(+)-68, 114828-02-3; 69, 131103-14-5; (+)-70, 124516-70-7; (+)-71, 114828-03-4; (+)-72, 124516-71-8; (+)-73, 87925-07-3; (±)-iia, 131067-82-8; (±)-iii, 131067-83-9; (±)-iv, 131067-84-0; (±)-iv alcohol, 131067-85-1; $EtO_2C(CH_2)_2CO_2H$, 131067-86-2; $EtO_2C(CH_2)_2COCl$, 1070-34-4; (Z)-$HO(CH_2)_2CH{=}CHC_2H_5$, 14794-31-1; $Cl(CH_2)_2COCl$, 928-96-1; $CH_2{=}CH_2$, 625-36-5; $Cl(CH_2)_2CO(CH_2)_2Cl$, 74-85-1; $HC{\equiv}C(CH_2)_4OH$, 3592-25-4; $C_2H_5C{\equiv}C(CH_2)_4OH$, 928-90-5; succinic anhydride, 41547-21-1, 108-30-5.

Phyllanthoside–Phyllanthostatin Synthetic Studies. 8. Total Synthesis of (+)-Phyllanthoside. Development of the Mitsunobu Glycosyl Ester Protocol

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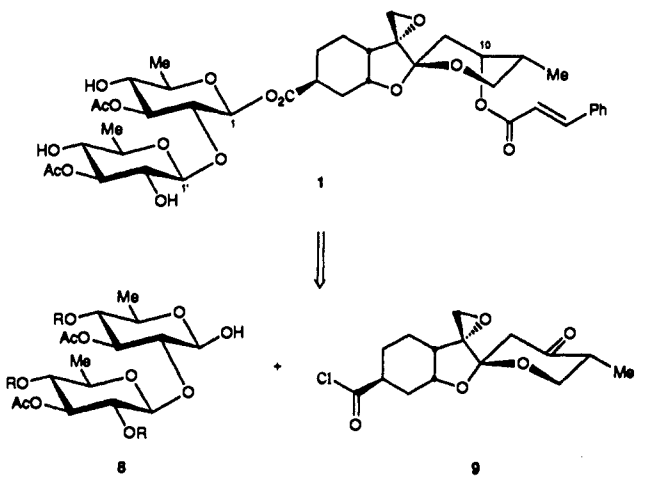
Contribution from the Department of Chemistry, the Laboratory for Research on the Structure of Matter, and the Monell Chemical Senses Center, University of Pennsylvania, Philadelphia, Pennsylvania 19104. *Received June 8, 1990*

Abstract: The first total syntheses of the antineoplastic glycoside (+)-phyllanthoside (**1**) and the parent disaccharide (−)-phyllanthose (**5**) have been achieved. Stereoselective Koenigs–Knorr coupling of two 6-deoxyglucose derivatives, bromide **54** and alcohol **55**, generated the uncommon $1' \rightarrow 2\beta$ glycosidic linkage of (−)-phyllanthose. A stereochemically convergent Mitsunobu reaction of protected disaccharide **87** with aglycon carboxylic acid **80**, prepared via asymmetric synthesis, then led to **1** of high enantiomeric purity. The Mitsunobu procedure comprises an efficient general method for stereospecific assembly of β-glycosyl esters.

Phyllanthoside (**1**)[1] and phyllanthostatins 1–3 (**2–4**)[1,2] comprise an architecturally novel family of antineoplastic glycosides,[3,4] isolated and characterized by Kupchan, Pettit, and their coworkers. The preceding paper in this issue details our syntheses of the aglycons in this series: phyllanthocin (**6a**), the aglycon methyl ester of **1–3** and phyllanthocindiol (**6b**), derived from phyllanthostatin 3 (**4**).[5,6] Novel features of the four glycoside

Scheme I



structures likewise present notable synthetic challenges. The disaccharide units, derived in each case from (−)-phyllanthose (**5**), are coupled to the aglycons by an unusual β-glycosyl ester moiety. Phyllanthose in turn is a dehydro dimer of 6-deoxyglucose, linked via a $1' \rightarrow 2\beta$ glycosidic bond.

Herein we record the completion of the first total syntheses of (−)-phyllanthose (**5**), (+)-phyllanthoside (**1**), and the α-glycosyl ester analogue of **1**; crucial to success was the development of the Mitsunobu glycosyl ester protocol.[7] This venture marked the culmination of our phyllanthocin synthetic studies; it also served as a prelude to the now complete constructions of phyllanthostatins 1–3. A full account of the phyllanthostatin efforts appears in the following paper in this issue.[8]

Phyllanthoside: An Initial Retrosynthetic Analysis. With a viable, stereocontrolled route to (+)-phyllanthocin in hand,[6a] the central issues in the synthesis of phyllanthoside (**1**) became the preparation of the disaccharide and its coupling to the aglycon.

(1) Kupchan, S. M.; La Voie, E. J.; Branfman, A. R.; Fei, B. Y.; Bright, W. M.; Bryan, R. F. *J. Am. Chem. Soc.* **1977**, *99*, 3199.

(2) The structures of these complex glycosides as well as the parent disaccharide phyllanthose (**5**) were based on detailed analysis of their 400-MHz ^1H NMR, 100-MHz ^{13}C NMR, and mass spectra, see: (a) Pettit, G. R.; Cragg, G. M.; Gust, D.; Brown, P. *Can. J. Chem.* **1982**, *60*, 544. Pettit, G. R.; Cragg, G. M.; Gust, D.; Brown, P.; Schmidt, J. M. *Can. J. Chem.* **1982**, *60*, 939. Pettit, G. R.; Cragg, G. M.; Niven, M. L.; Nassimbeni, L. R. *Can. J. Chem.* **1983**, *61*, 2630. Further evidence for phyllanthose (**5**) derived from the X-ray crystal structure of phyllanthose peracetate (**7**), see: (b) Pettit, G. R.; Cragg, G. M.; Suffness, M. I.; Gust, D.; Boettner, F. E.; Williams, M.; Saenz-Renauld, J. A.; Brown, P.; Schmidt, J. M.; Ellis, P. D. *J. Org. Chem.* **1984**, *49*, 4258. (c) Pettit, G. R.; Cragg, G. M.; Suffness, M. I. *J. Org. Chem.* **1985**, *50*, 5060.

(3) See, for example: Powis, G.; Moore, D. J. *Proc. Assoc. Cancer Res.* **1985**, *26*, 354. Also, see: refs 1 and 2.

(4) Phyllanthoside (**1**) and phyllanthostatin 1 (**2**) are in phase 1 clinical trials under the auspices of the NCI-EORTC. Both compounds inhibit human breast cancer cell lines with ED50s (μg/mL) against P388 of 0.27 and 0.19, respectively. Against P388 in vivo, the respective T/C values are 152% and 162–190% at doses of 6.68 and 4–16 mg/kg. Personal communication from Dr. Charles K. Grieshaber, Chief, Toxicology Branch, Developmental Therapeutics Program, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892.

(5) Smith, A. B., III; Fukui, M.; Vaccaro, H. A.; Empfield, J. R. *J. Am. Chem. Soc.*, preceding paper in this issue.

(6) For the preceding papers in this series, see: (a) (+)-Phyllanthocin (**6a**): Smith, A. B., III; Fukui, M. *Abstracts of Papers*, 187th National Meeting of the American Chemical Society, St. Louis, MO; American Chemical Society: Washington, DC, 1984; ORGN 6. Smith, A. B., III; Fukui, M. *J. Am. Chem. Soc.* **1987**, *109*, 1269. Smith, A. B., III; Empfield, J. R.; Vaccaro, H. A. *Tetrahedron Lett.* **1989**, *30*, 7325. (b) (+)-Phyllanthoside (**1**): Smith, A. B., III; Fukui, M., Rivero, R. A. *Abstracts of Papers*, 189th National Meeting of the American Chemical Society, Miami Beach, FL; American Chemical Society: Washington, DC, 1985; ORGN 82. Smith, A. B., III; Rivero, R. A. *J. Am. Chem. Soc.* **1987**, *109*, 1272. (c) (−)-Phyllanthostatin 1 (**2**): Smith, A. B., III; Hale, K. J.; Vaccaro, H. A. *J. Chem. Soc., Chem. Commun.* **1987**, 1026. (d) (+)-Phyllanthostatin 2 (**3**): Smith, A. B., III; Hale, K. J.; Vaccaro, H. A. *Tetrahedron Lett.* **1987**, *28*, 5591. (e) (+)-Phyllanthostatin 3 (**4**) and (+)-phyllanthocindiol methyl ester (**6b**): Vaccaro, H. A.; Rivero, R. A.; Smith, A. B., III *Tetrahedron Lett.* **1989**, *30*, 1465.

(7) Smith, A. B., III; Hale, K. J.; Rivero, R. A. *Tetrahedron Lett.* **1986**, *27*, 5813.

(8) Smith, A. B., III; Hale, K. J.; Vaccaro, H. A.; Rivero, R. A. *J. Am. Chem. Soc.*, following paper in this issue.

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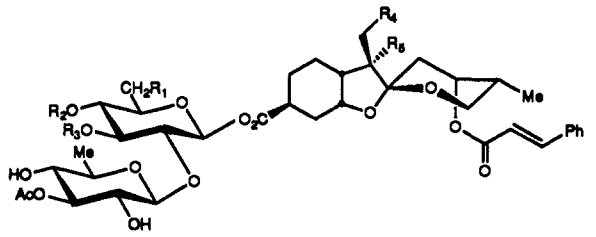
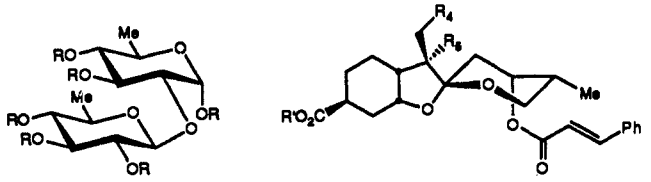


1 Phyllanthoside: $R_1 = R_2 = H$, $R_3 = Ac$, R_4, $R_5 = O$ (epoxide)
2 Phyllanthostatin 1: $R_1 = R_3 = H$, $R_2 = Ac$, R_4, $R_5 = O$ (epoxide)
3 Phyllanthostatin 2: $R_1 = OH$, $R_2 = H$, $R_3 = Ac$, R_4, $R_5 = O$ (epoxide)
4 Phyllanthostatin 3: $R_1 = R_2 = H$, $R_3 = Ac$, $R_4 = R_5 = OH$



5 Phyllanthose: R = H
7 R = Ac

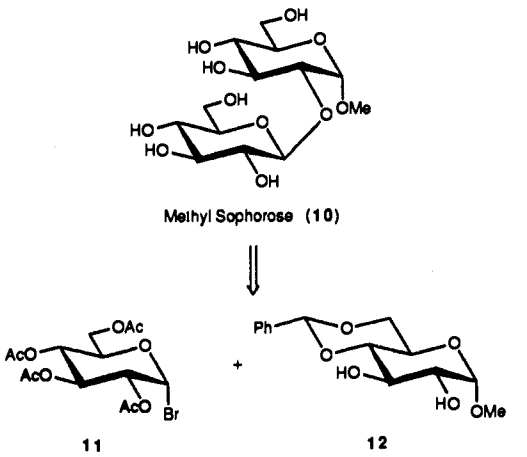
6a Phyllanthocin R' = Me, R_4, $R_5 = O$ (epoxide)
6b Phyllanthocindiol R' = H, $R_4 = R_5 = OH$

For generation of the β-glycosyl ester linkage,[9] we envisioned acylation of a suitably protected phyllanthose derivative **8** with an acid chloride **9** prepared from a phyllanthocin precursor (Scheme I). The stereoselectivity of this process would presumably depend upon the anomeric composition of the disaccharide lactol. A further concern, which would seriously constrain the choice of hydroxyl protecting groups (vide infra), involved the propensity of the phyllanthoside–phyllanthostatin acetates to undergo migration and solvolysis under mildly acidic or basic conditions.[2c]

Phyllanthose (**5**), the disaccharide constituent of phyllanthoside, comprises two 6-deoxyglucose units joined by the rare $1' \rightarrow 2\beta$ linkage. Methylsophorose (**10**), synthesized first in 1936 by Freudenberg[10a] and more recently by Coxon[10b] and Takeo,[10c] shares this novel coupling; these syntheses employed the Koenigs–Knorr condensation of α-bromotetraacetylglucose (**11**)[11] with the 4,6-benzylidene derivative of β-methylglucose (**12**) in the key step (Scheme II).[12] The conversion of methylsophorose to phyllanthose would first entail deoxygenation of the C(6) and C(6′) hydroxyls. Generation of a disaccharide (e.g., **13**) bearing the acetate moieties of the natural product would then require selective acetylation at C(3) and C(3′), followed by protection of the remaining hydroxyls. Rather than engage in a search for selective derivatization reactions, we decided to construct **13** directly via coupling of suitably protected monosaccharides.

From the retrosynthetic perspective, disconnection of the glycoside bond in the *O*-allyl derivative **13** leads to activated sugar **14** and nucleophilic sugar **15** (Scheme III). In the synthetic direction, selective removal of the allyl group[13] in **13** would permit coupling to the aglycon acid chloride (**9**) en route to phyllanthoside, whereas complete deprotection of **13** would secure the first synthesis of phyllanthose (**5**).

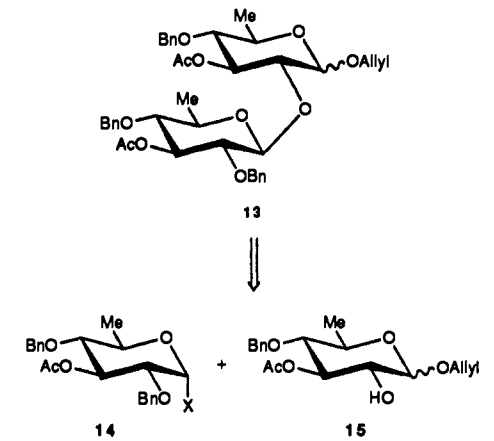
Scheme II



Methyl Sophorose (10)

11 12

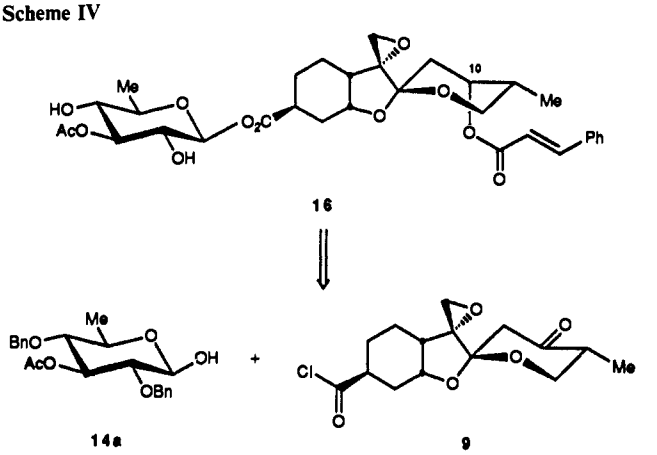
Scheme III



13

14 15

Scheme IV



16

14a 9

Glycosyl Ester Formation and Protecting Group Selection: A Model Study. To explore the feasibility of the glycosyl esterification as well as the suitability of possible protecting groups, we elected to carry out a model study. An ideal target appeared to be the monosaccharide analogue of phyllanthoside (i.e., **16**; Scheme IV).[14] To assure complete positional integrity of the acetates during the deprotection step, we selected the benzyl ether unit for the sugar hydroxyls. However, this choice precluded union with a fully endowed aglycon, given the anticipated interference from hydrogenation of the cinnamoyl moiety during debenzylation. To circumvent this problem, the benzyl groups would be exchanged for triethylsilyl ethers after coupling, followed by reduction of the C(10) carbonyl and cinnamoylation of the resulting axial hydroxyl.

(9) Existing methods for construction of β-glycosyl esters are not generally applicable to complex, multifunctional molecules. See, for example: (a) Bugiaesi, R.; Shen, T. Y. *Carbohydr. Res.* **1971**, *19*, 179. (b) Korwhauser, A.; Keglevic, D. *Carbohydr. Res.* **1969**, *11*, 407. (c) Fletcher, H. G. *Methods Carbohydr. Chem.* **1963**, *2*, 237. (d) Keglevic, D.; Valetokovec, S.; Roglic, G.; Goles, D.; Plavsic, F. *Carbohydr. Res.* **1973**, *29*, 25. (e) Pederson, C.; Fletcher, H. G. *J. Am. Chem. Soc.* **1960**, *82*, 3215. (f) Pfeffer, P. E.; Rothman, E. S.; Moore, G. G. *J. Org. Chem.* **1976**, *41*, 2925. (g) Ogawa, T.; Nozaki, M.; Matsui, M. *Carbohydr. Res.* **1978**, *60*, C7–C10. (h) Shoda, S.; Mukaiyama, T. *Chem. Lett.* **1982**, 861. (i) Schmidt, R. R.; Michel, J. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 731. (j) Schmidt, R. R. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 212, and references cited therein.

(10) (a) Freudenberg, K.; Soff, K. *Chem. Ber.* **1936**, *69*, 1245. (b) Coxon, B.; Fletcher, H. G. *J. Org. Chem.* **1969**, *26*, 241. (c) Takeo, K. *Carbohydr. Res.* **1979**, *77*, 131. (d) Takeo, K. *Carbohydr. Res.* **1983**, *112*, 73.

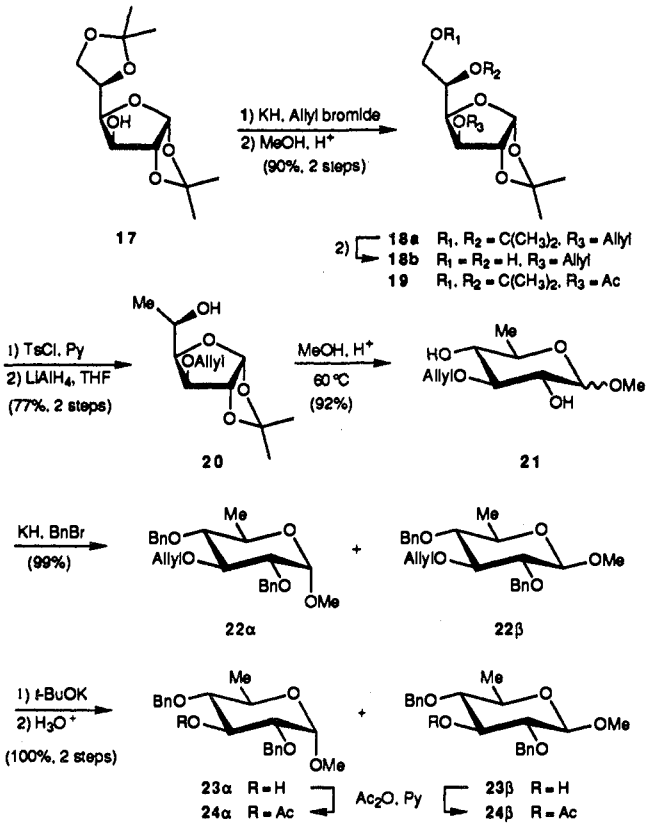
(11) Fletcher, H. G.; Hudson, C. S. *J. Am. Chem. Soc.* **1950**, *72*, 4173.

(12) Freudenberg, K.; Toeffer, H.; Anderson, C. C. *Chem. Ber.* **1928**, *61*, 1750.

(13) Ogawa, T.; Horisaki, T. *Carbohydr. Res.* **1983**, *123*, C1–C4.

(14) A further impetus for the model study was the possible biological activity of the monosaccharide analogue **16**.

Scheme V



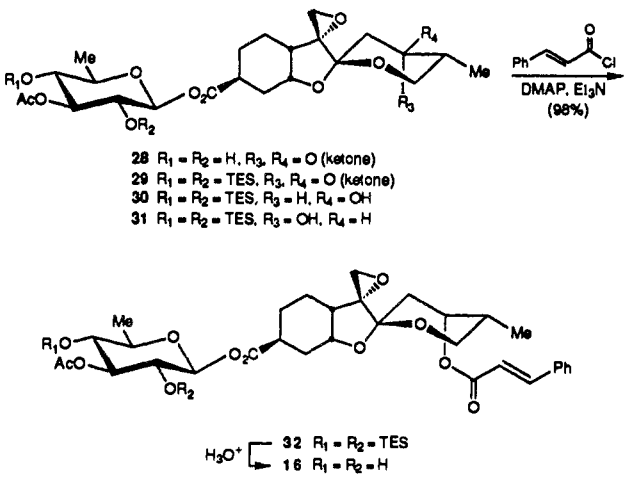
Hydrolysis of the silyl ethers would then complete the model synthesis. The lability of the triethylsilyl ethers prevented their use in place of benzyl from the outset.

The requisite monosaccharide fragment of phyllanthose was 6-deoxyglucose, acetylated at the C(3) position.[15] The use of di-*O*-isopropylidene-D-glucose (**17**, Scheme V) as starting material facilitated the selective protection of the C(3) hydroxyl and also provided suitable functionality at C(5) and C(6). Unfortunately, the vigorous conditions required for hydrolysis of the isopropylidene ketals precluded the intermediacy of acetate **19**.[16]

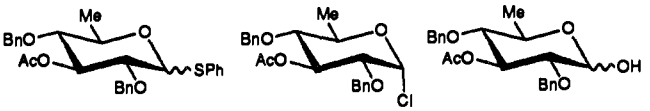
Recognizing the need for a C(3) hydroxyl protecting group, we turned to the more robust allyl ether unit.[17] Allylation at the C(3) position followed by selective hydrolysis of the 5,6-isopropylidene furnished diol **18b** in 90% yield for the two steps. Selective tosylation of the primary hydroxyl, reduction with $LiAlH_4$, and methanolysis then provided **21**, as a 1:1 anomeric mixture. The latter could easily be separated by flash chromatography after benzylation to furnish pure **22**α and **22**β in 70% overall yield (four steps). To simplify characterization the anomers were carried forward independently. The allyl groups, having served their purpose, were removed by isomerizing the terminal olefins to the corresponding enol ethers with *t*-BuOK; hydrolysis with aqueous acid then provided **23**α and **23**β almost quantitatively, whereupon acetylation afforded **24**α and **24**β.

Conversion of **24**α and **24**β to the free lactols proved unexpectedly difficult; in strong aqueous acid, the acetates hydrolyzed more rapidly than the methyl acetals. Glucoside **24**β did undergo clean conversion to thioglucosides **25** in 72% yield,[18] but the α-anomer reacted sluggishly and inefficiently.[19] Fortunately, **24**α

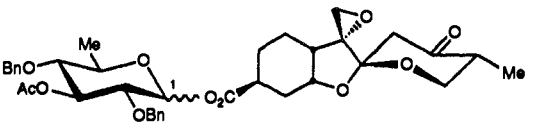
Scheme VI



did furnish chloro sugar **26** in 78–98% yield upon treatment with thionyl chloride.[20,21] Hydrolyses of **25** and **26**, via treatment with aqueous mercuric chloride and silver oxide, respectively, afforded lactol **14a** in 80–98% yield.



High-field ^1H NMR analysis revealed that **14a** existed as a 1:1 mixture of anomeric lactols. The β-anomer was anticipated to be more nucleophilic;[22] accordingly, acid chloride **9** was allowed to react with 2 equiv of **14a** in the presence of triethylamine to afford an 8:1 mixture of **27**β and **27**α in 63% yield. The esters could be separated either by preparative TLC or HPLC. DCC-promoted coupling of **14a** with the aglycon acid gave similar results.



27β equatorial ester
27α axial ester

The α- and β-glycosyl esters were easily identified via their 250-MHz ^1H NMR spectra, wherein the C(1) protons of the β- and α-anomers (**27**β and **27**α) appeared as doublets centered at δ 5.63 and 6.32. In general, the anomeric protons of β-glycosides resonate 0.5–1.0 ppm upfield of the corresponding α-glycoside

(15) Several methods exist for preparing 6-deoxyglucose derivatives differentiated at the C(3) position; all of these employ di-*O*-isopropylidene-D-glucose as starting material. See: deBelder, A. N. *Adv. Carbohydr. Chem.* **1984**, *49*, 843.

