), 1.85 (1H, dt, J = 15.2, 3.1 Hz), 2.23 (1H, ddd, J = 8.8, 11.7, 15.2 Hz), 2.96 (1H, d, J = 6.5 Hz), 3.25 (1H, d, J = 4.1 Hz), 3.47 (1H, dd, J = 8.6, 9.8 Hz), 3.53 (1H, dd, J = 5.8, 10.2 Hz), 3.80 (1H, t, 8.9 Hz), 3.88 (1H, ddd, J = 2.3, 5.7, 9.8 Hz), 4.03 (1H, dt, 8.7, 3.9 Hz), 4.28 (1H, ddd, J = 3.0, 6.95, 11.6 Hz). ^{13}C NMR ($CDCl_3$): δ 25.59, 26.47, 28.66, 109.13. HRMS (FAB, NaI): calcd for $C_{58}H_{66}O_{11}$ (M + Na) 961.4503; found 961.4503. [α]$_D$: +16.7° (c 1.35, $CHCl_3$).

3,4,5-Trimethoxybenzoate 17. The regioselective mono-MPM protection of diol **14** (29.6 mg, 31.5 μmol) was performed according to an earlier procedure (cf. acetate **11**). Preparative TLC (0.5 mm, 20% Et_2O/benzene) yielded the desired O.1′ mono-MPM ether and its O.2′ regioisomer as colorless oils [O.1′ MPM ether: 21.1 mg, 19.9 μmol, 63% yield; O.2′ MPM ether: 6.05 mg, 5.7 μmol, 18% yield]. The mixed anhydride 3,4,5-trimethoxybenzoyl 2,4,6-trichlorobenzoate was prepared according to the procedure of Yamaguchi.[19] A stirred solution of the O.1′ MPM ether (56.4 mg, 53.2 μmol) and the mixed anydride (250 mg, 0.532 mmol) in toluene (2 mL) was treated at 50 °C with DMAP (66 mg, 0.538 mmol). The reaction mixture was stirred for 6 h. Aqueous workup (Et_2O) and silica gel chromatography (12%–30% EtOAc/hexanes) yielded the 3,4,5-trimethoxybenzoate **17** as a colorless oil (62.25 mg, 49.7 μmol, 93% yield). IR (neat): 1712 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.29 (3H, s), 1.36 (3H, s), 1.87 (1H, ddd, J = 3.8, 10.3, 15.0 Hz), 2.14 (1H, ddd, J = 4.0, 12.3, 15.0 Hz), 3.28 (1H, dd, J = 1.9, 10.3 Hz), 3.37 (1H, ddd, J = 2.1, 3.1, 9.6 Hz), 3.70 (3H, s), 3.72 (6H, s), 3.88 (1H, dd, J = 6.2, 8.5 Hz), 4.09 (1H, ddd, J = 1.9, 4.4, 10.0 Hz), 4.13 (1H, dd, J = 3.5, 8.1 Hz), 5.79 (1H, dd, J = 1.9, 8.1 Hz). ^{13}C NMR ($CDCl_3$): δ 25.04, 25.67, 26.70, 55.20, 56.09, 60.89, 107.22, 108.99, 113.67, 142.36, 152.93, 159.12, 165.49. HRMS (FAB, NaI): calcd for $C_{76}H_{84}O_{16}$ (M + Na) 1275.5657; found 1275.5684. [α]$_D$: −6.2° (c 2.33, $CHCl_3$).

β-*C*-Mannoside Derivative 18. The transformation of 3,4,5-trimethoxybenzoate **17** (70.7 mg, 56.4 μmol) to the corresponding tetrahydropyran–MMTr ether (25.4 mg, 18.9 μmol, 34% yield) was performed according to an earlier procedure (cf. C-disaccharide **13**). A stirred solution of the tetrahydropyran in CH_2Cl_2 (1.5 mL) was treated at −78 °C under N_2 with DIBAL-H (120 μL of a 1 M solution in hexanes). The reaction mixture was stirred for 50 min and then diluted with Et_2O (12 mL) at room temperature and treated with crushed Glauber's salt (400 mg) for 45 min. Preparative TLC (0.5 mm, 25% EtOAc/hexanes) yielded the β-C-mannoside derivative **18** as a colorless oil (17.35 mg, 15.0 μmol, 80% yield). IR (neat): 3500 cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.20 (1H, ddd, J = 5.8, 10.5, 14.7 Hz), 2.28 (1H, ddd, J = 4.6, 7.9, 14.7 Hz), 2.46 (1H, d, J = 3.7 Hz), 3.20 (1H, dd, J = 4.2, 10.0 Hz), 3.34 (1H, ddd, J = 1.8, 4.2, 9.8 Hz), 3.48 (1H, dd, J = 1.7, 9.9 Hz), 3.50 (1H, dd, J = 3.3, 9.2 Hz), 3.55 (1H, br dd, J = 6.25, 7.7 Hz), 3.59 (1H, dd, J = 2.3, 10.5 Hz), 3.72 (3H, s), 3.77 (1H, dd, J = 5.8, 9.4 Hz), 3.86 (1H, t, J = 9.0 Hz), 4.05 (1H, m), 4.34 (1H, ddd, J = 4.8, 5.5, 10.7 Hz). ^{13}C NMR ($CDCl_3$): δ 27.09, 55.13, 113.02, 144.23, 144.74, 158.43. HRMS (FAB, NaI): calcd for $C_{75}H_{76}O_{11}$ (M + Na) 1175.5285; found 1175.5293. [α]$_D$: +23° (c 1.39, $CHCl_3$).