(16) Black, S. A.; Slessor, K. N.; Tracy, A. S. *Can. J. Chem.* **1972**, *50*, 1912.

(17) The allyl ether protecting group has been widely used in carbohydrate chemistry; see, for example: Cunningham, J.; Gigg, R.; Warren, C. D. *Tetrahedron Lett.* **1964**, 1191.

(18) Hanessian, S.; Guindon, Y. *Carbohydr. Res.* **1980**, *86*, C3–C6.

(19) Presumably, the strong Lewis acid required for this reaction was problematic vis-a-vis the acid-labile benzyl ether. Whereas the reaction of **24**β was complete within 20 min, **24**α was much less reactive. The difference in reaction times can be rationalized in terms of the anomeric effect. For discussion, see: Deslongchamps, P.; Atlanti, P.; Frehel, D. *Can. J. Chem.* **1974**, *52*, 3651.

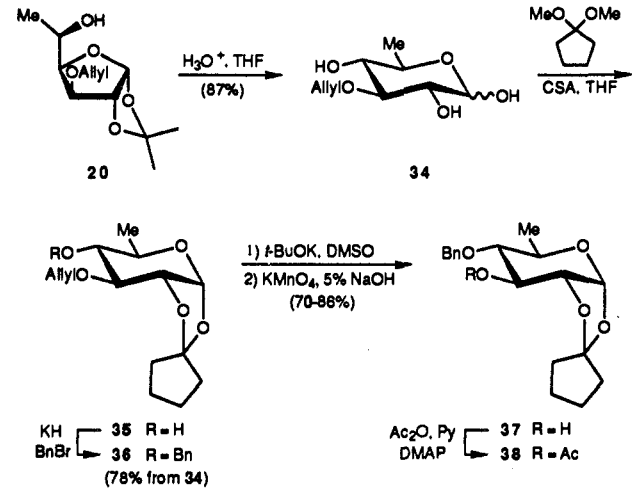
(20) Straus, F.; Heinze, H. *Ann. Chem.* **1932**, *493*, 191.

(21) This capricious reaction required the use of freshly distilled reagents.

(22) It has been proposed that the anomeric effect arises from the unfavorable interaction of nonbonding electron pairs on the ring sugar and the acetal oxygen in β-glycosides. The most favorable (lowest energy) conformation of the β-glycoside i has one such eclipsing interaction, while the α-glycoside ii has no eclipsed lone pairs. For this reason β-glycosides are more nucleophilic. See, for example: Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Baldwin, J. E., Ed.; Pergamon: New York, 1983. Kirby, A. J. *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*; Springer-Verlag: Berlin, 1983.

i ii

Scheme VII



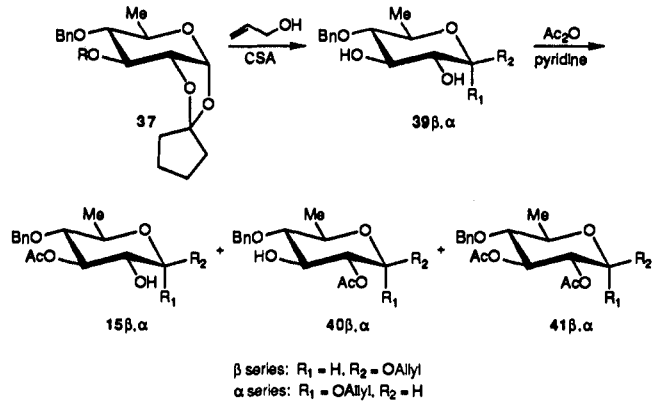
protons.[23] The coupling constants ($J_{1,2}$ = 8.2 and 3.7 Hz, respectively) provided further evidence for the anomeric configurations of **27**β and **27**α.[24]

With the desired β-glycosyl ester in hand, completion of the model study proved straightforward (Scheme VI). Following removal of the benzyl groups at C(2) and C(4) by hydrogenolysis, silylation of the resultant diol (**28**) with triethylsilyl chloride provided **29** in 91% yield. The selection of the triethylsilyl groups reflected the expectation that desilylation could be effected without acetate migration;[25] to verify this hypothesis, **29** was uneventfully reconverted to **28** upon exposure to aqueous acid. Reduction of the C(10) carbonyl of **29** afforded axial alcohol **31** as the major product (4:1 ratio), which on cinnamoylation gave ester **32**.[26] Finally, removal of the silyl protecting groups under mildly acidic conditions[25] provided diol **16**, the desired monosaccharide analogue of phyllanthoside.

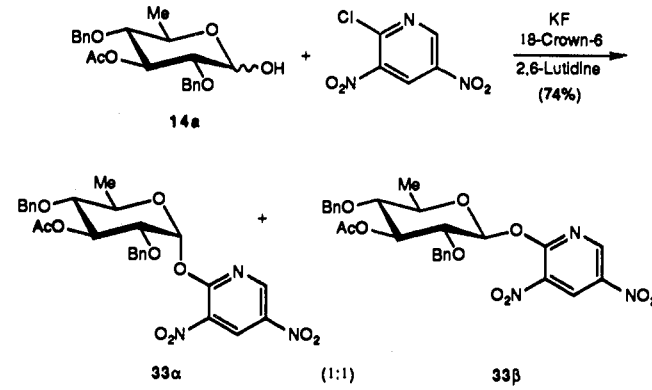
In summary, the model study substantiated not only our strategy for coupling the aglycon and sugar moieties but also the choice of protecting groups for the C(2'), C(4), and C(4') hydroxyls of phyllanthoside. We turned next to preparation of the requisite disaccharide.

Phyllanthose Synthetic Studies: Mukaiyama Glycosidation. The construction of a disaccharide such as **13** would require stereoselective β-glycosidation, without the intervention of neighboring group participation by the C(2) acetate group of the activated sugar.[27,28] Whereas most β-glycosidation methodologies are inapplicable to complex, multifunctional molecules, Mukaiyama in the late 1970s developed a mild procedure which affords very good β-selectivities (>6:1) in disaccharide formation.[29] The protocol involves the intermediacy of the 3,5-dinitro-2-pyridyl derivative of tetrabenzylglucose as the activated sugar. Confident that extension of this method would secure the desired β-glycoside bond, we set out to prepare the analogous activated sugar **33**α.

Scheme VIII

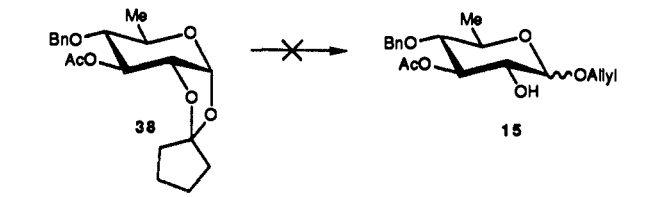


Reaction of lactol **14a**, previously prepared in our model study, with 2-chloro-3,5-dinitropyridine in the presence of KF, 18-crown-6, and 2,6-lutidine afforded a 1:1 mixture of **33**α and **33**β in 74% yield.[29] The products were easily separable by flash chromatography. Although only the α-anomer could be employed in the subsequent glycosidation reaction, in principle it would appear feasible to reconvert **33**β to **14a**.



The synthesis of the nucleophilic sugar **15** began with glucose derivative **20** (Scheme VII), also prepared in our model study. Hydrolysis of the 1,2-isopropylidene moiety afforded dihydroxy lactol **34**. Formation of the cyclopentylidene ketal **35**[30,31] followed by benzylation of the remaining hydroxyl then provided **36** in 68% yield for the three steps. The allyl group was next removed by isomerization of the terminal olefin to the corresponding enol ether, followed by treatment with $KMnO_4$ in aqueous base, to afford alcohol **37** in 70–86% yield.[17] The use of basic permanganate was dictated by the presumed lability of the cyclopentylidene moiety under normal acidic hydrolysis conditions. Acetylation of **37** then afforded **38**.

Numerous attempts to convert **38** to allyl glycoside **15** were completely unsuccessful. Although it was possible to form the allyl glycoside linkage, dreadful mixtures of deacetylation and acetate migration products resulted.



Alternatively, glucosides **39**β and **39**α were prepared in 80–90% yield (ca. 1:1 ratio) by treatment of **37** with allyl alcohol and camphorsulfonic acid in benzene at reflux (Scheme VIII). Se-

(23) Jackman, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*; Pergamon: Oxford, 1969; pp 238–241, and references cited therein.

(24) Karplus, M. *J. Am. Chem. Soc.* **1963**, *85*, 2870.

(25) Hart, T. W.; Metcalfe, D. A.; Scheinmann, F. *J. Chem. Soc., Chem. Commun.* **1979**, 156.

(26) Hassner, A.; Krepski, L. R.; Alexanian, V. *Tetrahedron* **1978**, *34*, 2069.

(27) (a) Paulsen, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 155–224, and references cited therein. (b) For examples of C(3) participation in the D-*gluco* series of sugars, see: Nishimura, D.; Hasegawa, A.; Nakajima, M. *Agric. Biol. Chem.* **1972**, *36*, 1767. Flowers, H. M. *Carbohydr. Res.* **1971**, *18*, 211. For examples of C(3) participation in non-*gluco* sugars, see: Flowers, H. M.; Dejter-Juszynski, M. *Carbohydr. Res.* **1975**, *41*, 308, and references cited therein. For a review, see: Bochkov, A. F.; Zaikov, G. E. *Chemistry of the O-Glycosidic Bond: Formation and Cleavage*; Schuerch, C., Ed.; Pergamon Press: New York, 1979.

(28) Schmidt and Danishefsky have recently developed elegant procedures for generation of β-glycosides without neighboring group participation, see: Schmidt, R. R. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 213. Halcomb, R. L.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1989**, *111*, 6661.

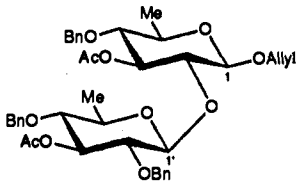
(29) Shoda, A.; Mukaiyama, T. *Chem. Lett.* **1979**, 847.

(30) Diol **35** was protected as the cyclopentylidene ketal rather than the more robust isopropylidene to permit deprotection under relatively mild conditions.

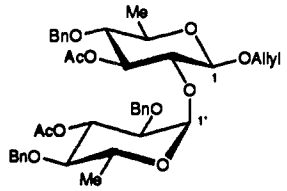
(31) Van Heeswijk, W. A. R.; Goedhart, J. B.; Vliegenthart, J. E. G. *Carbohydr. Res.* **1977**, *58*, 337.

lective acetylations at C(3) of **39**β and **39**α were then explored in separate experiments to provide the desired monoacetates **15**β and **15**α in 27% and 36% yields, respectively. Comparable amounts of the C(2) monoacetates (**40**β,α) and diacetates (**41**β,α) were also produced. A small consolation of this venture was that both **15**β and **15**α were easily separated from the respective by-products by flash chromatography. The undesired acetates and diacetates could be recycled by exposure to potassium carbonate in methanol, improving the yields of **15**β and **15**α to 90% and 92% based on recovered diol. Either of the nucleophilic sugars (i.e., **15**β or **15**α) could be used in the subsequent glycosidation reaction.

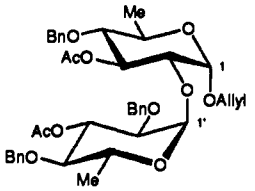
Unfortunately, coupling of activated sugar **33**α with **15**β under the conditions described by Mukaiyama (i.e., $BF_3{\cdot}Et_2O$, 4 Å molecular sieves, −20 °C) afforded the requisite β-linked disaccharide **13** in only 5% yield; the major product, α-anomer **42**, was isolated in 54% yield. Similar reaction of **33**α with **15**α gave α-glycoside **43** in 53% yield.



13



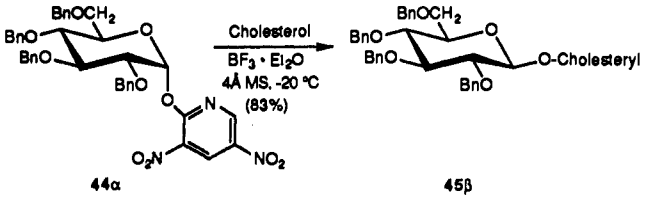
42



43

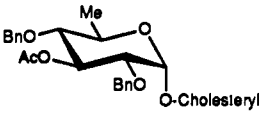
The 250-MHz ^1H NMR characteristics of the C(1′) anomeric protons again revealed the configurations of the disaccharide linkages. For **42** and **43** these protons appeared as doublets centered at δ 5.50 and 4.97, whereas the H(1′) doublet for **13** was centered at δ 4.65. As noted earlier, the anomeric protons of β-glycosides generally resonate 0.5–1.0 ppm upfield of the corresponding α-glycoside protons.[23] The axial–equatorial coupling constants for **42** and **43** ($J_{1',2'}$ = 3.9 and 3.8 Hz, respectively) and the axial–axial coupling for **13** ($J_{1',2'}$ = 8.0 Hz) were also fully in accord with the assigned configurations.[24]

The remarkable α-selectivity expressed in the reactions of **33**α with the nucleophilic sugars contrasts markedly with the results reported by Mukaiyama. To confirm the viability of our experimental procedure, we repeated a published example. As reported by Mukaiyama, reaction of tetrabenzyl-(3,5-dinitro-2-pyridyl)-α-glucoside (**44**α) with cholesterol furnished the β-glucoside (**45**β) in 83% yield.[29]

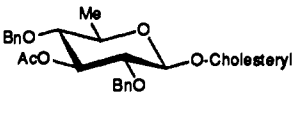


44α **45**β

Although the Mukaiyama protocol was clearly unsuitable for preparation of the desired disaccharide, these intriguing results led us to investigate the origins of the unexpected reversal of selectivity. The possible influence of the nucleophilic sugar was explored by coupling **33**α with cholesterol; again the α-anomer predominated, in a 2:1 mixture of **46**α and **46**β. To examine the role of the leaving group, we employed **26**, the chloro analogue of **33**α, which was available from the earlier model study. Exposure of **26** to excess cholesterol in the presence of $AgCO_3$ likewise furnished a 3:1 mixture of **46**α and **46**β, in 94% yield. This result suggested that similar pathways were followed in the predominant α-glycosidations of both activated sugars.

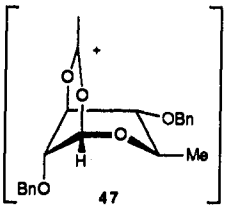


46α



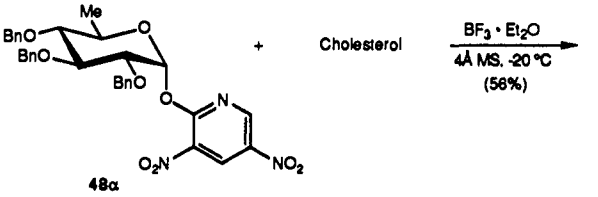
46β

These observations dictated the surprising conclusion that the deoxygenation of C(6) and/or the presence of the C(3) acetate moiety in **33**α and **26** were responsible for the α-selectivity. Our initial hypothesis involved participation of the acetoxy group through a boatlike intermediate. The resultant bicyclic oxonium ion **47** would then undergo nucleophilic attack preferentially from the α-face, affording α-glucosides stereoselectively. Whereas neighboring group participation by C(2) esters and amides is particularly well established,[27a] assistance by a group at the C(3) position has also been observed in the presence of nonparticipating C(2) functionality such as an ether. The latter effect has been noted for both C(3) esters and amides in D-gluco sugars and is more prevalent for substrates containing axial substituents at C(3).[27b]

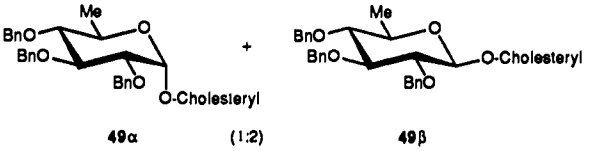


47

To test this possibility we prepared **48**α, the 6-deoxy analogue of the Mukaiyama activated sugar, with the expectation that coupling to cholesterol would proceed with high β-selectivity. In the event, however, a 2:1 mixture of **49**β and **49**α resulted, suggesting that both acetate participation and C(6) deoxygenation had contributed to the α-selectivity in glycosidation of **33**α and **26**. Although the influence of C(6) substituents upon the stereochemical outcome of glycosidation has been well documented,[32] to our knowledge no studies of 6-deoxyglucose derivatives have been published.[33]



48α

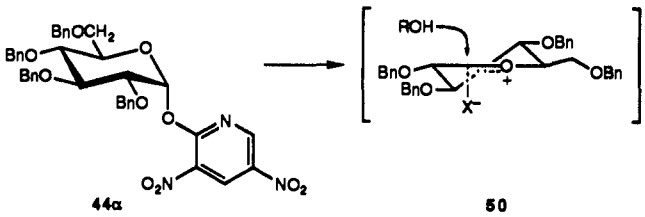


49α (1:2) **49**β

Collectively our results support an intimate ion pair mechanism for the Mukaiyama glycosidation of fully oxygenated glucose derivatives (e.g., **44**α). In methylene chloride solvent, incomplete dissociation leads to the intimate ion pair **50**, which preferentially undergoes nucleophilic attack from the β-face. In contrast, the tribenzyl 6-deoxyglucose derivative (**48**α) apparently reacts in part by an S_N1 mechanism, with complete dissociation of the ion pair. Nucleophilic attack on oxonium ion **51** from the β-face furnishes the equatorial β-glycoside through a twist-boat conformation,

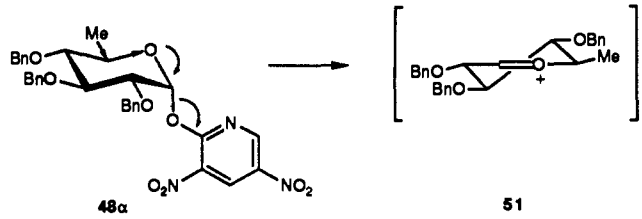
(32) Frechet, J. M.; Schuerch, C. *J. Am. Chem. Soc.* **1972**, *94*, 604.

(33) A similar effect has been noted for L-rhamnosyl halides. These are considerably more reactive than the corresponding D-mannosyl halides, see: Paulsen, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 165. Also, see: Eby, R.; Schuerch, C. *Carbohydr. Res.* **1974**, *34*, 79. Lucas, T. J.; Schuerch, C. *Carbohydr. Res.* **1975**, *39*, 39. Kronrer, F. J.; Schuerch, C. *Carbohydr. Res.* **1973**, *27*, 379.



44α 50

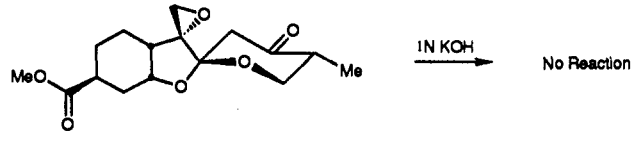
whereas attack from the α-face affords the axial α-glycoside via a more favorable chairlike transition state. The intervention of the S_N1 process presumably reflects the enhanced cation stabilization associated with C(6) deoxygenation. Finally, the α-selective glycosidations of **33α** and **26** appear to proceed largely via the S_N1 pathway, facilitated by participation of the C(3) acetoxy group.



48α 51

A Revised Strategy for Phyllanthose: Exploitation of the Koenigs–Knorr Glycosidation. Recognizing that the Mukaiyama protocol could not provide the desired β-disaccharide, we designed a new strategy based upon the Koenigs–Knorr reaction (Scheme IX).[34] For success this tactic would require neighboring group assistance from an acetate at C(2) to generate the critical β-linkage in **53**. Retrosynthetically such a scenario entails the preparation of bromo sugar **54** and nucleophilic sugar **55**. Deprotection of the C(1) anomeric position of **53** would then afford disaccharide **52**, poised for coupling with the aglycon acid. Alternatively, complete unmasking of **52** would secure the first synthesis of (−)-phyllanthose (**5**). For union of disaccharide **52** with aglycon derivative **9** (Scheme X), we planned to employ the acylation procedure developed during our model study. A disadvantage of the Koenigs–Knorr approach was that the disaccharide intermediate could not be acetylated at C(3) and C(3′) as in the natural product; instead, these hydroxyls would be protected as benzyl ethers, with acetates at all remaining sites. This in turn would necessitate a protecting group interchange after formation of glycosyl ester **57β**. Specifically, replacement of the acetates with triethylsilyl ethers and subsequent substitution of acetates for the benzyl ethers would lead to **56**. Reduction, cinnamoylation, and hydrolysis of the silyl ethers would then afford phyllanthoside (**1**).

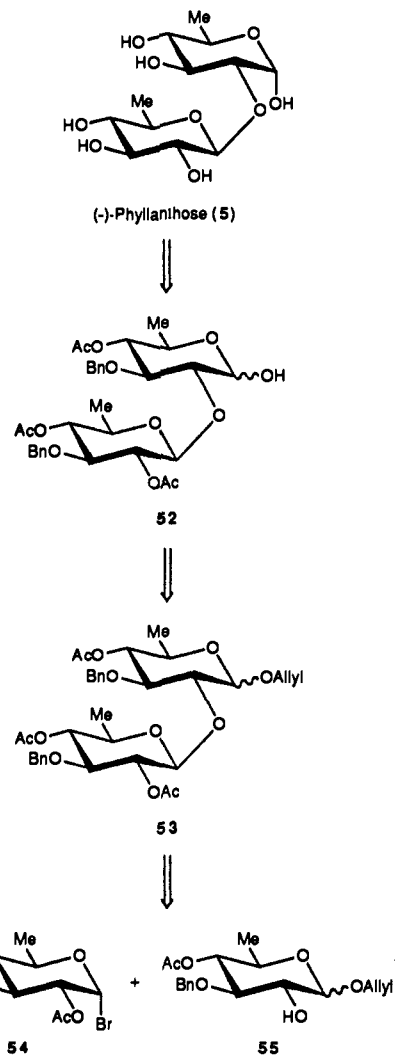
The viability of this scenario appeared to depend on two important factors. First, a favorable ratio of the lactol anomers (**52**) would be essential for efficient generation of the β-glycosyl ester. Second, chemoselective hydrolysis of the C(2′), C(4), and C(4′) acetates in the presence of the newly formed glycosyl ester linkage of **57β** would be required. Although the latter operation would appear problematic, we had earlier demonstrated that methyl ester **58** was inert to 1 N KOH at room temperature. Accordingly, we anticipated that acetate hydrolysis conditions (i.e., K_2CO_3 or KOH in MeOH) would leave the β-glycosyl ester intact.



58

Synthesis of (−)-Phyllanthose and (+)-Phyllanthose Peracetate. The Koenigs–Knorr synthesis of the disaccharide (−)-phyllanthose (**5**) began with the preparation of glycosyl bromide **54** (Scheme

Scheme IX



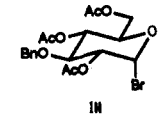
XI).[35] Acid hydrolysis of the isopropylidene moiety of glucofuranose **59**[36] furnished lactol **60**, which served as a common intermediate en route to both sugar units of **5**. Peracetylation afforded **61** as a mixture of anomers, which in turn was brominated to give **54**. Careful monitoring of the latter reaction was required to prevent secondary benzyl ether cleavage. In this fashion, **54** could be prepared in three steps and 62% overall yield from **59**.[37]

With **54** in hand, we turned to the synthesis of the protected nucleophilic sugars (Scheme XII). To this end, common intermediate **60** was converted to the cyclopentylidene derivative **62** (65% yield), accompanied by the undesired isomer **63** (17%).[38] Acetylation of **62** followed by glycosidation with allyl alcohol afforded a 1:1 mixture of **55β** and **55α** in 82–96% yield. These anomers were easily separable by flash chromatography. To facilitate product isolation and characterization, the nucleophilic sugars so obtained were carried forward separately.

Initial efforts to couple **54** with either of the nucleophilic sugars, via silver reagents such as $AgCO_3$ and $AgClO_4$, gave unsatisfactory

(34) (a) Koenigs, W.; Knorr, E. *Chem. Ber.* **1901**, *34*, 957. (b) Helferich, B.; Weiss, K. *Chem. Ber.* **1956**, *89*, 314. Helferich, B.; Zinner, J. *Chem. Ber.* **1962**, *95*, 2604. (c) Paulsen, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 155, and references cited therein.

(35) The synthesis of **54** was modeled after a published preparation of III: Finan, P. A.; Warren, C. D. *J. Chem. Soc.* **1962**, 3089.



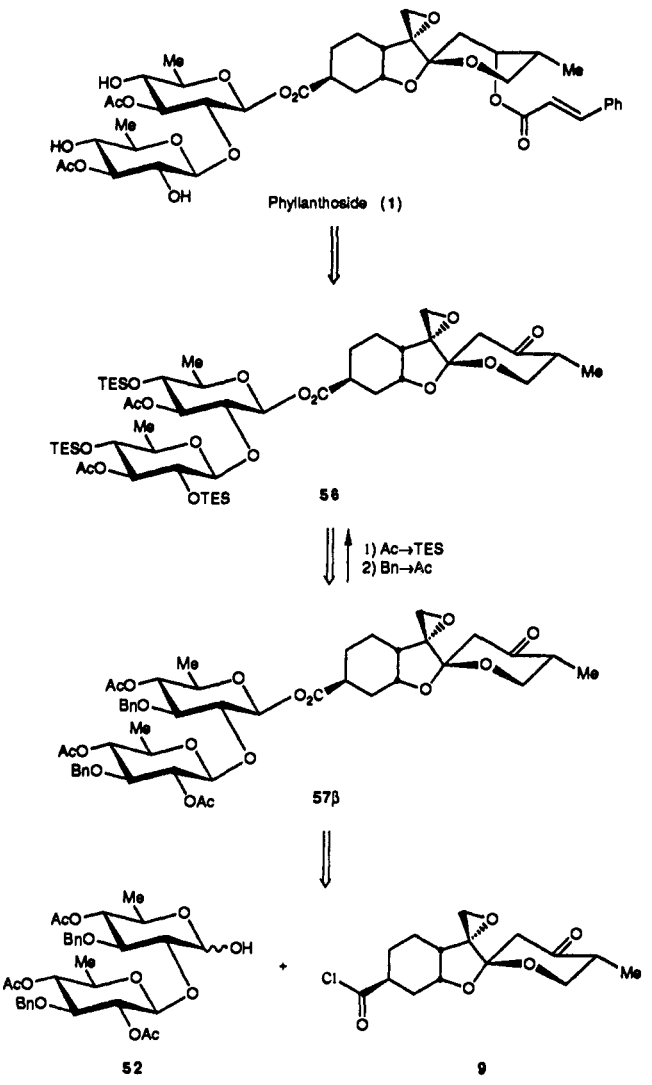
III

(36) Wolfrom, M. L.; Hanessian, S. *J. Org. Chem.* **1962**, *27*, 2107.

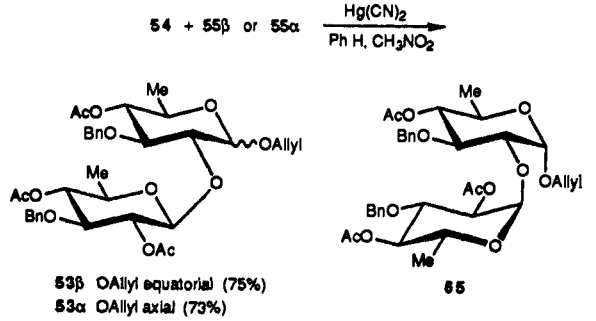
(37) Although glycosyl bromide **54** proved to be fairly unstable, it could be stored as a solid in the freezer for up to 1 week without excessive decomposition. Best results were obtained by using freshly prepared material.

(38) Although not explored, reconversion of **63** to **60** should be feasible.

Scheme X



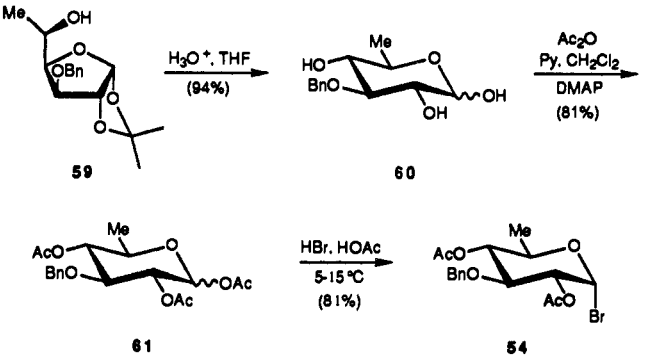
results. However, the Helferich modification[34b] of the Koenigs–Knorr process, employing $Hg(CN)_2$ for halide abstraction, furnished **53**β and **53**α in 75% and 73% yields from **55**β and **55**α, respectively. The latter reaction also afforded a minor amount (<12%) of α-glycoside **65**.



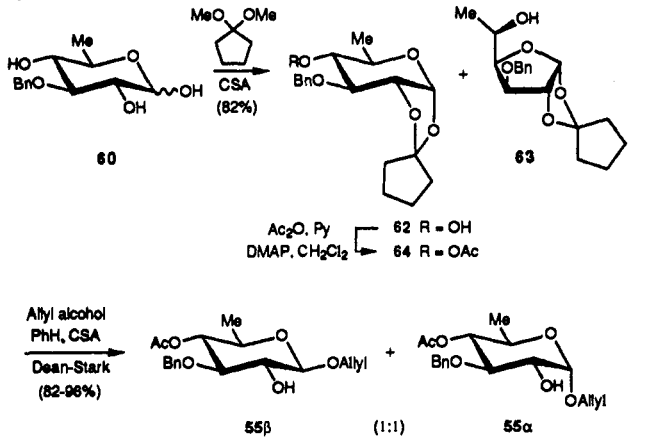
Structural assignments for the disaccharides initially evolved from spectroscopic observations; as before the chemical shifts and coupling constants of the C(1′) anomeric protons were particularly diagnostic. For **53**β and **53**α, these protons appeared as doublets centered at δ 4.77 and 4.63 with coupling constants ($J_{1',2'}$) of 9.0 and 9.4 Hz, respectively. In contrast, the corresponding doublet for **65** was centered at δ 4.95 with a coupling constant of 3.3 Hz. All of these observations fully support the proposed structures.[23,24]

To establish rigorously the stereochemical integrity of the β-glycoside linkages, each anomer of **53** was individually converted (Scheme XIII) to (−)-phyllanthose (**5**), the parent disaccharide previously isolated by Pettit.[2a] The allyl group was selectively

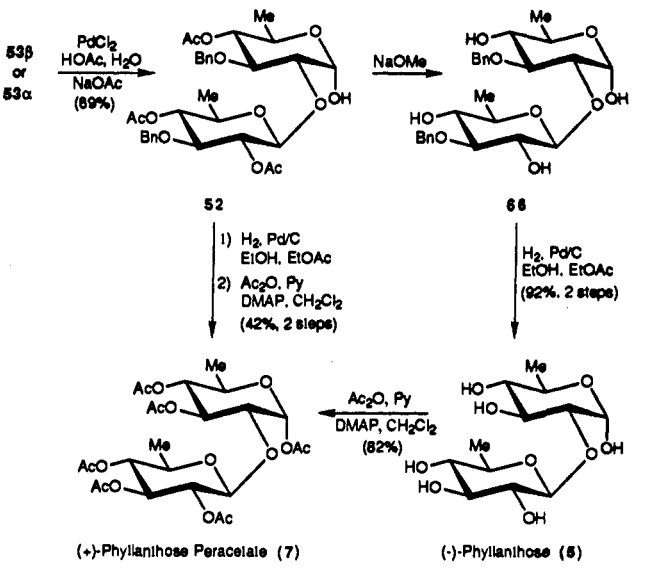
Scheme XI



Scheme XII

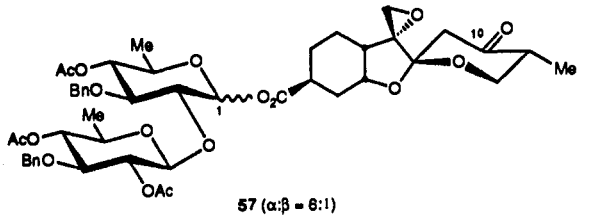


Scheme XIII



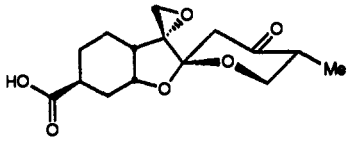
removed by treatment with $PdCl_2$[13] to afford lactol **52** in 89% yield. Although the conversion of **52** to phyllanthose appeared to proceed uneventfully, full characterization of the free sugar proved difficult due to its low solubility. Accordingly, we elected to prepare and characterize fully the peracetate derivative (**7**).[2b] The latter was generated in two ways. Hydrogenolysis of the benzyl groups in **52** followed by peracetylation provided (+)-phyllanthose peracetate (**7**). Alternatively, **52** was transformed to synthetic (−)-phyllanthose (**5**) via acetate methanolysis, followed by hydrogenolysis. The yield for the two steps was 92%. Acetylation of synthetic phyllanthose under the conditions of Pettit[2b] then furnished peracetate **7**. Both samples of synthetic (+)-phyllanthose peracetate were identical in all respects (^1H NMR, IR, MS, mp, and chiroptical properties) with an authentic sample kindly provided by Professor Pettit (Arizona State University).

The Mitsunobu Reaction: An Efficient Synthesis of Glycosyl Esters. With a viable route to the disaccharide now secure, we turned to our main goal, the synthesis of phyllanthoside (**1**). The key operation, coupling of disaccharide **52** with acid chloride **9** as in our model study, would be followed by protecting group interchange, reduction of the C(10) carbonyl, cinnamoylation, and final deprotection (Scheme IX). Condensation of **52** with **9** via the procedure developed previously did afford a mixture of **57β** and **57α** in 77% yield; however, the ratio was a very disappointing 1:6. DCC-mediated esterification of the corresponding acid gave similar results. The glycosyl esters were separable by flash chromatography, and, as in previous examples, the initial structural assignments were based upon ^{1}H NMR chemical shifts and coupling constants of the C(1) anomeric protons.[23,24]



57 (α:β = 6:1)

The unfavorable mixture of glycosyl esters suggested that lactol **52** existed predominantly as the α-anomer. NMR analysis confirmed this supposition, indicating an α:β ratio >20:1 in $CDCl_3$. Accordingly, we sought to employ a different coupling method that would exploit the anomeric configuration of **52**. Previous work by Castro and Gross[39] demonstrated that α-glycosyl tris(dimethylamino)phosphonium salts are versatile intermediates for the stereocontrolled preparation of β-glycosides. In particular, these species generally undergo nucleophilic displacement with inversion of configuration. This mode of hydroxyl activation therefore seemed conceptually ideal for the stereocontrolled construction of **57β** from **52** and carboxylic acid **80**. However, further examination of the literature revealed that phosphonium salts are poor substrates for ester synthesis;[40] moreover, we found no examples of their conversion into glycosyl esters. We therefore sought an alternative approach to glycosyl activation that would be conducive to the synthesis of 1-*O*-acyl aldoses.



80

At this juncture, we elected to investigate the Mitsunobu reaction.[41] This protocol had been employed for glycoside and nucleoside synthesis, but there were no previous reports of its use in glycosyl ester formation.[42] We therefore examined the scope of this process to evaluate its suitability for the phyllanthoside venture (Table I).[7]

Initially we studied a model reaction of α-lactol **52** with benzoic acid, mediated by triphenylphosphine (TPP) and diethyl azodicarboxylate (DEAD) in dry THF. This proceeded almost instantaneously at room temperature, affording β-glycosyl ester **67** as the sole product in 95% yield. In contrast, ambient-temperature Mitsunobu coupling of α-hemiacetal **68** with cyclohexanecarboxylic acid furnished a 1:1 mixture of anomers in a meager 36% yield. Fortunately, the yield and stereoselectivity could be markedly improved, merely by initiating the reaction at lower temperature (−50 °C) with gradual warming to room temperature over a period of 2 h. This simple modification provided exclusively the β-glycosyl ester **69** in 85% yield; none of the α-glycosyl ester could be detected. In the earlier experiment, the glycosyl phosphonium ion intermediate presumably decomposed at room temperature, generating triphenylphosphine oxide and the corresponding glycosyl oxonium ion. The latter, probably formed irreversibly, then combined nonstereoselectively with the carboxylate anion.

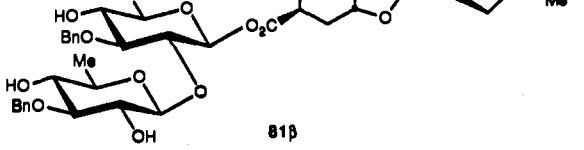
Low-temperature conditions also facilitated the coupling of α-hemiacetal **70** with cyclohexanecarboxylic acid, which again proceeded with inversion to give β-glycosyl ester (**71**) in 64% yield. Indeed, glycosidations of pyranose anomer mixtures *usually* proceeded with inversion (entries 4–6). However, this was not the case with entry 7. In our original communication we indicated that lactol **78** existed as a 2:1 mixture of α/β-anomers, based upon 250-MHz ^{1}H NMR analysis in deuteriochloroform.[7] In that solvent, accurate determination of the anomeric composition was complicated by extensive overlap and broadening of the anomeric proton signals. A more extensive ^{1}H NMR study of **78** at 500 MHz in dry, deuterated THF has now revealed that **78** in fact comprises a 1:2.5 mixture of α- and β-anomers. The resultant mixture of glucosyl benzoates (1:4, α/β) clearly did not arise via S_N2-type displacement at the anomeric center.

This brief study establishes that Mitsunobu glycosidation is a very effective method for preparing complex glycosyl esters. Its notable attributes include generally stereospecific coupling and essentially neutral reaction conditions, compatible with sensitive functionalities such as epoxides, β-alkoxy ketones, and conjugated olefins.

Given the anomeric configuration of lactol **52**, Mitsunobu coupling with acid **80**, an intermediate in our synthesis of phyllanthocin,[5,6a] was expected to furnish the requisite β-glycosyl ester. In the event, the Mitsunobu protocol outlined above rapidly and cleanly afforded β-glycosyl ester **57β** in 90% yield.

Disaccharide Refunctionalization: Conclusion of the Phyllanthoside Synthetic Venture. Completion of the phyllanthoside synthesis next entailed removal of the C(2′), C(4), and C(4′) acetates of **57β** in the presence of the newly formed glycosyl ester. Contrary to expectations (vide supra), the remarkably labile glycosyl ester linkage was cleaved prior to deacetylation under a variety of hydrolytic conditions.[43,44]

In an effort to circumvent this problem, we explored the coupling of lactol **66**, in which the C(2′), C(4), and C(4′) hydroxyl groups were left unprotected. Mitsunobu reaction of **66** with **80** did furnish a 2:1 mixture of the desired glycosyl ester **81β** and the α-anomer **81α** in a modest 40% yield. To facilitate purification and characterization, the mixture of **81β** and **81α** was peracetylated; the major product proved to be identical with glycosyl ester **57β**, obtained by coupling lactol **52** with **80**. However, the reaction was not clean and required the use of excess acid, which could not be recovered. Dissatisfied with this approach, we next



81β

(39) Chrétien, F.; Chapleur, Y.; Castro, B.; Gross, B. *J. Chem. Soc., Perkin Trans. 1* **1980**, 381.

(40) Toubiana, R.; Pizza, C.; Chapeur, Y.; Castro, B. *J. Carbohydr., Nucleosides, Nucleotides* **1978**, *5*, 127.

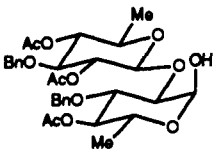
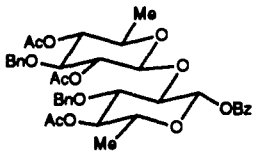
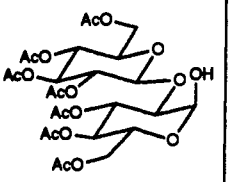
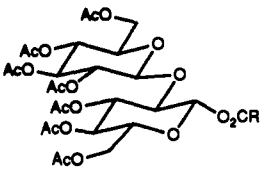
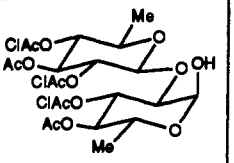
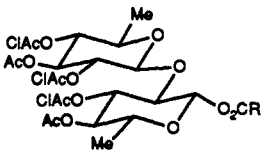
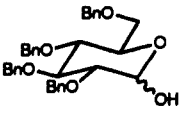
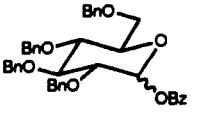
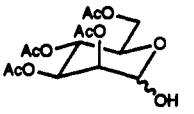
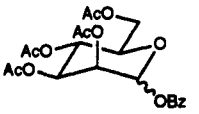
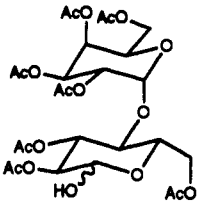
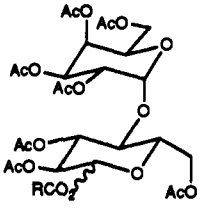
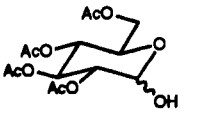
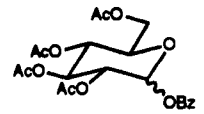
(41) (a) Mitsunobu, O.; Wada, M.; Sano, T. *J. Am. Chem. Soc.* **1972**, *94*, 979. (b) Mitsunobu, O.; Egushi, M. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 3427. (c) Mitsunobu, O. *Synthesis* **1973**, 740.

(42) Mitsunobu activation of anomeric hydroxyl groups has been employed for the synthesis of nucleosides, disaccharides, glycosyl fluorides, phenolic glycosides, and glycosides of aliphatic alcohols; see, for example: Szarek, W. A.; Depew, C.; Jarrell, H. C.; Jones, J. K. N. *J. Chem. Soc., Chem. Commun.* **1975**, 648. Schorkhuber, W.; Zbiral, E. *Ann. Chem.* **1980**, 1455. Kunz, H.; Sager, W. *Helv. Chim. Acta* **1985**, *68*, 283. Grynkiewicz, G. *Carbohydr. Res.* **1977**, *53*, C11. Garegg, P. J.; Inverson, T.; Norberg, T. *Carbohydr. Res.* **1979**, *73*, 313. Szarek, W. A.; Jarrell, H. D.; Jones, J. K. N. *Carbohydr. Res.* **1977**, *57*, C13. Grynkiewicz, G.; Zamojski, A. *Synth. Commun.* **1978**, *8*, 491.

(43) (a) Plattner, J. J.; Gless, R. D.; Rapoport, H. *J. Am. Chem. Soc.* **1972**, *94*, 8613. (b) Nielson, T.; Werstiuk, E. S. *Can. J. Chem.* **1971**, *49*, 493. (c) Mori, K.; Tominaga, M.; Takigawa, T.; Matsui, M. *Synthesis* **1973**, 740.

(44) This result, although unexpected, was not without precedent; glycosyl esters have previously been cleaved in the presence of other esters. See, for example: Bullock, C.; Hough, L.; Richardson, A. C. *J. Chem. Soc., Chem. Commun.* **1967**, 1276.

Table I. Preparation of Glycosyl Esters via the Mitsunobu Reaction

Entry	Substrate	Reagents and Conditions[1]	Products[2]	Isolated Yield (Anomer Ratio: β/α)[3]
1	 **52**	Benzoic acid (1 equiv) TPP, DEAD THF, rt	 **67**	95% (exclusively β)
2	 **68**	Cyclohexanecarboxylic acid (1.3 equiv) TPP, DIAD, THF -50 °C → rt	 **69**	85% (exclusively β)
3	 **70**	Cyclohexanecarboxylic acid (2 equiv) TPP, DIAD, THF -50 °C → rt	 **71**	64% (exclusively β)
4	 **72**	Benzoic acid (1.3 equiv) TPP, DIAD, THF -50 °C → rt	 **73**	54% (4:1)
5	 **74**	Benzoic acid (1.3 equiv) TPP, DIAD, THF -50 °C → rt	 **75**	51% (4:1)
6	 **76**	Cyclohexanecarboxylic acid (1.3 equiv) TPP, DIAD, THF -40 °C → rt	 **77**	63% (4.5:1)
7	 **78**	Benzoic acid (1.3 equiv) TPP, DIAD, THF -50 °C → rt	 **79**	80% (4:1)

[1] TPP = triphenylphosphine
DIAD = diisopropyl azodicarboxylate

[2] **69**, **71**, **77**: R = cyclohexyl

[3] Determined by 250-MHz ^{1}H NMR

prepared a refunctionalized disaccharide unit.

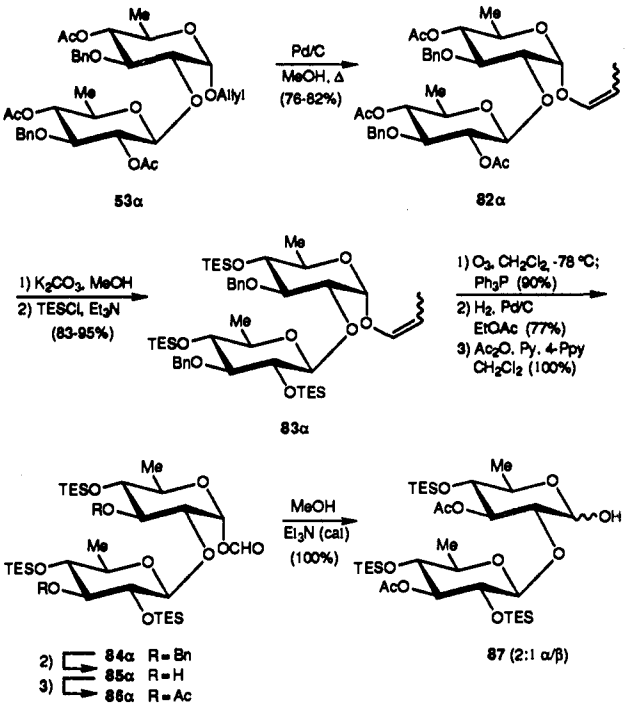
This effort constituted a reprise of our original plan, wherein the disaccharide moiety would incorporate the C(3) and C(3′) acetates of the natural product, with triethylsilyl ethers at the C(2′), C(4), and C(4′) positions. Critical for success would be protection of the C(1) anomeric hydroxyl with a group that could be removed in the presence of the labile silyl ethers. The allyl group explored earlier was clearly not suitable, per se. However, if the allyl ether could be transformed to a formate ester, then selective hydrolysis of the latter could reasonably be envisioned.[45]

Toward this end, treatment of disaccharide **53**α with a catalytic amount of Pd on carbon in methanol afforded enol ether **82**α as a 4:1 mixture of *Z*:*E* isomers in 76–82% yield (Scheme XIV).[46] A small amount of lactol **52** was also produced by enol ether

(45) Formate esters are known to hydrolyze faster than acetate esters. See: (a) Zemlicka, J.; Beranek, J.; Smit, J. *Collect. Czech. Chem. Commun.* **1962**, *27*, 2784. (b) Reese, C. B.; Stewart, J. C. M. *Tetrahedron Lett.* **1986**, *27*, 4273.

(46) Boss, R.; Scheffold, R. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 558.

Scheme XIV



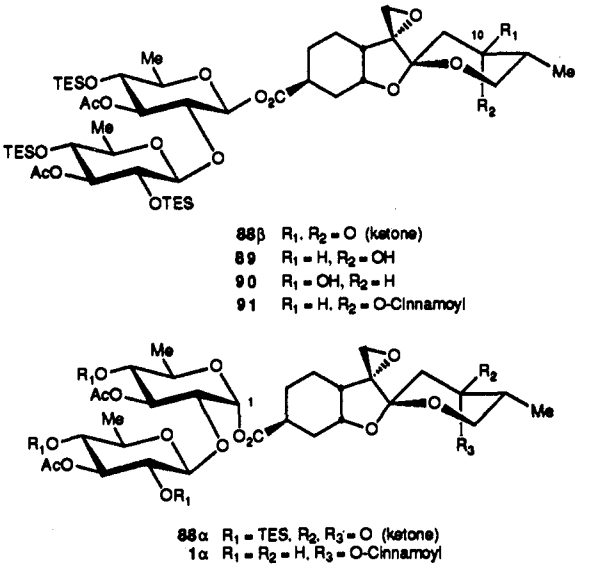
hydrolysis. Deacetylation of **82**α and triethylsilyl ether formation furnished **83**α in 83–95% yield.[25] Ozonolysis of the enol ether then generated formate ester **84**α in 90% yield. Overoxidation was suppressed via rigorous temperature control during the addition of 1 equiv of ozone at −78 °C, followed by immediate destruction of the ozonide with triphenylphosphine. Hydrogenolysis of the benzyl ethers with 10% Pd on carbon in freshly distilled ethyl acetate afforded **85**α in 77% yield.[47] Diacetylation, although initially difficult, could be effected via 4-pyrrolidinopyridine catalysis,[26] to afford **86**α quantitatively. Finally, methanolysis of the formate ester afforded lactol **87** in 44–53% yield overall from **53**α. The lactol existed as a 2:1 mixture of α/β-anomers, as determined by 250-MHz ^{1}H NMR analysis. The same reaction sequence transformed disaccharide **53**β to **87** in comparable yield.