α-Glucopyranosyl β-*C*-Mannopyranoside 4. The transformation of β-C-mannoside **18** (2.5 mg, 2.17 μmol) to α-glucopyranosyl β-C-mannopyranoside **4** was accomplished according to an earlier procedure (cf. α,α-C-trehalose (**1**)). ^1H NMR (pyridine-d_5): δ 2.82 (1H, ddd, J = 5.8, 10.8, 14.5 Hz), 3.05 (1H, ddd, J = 4.0, 8.0, 14.5 Hz), 3.93 (1H, ddd, J = 2.75, 6.4, 9.55 Hz), 4.85 (1H, ddd, J = 4.1, 5.8, 10.8 Hz). ^{13}C NMR (CD_3OD): δ 27.86, 63.21, 63.32, 69.03, 71.60, 72.51, 73.02, 74.13, 75.05, 75.20, 76.60, 77.09, 82.12. HRMS (FAB, NaI): calcd for $C_{13}H_{24}O_{10}$ (M + Na) 363.1267; found 363.1282. [α]$_D$: +9.4° (c 0.48, H_2O).

Acetylenic Alcohol 20. Acetylenic iodide **19** (1.32 g, 1.92 mmol) and the aldehyde derived from threitol **7** (330 mg, 1.33 mmol) were coupled according to an earlier procedure (cf. acetylenic alcohol **8**), yielding acetylenic alcohol **20** and its C.3′ epimer as an inseparable 1:1 mixture of isomers (700 mg, 0.86 mmol, 65% yield). A stirred solution of the acetylenic alcohols and powdered 3-Å molecular sieves (560 mg) in CH_2Cl_2 (11 mL) was treated at room temperature with Dess–Martin periodinane (560 mg, 1.32 mmol). The reaction mixture was stirred for 25 min, diluted with Et_2O (75 mL), and filtered over Celite. Aqueous workup (Et_2O) yielded the crude acetylenic ketone as a white solid (621 mg, 0.77 mmol, 89% yield), which was used without further purification. A stirred solution of $TbCl_3{\cdot}6H_2O$ (1.44 g, 3.85 mmol) in MeOH (20 mL) was treated with $LiBH_4$ (84 mg, 3.85 mmol). The reaction mixture was stirred at 0 °C for 5 min, followed by the slow addition of acetylenic ketone in THF (2 mL). The reaction mixture was stirred for 15 min and quenched at 0 °C with saturated NH_4Cl. Aqueous workup (CH_2Cl_2) and silica gel chromatography (14%–30% EtOAc/hexanes) yielded acetylenic alcohol **20** and its C.3′ epimer as an inseparable 6:1 mixture of isomers (614 mg, 0.75 mmol, 98% yield), a white solid. IR (neat): 3451 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.34 (3H, s), 1.40 (3H, s), 2.56 (1H, d, J = 6.2 Hz), 2.57 (1H, ddd, J = 2.2, 5.9, 17.0 Hz), 2.73 (1H, ddd, J = 2.0, 3.3, 17.0 Hz), 3.59 (1H, t, 8.9 Hz), 3.78 (1H, dd, J = 7.4, 8.4 Hz), 3.97 (1H, dd, J = 6.5, 8.4 Hz), 4.27 (1H, dt, J = 7.35, 6.3 Hz), 4.34 (1H, m). ^{13}C NMR ($CDCl_3$): δ 22.24, 25.63, 26.45, 109.20. HRMS (FAB, NaI): calcd for $C_{51}H_{56}O_9$ (M + Na) 835.3822; found 835.3818.