The synthesis of refunctionalized disaccharide **87** set the stage for the crucial Mitsunobu coupling. Glycosidation of **87** (2:1 α/β anomer ratio) with **80** in this fashion afforded a 2:1 mixture of **88**β and **88**α in 55% yield; the yield based on recovered lactol was 94%. The anomers were readily separable by preparative HPLC.

Completion of the synthesis of (+)-phyllanthoside then required stereoselective reduction of the C(10) carbonyl group in **88**β, acylation of the resultant axial alcohol (**89**), and removal of the triethylsilyl ethers. Following our model study, treatment of **88**β with sodium borohydride afforded predominantly the axial epimer (ca. 6:1). Cinnamoylation followed by desilylation then gave (+)-phyllanthoside (**1**), identical in all respects (NMR, IR, MS, TLC, and mmp) with an authentic sample {synthetic **1**: mp 125–127 °C; $[\alpha]^{22}_D$ +19.5° (*c* 0.6, $CHCl_3$); natural **1**: mp 125–127 °C; $[\alpha]^{22}_D$ +19.6° (*c* 1.2, $CHCl_3$)} provided by Professor George Pettit.

Synthesis of α-Phyllanthoside. α-Phyllanthoside, a potentially important analogue of **1**, was similarly prepared from **88**α. Stereoselective reduction of the ketone moiety in **88**α, followed by cinnamoylation and hydrolysis of the triethylsilyl ethers, furnished (+)-α-phyllanthoside (**1**α) in 71% yield for the three steps.

(47) This reaction was carefully monitored to minimize hydrolysis of the silyl ethers and the formate ester.



Summary. The first total syntheses of (−)-phyllanthose and (+)-phyllanthoside have been achieved. Key features of the scheme include the Koenigs–Knorr disaccharide construction and Mitsunobu coupling of the aglycon and sugar. Importantly, the Mitsunobu protocol comprises a simple, highly efficient new method for the stereoselective generation of β-glycosyl esters.

Experimental Section[48]

Allyl Ether 18a. Under argon, a suspension of KH (1.37 g, 2 equiv) in THF (20 mL) was cooled to 0 °C, and a solution of di-*O*-isopropylidene-D-glucose (**17**) (4.43 g, 17.0 mmol) in THF (70 mL) was added slowly over 30 min. After 5 min at 0 °C, allyl bromide (3.0 mL, 2 equiv) was added. The reaction was stirred at room temperature for 1 h, cooled to 0 °C, and quenched by slow addition to a mixture of ice and saturated NH_4Cl solution (75 mL). The resultant mixture was extracted twice with chloroform, and the combined extracts were dried over $MgSO_4$ and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (3:17) as eluant, gave 4.87 g (95% yield) of **18a** as an oil: IR ($CHCl_3$) 2990 (s, br), 2940 (s, br), 2900 (s, br), 1650 (w), 1455 (m), 1380–1390 (s), 1340 (m), 1200–1280 (s, br), 990–1070 (s, br), 940 (s, br), 885 (s), 850 (s, br), 630 (m) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.28 (s, 3 H), 1.35 (s, 3 H), 1.41 (s, 3 H), 1.47 (s, 3 H), 3.92–4.13 (comp m, 6 H), 4.28 (m, 1 H), 4.52 (d, J = 4.3 Hz, 1 H), 5.16 (m, 1 H), 5.27 (m, 1 H), 5.77–5.94 (m, 2 H).

Diol 18b. To a solution of ketal **18a** (4.1 g, 13.7 mmol) in methanol (80 mL) was added 2 N H_2SO_4 (6.0 mL) at room temperature. After 20 h, the reaction was quenched with solid $NaHCO_3$. The resultant

(48) **Materials and Methods.** Reactions were carried out under an argon atmosphere, with freshly distilled solvents in vacuum-flamed glassware, unless otherwise noted. All solvents were reagent grade. Ether and THF were distilled from sodium and benzophenone. Precoated silica gel plates (250 μm) with a fluorescent indicator (E. Merck) were used for analytical thin-layer chromatography. *n*-Butyllithium was standardized by titration with diphenylacetic acid. ^{1}H and ^{13}C NMR spectra were recorded in deuteriochloroform solutions with a Bruker WP250, AM250 (250 MHz), or AM500 (500 MHz) spectrometer. Chemical shifts are reported in δ values relative to tetramethylsilane. All infrared spectra were recorded on a Perkin-Elmer Model 283B spectrophotometer. Optical rotations were measured with a Perkin-Elmer 241 polarimeter. Melting points were determined on either a Thomas-Hoover instrument or a Bristoline micro hot stage apparatus and are corrected. Microanalyses were performed by the Rockefeller University Microanalytical Laboratories under the direction of S. T. Bella or by Robertson Labs, Madison, NJ. High-resolution mass spectra were measured by the University of Pennsylvania Mass Spectrometry Service Center on a Hitachi-Perkin Elmer RMH-2 or a VG 70-70 Micromass spectrometer interfaced with a Kratos DS-50-s data system. Gas–liquid chromatography (GLC) analyses were performed on a Hewlett-Packard 5790A chromatograph equipped with a Hewlett Packard 25 m × 0.2 mm × 0.33 μm Ultra I (cross-linked methylsilicone) column. Chromatograms were recorded on a Hewlett-Packard 3390a integrator. High-pressure liquid chromatography (HPLC) was performed on a Waters analytical chromatograph equipped with a Model 6000A solvent delivery system, a U6K injector, and a R-400 refractive index detector or a Model 440 absorbance detector. A 4.6 mm × 25 cm column packed with 5 μm Ultrasphere-Si was employed. Chromatograms were recorded on a Hewlett-Packard 3390a integrator.

mixture was filtered through a Celite pad, and the solids were washed with ethyl acetate. Following concentration in vacuo, the residue was diluted with ethyl acetate, and the mixture was filtered again. Concentration in vacuo and flash chromatography, with ethyl acetate–hexane (1:1, then 2:1, then 1:0) as eluant, furnished 3.40 g (95% yield) of **18b** as an oil: IR ($CHCl_3$) 3200–3700 (m, br), 3000 (s, br), 2940 (s), 2880 (m, br), 1650 (w), 1460 (m), 1390 (s), 1380 (s), 1350 (m), 1300 (m), 1210–1270 (s, br), 1170 (s), 1000–1110 (s, br), 940 (s), 890 (s), 860 (s, br) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.30 (s, 3 H), 1.47 (s, 3 H), 2.24–2.44 (br s, 1 H), 2.84 (br m, 1 H), 3.65–3.87 (m, 2 H), 3.98–4.22 (comp m, 5 H), 4.56 (d, J = 4.5 Hz, 1 H), 5.22 (dd, J = 9.5 and 1.5 Hz, 1 H), 5.30 (dq, J = 15.0 and 1.5 Hz, 1 H), 5.81–5.97 (m, 2 H).

Alcohol (+)-20. A solution of diol **18b** (4.0 g, 15.3 mmol) and DMAP (catalytic amount) in methylene chloride (125 mL) and pyridine (25 mL) was cooled to −18 °C under argon, and *p*-toluenesulfonyl chloride (3.52 g, 1.2 equiv) was added in two portions, 3 h apart. The reaction mixture was stirred at room temperature for 4 days, diluted with methylene chloride (150 mL), washed three times with 4 N HCl and then with saturated $NaHCO_3$, and dried over $MgSO_4$. Removal of solvent in vacuo and purification by flash chromatography, with ethyl acetate–hexane (27:73, then 1:2) as eluant, afforded 5.61 g (89% yield) of the monotosylate as an oil.

Under argon, a suspension of $LiAlH_4$ (0.7 g, excess) in THF (10 mL) was cooled to 0 °C, and a solution of the tosylate (5.6 g, 13.5 mmol) in THF (40 mL) was added slowly. The reaction mixture was stirred at room temperature for 8 h, then cooled to 0 °C, and carefully quenched with water. The resultant white precipitate was dissolved in 4 N HCl, and the solution was extracted three times with ether. After drying over $MgSO_4$ and concentration in vacuo, the product was purified by flash chromatography, with ethyl acetate–hexane (27:73, then 1:2) as eluant, to give 2.85 g (86% yield) of **20** as an oil.

Tosylate derivative of 18b: IR ($CHCl_3$) 3320–3640 (m, br), 2990 (m), 2930 (m), 1600 (w), 1455 (m), 1360–1380 (s, br), 1310 (m), 1290 (m), 1210–1260 (m, br), 1180 (s), 1160 (s), 1070–1100 (s, br), 960–1030 (s, br), 880–900 (m, br), 850 (m), 830 (m), 810 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.30 (s, 3 H), 1.46 (s, 3 H), 2.44 (s, 3 H), 3.98–4.29 (comp m, 8 H), 4.53 (d, J = 4.5 Hz, 1 H), 5.20 (dd, J = 11.0 and 1.0 Hz, 1 H), 5.27 (dq, J = 16.0 and 1.0 Hz, 1 H), 5.78–5.94 (m, 2 H), 7.33 (d, J = 9.3 Hz, 2 H), 7.78 (d, J = 9.3 Hz, 2 H).

Alcohol 20: $[\alpha]^{22}_D$ +60.7° (c 2.72, $CHCl_3$); IR ($CHCl_3$) 3600–3300 (m), 3090 (w), 3000 (s), 2950 (s), 2900 (m), 1645 (w), 1460 (m), 1420 (m), 1390 (s), 1380 (s), 1350 (m), 1300 (m), 1260–1230 (s), 1170 (s), 1070 (s), 1020 (s), 940 (s), 890 (s), 860 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.30 (d, J = 6.4 Hz, 3 H), 1.30 (s, 3 H), 1.47 (s, 3 H), 2.30 (br s, 1 H), 3.91–4.22 (comp m, 5 H), 4.52 (d, J = 3.8 Hz, 1 H), 5.23 (dd, J = 11.3 and 1.1 Hz, 1 H), 5.32 (dd, J = 17.2 and 1.3 Hz, 1 H), 5.90 (m, 1 H), 5.95 (d, superimposed on m, J = 3.8 Hz, 1 H).

Diol 21. A solution of alcohol **20** (2.6 g, 10.6 mmol) in 0.35 M methanolic HCl (30 mL) was stirred for 4 days at room temperature. The reaction was then basified to pH 8.0 with NH_4OH. Following evaporation of solvent, the mixture was extracted with ethyl acetate, and the combined extracts were washed with brine and dried over $MgSO_4$. Removal of solvent in vacuo afforded 2.13 g (92% yield) of **21** as a 1:1 mixture of anomers: IR ($CHCl_3$) 3580 (s), 3480 (m), 3080 (w), 3020 (s), 2940 (s), 2910 (s), 2840 (m), 1645 (w), 1455 (m), 1410 (m), 1385 (m), 1340 (m), 1235 (s), 1195 (s), 1150–1030 (s), 930 (s), 840 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.25, 1.30 (diastereomers, d, d, J = 6.3 Hz, J = 6.1 Hz, 3 H), 2.5 (br s, 2 H), 3.10–3.28 (m, 1 H), 3.41, 3.54 (diastereomers, s, s, 3 H), 3.42 (m, 1 H), 3.52–3.71 (m, 2 H), 4.13, 4.65 (diastereomers, d, d, J = 7.7 Hz, J = 3.8 Hz, 1 H), 4.21 (m, 1 H), 4.41 (m, 1 H), 5.18 (dd, J = 9.4 and 0.8 Hz, 1 H), 5.28 (dd, J = 18.8 and 1.5 Hz, 1 H), 5.93 (m, 1 H); high-resolution mass spectrum (CI, NH_3) m/z 236.1472 [$(M + NH_4)^+$, calcd for $C_{10}H_{22}NO_5$ 236.1498].

Dibenzyl Ethers (+)-22α and (+)-22β. To a suspension of KH (0.74 g, 2.0 equiv) in THF (2.0 mL) at room temperature under argon was added a solution of diol **21** (350 mg, 1.61 mmol) and BnBr (0.85 mL, 2 equiv) in THF (10 mL). After 2 h at room temperature, the reaction was quenched with saturated NH_4Cl solution. The mixture was extracted three times with ethyl acetate, and the combined extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (7:93) as eluant, afforded 212 mg (33% yield) of the less polar **22α** and 424 mg (66% yield) of the more polar **22β**, both as white solids.

22β: mp 54 °C; $[\alpha]^{22}_D$ +9.2° (c 1.0, $CHCl_3$); IR ($CHCl_3$) 3095 (m), 3040 (m), 3010 (s), 2940 (m), 1500 (m), 1460 (m), 1395 (m), 1385 (m), 1350 (m), 1310 (m), 1280 (m), 1235 (m), 1200 (m), 1155 (m), 1070 (s), 930 (m), 700 (s) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.31 (d, J = 6.2 Hz, 3 H), 3.14 (dd, $J_1 = J_2$ = 9.1 Hz, 1 H), 3.30–3.40 (m, 2 H), 3.47 (dd, $J_1 = J_2$ = 8.7 Hz, 1 H), 3.55 (s, 3 H), 4.24 (d, superimposed on m, J = 7.7 Hz, 1 H), 4.26 (m, 1 H), 4.39 (ddt, J = 12.3, 5.7 and 1.4 Hz, 1 H), 4.76 (ABq, J_{AB} = 10.9 Hz, $\Delta\nu_{AB}$ = 64 Hz, 2 H), 4.81 (ABq, J_{AB} = 10.9 Hz, $\Delta\nu_{AB}$ = 47 Hz, 2 H), 5.15 (dq, J = 10.3 and 1.8 Hz, 1 H), 5.27 (dq, J = 17.2 and 1.7 Hz, 1 H), 5.96 (m, 1 H), 7.27–7.41 (comp m, 10 H); high-resolution mass spectrum (CI, NH_3) m/z 367.1946 [$(M - OCH_3)^+$, calcd for $C_{23}H_{27}O_4$ 367.1909]. Anal. Calcd for $C_{24}H_{30}O_5$: C, 72.32; H, 7.59. Found: C, 72.16; H, 7.35.

22α: mp 105–106 °C; $[\alpha]^{22}_D$ +37.2° (c 1.67, $CHCl_3$); IR ($CHCl_3$) 3080 (m), 3020 (m), 2930 (m), 1645 (w), 1500 (w), 1460 (m), 1370 (m), 1230 (m), 1200 (m), 1140 (m), 1080 (s), 1055 (s), 1010 (m), 930 (m), 700 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.22 (d, J = 6.3 Hz, 3 H), 3.06 (dd, $J_1 = J_2$ = 9.3 Hz, 1 H), 3.24 (s, 3 H), 3.44 (dd, J = 9.6 and 3.6 Hz, 1 H), 3.68 (m, 1 H), 3.80 (dd, $J_1 = J_2$ = 9.2 Hz, 1 H), 4.31 (ddt, J = 12.4, 5.7, and 1.4 Hz, 1 H), 4.44 (ddt, J = 12.5, 5.7, and 1.4 Hz, 1 H), 4.50 (d, J = 3.6 Hz, 1 H), 4.73 (ABq, J_{AB} = 12.2 Hz, $\Delta\nu_{AB}$ = 31 Hz, 2 H), 4.75 (ABq, J_{AB} = 10.2 Hz, $\Delta\nu_{AB}$ = 69 Hz, 2 H), 5.18 (dq, J = 10.5 and 1.8 Hz, 1 H), 5.42 (dq, J = 17 and 1.7 Hz, 1 H), 6.01 (m, 1 H), 7.28–7.40 (comp m, 10 H); high-resolution mass spectrum (CI, NH_3), m/z 416.2422 [$(M + NH_4)^+$, calcd for $C_{24}H_{34}NO_5$ 416.2437]. Anal. Calcd for $C_{24}H_{30}O_5$: C, 72.32; H, 7.59. Found: C, 72.13; H, 7.30.

Alcohol (+)-23α. To a solution of **22α** (220 mg, 0.533 mmol) in DMSO (4.0 mL) at room temperature under argon was added *t*-BuOK (68 mg, 1.1 equiv). The reaction was then heated to 100 °C for 20 min and quenched with water. The mixture was extracted with ether, and the combined extracts were concentrated in vacuo. The crude enol ether was dissolved in THF (40 mL) and treated with 2 N H_2SO_4 (10 mL). After 24 h at room temperature, the reaction was quenched with concentrated NH_4OH. After removal of ca. half the solvent in vacuo, the mixture was extracted three times with ether, and the combined extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (1:3) as eluant, provided 190 mg (96% yield) of **23α** as an oil: $[\alpha]^{22}_D$ +68.3° (c 2.7, $CHCl_3$); IR ($CHCl_3$) 3600–3300 (m), 3580 (m), 3080 (m), 3060 (m), 3010 (s), 2930 (s), 2910 (s), 2840 (m), 1500 (m), 1455 (s), 1370 (m), 1320 (m), 1240 (m), 1195 (s), 1150 (s), 1070 (s), 995 (m), 900 (m), 700 (s) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.25 (d, J = 6.1 Hz, 3 H), 2.47 (d, J = 1.8 Hz, 1 H), 3.06 (dd, $J_1 = J_2$ = 9.2 Hz, 1 H), 3.32 (s, 3 H), 3.37 (dd, J = 9.6 and 3.6 Hz, 1 H), 3.71 (m, 1 H), 4.03 (td, J = 9.6 and 1.8 Hz, 1 H), 4.55 (d, J = 3.6 Hz, 1 H), 4.68 (s, 2 H), 4.75 (ABq, J_{AB} = 11.2 Hz, $\Delta\nu_{AB}$ = 55 Hz, 2 H), 7.26–7.40 (comp m, 10 H); high-resolution mass spectrum (CI, NH_3) m/z 376.2115 [$(M + NH_4)^+$, calcd for $C_{21}H_{30}NO_5$ 376.2124].

Alcohols (+)-23α and (+)-23β. Following the procedure described above for **23α**, a 2:1 mixture of dibenzyl ethers **22α** and **22β** (1.5 g, 3.77 mmol) was treated with *t*-BuOK (633 mg, 1.5 equiv) in DMSO (25 mL). Flash chromatography, with ethyl acetate–hexane (1:3) as eluant, gave 480 mg (36% yield) of the less polar **23β** and 865 mg (64% yield) of the more polar **23α**, both as oils.

23β: $[\alpha]^{22}_D$ +22.9° (c 4.3, $CHCl_3$); IR ($CHCl_3$) 3600–3300 (m), 3580 (m), 3090 (w), 3060 (m), 3010 (m), 2940 (m), 1500 (m), 1455 (m), 1380 (m), 1360 (m), 1330 (m), 1295 (m), 1230 (m), 1195 (m), 1070 (s), 1030 (s), 1000 (m), 900 (m), 700 (s) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.32 (d, J = 6.1 Hz, 3 H), 2.47 (d, J = 2.1 Hz, 1 H), 3.11 (dd, $J_1 = J_2$ = 9.1 Hz, 1 H), 3.22 (dd, J = 9.2 and 7.9 Hz, 1 H), 3.39 (m, 1 H), 3.55 (s, 3 H), 3.69 (td, J = 9.2 and 2.1 Hz, 1 H), 4.27 (d, J = 7.9 Hz, 1 H), 4.66 (dd, J = 11.5 and 3.5 Hz, 2 H), 4.92 (dd, $J_1 = J_2$ = 11.8 Hz, 2 H), 7.26–7.40 (comp m, 10 H); high-resolution mass spectrum (CI, NH_3) m/z 376.2098 [$(M + NH_4)^+$, calcd for $C_{21}H_{30}NO_5$ 376.2124].

Acetate (+)-24α. A solution of alcohol **23α** (332 mg, 0.927 mmol) and DMAP (catalytic) in pyridine (7.0 mL) at room temperature was treated with acetic anhydride (1.0 mL, excess). After 20 min, the reaction mixture was diluted with ether, washed with 2 N H_2SO_4, saturated $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (3:17) as eluant, gave 353 mg (95% yield) of **24α** as a white solid: mp 73–74 °C; $[\alpha]^{22}_D$ +52.4° (c 0.41, $CHCl_3$); IR ($CHCl_3$) 3080 (m), 3020 (m), 2940 (m), 2850 (m), 1750 (s), 1500 (m), 1460 (m), 1380 (m), 1365 (m), 1245 (s), 1170 (m), 1080 (s), 915 (m), 700 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.24 (d, J = 6.2 Hz, 3 H), 1.96 (s, 3 H), 3.13 (dd, $J_1 = J_2$ = 9.4 Hz, 1 H), 3.37 (s, 3 H), 3.43 (dd, J = 9.9 and 3.6 Hz, 1 H), 3.79 (m, 1 H), 4.58 (comp m, 5 H), 5.48 (dd, $J_1 = J_2$ = 9.7 Hz, 1 H), 7.22–7.40 (comp m, 10 H); high-resolution mass spectrum (CI, isobutane) m/z 401.1977 [$(M + H)^+$, calcd for $C_{23}H_{29}O_6$ 401.1964]. Anal. Calcd for $C_{23}H_{28}O_6$: C, 68.96; H, 7.05. Found: C, 68.69; H, 6.84.

Acetate (+)-24β. To a solution of alcohol **23β** (70 mg, 0.196 mmol) and DMAP (catalytic) in pyridine (1.0 mL) at room temperature was added acetic anhydride (5 drops). After 15 min, the reaction mixture was diluted with ether, washed twice with 2 N H_2SO_4, washed with saturated $NaHCO_3$ and brine, and dried over $MgSO_4$. Concentration in vacuo provided 78 mg (100% yield) of crude acetate which solidified on standing. Recrystallization from ethyl acetate–hexane then gave

analytically pure **24β**: mp 71 °C; $[\alpha]^{22}_D$ +16.2° (*c* 1.51, $CHCl_3$); IR ($CHCl_3$) 3020 (m), 2940 (m), 2900 (m), 1745 (s), 1500 (w), 1460 (m), 1390 (m), 1370 (m), 1245 (s), 1170 (m), 1080 (s), 1005 (m), 915 (m), 700 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.31 (d, *J* = 6.1 Hz, 3 H), 1.86 (s, 3 H), 3.17 (dd, $J_1 = J_2$ = 9.5 Hz, 1 H), 3.28 (dd, *J* = 9.5 and 7.8 Hz, 1 H), 3.45 (m, 1 H), 3.58 (s, 3 H), 4.33 (d, *J* = 7.8 Hz, 1 H), 4.57 (s, 2 H), 4.71 (ABq, J_{AB} = 12 Hz, $\Delta\nu_{AB}$ = 63 Hz, 2 H), 5.21 (dd, $J_1 = J_2$ = 9.5 Hz, 1 H), 7.21–7.42 (comp m, 10 H); high-resolution mass spectrum (CI, NH_3) *m/z* 401.1882 [$(M + H)^+$, calcd for $C_{23}H_{29}O_6$ 401.1964]. Anal. Calcd for $C_{23}H_{28}O_6$: C, 68.96; H, 7.05. Found: C, 68.78; H, 6.84.

Thioglucoside (+)-25. Under argon, tetra-*n*-butylammonium iodide (155 mg, 1.2 equiv), TMSSPh (0.33 mL, 5 equiv), and zinc iodide (335 mg, 3 equiv) were added to a solution of **24β** (140 mg, 0.35 mmol) in methylene chloride (3.0 mL). The reaction mixture was heated to 60 °C for 30 min, then diluted with methylene chloride, washed three times with 10% $Ba(OH)_2$, washed with 5% HCl and brine, and dried over $MgSO_4$. Following evaporation of solvent in vacuo, the product was purified by flash chromatography, eluting with ethyl acetate–hexane (3:7), to give 120 mg (72% yield) of **25** as a mixture of anomers. An analytical sample of the α-thioglycoside was obtained via selective crystallization from ethyl acetate–hexane: mp 130 °C; $[\alpha]^{22}_D$ +163° (*c* 0.36, $CHCl_3$); IR ($CHCl_3$) 3060 (w), 3020 (m), 2940 (m), 2880 (m), 1755 (s), 1590 (w), 1490 (m), 1460 (m), 1440 (m), 1370 (m), 1240 (s), 1080 (s), 1030 (s), 910 (w), 700 (s) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.25 (d, *J* = 6.2 Hz, 3 H), 2.00 (s, 3 H), 3.21 (dd, $J_1 = J_2$ = 9.3 Hz, 1 H), 3.66 (dd, *J* = 9.3 and 5.4 Hz, 1 H), 4.35 (dq, *J* = 9.3 and 6.2 Hz, 1 H), 4.62 (s, 2 H), 4.64 (ABq, J_{AB} = 12.3 Hz, $\Delta\nu_{AB}$ = 46 Hz, 2 H), 5.42 (dd, $J_1 = J_2$ = 9.3 Hz, 1 H), 5.55 (d, *J* = 5.4 Hz, 1 H), 7.23–7.38 (comp m, 13 H), 7.45 (m, 2 H); high-resolution mass spectrum (CI, isobutane) *m/z* 479.1895 [$(M + H)^+$, calcd for $C_{28}H_{31}O_5S$ 479.1892]. Anal. Calcd for $C_{28}H_{30}O_5S$: C, 70.27; H, 6.32. Found: C, 70.58; H, 6.30.

Chloro Sugar 26. A solution of methyl glucoside **24α** (30 mg, 0.075 mmol) in freshly distilled acetyl chloride (1.0 mL) was treated with freshly distilled thionyl chloride (0.06 mL) at room temperature under argon. The reaction mixture was heated to 45 °C for 16 h and then concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (1:4) as eluant, afforded 27 mg (89% yield) of the unstable chloro sugar **26**: IR ($CHCl_3$) 3060 (w), 3020 (m), 3010 (m), 2920 (m), 2870 (m), 1750 (s), 1495 (w), 1450 (m), 1365 (m), 1230 (s), 1110 (s), 1070 (s), 1030 (m), 970 (m), 700 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.31 (d, *J* = 6.2 Hz, 3 H), 2.00 (s, 3 H), 3.22 (dd, $J_1 = J_2$ = 9.4 Hz, 1 H), 3.62 (dd, *J* = 9.4 and 3.8 Hz, 1 H), 4.17 (m, 1 H), 4.60 (s, 2 H), 4.62 (ABq, J_{AB} = 12.3 Hz, $\Delta\nu_{AB}$ = 24.5 Hz, 2 H), 5.53 (dd, $J_1 = J_2$ = 9.4 Hz, 1 H), 5.97 (d, *J* = 3.8 Hz, 1 H), 7.22–7.50 (comp m, 10 H).

Lactol 14a. (a) From 25. To a solution of thioglucoside **25** (240 mg, 0.502 mmol) in THF (24 mL) at room temperature were added water (12 mL) and mercuric acetate (740 mg, 5 equiv). The reaction mixture was heated to 55 °C for 5 h. After filtration through a Celite pad, the precipitates were washed with ether. The filtrate was extracted with ether, and the combined ethereal solutions were washed twice with 5% HCl, washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (7:15) as eluant, gave 185 mg (95% yield) of **14a** as a 1:1 mixture of anomers: IR ($CHCl_3$) 3600 (w), 3500–3300 (w), 3060 (w), 3010 (m), 2920 (m), 2900 (m), 1745 (s), 1500 (w), 1455 (m), 1360 (m), 1240 (m), 1075 (s), 1030 (m), 920 (w), 700 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.27, 1.32 (diastereomers, d, d, *J* = 6.4 Hz, *J* = 6.3 Hz, 3 H), 1.91, 1.97 (diastereomers, s, s, 3 H), 3.10–3.32 (m, 2 H), 3.45–3.58, 4.10 (diastereomers, m, m, 1 H), 4.61–4.80 (comp m, 5 H), 4.87 (d, *J* = 12.3 Hz, 1 H), 5.21, 5.46 (diastereomers, dd, dd, $J_1 = J_2$ = 9.3 Hz, $J_1 = J_2$ = 9.3 Hz, 1 H), 7.22–7.44 (comp m, 10 H); high-resolution mass spectrum (CI, NH_3) *m/z* 387.1836 [$(M + H)^+$, calcd for $C_{22}H_{27}O_6$ 387.1808]. Anal. Calcd for $C_{22}H_{26}O_6$: C, 68.38; H, 6.78. Found: C, 68.27; H, 6.85.

Lactol 14a. (b) From 26. To a mixture of chloro sugar **26** (100 mg, 0.248 mmol), water (1.0 mL), and CH_3CN (3.0 mL) at room temperature were added Ag_2O (57 mg, 1 equiv) and $BaCO_3$ (30 mg). The reaction was heated to 45 °C for 4 h and then filtered. The filtrate was extracted twice with ether, and the combined extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (7:13) as eluant, gave 94 mg (98% yield) of **14a** as a 1:1 mixture of anomers.

Glycosyl Esters (+)-27β and 27α. Under argon, a solution of lactol **14a** (90 mg, 0.233 mmol) and DMAP (catalytic) in methylene chloride (3.0 mL) and triethylamine (0.3 mL) was added to acid chloride **9** (45 mg, 0.143 mmol) at room temperature. After 3 h, the solvent was evaporated in vacuo, and the residue was purified by flash chromatography, with ethyl acetate–hexane (1:3) as eluant, to give 60 mg (63% yield) of the glycosyl esters. Separation by preparative by HPLC [ethyl acetate–hexane (1:3)] then furnished pure **27β** and **27α** (8:1 ratio).

27β: $[\alpha]^{22}_D$ +46.6° (*c* 1.43, $CHCl_3$); IR ($CHCl_3$) 3020 (m), 3010 (m), 2960 (m), 2880 (m), 1750 (s), 1725 (s), 1500 (w), 1455 (m), 1385 (m), 1240 (s), 1170 (s), 1080 (s), 1030 (s), 970 (m), 700 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.98 (d, *J* = 6.6 Hz, 3 H), 1.20–1.42 (m, 2 H), 1.30 (d, *J* = 6.2 Hz, 3 H), 1.60–1.83 (m, 2 H), 1.88 (s, 3 H), 1.90–2.08 (m, 2 H), 2.30 (m, 1 H), 2.43 (q, *J* = 9.0 Hz, 2 H), 2.50–2.65 (m, 2 H), 3.05 (ABq, J_{AB} = 5.1 Hz, $\Delta\nu_{AB}$ = 22 Hz, 2 H), 3.22 (dd, $J_1 = J_2$ = 9.3 Hz, 1 H), 3.51 (dd, *J* = 9.3 and 8.2 Hz, 1 H), 3.62 (dd, *J* = 11.4 and 6.1 Hz, 1 H), 3.72 (dd, $J_1 = J_2$ = 9.2 Hz, 1 H), 3.89 (dd, *J* = 11.0 and 6.2 Hz, 1 H), 4.39 (br q, *J* = 3.5 Hz, 1 H), 4.55–4.62 (m, 2 H), 4.64 (ABq, J_{AB} = 11.8 Hz, $\Delta\nu_{AB}$ = 28.3 Hz, 2 H), 5.27 (dd, $J_1 = J_2$ = 9.3 Hz, 1 H), 5.63 (d, *J* = 8.2 Hz, 1 H), 7.22–7.38 (comp m, 10 H); high-resolution mass spectrum (CI, NH_3) *m/z* 665.3008 [$(M + H)^+$, calcd for $C_{37}H_{45}O_{11}$ 665.2961].

27α: $[\alpha]^{22}_D$ +87.5° (*c* 1.03, $CHCl_3$); IR ($CHCl_3$) 3020 (m), 2940 (m), 2880 (m), 1745 (s), 1500 (w), 1460 (m), 1380 (m), 1240 (s), 1170 (s), 1075 (s), 995 (m), 975 (m), 950 (m), 700 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.99 (d, *J* = 6.6 Hz, 3 H), 1.20–1.40 (m, 2 H), 1.28 (d, superimposed on m, *J* = 6.2 Hz, 3 H), 1.60–1.70 (m, 2 H), 1.93–2.04 (m, 2 H), 1.97 (s, superimposed on m, 3 H), 2.33 (m, 1 H), 2.40 (d, *J* = 4.7 Hz, 2 H), 2.55 (m, 1 H), 2.70 (m, 1 H), 3.05 (ABq, J_{AB} = 5.1 Hz, $\Delta\nu_{AB}$ = 22.5 Hz, 2 H), 3.19 (dd, $J_1 = J_2$ = 9.5 Hz, 1 H), 3.55 (dd, *J* = 9.9 and 3.7 Hz, 1 H), 3.81 (q, *J* = 10.9 Hz, 2 H), 3.92 (m, 1 H), 4.34 (br q, *J* = 3.4 Hz, 1 H), 4.52 (ABq, J_{AB} = 11.9 Hz, $\Delta\nu_{AB}$ = 40.3 Hz, 2 H), 4.60 (s, 2 H), 5.41 (dd, $J_1 = J_2$ = 9.7 Hz, 1 H), 6.32 (d, *J* = 3.7 Hz, 1 H), 7.20–7.38 (comp m, 10 H); high-resolution mass spectrum (CI, NH_3) *m/z* 665.3006 [$(M + H)^+$, calcd for $C_{37}H_{45}O_{11}$ 665.2961].

Diol (+)-28. A suspension of 10% Pd/carbon (35 mg) in ethanol (3.0 mL) at room temperature was flushed with hydrogen, and a solution of glycosyl ester **27β** (60 mg, 0.0904 mmol) in ethanol (1.0 mL) was added. After 18 h, the reaction mixture was diluted with ethyl acetate and filtered through a Celite pad. Concentration in vacuo gave 41 mg (94% yield) of **28** as an oil: $[\alpha]^{22}_D$ +48.4° (*c* 1.2, $CHCl_3$); IR ($CHCl_3$) 3650–3200 (m), 3010 (m), 2930 (m), 1740 (s), 1720 (s), 1450 (m), 1380 (m), 1240 (s), 1160 (s), 1070 (s), 990 (m), 970 (m), 900 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.97 (d, *J* = 6.6 Hz, 3 H), 1.33 (d, *J* = 6.1 Hz, 3 H), 1.30–1.42 (m, 2 H), 1.60–1.86 (m, 2 H), 2.05 (m, 2 H), 2.19 (s, 3 H), 2.30–2.50 (m, 3 H), 2.56–2.72 (comp m, 4 H), 3.07 (ABq, J_{AB} = 5.1 Hz, $\Delta\nu_{AB}$ = 21.4 Hz, 2 H), 3.35 (m, 1 H), 3.50–3.80 (m, 3 H), 3.88 (dd, *J* = 10.9 and 7.2 Hz, 1 H), 4.38 (m, 1 H), 4.88 (dd, $J_1 = J_2$ = 9.3 Hz, 1 H), 5.57 (d, *J* = 8.1 Hz, 1 H); high-resolution mass spectrum (CI, NH_3) *m/z* 485.2020 [$(M + H)^+$, calcd for $C_{23}H_{33}O_{11}$ 485.2023].

Bis(triethylsilyl) Ether (+)-29. Under argon, a solution of diol **28** (12.6 mg, 0.026 mmol), DMAP (catalytic amount), and imidazole (catalytic amount) in DMF (1.0 mL) at room temperature was treated with triethylchlorosilane and triethylamine (0.25 mL, 1:1 mixture). After 5 h, the reaction was quenched with saturated $NaHCO_3$. The mixture was extracted twice with ether, and the combined extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (1:4) as eluant, furnished 18.1 mg (97% yield) of **29** as an oil: $[\alpha]^{22}_D$ +43.8° (*c* 1.81, $CHCl_3$); IR ($CHCl_3$) 2960 (s), 2920 (s), 2880 (s), 1745 (s), 1720 (s), 1460 (m), 1410 (w), 1380 (m), 1240 (s), 1220 (s), 1160 (s), 1090 (s), 1010 (m), 970 (m), 940 (w), 800 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.50–0.70 (comp m, 12 H), 0.88–1.04 (comp m, 21 H), 1.24 (d, *J* = 6.0 Hz, 3 H), 1.21–1.42 (m, 2 H), 1.60–1.83 (m, 2 H), 1.95–2.10 (m, 2 H), 2.14 (s, 3 H), 2.30–2.50 (m, 2 H), 2.51–2.72 (m, 2 H), 3.06 (ABq, J_{AB} = 5.0 Hz, $\Delta\nu_{AB}$ = 19.6 Hz, 2 H), 3.36 (dd, $J_1 = J_2$ = 9.1 Hz, 1 H), 3.50 (m, 2 H), 3.63 (dd, *J* = 9.1 and 8.0 Hz, 1 H), 3.72 (dd, $J_1 = J_2$ = 10.8 Hz, 1 H), 3.88 (m, 1 H), 4.38 (m, 1 H), 5.03 (dd, $J_1 = J_2$ = 9.0 Hz, 1 H), 5.51 (d, *J* = 7.9 Hz, 1 H); high-resolution mass spectrum (CI, NH_3) *m/z* 712.3702 (M^+, calcd for $C_{35}H_{60}O_{11}Si_2$ 712.3674).

Equatorial Alcohol (+)-30 and Axial Alcohol (+)-31. A solution of ketone **29** (16.1 mg, 0.0226 mmol) in methanol (1.0 mL) was cooled to −20 °C under argon, and sodium borohydride (2.0 mg, excess) was added. After 20 min, the reaction was quenched with saturated NH_4Cl. The mixture was extracted three times with ether, and the combined extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (1:4, then 3:7) as eluant, gave 8.3 mg (51% yield) of the less polar axial alcohol **31** and 2.0 mg (12% yield) of the more polar equatorial alcohol **30**, both as oils.

30: $[\alpha]^{22}_D$ +41.5° (*c* 0.81, $CHCl_3$); IR ($CHCl_3$) 3550 (w), 3040 (m), 3020 (m), 2960 (s), 2940 (s), 2880 (s), 1755 (s), 1460 (m), 1420 (m), 1390 (m), 1370 (m), 1240 (s), 1160 (s), 1110–1090 (s), 1020 (m), 950 (m), 860 (m), 800 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.55–0.68 (comp m, 12 H), 0.85–1.00 (comp m, 21 H), 1.20–1.32 (m, 3 H), 1.26 (d, superimposed on m, *J* = 6.1 Hz, 3 H), 1.40 (m, 2 H), 1.60–1.90 (m, 3 H), 1.90–2.10 (m, 2 H), 2.14 (s, 3 H), 2.40 (m, 1 H), 2.54 (m, 1 H), 2.93 (s, 2 H), 3.09 (d, *J* = 10.3 Hz, 1 H), 3.32–3.56 (m, 3 H), 3.60–3.87

(m, 2 H), 4.45 (m, 1 H), 5.03 (dd, $J_1 = J_2 = 9.1$ Hz, 1 H), 5.53 (d, $J = 8.0$ Hz, 1 H); high-resolution mass spectrum (FAB, NBA matrix) m/z 715.3940 [$(M + H)^+$, calcd for $C_{35}H_{63}O_{11}Si_2$ 715.3909].

31: $[\alpha]^{22}_D$ +25.5° (c 0.02, $CHCl_3$); IR ($CHCl_3$) 3600–3300 (w), 3020 (m), 2970 (s), 2940 (s), 2880 (m), 1755 (s), 1470 (w), 1240 (s), 1110–1090 (s), 1050 (m), 990 (m), 800 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.52–0.78 (comp m, 12 H), 0.78–1.03 (comp m, 21 H), 1.26 (d, $J = 6.2$ Hz, 3 H), 1.20–1.50 (comp m, 5 H), 1.60–2.10 (comp m, 5 H), 2.13 (s, 3 H), 2.38 (m, 1 H), 2.65 (m, 1 H), 2.95 (ABq, $J_{AB} = 3.4$ Hz, $\Delta\nu_{AB} = 5.7$ Hz, 2 H), 3.38 (dd, $J_1 = J_2 = 9.2$ Hz, 1 H), 3.41–3.70 (comp m, 5 H), 4.37 (m, 1 H), 5.04 (dd, $J_1 = J_2 = 9.1$ Hz, 1 H), 5.52 (d, $J = 8.0$ Hz, 1 H); high-resolution mass spectrum (CI, NH_3) m/z 715.3902 [$(M + H)^+$, calcd for $C_{35}H_{63}O_{11}Si_2$ 715.3909].

Cinnamate (+)-32. Under argon, a solution of alcohol **31** (8.0 mg, 0.0112 mmol) and 4-pyrrolidinopyridine (catalytic amount) in pyridine (0.5 mL) and triethylamine (0.25 mL) at room temperature was treated with *trans*-cinnamoyl chloride (10 mg, excess). After 12 h at room temperature, the reaction was quenched with saturated $NaHCO_3$. The mixture was extracted three times with ether, and the combined extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (1:4) as eluant, furnished 9.3 mg (98% yield) of **32** as an oil: $[\alpha]^{22}_D$ +10.7° (c 1.12, $CHCl_3$); IR ($CHCl_3$) 3020 (m), 3010 (m), 2960 (s), 2880 (m), 1750 (s), 1710 (s), 1640 (m), 1465 (m), 1450 (m), 1380 (m), 1310 (m), 1240 (s), 1160 (m), 1120–1080 (s), 910 (m), 800 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.32–0.51 (comp m, 6 H), 0.55–0.68 (comp m, 6 H), 0.78–0.90 (comp m, 13 H), 0.91–1.02 (comp m, 8 H), 1.23 (d, superimposed on m, $J = 6.2$ Hz, 3 H), 1.10–1.50 (m, 3 H), 1.61–1.71 (m, 3 H), 1.71–2.08 (m, 3 H), 2.12 (s, 3 H), 2.39 (m, 1 H), 2.55 (m, 1 H), 2.95 (s, 2 H), 3.22–3.32 (m, 2 H), 3.39–3.50 (m, 2 H), 3.97 (dd, $J_1 = J_2 = 9.2$ Hz, 1 H), 4.43 (m, 1 H), 4.94 (dd, $J_1 = J_2 = 9.2$ Hz, 1 H), 5.20 (m, 1 H), 5.42 (d, $J = 8.0$ Hz, 1 H), 6.50 (d, $J = 16.1$ Hz, 1 H), 7.42 (m, 3 H), 7.59 (m, 2 H), 7.80 (d, $J = 16.1$ Hz, 1 H): high-resolution mass spectrum (CI, NH_3) m/z 845.4330 [$(M + H)^+$, calcd for $C_{44}H_{69}O_{12}Si_2$ 845.4327].

Diol (+)-16. Bis(triethylsilyl) ether **32** (7.1 mg, 0.0084 mmol) was dissolved in AcOH–H_2O–THF (6:3:1, 1.0 mL) at room temperature. After 7 h, the reaction mixture was diluted with methylene chloride, washed with saturated $NaHCO_3$, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (7:3) as eluant, gave 3.2 mg (62% yield) of **16** as an oil: $[\alpha]^{22}_D$ +41.3° (c 0.32, $CHCl_3$); IR ($CHCl_3$) 3600–3300 (m), 3020 (m), 3010 (m), 2940 (s), 1745 (s), 1730 (s), 1710 (s), 1660 (m), 1450 (m), 1380 (m), 1310 (s), 1250 (s), 1170 (s), 1075 (s), 1050 (s), 1030 (s), 990 (m), 950 (m), 900 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.86 (d, $J = 7.0$ Hz, 3 H), 1.20–1.40 (m, 3 H), 1.28 (d, superimposed on m, $J = 6.1$ Hz, 3 H), 1.60–1.70 (m, 2 H), 1.78 (ddd, $J = 14.0$, 11.0, and 3.5 Hz, 1 H), 1.86–2.05 (comp m, 4 H), 2.20 (s, 3 H), 2.32 (m, 1 H), 2.55 (m, 2 H), 2.94 (ABq, $J_{AB} = 2.9$ Hz, $\Delta\nu_{AB} = 6.2$ Hz, 2 H), 3.23 (m, 2 H), 3.45 (m, 2 H), 3.93 (dd, $J_1 = J_2 = 9.2$ Hz, 1 H), 4.42 (m, 1 H), 4.75 (dd, $J_1 = J_2 = 9.2$ Hz, 1 H), 5.10 (m, 1 H), 5.41 (d, $J = 8.2$ Hz, 1 H). 6.50 (d, $J = 16.2$ Hz, 1 H), 7.38 (m, 3 H), 7.56 (m, 2 H), 7.76 (d, $J = 16.2$ Hz, 1 H); high-resolution mass spectrum (FAB, NBA matrix) m/z 617.2623 [$(M + H)^+$, calcd for $C_{32}H_{41}O_{12}$ 617.2586].

3,5-Dinitropyridyl Derivatives (+)-33α and (+)-33β. Under argon, a solution of lactol **14a** (210 mg, 0.544 mmol), anhydrous KF (catalytic amount), and 18-crown-6 (catalytic amount) in THF (8.0 mL) and triethylamine (1.0 mL) at room temperature was treated with 2-chloro-3,5-dinitropyridine (222 mg, 2.0 equiv). After 3 h, the reaction mixture was diluted with ether, washed twice with 4 N HCl, washed with 2 N NaOH and brine, and dried over $MgSO_4$. Following concentration in vacuo, the product was purified by flash chromatography, with ethyl acetate–hexane (3:17) as eluant, to give 109 mg (36% yield) of the less polar **33α** as an oil and 117 mg (38% yield) of the more polar **33β** as a solid.

33α: $[\alpha]^{22}_D$ +310° (c 1.26, $CHCl_3$); IR ($CHCl_3$) 3080 (w), 3020 (w), 2920 (w), 2870 (w), 1755 (m), 1610 (s), 1545 (m), 1455 (m), 1410 (m), 1345 (s), 1310 (m), 1240 (s), 1080 (s), 950 (m), 910 (m), 830 (m), 700 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.29 (d, $J = 6.3$ Hz, 3 H), 2.01 (s, 3 H), 3.32 (dd, $J_1 = J_2 = 9.1$ Hz, 1 H), 3.73 (dd, $J = 9.1$ and 3.8 Hz, 1 H), 4.18 (m, 1 H), 4.60 (ABq, $J_{AB} = 12.2$ Hz, $\Delta\nu_{AB} = 8.0$ Hz, 2 H), 4.65 (s, 2 H), 5.65 (dd, $J_1 = J_2 = 9.1$ Hz, 1 H), 5.93 (d, $J = 3.8$ Hz, 1 H), 7.15–7.43 (comp m, 10 H), 9.10 (d, $J = 2.5$ Hz, 1 H), 9.14 (d, $J = 2.5$ Hz, 1 H); high-resolution mass spectrum (CI, NH_3) m/z 571.2066 [$(M + NH_4)^+$, calcd for $C_{27}H_{31}N_4O_{10}$ 571.2040].

33β: mp 160 °C dec; $[\alpha]^{22}_D$ +48.4° (c 2.0, $CHCl_3$); IR ($CHCl_3$) 3100 (w), 3020 (m), 2960 (m), 2940 (m), 2880 (m), 1750 (m), 1610 (s), 1550 (m), 1460 (m), 1415 (m), 1340 (s), 1310 (m), 1240 (s), 1080 (s), 1020 (m), 910 (m), 840 (m), 700 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.31 (d, $J = 6.2$ Hz, 3 H), 1.91 (s, 3 H), 3.31 (dd, $J_1 = J_2 = 9.3$ Hz, 1 H), 3.72 (m, 1 H), 3.78 (dd, $J_1 = J_2 = 9.3$ Hz, 1 H), 4.61 (s, 2 H), 4.69 (ABq, $J_{AB} = 12$ Hz, $\Delta\nu_{AB} = 23$ Hz, 2 H), 5.35 (dd, $J_1 = J_2 = 9.3$ Hz, 1 H), 6.23 (d, $J = 7.9$ Hz, 1 H), 7.22–7.39 (comp m, 10 H), 9.08 (d, $J = 2.6$ Hz, 1 H), 9.27 (d, $J = 2.6$ Hz, 1 H); high-resolution mass spectrum (CI, NH_3) m/z 571.2062 [$(M + NH_4)^+$, calcd for $C_{27}H_{31}N_4O_{10}$ 571.2040]. Anal. Calcd for $C_{27}H_{27}N_3O_{10}$: C, 58.59; H, 4.92. Found: C, 58.37; H, 4.84.