***cis*-Alkene 21.** The transformation of acetylenic alcohol **20** and its C.3′ epimer (203.2 mg, 0.250 mmol) to *cis*-alkene **21** and its C.3′ epimer (174 mg, 0.193 mmol, 77% yield) was performed according to an earlier procedure (cf. *cis*-alkene **9**). An analytical sample of **21** was obtained by preparative TLC (0.5 mm, 14% *tert*-butyl methyl ether/benzene) of the *cis*-allylic alcohol precursor. IR (neat): 2865 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.31 (3H, s), 1.35 (3H, s), 2.15 (1H, m), 2.74 (1H, br dd, J = 5.8, 15.5 Hz), 3.39 (1H, ddd, J = 2.0, 4.1, 9.4 Hz), 3.41 (1H, t, J = 5.6 Hz), 3.80 (1H, dd, J = 6.3, 8.0 Hz), 5.51 (1H, ddt, J = 9.4, 11.2, 1.8 Hz), 5.89 (1H, br ddd, J = 5.6, 8.5, 11.2 Hz). ^{13}C NMR ($CDCl_3$): δ 25.80, 26.59, 30.22, 108.80, 131.26. HRMS (FAB, NaI): calcd for $C_{58}H_{64}O_9$ (M + Na) 927.4448; found 927.4459. $[\alpha]_D$: −14.7° (*c* 1.00, $CHCl_3$).

***α,β-C*-Trehalose (2) and α-Mannopyranosyl *β-C*-Glucopyranoside 5.** A stirred solution of OsO_4 (80.3 mg, 0.316 mmol) in toluene (0.8 mL) and CH_2Cl_2 (0.5 mL) was treated at −78 °C under N_2 with *N,N*′-diisopropylethylenediamine (57 μL, 0.313 mmol) in CH_2Cl_2 (0.7 mL). The reaction mixture was stirred for 20 min, followed by dropwise addition at −78 °C of *cis*-alkene **21** and its C.3′ epimer (258 mg, 0.285 mmol) in CH_2Cl_2 (1 mL). The reaction was stirred for 16 h and then warmed to room temperature and worked up according to an earlier procedure (cf. *erythro*-diol **10**). Purification by silica gel chromatography (12%–25% EtOAc/hexanes) yielded as the major product the desired *erythro*-diol as a colorless oil (184.7 mg, 0.197 mmol, 69% yield). The transformation of the *erythro*-diol (41.9 mg, 44.6 μmol) to α,β-*C*-trehalose (**2**) (4.2 mg, 12.2 μmol, 27% yield), a colorless oil, was performed according to an earlier procedure (cf. *C*-disaccharide **13**). α-Mannopyranosyl β-*C*-glucopyranoside **5** was obtained by deprotecting the appropriate intermediate. ***α,β-C*-Trehalose (2).** ^1H NMR (D_2O): δ 1.75 (1H, ddd, J = 7.0, 9.5, 15.4 Hz), 2.06 (1H, ddd, J = 3.6, 4.1, 15.4 Hz), 3.14 (1H, dd, J = 8.9, 9.7 Hz), 3.21 (1H, dd, J = 8.9, 9.4 Hz), 3.29 (1H, t, J = 8.9 Hz), 3.32 (1H, ddd, J = 3.6, 7.0, 9.7 Hz), 3.47 (1H, dd, J = 8.9, 9.8 Hz), 3.57 (1H, dd, J = 5.9, 9.8 Hz), 3.69 (1H, dd, J = 2.2, 12.0 Hz), 3.72 (1H, dd, 1.9, 12.3 Hz), 4.13 (1H, ddd, J = 4.1, 5.9, 9.6 Hz). ^{13}C NMR (CD_3OD): δ 28.09, 63.33, 63.42, 72.16, 72.67, 73.04, 74.70, 74.86, 75.12, 75.18, 79.19, 79.84, 81.65. HRMS (FAB, NaI): calcd for $C_{13}H_{24}O_{10}$ (M + Na) 363.1267; found 363.1284. $[\alpha]_D$: +33° (*c* 1.02, H_2O). ***α*-Mannopyranosyl *β-C*-Glucopyranoside 5.** ^1H NMR (CD_3OD): δ 1.95 (1H, ddd, J = 7.0, 7.7, 14.7 Hz), 2.05 (1H, ddd, 3.1, 6.2, 14.7 Hz), 3.78 (1H, dd, J = 2.2, 3.3 Hz), 3.82 (2H, dt, J = 11.4, 1.85 Hz), 4.19 (1H ddd, J = 2.6, 6.25, 7.7 Hz). ^{13}C NMR (CD_3OD): δ 32.16, 63.21, 63.26, 69.61, 72.05, 72.76, 72.82, 75.02, 76.00, 76.18, 78.67, 79.82, 81.80. HRMS (FAB, NaI): calcd for $C_{13}H_{24}O_{10}$ (M + Na) 363.1267; found 363.1247. $[\alpha]_D$: +8.0° (*c* 0.64, H_2O).