Lactol 34. A solution of alcohol **20** (2.8 g, 11.4 mmol) in 2 N H_2SO_4 (20 mL) and THF (40 mL) was heated to 60 °C for 44 h. The reaction mixture then was neutralized with aqueous NH_4OH. Following concentration in vacuo, the resultant precipitates were washed three times with ethyl acetate, and the combined filtrates were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (3:1) as eluant, afforded 2.02 g (87% yield) of a mixture of α- and β-lactols **34** as a colorless oil: IR ($CHCl_3$) 3600 (s), 3520 (s), 3090 (m), 3020 (s), 2990 (s), 2920 (s), 1645 (w), 1450 (m) 1385 (s), 1235 (s), 1140–1010 (s), 930 (s), 845 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.25, 1.32 (diastereomers, d, d, $J = 6.3$ Hz, $J = 6.1$ Hz, 3 H), 1.70–2.40 (br s, 3 H), 3.15–3.29 (m, 1 H), 3.42, 3.94 (diastereomers, m, m, 1 H), 3.50 (dd, $J_1 = J_2 = 9.2$ Hz, 1 H), 3.92 (m, 1 H), 4.27 (m, 1 H), 4.46 (m, 1 H), 4.60, 5.22 (diastereomers, d, d, $J = 8.2$ Hz, $J = 3.8$ Hz, 1 H), 5.23 (dd, $J = 10.2$ and 0.8 Hz, 1 H), 5.31 (dd, $J = 18.6$ and 1.4 Hz, 1 H), 5.98 (m, 1 H); high-resolution mass spectrum (CI, NH_3) m/z 222.1343 [$(M + NH_4)^+$, calcd for $C_9H_{20}NO_5$ 222.1341].

Cyclopentylidene Ketal (+)-35. Under argon, a solution of lactols **34** (677 mg, 3.32 mmol) in THF (10 mL) at room temperature was treated with CSA (catalytic amount) and 1,1-dimethoxycyclopentane (2.0 mL, excess). The reaction was stirred for 45 h and quenched with pyridine (3 drops). After concentration in vacuo, the product was purified by flash chromatography, with ethyl acetate–hexane (3:22) as eluant, to give 720 mg (80% yield) of **35** as a colorless oil: $[\alpha]^{22}_D$ +45.1° (c 0.8, $CHCl_3$); IR ($CHCl_3$) 3580 (m), 3600–3300 (m), 3020 (s), 2990 (s), 2960 (s), 2890 (s), 1650 (w), 1460 (m), 1440 (m), 1340 (s), 1240 (s), 1180 (s), 1140–1000 (s), 930 (s), 855 (m), 810 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.23 (d, $J = 6.3$ Hz, 3 H), 1.72 (comp m, 6 H), 1.89–2.11 (m, 3 H), 3.30 (dd, $J = 9.1$ and 7.8 Hz, 1 H), 3.57 (dd, $J = 7.5$ and 6.0 Hz, 1 H), 3.82 (m, 1 H), 4.03 (dd, $J_1 = J_2 = 5.0$ Hz, 1 H), 4.13 (ddt, $J = 12.8$, 5.9 and 0.5 Hz, 1 H), 4.28 (ddt, $J = 12.8$, 5.9 and 0.5 Hz, 1 H), 5.21 (br d, $J = 10.2$ Hz, 1 H), 5.29 (br d, $J = 17.2$ Hz, 1 H), 5.43 (d, $J = 4.8$ Hz, 1 H), 5.92 (m, 1 H); high-resolution mass spectrum (CI, NH_3) m/z 270.1494 (M^+, calcd for $C_{14}H_{22}O_5$ 270.1467).

Benzyl Ether (+)-36. To a suspension of KH (1.54 g, 2.0 equiv) in THF (3.0 mL) at room temperature under argon was added a solution of alcohol **35** (1.80 g, 6.67 mmol), BnBr (1.8 mL, 2.0 equiv), and 18-crown-6 (25 mg) in THF (15 mL). After 5 h, the reaction was quenched with saturated NH_4Cl. The mixture was extracted three times with ether, and the combined extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (1:9) as eluant, furnished 2.32 g (97% yield) of **36** as a colorless oil: $[\alpha]^{22}_D$ +75.6° (c 1.5, $CHCl_3$); IR ($CHCl_3$) 3080 (m), 3020 (s), 2980 (s), 2880 (s), 1650 (w), 1500 (m), 1460 (s), 1440 (m), 1395 (m), 1340 (s), 1120–1060 (s), 1000 (s), 930 (s), 720 (m), 700 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.27 (d, $J = 6.2$ Hz, 3 H), 1.61–1.78 (comp m, 6 H), 1.93–2.04 (m, 2 H), 3.19 (dd, $J = 9.2$ and 4.8 Hz, 1 H), 3.76 (dd, $J_1 = J_2 = 4.2$ Hz, 1 H), 3.88 (m, 1 H), 4.08–4.26 (m, 3 H), 4.70 (ABq, $J_{AB} = 11.4$ Hz, $\Delta\nu_{AB} = 52$ Hz, 2 H), 5.23 (br d, $J = 11.2$ Hz, 1 H), 5.33 (br d, $J = 18.1$ Hz, 1 H), 5.44 (d, $J = 5.0$ Hz, 1 H), 5.95 (m, 1 H), 7.28–7.38 (comp m, 5 H); high-resolution mass spectrum (CI, NH_3) m/z 360.1938 (M^+, calcd for $C_{21}H_{28}O_5$ 360.1937).

Alcohol (+)-37. A solution of **36** (1.15 g, 3.19 mmol) in DMSO (22 mL) was heated to 100 °C, and t-BuOK (430 mg, 1.2 equiv) was added. After 20 min at 100 °C, TLC analysis showed complete isomerization to the corresponding enol ether. The reaction was then quenched with water, the mixture was extracted with ether, and the combined extracts were dried over $MgSO_4$. The solvent was removed in vacuo, and the residual yellow oil was dissolved in 0.5 N methanolic NaOH (40 mL). The solution was treated with 4% aqueous $KMnO_4$ until the reaction was complete by TLC analysis (40% ethyl acetate–hexane). The mixture was then filtered through a Celite plug, and the precipitates were washed with ether. After removal of solvent in vacuo, the residue was extracted three times with ether, and the combined extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (2:3) as eluant, gave 804 mg (79% yield) of **37** as a colorless oil: $[\alpha]^{22}_D$ +81.9° (c 0.56, $CHCl_3$); IR ($CHCl_3$) 3600 (m), 3600–3300 (m), 3020 (m), 3000 (m), 2950 (m), 1500 (m), 1460 (m), 1390 (m), 1380 (m), 1250 (m), 1230 (s), 1175 (s), 1055 (s), 1010 (s), 880 (m), 800 (m), 700 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.31 (d, $J = 6.2$ Hz, 3 H), 1.60–1.81 (comp m, 6 H), 1.94–2.03 (m, 2 H), 2.21 (d, $J = 5.2$ Hz, 1 H), 3.12 (dd, $J = 9.2$ and 5.9 Hz, 1 H), 3.73–4.08 (m, 3 H), 4.72 (ABq, $J_{AB} = 11.5$ Hz, $\Delta\nu_{AB} = 17.8$ Hz, 2 H), 5.45 (d, $J = 4.8$ Hz, 1 H), 7.28–7.36 (comp m, 5 H); high-resolution

mass spectrum (EI, NH_3) m/z 320.1635 (M^+, calcd for $C_{18}H_{24}O_5$ 320.1624).

Acetate (+)-38. A solution of alcohol **37** (30 mg, 0.0938 mmol) and DMAP (catalytic amount) in methylene chloride (1.0 mL) containing pyridine (3 drops) at room temperature was treated with acetic anhydride (5 drops, excess). After 10 min, the reaction was quenched with water. The mixture was extracted twice with ether, and the combined extracts were washed with 5% HCl and brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (3:17) as eluant, gave 30 mg (88% yield) of **38** as a colorless oil: $[\alpha]^{22}_D$ +143° (c 1.24, $CHCl_3$); IR ($CHCl_3$) 3020 (m), 2980 (m), 2880 (m), 1745 (s), 1500 (w), 1455 (m), 1370 (m), 1350 (m), 1240–1220 (s), 1100 (s), 1030 (s), 970 (m), 695 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.22 (d, J = 6.3 Hz, 3 H), 1.62–1.75 (comp m, 6 H), 2.01–2.11 (m, 2 H), 2.08 (s, superimposed on m, 3 H), 3.14 (ddd, J = 9.1, 2.6 and 0.9 Hz, 1 H), 3.88 (m, 1 H), 4.08 (m, 1 H), 4.68 (ABq, J_{AB} = 11.9 Hz, $\Delta\nu_{AB}$ = 52 Hz, 2 H), 5.33 (dd, $J_1 = J_2$ = 3.1 Hz, 1 H), 5.46 (d, J = 4.9 Hz, 1 H), 7.28–7.37 (comp m, 5 H); high-resolution mass spectrum (EI, NH_3) m/z 362.1704 (M^+, calcd for $C_{20}H_{26}O_6$ 362.1729).

Glycosides (−)-39β and (+)-39α. To a solution of alcohol **37** (824 mg, 2.58 mmol) in allyl alcohol (12 mL) at room temperature was added acetyl chloride (0.25 mL). The reaction mixture was stirred for 3 days and then concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (2:3) as eluant, afforded 323.7 mg (43% yield) of **39β** and 338 mg (45% yield) of **39α**, both as solids.

39β: mp 92–93 °C; $[\alpha]^{22}_D$ −16.9° (c 0.9, $CHCl_3$); IR ($CHCl_3$) 3580 (m), 3550–3300 (m), 3080 (w), 3060 (w), 3000 (m), 2880 (m), 1500 (w), 1455 (m), 1380 (m), 1240 (m), 1170 (m), 1100 (s), 1065 (s), 1015 (s), 930 (m), 700 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.37 (d, J = 6.2 Hz, 3 H), 2.56 (d, J = 2.3 Hz, 1 H), 2.62 (d, J = 2.4 Hz, 1 H), 3.15 (dd, $J_1 = J_2$ = 11.0 Hz, 1 H), 3.38–3.47 (m, 2 H), 3.67 (td, J = 9.1 and 2.2 Hz, 1 H), 4.26 (ABxyz, J_{AB} = 12.5 Hz, J_{AX} = 7.7 Hz, $J_{AY} = J_{AZ}$ = 1.2 Hz, $\Delta\nu_{AB}$ = 68 Hz, 2 H), 4.30 (d, J = 7.8 Hz, 1 H), 4.78 (ABq, J_{AB} = 11.1 Hz, $\Delta\nu_{AB}$ = 34.2 Hz, 2 H), 5.22 (br d, J = 11.3 Hz, 1 H), 5.32 (br d, J = 17.3 Hz, 1 H), 5.95 (m, 1 H), 7.28–7.40 (comp m, 5 H); high-resolution mass spectrum (CI, NH_3) m/z 294.1449 (M^+, calcd for $C_{16}H_{22}O_5$ 294.1467). Anal. Calcd for $C_{16}H_{22}O_5$: C, 65.26; H, 7.53. Found: C, 65.08; H, 7.34.

39α: mp 71–72 °C; $[\alpha]^{22}_D$ +149° (c 0.8, $CHCl_3$); IR ($CHCl_3$) 3550 (m), 3500–3300 (m), 3080 (w), 3050 (w), 2995 (m), 2900 (m), 2860 (m), 1490 (w), 1450 (m), 1380 (m), 1230 (m), 1140 (s), 1100 (s), 1050 (s), 990 (s), 920 (m), 690 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.29 (d, J = 6.3 Hz, 3 H), 2.18 (d, J = 10.0 Hz, 1 H), 2.68 (br s, 1 H), 3.08 (dd, $J_1 = J_2$ = 9.2 Hz, 1 H), 3.52 (td, J = 3.9 and 9.7 Hz, 1 H), 3.78 (m, 1 H), 3.85 (br dd, $J_1 = J_2$ = 9.3 Hz, 1 H), 4.10 (ABxyz, J_{AB} = 11.8 Hz, J_{AX} = 6.6 Hz, $J_{AY} = J_{AZ}$ = 1.2 Hz, $\Delta\nu_{AB}$ = 51 Hz, 2 H), 4.79 (ABq, J_{AB} = 11.1 Hz, $\Delta\nu_{AB}$ = 42 Hz, 2 H), 4.85 (d, superimposed on ABq, J = 3.9 Hz, 1 H), 5.21 (br d, J = 11.3 Hz, 1 H), 5.30 (br d, J = 16.8 Hz, 1 H), 5.92 (m, 1 H), 7.28–7.38 (comp m, 5 H); high-resolution mass spectrum (EI, NH_3) m/z 312.1811 [$(M + NH_4)^+$, calcd for $C_{16}H_{26}NO_5$ 312.1803]. Anal. Calcd for $C_{16}H_{22}O_5$: C, 65.26; H, 7.53. Found: C, 65.04; H, 7.36.

Acetates (+)-41α, (+)-40α, and (+)-15α. To a solution of diol **39α** (110 mg, 0.374 mmol) and DMAP (catalytic amount) in methylene chloride (4.0 mL) and pyridine (0.5 mL) at room temperature was added acetic anhydride (0.045 mL, 1.27 equiv). After 20 min, the reaction mixture was concentrated in vacuo, and the product was purified by flash chromatography, with ethyl acetate–hexane (3:7, then 2:3) as eluant, to give 42 mg (30% yield) of **41α**, 33 mg (26% yield) of **40α**, and 45 mg (36% yield) of **15α**, all as oils.

41α: $[\alpha]^{22}_D$ +102° (c 1.98, $CHCl_3$); IR ($CHCl_3$) 3060 (m), 3020 (m), 2960 (m), 2930 (m), 2880 (m), 1750 (s), 1645 (w), 1500 (m), 1455 (m), 1370 (s), 1250 (s), 1050 (s), 930 (m), 700 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.29 (d, J = 6.2 Hz, 3 H), 1.97 (s, 3 H), 2.06 (s, 3 H), 3.25 (dd, $J_1 = J_2$ = 9.5 Hz, 1 H), 3.91 (m, 1 H), 3.99 (br dd, J = 13.2 and 5.0 Hz, 1 H), 4.17 (br dd, J = 13.2 and 5.0 Hz, 1 H), 4.61 (s, 2 H), 4.82 (dd, J = 9.2 and 3.8 Hz, 1 H), 4.95 (d, J = 3.8 Hz, 1 H), 5.18 (br d, J = 10.4 Hz, 1 H), 5.30 (br d, J = 16.2 Hz, 1 H), 5.55 (dd, J = 10.1 and 9.3 Hz, 1 H), 5.88 (m, 1 H), 7.28–7.39 (comp m, 5 H); high-resolution mass spectrum (CI, NH_3) m/z 379.1746 [$(M + H)^+$, calcd for $C_{20}H_{27}O_7$ 379.1757].

40α: $[\alpha]^{22}_D$ +121° (c 2.3, $CHCl_3$); IR ($CHCl_3$) 3600–3300 (m), 3080 (m), 3060 (m), 3020 (m), 3010 (m), 2930 (m), 2920 (m), 2870 (m), 1745 (s), 1645 (w), 1500 (m), 1370 (m), 1245 (s), 1155 (m), 1110 (m), 1055 (s), 995 (m), 930 (m), 700 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.30 (d, J = 6.3 Hz, 3 H), 2.12 (s, 3 H), 2.27 (d, J = 3.6 Hz, 1 H), 3.13 (d, J = 9.2 Hz, 1 H), 3.81 (m, 1 H), 3.96 (br dd, J = 13.2 and 4.1 Hz, 1 H), 4.05–4.19 (m, 2 H), 4.70 (dd, J = 10.0 and 3.5 Hz, 1 H), 4.80 (ABq, J_{AB} = 11.3 Hz, $\Delta\nu_{AB}$ = 30.3 Hz, 2 H), 4.97 (d, J = 3.5 Hz, 1 H), 5.18 (br d, J = 11.0 Hz, 1 H), 5.27 (dq, J = 16.8 and 1.6 Hz, 1 H), 5.86 (m, 1 H), 7.27–7.40 (comp m, 5 H); high-resolution mass spectrum (CI, NH_3) m/z 337.1693 [$(M + H)^+$, calcd for $C_{18}H_{25}O_6$ 337.1651].

15α: $[\alpha]^{22}_D$ +119° (c 3.4, $CHCl_3$); IR ($CHCl_3$) 3570 (m), 3500–3300 (w), 3090 (m), 3070 (m), 3030 (m), 3010 (m), 2990 (m), 2940 (m), 2880 (m), 1745 (s), 1650 (w), 1500 (m), 1455 (m), 1410 (m), 1380 (m), 1240 (s), 1140 (m), 1055 (s), 935 (m), 700 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.28 (d, J = 6.3 Hz, 3 H), 2.05 (s, 3 H), 2.13 (d, J = 11.5 Hz, 1 H), 3.20 (dd, $J_1 = J_2$ = 9.5 Hz, 1 H), 3.57 (ddd, J = 11.5, 9.4, and 3.9 Hz, 1 H), 3.82 (m, 1 H), 4.02 (br dd, J = 13.3 and 6.2 Hz, 1 H), 4.21 (br dd, J = 12.8 and 5.4 Hz, 1 H), 4.61 (s, 2 H), 4.38 (d, J = 3.9 Hz, 1 H), 5.20–5.35 (m, 3 H), 5.90 (m, 1 H), 7.20–7.41 (comp m, 5 H); high-resolution mass spectrum (CI, NH_3) m/z 337.1647 [$(M + H)^+$, calcd for $C_{18}H_{25}O_6$ 337.1651].

Acetates (−)-41β, (−)-40β, and (−)-15β. A solution of diol **39β** (140 mg, 0.467 mmol) and DMAP (catalytic amount) in methylene chloride (4.0 mL) and pyridine (0.5 mL) at room temperature was treated with acetic anhydride (0.06 mL, 1.33 equiv). After 20 min, the reaction mixture was concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (3:7, then 2:3) as eluant, furnished 50 mg (28% yield) of **41β** as an oil, 71 mg (44% yield) of **40β** as a white solid, and 43 mg (27% yield) of **15β** as an oil.

41β: $[\alpha]^{22}_D$ −59.5° (c 1.69, $CHCl_3$); IR ($CHCl_3$) 3070 (m), 3020 (m), 2940 (m), 2880 (m), 1750 (s), 1650 (w), 1500 (m), 1455 (m), 1430 (m), 1405 (m), 1380 (m), 1365 (m), 1250 (s), 1170 (s), 1070 (s), 990 (m), 930 (m), 700 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.34 (d, J = 6.1 Hz, 3 H), 1.95 (s, 3 H), 2.04 (s, 3 H), 3.31 (dd, $J_1 = J_2$ = 9.3 Hz, 1 H), 3.49 (m, 1 H), 4.08 (ddt, J = 13.3, 5.3, and 1.3 Hz, 1 H), 4.32 (ddt, J = 13.2, 4.9, and 1.5 Hz, 1 H), 4.50 (d, J = 8.1 Hz, 1 H), 4.61 (s, 2 H), 4.92 (dd, J = 9.7 and 8.0 Hz, 1 H), 5.20 (dd, superimposed on m, $J_1 = J_2$ = 8.0 Hz, 1 H), 5.15–5.31 (m, 2 H), 5.85 (m, 1 H), 7.20–7.41 (comp m, 5 H); high-resolution mass spectrum (CI, NH_3) m/z 396.2021 [$(M + NH_4)^+$, calcd for $C_{20}H_{30}N_7$ 396.2022].

40β: mp 77–78 °C; $[\alpha]^{22}_D$ −34.5° (c 0.8, $CHCl_3$); IR ($CHCl_3$) 3600–3300 (m), 3080 (m), 3010 (m), 2940 (m), 2880 (m), 1750 (s), 1455 (m), 1400 (m), 1375 (m), 1245 (s), 1170 (m), 1060 (s), 1025 (m), 930 (m), 695 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.35 (d, J = 6.1 Hz, 3 H), 2.12 (s, 3 H), 2.53 (d, J = 4.2 Hz, 1 H), 3.17 (dd, $J_1 = J_2$ = 9.2 Hz, 1 H), 3.39 (m, 1 H), 3.71 (td, J = 9.1 and 4.0 Hz, 1 H), 4.07 (ddt, J = 13.3, 7.3, and 1.3 Hz, 1 H), 4.32 (ddt, J = 13.3, 4.9, and 1.6 Hz, 1 H), 4.41 (d, J = 8.0 Hz, 1 H), 4.80 (ABq, J_{AB} = 11.2 Hz, $\Delta\nu_{AB}$ = 29 Hz, 2 H), 4.73 (dd, J = 9.5 and 7.9 Hz, 1 H), 5.18 (dq, J = 11.0 and 1.4 Hz, 1 H), 5.28 (dq, J = 17.2 and 1.7 Hz, 1 H), 5.86 (m, 1 H), 7.23–7.39 (comp m, 5 H); high-resolution mass spectrum (CI, NH_3) m/z 337.1664 [$(M + H)^+$, calcd for $C_{18}H_{25}O_6$ 337.1651]. Anal. Calcd for $C_{18}H_{24}O_6$: C, 64.25; H, 7.19. Found: C, 64.22; H, 6.97.

15β: $[\alpha]^{22}_D$ −21.6° (c 0.78, $CHCl_3$); IR ($CHCl_3$) 3600–3300 (m), 3080 (m), 3020 (m), 2940 (m), 2880 (m), 1740 (s), 1500 (w), 1455 (m), 1380 (m), 1240 (s), 1170 (m), 1075 (s), 995 (m), 940 (m), 700 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.34 (d, J = 6.2 Hz, 3 H), 2.07 (s, 3 H), 2.47 (d, J = 3.0 Hz, 1 H), 3.25 (dd, $J_1 = J_2$ = 9.3 Hz, 1 H), 3.40–3.58 (m, 2 H), 4.13 (ddt, J = 12.7, 6.4, and 1.2 Hz, 1 H), 4.38 (d, superimposed on m, J = 8.0 Hz, 1 H), 4.32–4.42 (m, 1 H), 4.63 (s, 2 H), 5.13 (dd, $J_1 = J_2$ = 9.4 Hz, 1 H), 5.22 (dq, J = 10.3 and 1.4 Hz, 1 H), 5.32 (dq, J = 17.3 and 1.5 Hz, 1 H), 5.91 (m, 1 H), 7.22–7.38 (comp m 5 H); high-resolution mass spectrum (CI, NH_3) m/z 337.1678 [$(M + H)^+$, calcd for $C_{18}H_{25}O_6$ 337.1651].

Mukaiyama Coupling of 15β with 33α. Under argon, a solution of **33α** (75 mg, 0.140 mmol) and **15β** (70 mg, 1.5 equiv) in methylene chloride (2.0 mL) containing a few activated 4Å molecular sieves was cooled to −20 °C and $BF_3{\cdot}OEt_2$ (20 μL, 1.16 equiv) was added dropwise. After 2 h at −20 °C, the reaction was warmed to room temperature for 5 h and then quenched with saturated $NaHCO_3$. The mixture was extracted three times with ether, and the combined extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (3:17) as eluant, gave 5 mg (5% yield) of the less polar disaccharide **13** and 54 mg (54% yield) of the more polar disaccharide **42**, both as oils.

13: $[\alpha]^{22}_D$ +8.3° (c 0.70, $CHCl_3$); IR ($CHCl_3$); IR ($CHCl_3$) 3020 (m), 2940 (m), 2870 (m), 1745 (s), 1500 (w), 1455 (w), 1370–1360 (m), 1240 (s), 1170 (m), 1075 (s), 790 (m), 700 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.30 (d, J = 6.3 Hz, 3 H), 1.32 (d, J = 6.9 Hz, 3 H), 1.77 (s, 3 H), 1.89 (s, 3 H), 3.18 (dd, $J_1 = J_2$ = 9.1 Hz, 1 H), 3.23 (dd, $J_1 = J_2$ = 9.1 Hz, 1 H), 3.28 (dd, J = 9.1 and 8.0 Hz, 1 H), 3.41 (m, 1 H), 3.51 (m, 1 H), 3.73 (dd, J = 9.1 and 8.0 Hz, 1 H), 4.12 (br dd, J = 13.0 and 5.6 Hz, 1 H), 4.42–4.60 (comp m, 7 H), 4.65 (d, J = 8.0 Hz, 1 H), 4.74 (d, J = 12.3 Hz, 1 H), 5.14 (dd, $J_1 = J_2$ = 9.1 Hz, 1 H), 5.18 (dd, J = 11.1 and 1.7 Hz, 1 H), 5.35 (dd, $J_1 = J_2$ = 9.2 Hz, 1 H), 5.38 (dd, J = 16.8 and 1.7 Hz, 1 H), 5.92 (m, 1 H), 7.30–7.43 (comp m, 15 H); high-resolution mass spectrum (FAB, NBA matrix) m/z 727.3045 [$(M + Na)^+$, calcd for $C_{40}H_{48}O_{11}Na$ 727.3094].

42: $[\alpha]^{22}_D$ +57.9° (*c* 0.62, $CHCl_3$); IR ($CHCl_3$) 3020 (m), 2940 (m), 2880 (m), 1750 (s), 1570 (w), 1500 (w), 1460 (m), 1380 (m), 1360 (m), 1240 (s), 1170 (m), 1080 (s), 1030 (s), 700 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.27 (d, J = 6.2 Hz, 3 H), 1.32 (d, J = 6.2 Hz, 3 H), 1.90 (s, 3 H), 1.98 (s, 3 H), 3.14 (dd, $J_1 = J_2$ = 9.0 Hz, 1 H), 3.21 (dd, $J_1 = J_2$ = 9.0 Hz, 1 H), 3.42 (dd, J = 9.0 and 3.9 Hz, 1 H), 3.49 (m, 1 H), 3.71 (dd, J = 9.0 and 7.9 Hz, 1 H), 3.82 (m, 1 H), 3.93 (br dd, J = 12.0 and 6.1 Hz, 1 H), 4.32 (br dd, J = 12.0 and 4.9 Hz, 1 H), 4.50–4.62 (comp m, 5 H), 4.57 (ABq, J_{AB} = 12.2 Hz, $\Delta\nu_{AB}$ = 46.5 Hz, 2 H), 5.19 (dd, J = 11.0 and 1.3 Hz, 1 H), 5.24 (dd, J = 17.0 and 1.3 Hz, 1 H), 5.31 (dd, $J_1 = J_2$ = 9.1 Hz, 1 H), 5.41 (dd, $J_1 = J_2$ = 9.1 Hz, 1 H), 5.50 (d, J = 3.9 Hz, 1 H), 5.92 (m, 1 H), 7.21–7.43 (comp m, 15 H); high-resolution mass spectrum (FAB, NBA matrix) m/z 727.3108 [$(M + Na)^+$, calcd for $C_{40}H_{48}O_{11}Na$ 727.3094].

Mukaiyama Coupling of 15α with 33α. A solution of **33α** (60 mg, 0.112 mmol) and **15α** (80 mg, 0.238 mmol, 2.1 equiv) in methylene chloride (1.0 mL) containing a few activated 4Å molecular sieves was cooled to −20 °C under argon, and $BF_3{\cdot}OEt_2$ (14 μL, 1 equiv) was introduced slowly. The reaction was stirred for 30 min and quenched with saturated $NaHCO_3$. The mixture was extracted twice with ether, and the combined extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (1:4) as eluant, afforded 42 mg (53% yield) of **43** as an oil: $[\alpha]^{22}_D$ +82.7° (*c* 1.11, $CHCl_3$); 3080 (w), 3010 (m), 2980 (m), 2930 (m), 2880 (m), 1750 (s), 1645 (w), 1500 (w), 1455 (m), 1360 (m), 1240 (s), 1070 (s), 700 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.23 (d, J = 6.2 Hz, 3 H), 1.29 (d, J = 6.3 Hz, 3 H), 1.97 (s, 3 H), 2.04 (s, 3 H), 3.13 (q, J = 9.4 Hz, 2 H), 3.43 (dd, J = 9.4 and 3.8 Hz, 1 H), 3.57 (dd, J = 9.3 and 3.8 Hz, 1 H), 3.93 (m, 2 H), 4.11 (ABxy, J_{AB} = 12.0 Hz, J_{AX} = 5.7 Hz, J_{AY} = 0.3 Hz, $\Delta\nu_{AB}$ = 24 Hz, 2 H), 4.58 (comp m, 6 H), 4.83 (d, J = 3.8 Hz, 1 H), 4.97 (d, J = 3.8 Hz, 1 H), 5.18 (dd, J = 12.0 and 1.2 Hz, 1 H), 5.31 (dd, J = 16.2 and 1.2 Hz, 1 H), 5.45–5.68 (m, 2 H), 5.92 (m, 1 H), 7.20–7.45 (comp m, 15 H); high-resolution mass spectrum (FAB, NBA matrix) m/z 727.3024 [$(M + Na)^+$, calcd for $C_{40}H_{48}O_{11}Na$ 727.3094].

Mukaiyama Coupling of 44α with Cholesterol. A mixture of **44α** (15 mg, 0.0212 mmol), cholesterol (16 mg, 2 equiv), a few activated 4Å molecular sieves, and methylene chloride (1.0 mL) was cooled to −20 °C under argon, and $BF_3{\cdot}OEt_2$ (5 μL, 2 equiv) was introduced dropwise. After 5 min, the reaction was quenched with saturated $NaHCO_3$. The mixture was extracted twice with ether, and the combined extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (1:19, then 1:9) as eluant, gave 16 mg (83% yield) of **45β** as an oil.

45β: ^1H NMR (250 MHz, $CDCl_3$) δ 0.70 (s, 3 H), 0.88 (d, J = 4.5 Hz, 6 H), 0.92 (d, J = 5.5 Hz, 3 H), 0.90–1.70 (comp m, 26 H), 1.03 (s, 3 H), 1.78–2.08 (comp m, 7 H), 2.37 (m, 2 H), 3.41–3.77 (comp m, 8 H), 4.50–4.64 (m, 3 H), 4.70–5.02 (comp m, 6 H), 5.35 (br d, J = 4.0 Hz, 1 H), 7.13–7.36 (comp m, 20 H).

Mukaiyama Coupling of 33α with Cholesterol. Under argon, a mixture of **33α** (50 mg, 0.090 mmol), cholesterol (70 mg, 2.0 equiv), a few activated 4Å molecular sieves, and methylene chloride (1.0 mL) was cooled to −20 °C, and $BF_3{\cdot}OEt_2$ (14 μL, 1.25 equiv) was added slowly. After 20 min, the reaction was quenched with saturated $NaHCO_3$. The mixture was extracted three times with ether, and the combined extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (7:93) as eluant, furnished 14 mg (21% yield) of the less polar **46β** and 27 mg (39% yield) of the more polar **46α**, both as solids.

46β: mp 161–162 °C; $[\alpha]^{22}_D$ +8.1° (*c* 1.36, $CHCl_3$); IR ($CHCl_3$) 3020 (m), 2940 (s), 2850 (m), 1745 (m), 1460 (m), 1450 (m), 1380 (m), 1330 (m), 1240 (s), 1070 (s), 700 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.68 (s, 3 H), 0.86 (d, J = 6.6 Hz, 3 H), 0.87 (d, J = 6.6 Hz, 3 H), 0.91 (d, J = 6.4 Hz, 3 H), 0.9–1.7 (comp m, 18 H), 1.03 (s, superimposed on m, 3 H), 1.25 (s, superimposed on m, 3 H), 1.32 (d, J = 6.2 Hz, 3 H), 1.88 (s, 3 H), 1.81–1.93 (m, 1 H), 1.95–2.05 (comp m, 4 H), 2.21–2.48 (m, 2 H), 3.15 (dd, $J_1 = J_2$ = 9.1 Hz, 1 H), 3.30 (dd, J = 9.1 and 7.9 Hz, 1 H), 3.45 (m, 1 H), 3.56 (m, 1 H), 4.50–4.65 (comp m, 3 H), 4.74 (ABq, J_{AB} = 12.2 Hz, $\Delta\nu_{AB}$ = 57 Hz, 2 H), 5.18 (dd, $J_1 = J_2$ = 9.1 Hz, 1 H), 5.35 (br m, 1 H), 7.22–7.38 (comp m, 10 H); high-resolution mass spectrum (CI, NH_3) m/z 755.5290 [$(M + H)^+$, calcd for $C_{49}H_{71}O_6$ 755.5250]. Anal. Calcd for $C_{49}H_{70}O_6$: C, 77.92; H, 9.35. Found: C, 77.77; H, 9.24.

46α: mp 153–154 °C; $[\alpha]^{22}_D$ +56.5° (*c* 0.96, $CHCl_3$); IR ($CHCl_3$) 3040 (w), 3010 (m), 2940 (s), 2880 (s), 1745 (s), 1470 (m), 1460 (m), 1380 (m), 1240 (s), 1075 (s), 1030 (s), 700 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.68 (s, 3 H), 0.86 (d, J = 6.6 Hz, 3 H), 0.87 (d, J = 6.6 Hz, 3 H), 0.90 (d, J = 6.4 Hz, 3 H), 0.90–1.10 (comp m, 22 H), 1.00 (s, superimposed on m, 3 H), 1.34 (d, J = 6.2 Hz, 3 H), 1.86 (m, 3 H), 1.90–2.05 (m, 1 H), 2.00 (s, superimposed on m, 3 H), 2.27 (br m, 1 H), 2.42 (br m, 1 H), 3.13 (dd, $J_1 = J_2$ = 9.1 Hz, 1 H), 3.32–3.45 (br m, 1 H), 3.42 (dd, superimposed on br m, J = 9.1 Hz, 1 H), 3.92 (m, 1 H), 4.59 (s, 4 H), 4.88 (d, J = 3.9 Hz, 1 H), 5.32 (br m, 1 H), 5.52 (dd, $J_1 = J_2$ = 9.1 Hz, 1 H), 7.22–7.38 (comp m, 10 H); high-resolution mass spectrum (CI, NH_3) m/z 755.5252 [$(M + H)^+$, calcd for $C_{49}H_{71}O_6$ 755.5250]. Anal. Calcd for $C_{49}H_{70}O_6$: C, 77.92; H, 9.35. Found: C, 77.73; H, 9.22.

Coupling of Chloro Sugar 26 with Cholesterol. Under argon, a solution of chloro sugar **26** (130 mg, 0.323 mmol) and cholesterol (250 mg, 2 equiv) in benzene (5.0 mL) was treated with $AgCO_3$ (excess) and $AgClO_4$ (catalytic amount) at room temperature. After 5 min, the mixture was filtered through a plug of silica, and the filtrate was concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (1:19, then 1:9, then 3:17) as eluant, gave 227 mg (94% yield) of products, determined to be a 3:1 mixture of **46α** and **46β** by 250-MHz ^1H NMR analysis.

3,5-Dinitropyridyl Derivatives (+)-48α and (+)-48β.[29] Under argon, a solution of the lactol (50 mg, 0.112 mmol) and 2-chloro-3,5-dinitropyridine (34 mg, 1.4 equiv) in methylene chloride (0.75 mL) and 2,6-lutidine (0.5 mL) at room temperature was treated with anhydrous KF (catalytic amount), DMAP (catalytic amount), and 18-crown-6 (catalytic amount). After stirring for 16 h at room temperature, the reaction mixture was diluted with ether, and the solution was washed twice with 8% HCl, washed with 2 N NaOH and brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (3:17) as eluant, gave 12 mg (17% yield) of **48α**, 10 mg (14% yield) of **48β**, and 22 mg (44% yield) of the lactol, all as oils.

48β: $[\alpha]^{22}_D$ +23.4° (*c* 0.8, $CHCl_3$); IR ($CHCl_3$) 3090 (w), 3060 (w), 3010 (m), 2920 (m), 2860 (m), 1610 (s), 1550 (m), 1455 (m), 1410 (m), 1345 (s), 1300 (m), 1240 (m), 1080 (s), 1020 (m), 830 (m), 695 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.31 (d, J = 6.2 Hz, 3 H), 3.32 (dd, $J_1 = J_2$ = 9.2 Hz, 1 H), 3.67 (m, 1 H), 3.78 (dd, $J_1 = J_2$ = 9.0 Hz, 1 H), 3.85 (dd, $J_1 = J_2$ = 8.8 Hz, 1 H), 4.67 (d, J = 11.2 Hz, 1 H), 4.86–5.01 (comp m, 5 H), 6.18 (d, J = 8.8 Hz, 1 H), 7.20–7.42 (comp m, 15 H), 9.05 (d, J = 2.3 Hz, 1 H), 9.27 (d, J = 2.3 Hz, 1 H); high-resolution mass spectrum (CI, NH_3) m/z 601.2040 (M^+, calcd for $C_{32}H_{31}N_3O_9$ 601.2060).

48α: $[\alpha]^{22}_D$ +147° (*c* 0.63, $CHCl_3$); IR ($CHCl_3$) 3080 (m), 3060 (m), 3020 (m), 3010 (m), 2920 (m), 2870 (m), 1610 (s), 1540 (m), 1530 (m), 1455 (m), 1410 (m), 1345 (s), 1310 (m), 1240 (m), 1075 (s), 950 (m), 830 (m), 695 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.25 (d, J = 6.2 Hz, 3 H), 3.26 (dd, $J_1 = J_2$ = 9.4 Hz, 1 H), 3.67 (dd, J = 9.4 and 3.4 Hz, 1 H), 4.05 (m, 1 H), 5.15 (dd, $J_1 = J_2$ = 9.4 Hz, 1 H), 4.60 (d, J = 12.0 Hz, 1 H), 4.72 (ABq, J_{AB} = 12.0 Hz, $\Delta\nu_{AB}$ = 26.7 Hz, 2 H), 4.87–5.00 (m, 3 H), 6.82 (d, J = 3.4 Hz, 1 H), 7.18–7.40 (comp m, 15 H), 9.05 (d, J = 1.6 Hz, 1 H), 9.13 (d, J = 1.6 Hz, 1 H); high-resolution mass spectrum (CI, NH_3) m/z 601.2089 (M^+, calcd for $C_{32}H_{31}N_3O_9$ 601.2060).

Lactol: IR ($CHCl_3$) 3600 (w), 3600–3300 (w), 3060 (m), 3010 (m), 2900 (m), 2860 (m), 1600 (w), 1500 (w), 1360 (m), 1240 (m), 1070 (s), 1030 (m), 1000 (m), 700 (s) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.24, 1.32 (diastereomers, d, d, J = 6.3 Hz, J = 6.3 Hz, 3 H), 3.00–3.70 (comp m, 4 H), 3.88–4.07 (m, 1 H), 4.60–5.13 (ABq and anomeric H's, comp m, 7 H), 7.25–7.42 (comp m, 15 H); high-resolution mass spectrum (CI, NH_3) m/z 417.2092 [$(M - OH)^+$, calcd for $C_{27}H_{29}O_4$ 417.2066].

Mukaiyama Coupling of 48α with Cholesterol. A mixture of **48α** (15 mg, 0.025 mmol), cholesterol (19 mg, 2 equiv), a few activated 4Å molecular sieves, and methylene chloride (2.0 mL) was cooled to −20 °C under argon, and $BF_3{\cdot}OEt_2$ (9 μL, 3 equiv) was introduced dropwise. After 10 min, the reaction was quenched with saturated $NaHCO_3$. The mixture was extracted twice with ether, and the combined extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (3:47) as eluant, gave 13 mg (56% yield) of products, which comprised a 2:1 mixture of **49β** and **49α** as determined by HPLC [ethyl acetate–hexane (1:19)].

49β: $[\alpha]^{22}_D$ +5.5° (*c* 0.2, $CHCl_3$); IR ($CHCl_3$) 3010 (m), 2940 (s), 2880 (m), 1600 (w), 1450 (w), 1330 (m), 1225 (m), 1070 (s), 790 (m), 700 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.68 (s, 3 H), 0.86 (d, J = 6.6 Hz, 3 H), 0.86 (d, J = 6.6 Hz, 3 H), 0.91 (d, J = 6.3 Hz, 3 H), 1.01 (s, 3 H), 0.90–1.70 (comp m, 20 H), 1.28 (d, J = 6.2 Hz, 3 H), 1.80–2.10 (comp m, 6 H), 2.28–2.45 (m, 2 H), 3.18 (dd, $J_1 = J_2$ = 9.4 Hz, 1 H), 3.39 (dq, J = 9.4 and 6.2 Hz, 1 H), 3.42 (dd, J = 9.4 and 7.8 Hz, 1 H), 3.58 (br m, 1 H), 3.60 (dd, superimposed on br m, $J_1 = J_2$ = 9.4 Hz, 1 H), 4.48 (d, J = 7.8 Hz, 1 H), 4.62 (d, J = 10.9 Hz, 1 H), 4.71 (d, J = 10.8 Hz, 1 H), 4.77 (d, J = 10.9 Hz, 1 H), 4.86 (d, J = 10.9 Hz, 1 H), 4.92 (d, J = 10.9 Hz, 1 H), 4.97 (d, J = 10.8 Hz, 1 H), 5.34 (br d, J = 5.0 Hz, 1 H), 7.22–7.38 (comp m, 15 H); high-resolution mass spectrum (FAB, NBA matrix) m/z 803.5604 [$(M + H)^+$, calcd for $C_{54}H_{75}O_5$ 803.5614].

49α: $[\alpha]^{22}_D$ +43.0° (*c* 0.1, $CHCl_3$); IR ($CHCl_3$) 3090 (w), 3010 (m), 2940 (s), 2860 (s), 1600 (w), 1500 (m), 1460 (m), 1380 (m), 1360 (m), 1240 (m), 1070 (s), 1030 (s), 700 (s) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.68 (s, 3 H), 0.86 (d, *J* = 6.6 Hz, 3 H), 0.87 (d, *J* = 6.6 Hz, 3 H), 0.91 (d, *J* = 6.3 Hz, 3 H), 1.03 (s, 3 H), 1.25 (d, *J* = 6.3 Hz, 3 H), 0.95–1.62 (comp m, 19 H), 1.68–2.07 (comp m, 7 H), 2.25 (br dd, *J* = 13.2 and 3.8 Hz, 1 H), 2.42 (m, 1 H), 3.12 (dd, $J_1 = J_2$ = 9.2 Hz, 1 H), 3.45 (br m, 1 H), 3.51 (dd, *J* = 9.2 and 3.9 Hz, 1 H), 3.53 (m, 1 H), 3.97 (dd, $J_1 = J_2$ = 9.2 Hz, 1 H), 4.61 (d, *J* = 10.8 Hz, 1 H), 4.65 (d, *J* = 11.9 Hz, 1 H), 4.73–4.85 (m, 3 H), 4.90 (d, *J* = 10.8 Hz, 1 H), 5.00 (d, *J* = 10.8 Hz, 1 H), 5.32 (br d, *J* = 5.0 Hz, 1 H), 7.24–7.39 (comp m, 15 H); high-resolution mass spectrum (FAB, NBA matrix) *m/z* 803.5638 [(M + H)$^+$, calcd for $C_{54}H_{75}O_5$ 803.5614].

Lactol 60. A solution of alcohol **59** (2.4 g, 8.16 mmol) in THF–2 N H_2SO_4 (60 mL, 2:1) was heated to 60 °C. After 48 h, the reaction was basified to pH 8 with saturated NH_4OH. After concentration in vacuo, the mixture was diluted with ethyl acetate, and the inorganic salts were removed by filtration and washing with ethyl acetate. The filtrate was then washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (7:3) as eluant, furnished 1.94 g (94% yield) of **60** as a thick syrup: IR ($CHCl_3$) 3580 (m), 3400 (m), 3010 (m), 2900 (m), 1450 (m), 1355 (m), 1225 (m), 1120 (s), 1070 (s), 695 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.28, 1.30 (diastereomers, d, d, *J* = 7.0, 6.5 Hz, 3 H), 2.77, 2.80 (diastereomers, d, d, *J* = 4.0, 4.0 Hz, 1 H), 3.10, 3.63 (diastereomers m, m, 1 H), 3.18–3.51 (comp m, 3 H), 3.81, 3.91 (diastereomers, d, dq, *J* = 3.8, *J* = 7.0 and 6.3 Hz, 1 H), 4.45, 4.51 (diastereomers, dd, d, $J_1 = J_2$ = 4.0, *J* = 3.1 Hz, 1 H), 4.83 (diastereomers, ABq, ABq, J_{AB} = 10.5, 10.4 Hz, $\Delta\nu_{AB}$ = 55, 50 Hz. 2 H), 5.18, 5.41 (diastereomers, m, m, 1 H), 7.31–7.42 (comp m, 5 H); chemical ionization mass spectrum (CI, NH_3) *m/z* 272.1485 [(M + NH_4)$^+$, calcd for $C_{13}H_{22}NO_5$ 272.1498].

Triacetate (+)-61. A solution of lactol **60** (0.162 g, 0.638 mmol) and DMAP (catalytic amount) in methylene chloride (5.0 mL) and pyridine (0.5 mL) at room temperature was treated with acetic anhydride (0.7 mL, excess). After 10 min, the reaction mixture was diluted with ether, washed twice with 4 N HCl, washed with saturated $NaHCO_3$ and brine, and dried over $MgSO_4$. Following concentration in vacuo, the product was purified by flash chromatography, with ethyl acetate–hexane (1:4) as eluant, to afford 0.196 g (81% yield) of **61** as a 2:1 mixture of α- and β-anomers. Recrystallization from ethyl acetate–hexane provided an analytically pure sample of the α-anomer: mp 132–133 °C; $[\alpha]^{22}_D$ +114° (*c* 0.51, $CHCl_3$); IR ($CHCl_3$) 3020 (m), 2950 (m), 1760 (s), 1375 (m), 1225 (s), 1090 (m), 1050 (m), 930 (m), 695 (m), cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.19 (d, *J* = 6.3 Hz, 3 H), 2.01 (s, 6 H), 2.16 (s, 3 H), 3.92 (dd, $J_1 = J_2$ = 8.7 Hz, 1 H), 3.92 (m, superimposed on dd, 1 H), 4.68 (ABq, J_{AB} = 10.2 Hz, $\Delta\nu_{AB}$ = 20.6 Hz, 2 H), 4.90 (dd, $J_1 = J_2$ = 9.4 Hz, 1 H), 5.05 (dd, *J* = 9.4 and 4.5 Hz, 1 H), 6.26 (d, *J* = 4.5 Hz, 1 H), 7.23–7.41 (comp m, 5 H); high-resolution mass spectrum (CI, NH_3) *m/z* 380.1441 (M$^+$, calcd for $C_{19}H_{24}O_8$ 380.1470). Anal. Calcd for $C_{19}H_{24}O_8$: C, 59.99; H, 6.36. Found: C, 60.16; H, 6.25.

Glycosyl Bromide (+)-54. A solution of **61** (1.20 g, 3.15 mmol) in methylene chloride (5.0 mL) was cooled to −6 °C and a 30% solution of HBr in acetic acid (2.5 mL) was added dropwise. After 30 min at −6 °C, the reaction mixture was diluted with chloroform, washed with cold water, saturated $NaHCO_3$, and cold water, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (3:17) as eluant, gave 1.03 g (81% yield) of **54** as a white crystalline solid: mp 82–84 °C; $[\alpha]^{25}_D$ +183° (*c* 2.56, $CHCl_3$); IR ($CHCl_3$) 3020 (m), 3005 (m), 2940 (m), 1750 (s), 1495 (m), 1380 (s), 1370 (s), 1235 (s), 1110 (s), 1045 (s), 895 (m), 690 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.22 (d, *J* = 6.3 Hz, 3 H), 1.98 (s, 3 H), 2.10 (s, 3 H), 4.01 (dd, $J_1 = J_2$ = 9.5 Hz, 1 H), 4.08 (m, 1 H), 4.71 (ABq, J_{AB} = 11.9 Hz, $\Delta\nu_{AB}$ = 25 Hz, 2 H), 4.77 (dd, *J* = 9.5 and 3.9 Hz, 1 H), 4.93 (dd, $J_1 = J_2$ = 9.5 Hz, 1 H), 6.62 (d, *J* = 3.9 Hz, 1 H), 7.23–7.41 (comp m, 5 H); high-resolution mass spectrum (CI, isobutane) *m/z* 401.0578 (M$^+$, calcd for $C_{17}H_{21}O_6Br$ 401.0515).