***trans*-Alkene 22.** The transformation of acetylenic alcohol **20** and its C.3′ epimer (277 mg, 0.341 mmol) to their corresponding *trans*-allylic alcohols (231.5 mg, 0.284 mmol, 83% combined yield) was performed according to an earlier procedure (cf. *trans*-alkene **15**). A stirred solution of the minor allylic alcohol (41.5 mg, 50.9 μmol) was oxidized and reduced according to an earlier procedure (cf. acetylenic alcohol **20**) to yield exclusively the desired allylic alcohol (38.25 mg, 46.9 μmol, 92% yield) as a colorless oil. Benzylation of the *trans*-allylic alcohol (228 mg, 0.280 mmol) was performed according to an earlier procedure (cf. *trans*-alkene **15**) to yield the *trans*-alkene **22** as a white solid (233.5 mg, 0.258 mmol, 92% yield), mp (hexanes/EtOAc) 101–102.5 °C. IR (neat): 2863 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.36 (3H, s), 1.40 (3H, s), 2.34 (1H, dt, J = 16.0, 7.9 Hz), 2.63 (1H, br dd, J = 6.7, 16.0 Hz), 3.40 (1H, dd, J = 4.7, 6.45 Hz), 3.60 (1H, t, J = 7.9 Hz), 3.79 (1H, dd, J = 6.4, 8.2 Hz), 3.85 (1H, dd, J = 4.5, 7.8 Hz), 5.59 (1H, br dd, J = 7.9, 15.6 Hz), 5.79 (1H, dt, J = 15.6, 6.8 Hz). ^{13}C NMR ($CDCl_3$): δ 25.84, 26.62, 34.54, 108.72, 129.32, 131.56. HRMS (FAB, NaI): calcd for $C_{58}H_{64}O_9$ (M + Na) 927.4448; found 927.4418. $[\alpha]_D$: −20.2° (*c* 1.26, $CHCl_3$).

***β,β-C*-Trehalose (3).** The transformation of *trans*-alkene **22** (247 mg, 0.273 mmol) to the corresponding β-*C*-mannoside C.2′ alcohol (113.5 mg, 98.4 μmol, 36% yield) was performed according to an earlier procedure (cf. β-*C*-mannoside derivative **18**). The C.2′ alcohol (30.2 mg, 26.2 μmol) was oxidized to the ketone by the usual Swern procedure. A stirred solution of ketone in CH_2Cl_2 (1 mL) was treated at −78 °C under N_2 with triisobutylaluminum (105 μL of a 1 M hexanes solution). The reaction was stirred for 21 h, diluted with Et_2O (10 mL) at room temperature, and treated with crushed Glauber's salt (0.25 g). Preparative TLC (0.5 mm, 7% acetone/benzene) yielded the β-*C*-glucoside C.2′ alcohol (23.65 mg, 20.5 μmol, 78% yield) and the β-*C*-mannoside C.2′ alcohol (2.4 mg, 2.1 μmol, 8% yield) as colorless oils. The transformation of the β-*C*-glucoside C.2′ alcohol (24.6 mg, 21.3 μmol) to the β,β-*C*-trehalose (**3**) dihydrate (7.25 mg, 19.3 μmol, 90% yield), a colorless gum, was accomplished according to an earlier procedure (cf. α,α-*C*-trehalose (**1**)). ^1H NMR (D_2O): δ 1.77 (1H, m), 3.07 (1H, dd, J = 9.2, 9.6 Hz), 3.22 (1H, ddd, J = 2.0, 5.8, 9.0 Hz), 3.25 (1H, dd, J = 9.0, 9.6 Hz), 3.33 (1H, t, J = 9.0 Hz), 3.43 (1H, m), 3.54 (1H, dd, J = 5.8, 12.3 Hz), 3.75 (1H, dd, J = 2.0, 12.3 Hz). ^{13}C NMR (CD_3OD): δ 36.08, 63.27, 72.18, 75.80, 77.10, 79.92, 81.35. HRMS (FAB, NaI): calcd for $C_{13}H_{24}O_{10}$ (M + Na) 363.1267; found 363.1261. $[\alpha]_D$: −20.7° (*c* 0.73, H_2O).

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Supplementary Material Available: ^1H NMR and ^{13}C NMR spectra for all compounds (40 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.