Cyclopentylidene Ketals (+)-62 and (−)63. A solution of lactol **60** (6.7 g, 26.4 mmol), 1,1-dimethoxycyclopentane (9.0 mL, excess), and camphorsulfonic acid (350 mg, catalytic amount) in THF (75 mL) was stirred at room temperature for 20 h and then heated to 60 °C for an additional 6 h. Pyridine (25 mL) was added, and the solution was concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (3:17) as eluant, furnished 5.48 g (65% yield) of **62** as a solid and 1.43 g (17% yield) of **63** as a thick oil.

62: mp 77.5 °C; $[\alpha]^{22}_D$ +30.0° (*c* 0.59, $CHCl_3$); IR ($CHCl_3$) 3560 (m), 3500–3400 (m), 3010 (m), 2985 (s), 2920 (s), 2870 (m), 1495 (w), 1450 (m), 1330 (s), 1170 (s), 850 (m), 690 (m), cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.33 (d, *J* = 6.3 Hz, 3 H), 1.68–1.81 (comp m, 6 H), 1.85–2.09 (m, 2 H), 2.23 (d, *J* = 5.1 Hz, 1 H), 3.37 (m, 1 H), 3.65 (dd, *J* = 6.3 and 5.4 Hz, 1 H), 3.84 (m, 1 H), 4.12 (dd, $J_1 = J_2$ = 5.0 Hz, 1 H), 4.75 (ABq, J_{AB} = 11.8 Hz, $\Delta\nu_{AB}$ = 37.5 Hz, 2 H), 5.47 (d, *J* = 4.9 Hz, 1 H), 7.30–7.41 (comp m, 5 H). Anal. Calcd for $C_{18}H_{24}O_5$: C, 67.48; H, 7.55. Found: C, 67.53; H, 7.46.

63: $[\alpha]^{22}_D$ −29.9° (*c* 1.57, $CHCl_3$); IR ($CHCl_3$) 3600–3500 (m), 3010 (s), 2890 (s), 1495 (w), 1451 (m), 1340 (m), 1110 (s), 1080–1060 (s), 1030 (s), 895 (m), 695 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.27 (d, *J* = 6.4 Hz, 3 H), 1.71 (comp m, 6 H), 1.80–2.03 (comp m, 2 H), 2.25 (d, *J* = 6.3 Hz, 1 H), 3.95 (dd, *J* = 7.0 and 3.4 Hz, 1 H), 4.09 (m, 1 H), 4.12 (d, superimposed on m, *J* = 3.4 Hz, 1 H), 4.60 (d, *J* = 3.9 Hz, 1 H), 4.65 (ABq, J_{AB} = 11.8 Hz, $\Delta\nu_{AB}$ = 61.6 Hz, 2 H), 5.95 (d, *J* = 3.9 Hz, 1 H), 7.31–7.45 (comp m, 5 H); high-resolution mass spectrum (CI, NH_3) *m/z* 338.1944 [(M + NH_4)$^+$, calcd for $C_{18}H_{28}NO_5$ 338.1967].

Acetate (+)-64. A solution of alcohol **62** (3.46 g, 10.8 mmol) and DMAP (catalytic amount) in methylene chloride (10 mL) and pyridine (4.0 mL) was treated with acetic anhydride (3.0 mL, excess). After 20 min, the mixture was concentrated in vacuo, and the product was purified by flash chromatography, with ethyl acetate–hexane (3:22) as eluant, to give 3.89 g (99% yield) of **64** as a white crystalline solid: mp 77–78 °C; $[\alpha]^{22}_D$ +54.6° (*c* 0.67, $CHCl_3$); IR ($CHCl_3$) 3010 (m), 2985 (m), 1740 (s), 1495 (w), 1455 (m), 1380 (m), 1250 (s), 1100 (s), 970 (m), 695 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.25 (d, *J* = 6.2 Hz, 3 H), 1.65–1.81 (comp m, 6 H), 1.90–2.17 (m, 2 H), 2.08 (s, 3 H), 3.71 (dd, $J_1 = J_2$ = 3.6 Hz, 1 H), 3.94 (m, 1 H), 4.13 (m, 1 H), 4.74 (ABq, J_{AB} = 12.2 Hz, $\Delta\nu_{AB}$ = 19.7 Hz, 2 H), 4.75–4.84 (comp m, 1 H), 5.51 (d, *J* = 5.0 Hz, 1 H), 7.26–7.34 (comp m, 5 H). Anal. Calcd for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23. Found: C, 66.27; H, 7.17.

Alcohols (−)-55β and (+)-55α. A solution of **64** (2.0 g, 5.53 mmol), freshly distilled allyl alcohol (6.0 mL, excess), and camphorsulfonic acid (catalytic amount) in benzene (60 mL) was heated to reflux (ca. 95 °C) with azeotropic removal of water (Dean Stark trap) for 27 h. The mixture was then cooled to room temperature, quenched with saturated $NaHCO_3$, and extracted with ether. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ether–hexane (3:7) as eluant, afforded 0.850 g (46% yield) of the less polar **55β**, 0.647 g (35% yield) of the more polar **55α**, and 0.30 g (16% yield) of a mixture of the anomers, which were rechromatographed later.

55β: mp 57–58 °C; $[\alpha]^{25}_D$ −43.7° (*c* 5.9, $CHCl_3$); IR ($CHCl_3$) 3600 (w), 3010 (m), 2950–2800 (m), 1745 (s), 1495 (w), 1455 (m), 1385 (m), 1240 (s), 1170 (m), 1065 (s), 1030 (s), 940 (m), 695 (w) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.20 (d, *J* = 6.2 Hz, 3 H), 1.97 (s, 3 H), 2.70 (d, *J* = 2.0 Hz, 1 H), 3.43 (m, 1 H), 3.52 (dd, $J_1 = J_2$ = 9.3 Hz, 1 H), 3.63 (ddd, *J* = 9.3, 9.3, and 2.0 Hz, 1 H), 4.13 (ddd, *J* = 11.2, 6.4, and 0.3 Hz, 1 H), 4.32 (d, *J* = 7.6 Hz, 1 H), 4.38 (m, 1 H), 4.77 (ABq, J_{AB} = 12.2 Hz, $\Delta\nu_{AB}$ = 35 Hz, 2 H), 4.81 (dd, $J_1 = J_2$ = 8.5 Hz, 1 H), 5.23 (dd, *J* = 10.2 and 1.3 Hz, 1 H), 5.32 (dd, *J* = 15.7 and 1.5 Hz, 1 H), 5.86–6.02 (m, 1 H), 7.22–7.37 (comp m, 5 H). Anal. Calcd for $C_{18}H_{24}O_8$: C, 64.27; H, 7.19. Found: C, 64.36; H, 7.14.

55α: mp 80.5–81.5 °C; $[\alpha]^{25}_D$ +109° (*c* 3.92, $CHCl_3$); IR ($CHCl_3$) 3560 (w), 3005 (m), 2980 (m), 2900 (m), 1740 (s), 1495 (w), 1450 (m), 1380 (m), 1240 (s), 1140 (m), 1080 (s), 930 (m), 695 (w) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.15 (d, *J* = 6.3 Hz, 3 H), 1.99 (s, 3 H), 2.18 (d, *J* = 8.4 Hz, 1 H), 3.65–3.87 (m, 3 H), 4.07 (ddd, *J* = 12.8, 6.2, and 1.0 Hz, 1 H), 4.23 (dd, *J* = 12.8, 6.2, and 1.0 Hz, 1 H), 4.78 (ABq, J_{AB} = 11.7 Hz, $\Delta\nu_{AB}$ = 40 Hz, 2 H), 4.81 (dd, $J_1 = J_2$ = 7.7 Hz, 1 H), 4.91 (d, *J* = 3.5 Hz, 1 H), 5.25 (dd, *J* = 10.2 and 1.2 Hz, 1 H), 5.34 (dd, *J* = 15.7 and 1.4 Hz, 1 H), 5.86–6.02 (m, 1 H), 7.25–7.42 (comp m, 5 H). Anal. Calcd for $C_{18}H_{24}O_8$: C, 64.27; H, 7.19. Found: C, 64.32; H, 7.17.

Koenigs–Knorr Coupling of 55α and 54. Under argon, a mixture of **55α** (0.395 g, 1.18 mmol), **54** (0.590 g, 1.25 equiv), 4Å molecules sieves (0.5 g, crushed), and benzene–nitromethane (6.0 mL, 1:1) at room temperature was treated with $Hg(CN)_2$ (0.744 g, 2.0 equiv). After 1 h, the mixture was filtered through a Celite pad, and the precipitates were washed with ether. The solvent was removed in vacuo, and the product was purified by flash chromatography, with ether–hexane (7:13) as eluant, to give 0.563 g (73% yield) of **53α** and 0.093 g (12% yield) of **65**, both as solids.

53α: mp 137–139 °C; $[\alpha]^{22}_D$ +20.0° (*c* 2.6, $CHCl_3$); IR ($CHCl_3$) 3030 (s), 3020 (m), 3010 (m), 2980 (m), 2930 (m), 2870 (m), 1750 (s), 1645 (w), 1495 (m), 1455 (m), 1375 (s), 1305 (s), 1350–1330 (s), 1180 (s), 1120 (s), 1100–1020 (s), 930 (m), 910 (m), 890 (m), 690 (m), 650 (m), 595 (m), 550 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.11 (d, *J* = 6.3 Hz, 3 H), 1.21 (d, *J* = 6.3 Hz, 3 H), 1.76 (s, 3 H), 1.85 (s, 3 H), 1.99 (s, 3 H), 3.45 (m, 1 H), 3.63 (dd, $J_1 = J_2$ = 9.4 Hz, 1 H), 3.67 (dd, *J* = 9.4 and 3.4 Hz, 1 H), 3.85 (m, 1 H), 3.87 (dd, $J_1 = J_2$ = 9.4 Hz, 1 H), 4.01–4.23 (m, 2 H), 4.58 (s, 2 H), 4.62 (ABq, J_{AB} = 11.9 Hz, $\Delta\nu_{AB}$ = 65 Hz. 2 H), 4.63 (d, *J* = 9.4 Hz, 1 H), 4.72 (dd, $J_1 = J_2$ = 9.4 Hz, 1 H), 4.91 (dd, $J_1 = J_2$ = 9.4 Hz, 1 H), 4.98 (d, *J* = 3.4 Hz, 1 H),

5.12–5.27 (m, 2 H), 5.33 (dd, J = 15.3 and 1.3 Hz, 1 H), 5.86–6.03 (m, 1 H), 7.18–7.38 (comp m, 10 H). Anal. Calcd for $C_{35}H_{44}O_{12}$: C, 64.01; H, 6.75. Found: C, 64.26; H, 6.79.

65: mp 108–110 °C; $[\alpha]^{20}_D$ +135° (c 1.4, $CHCl_3$); IR ($CHCl_3$) 3010 (m), 2980 (m), 2920 (m), 2900 (m), 2860 (w), 1745 (s), 1495 (w), 1450 (m), 1370 (m), 1230 (s), 1120 (m), 1070 (m), 1045 (s), 980 (m), 930 (m), 690 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.98 (d, J = 6.2 Hz, 3 H), 1.14 (d, J = 6.2 Hz, 3 H), 1.89 (s, 3 H), 1.97 (s, 3 H), 2.08 (s, 3 H), 3.71–4.01 (comp m, 6 H), 4.18 (ddd, J = 10.5, 6.0, and 0.3 Hz, 1 H), 4.60 (d, J = 11.2 Hz, 1 H), 4.68 (d, J = 4.2 Hz, 1 H), 4.71–4.86 (comp m, 5 H), 4.95 (d, J = 3.3 Hz, 1 H), 5.20–5.29 (m, 2 H), 5.35 (dd, J = 15.3 and 1.3 Hz, 1 H), 5.83–6.01 (m, 1 H), 7.21–7.40 (comp m, 10 H); high-resolution mass spectrum (FAB, NBA matrix) m/z 657.2874 [$(M + H)^+$, calcd for $C_{35}H_{45}O_{12}$ 657.2920]. Anal. Calcd for $C_{35}H_{44}O_{12}$: C, 64.01; H, 6.75. Found: C, 63.86; H, 6.75.

Koenigs–Knorr Coupling of 55β and 54. Under argon, a mixture of **54** (1.19 g, 2.98 mmol), **55β** (1.5 g, 1.5 equiv), 4Å molecular sieves (0.8 g, crushed), and benzene–nitromethane (16 mL, 1:1) at room temperature was treated with $Hg(CN)_2$ (1.13 g, 1.5 equiv). After 1 h, the mixture was filtered through a Celite pad, the precipitates were washed with ether, and the filtrates were concentrated in vacuo. Flash chromatography, with ether–hexane (3:7, then 1:3, and 2:3) as eluant, gave 1.46 g (75% yield) of **53β** and 604 mg of recovered **55β**. Recrystallization from ethyl acetate–hexane provided colorless crystals: mp 150–152 °C; $[\alpha]^{23}_D$ −41.2° (c 2.5, $CHCl_3$); IR ($CHCl_3$) 3010 (m), 2995 (w), 2880 (w), 1750 (s), 1496 (w), 1455 (m), 1375 (m), 1230 (s), 1180 (m), 1080 (s), 1060 (s), 930 (w), 910 (w), 690 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.17 (d, J = 6.4 Hz, 3 H), 1.22 (d, J = 6.3 Hz, 3 H), 1.77 (s, 3 H), 1.85 (s, 3 H), 2.00 (s, 3 H), 3.33–3.50 (comp m, 2 H), 3.52–3.71 (m, 3 H), 4.11 (ddd, J = 12.5, 6.0 and 3.0 Hz, 1 H), 4.37–4.65 (comp m, 5 H), 4.77 (d, J = 9.0 Hz, 1 H), 4.70–4.94 (comp m, 3 H), 5.08 (dd, J = 9.3 and 8.5 Hz, 1 H), 5.22 (dd, J = 10.3 and 1.2 Hz, 1 H), 5.35 (dd, J = 15.5 and 1.2 Hz, 1 H), 5.86–6.02 (m, 1 H), 7.02–7.42 (comp m, 10 H). Anal. Calcd for $C_{35}H_{44}O_{12}$: C, 64.01; H, 6.75. Found: C, 63.92; H, 6.77.

Lactol (+)-52. To a solution of **53α** (1.1 g, 1.68 mmol) in acetic acid (7.0 mL) and water (8 drops) at room temperature were added $PdCl_2$ (453 mg) and NaOAc (453 mg). After 18 h at room temperature, the mixture was concentrated in vacuo. The residual solid was dissolved in ethyl acetate, and the solution was washed three times with saturated $NaHCO_3$, washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (7:13) as eluant, gave 930 mg (89% yield) of **52** as a solid. Similar treatment of disaccharide **53β** afforded **52** in 84% yield. Recrystallization from ethyl acetate–hexane afforded white needles: mp 171–172 °C $[\alpha]^{22}_D$ +4.1° (c 0.41, $CHCl_3$); IR ($CHCl_3$) 3600–3400 (w), 3010 (m), 2890 (w), 2870 (w), 1750 (s), 1495 (w), 1450 (m), 1375 (m), 1230 (s), 1170 (m), 1070 (s), 790 (m), 695 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.15 (d, J = 6.3 Hz, 3 H), 1.21 (d, J = 6.3 Hz, 3 H), 1.79 (s, 3 H), 1.91 (s, 3 H), 2.00 (s, 3 H), 3.10 (br d, J = 2.0 Hz, 1 H), 3.46 (m, 1 H), 3.62 (dd, J_1 = J_2 = 9.4 Hz, 1 H), 3.73 (dd, J = 9.4 and 3.4 Hz, 1 H), 3.85 (dd, J_1 = J_2 = 9.4 Hz, 1 H), 4.06 (m, 1 H), 4.47–4.81 (comp m, 6 H), 4.91 (dd, J_1 = J_2 = 9.5 Hz, 1 H), 5.11 (dd, J = 9.5 and 8.1 Hz, 1 H), 5.31 (br d, J = 1.9 Hz, 1 H), 7.21–7.40 (comp m, 10 H). Anal. Calcd for $C_{32}H_{40}O_{12}$: C, 62.32; H, 6.54. Found: C, 62.36; H, 6.53.

(+)-Phyllanthose Peracetate (7). (a) Via Phyllanthose (5). A solution of lactol **52** (300 mg, 0.487 mmol) in methanol (10 mL) at room temperature was treated with sodium methoxide (catalytic). After 18 h, the reaction was quenched with saturated NH_4Cl. The mixture was extracted with ethyl acetate, and the combined extracts were dried over $MgSO_4$ and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (1:1, then 3:2, then 3:1) as eluant, furnished 230 mg (96% yield) of 66. A suspension of 10% Pd/C (catalyst amount) in ethanol (2.0 mL) was flushed with hydrogen at room temperature, and a solution of 66 (45 mg, 0.09 mmol) in ethanol (3.0 mL) was then added. After stirring for 4 h under a hydrogen atmosphere, the mixture was filtered through a Celite pad, and the filtrate was concentrated in vacuo, affording 28 mg (98% yield) of crude phyllanthose (**5**). For ease of characterization, phyllanthose was peracetylated; crude phyllanthose (28 mg, 0.090 mmol) and DMAP (catalytic amount) were dissolved in pyridine (1.0 mL), and acetic anhydride (3 drops, excess) was added. After 6 h at room temperature, the reaction was quenched with saturated $NaHCO_3$. The mixture was extracted three times with ethyl acetate, and the combined extracts were washed twice with 5% HCl, washed with brine, and dried over $MgSO_4$. The solvent was removed in vacuo, affording 32 mg (62% for two steps) of crude phyllanthose peracetate (**7**). Recrystallization from acetone–hexane afforded pure **7** as a colorless solid: mp 225–226 °C; $[\alpha]^{22}_D$ +64.1° (c 0.8, $CHCl_3$); IR ($CHCl_3$) 3005 (m), 1755 (s), 1430 (w), 1375 (m), 1250 (s), 1220 (s), 1130 (w), 1060 (m), 1030 (m), 785 (w) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.17 (d, J = 6.2 Hz, 3 H), 1.21 (d, J = 6.3 Hz, 3 H), 1.98 (s, 3 H), 2.00 (s, 3 H), 2.03 (s, 3 H), 2.05 (s, 3 H), 2.07 (s, 3 H), 2.16 (s, 3 H), 3.55 (m, 1 H), 3.85 (dd, J = 9.9 and 3.8 Hz, 1 H), 3.92 (m, 1 H), 4.55 (d, J = 7.9 Hz, 1 H), 4.78 (q, J = 9.5 Hz, 2 H), 4.88 (dd, J = 9.7 and 8.0 Hz, 1 H), 5.08 (dd, J_1 = J_2 = 9.4 Hz, 1 H), 5.37 (dd, J_1 = J_2 = 9.8 Hz, 1 H), 6.21 (d, J = 3.8 Hz, 1 H); high-resolution mass spectrum (CI, NH_3) m/z 580.2234 [$(M + NH_4)^+$, calcd for $C_{24}H_{38}NO_{15}$ 580.2230].

(+)-Phyllanthose Peracetate (7). (b) Via Hydrogenolysis of 52 and Acetylation. A solution of **53α** (68 mg, 0.104 mmol) in acetic acid (2.0 mL) and water (0.2 mL) at room temperature was treated with $PdCl_2$ (70 mg) and NaOAc (70 mg). After 22 h the mixture was concentrated in vacuo. The residual solid was dissolved in ethyl acetate, and the solution was washed three times with saturated $NaHCO_3$, washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Crude **52**, obtained as an oil in this fashion, was dissolved in ethyl acetate (2.0 mL) and 10% Pd/C (catalytic amount) was added. After flushing the flask three times with hydrogen, the mixture was stirred for 24 h at room temperature under an atmosphere of hydrogen. The mixture was then diluted with ether and filtered through a Celite pad, and the filtrate was concentrated in vacuo. The resultant oil was then dissolved in methylene chloride (2.0 mL) and pyridine (0.5 mL), and acetic anhydride (excess) was added. After 1 h at room temperature, the reaction was quenched with saturated $NaHCO_3$. The mixture was extracted three times with ethyl acetate, and the combined extracts were washed twice with 5% HCl, washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (3:7, then 2:3) as eluant, afforded 22 mg (37%, 3 steps) of **7** as a colorless solid.

Glycosyl Esters (+)-57α and (+)-57β. Under argon, a solution of lactol **52** (110 mg, 0.179 mmol) and DMAP (catalytic amount) in methylene chloride (2.0 mL) and triethylamine (0.5 mL) at room temperature was treated with acid chloride **9** (21 mg, 0.067 mmol) in methylene chloride (2.0 mL). After stirring overnight at room temperature, the mixture was diluted with ether, washed twice with 2 N HCl, washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (3:7) as eluant, afforded 38 mg (64% yield) of the less polar **57α**, 7.6 mg (13% yield) of the more polar **57β**, and 1.3 mg of recovered **52**, all as oils.

57α: $[\alpha]^{22}_D$ +55.7° (c 0.9, $CHCl_3$); IR ($CHCl_3$) 3020 (m), 2930 (m), 1750 (s), 1725 (s), 1460 (m), 1375 (m), 1240 (s), 1160 (m), 1070 (s), 1030 (m), 970 (m), 940 (m), 920 (m), 700 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.01 (d, J = 6.6 Hz, 3 H), 1.13 (d, J = 6.3 Hz, 3 H), 1.15 (d, J = 5.8 Hz, 3 H), 1.20–1.41 (comp m, 4 H), 1.62–1.80 (m, 1 H), 1.74 (s, superimposed on m, 3 H), 1.94 (s, 3 H), 1.99 (s, 3 H), 2.07 (m, 1 H), 2.32–2.48 (m, 3 H), 2.55–2.71 (m, 2 H), 3.10 (ABq, J_{AB} = 5.1 Hz, $\Delta\nu_{AB}$ = 19.7 Hz, 2 H), 3.41 (m, 1 H), 3.58 (dd, J_1 = J_2 = 9.4 Hz, 1 H), 3.78–3.92 (comp m, 5 H), 4.45 (m, 1 H), 4.55–4.62 (comp m, 4 H), 4.75–4.88 (m, 3 H), 5.02 (dd, J = 9.5 and 8.1 Hz, 1 H), 6.23 (d, J = 3.4 Hz, 1 H), 7.15–7.39 (comp m, 10 H); high-resolution mass spectrum (CI, isobutane) m/z 895.3813 [$(M + H)^+$, calcd for $C_{47}H_{59}O_{17}$ 895.3752].

57β: $[\alpha]^{22}_D$ +37.5° (c 0.82, $CHCl_3$); IR ($CHCl_3$) 3020 (m), 2990 (m), 2880 (m), 1750 (s), 1490 (w), 1450 (m), 1370 (m), 1230 (s), 1160 (m), 1070 (s), 990 (m), 970 (m), 940 (m), 900 (w), 695 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.96 (d, J = 6.6 Hz, 3 H), 1.15 (d, J = 6.1 Hz, 3 H), 1.16 (d, J = 6.0 Hz, 3 H), 1.25–1.41 (m, 2 H), 1.62–1.78 (m, 2 H), 1.81–2.22 (m, 2 H), 1.98 (s, 6 H), 2.01 (s, 3 H), 2.23–2.50 (m, 3 H), 2.51–2.72 (m, 2 H), 3.07 (ABq, J_{AB} = 5.0 Hz, $\Delta\nu_{AB}$ = 16.7 Hz, 2 H), 3.37 (m, 1 H), 3.51–3.68 (comp m, 4 H), 3.73 (dd, J_1 = J_2 = 9.2 Hz, 1 H), 3.88 (m, 1 H), 4.40 (m, 1 H), 4.51–4.62 (m, 3 H), 4.75–4.87 (comp m, 4 H), 4.97 (dd, J_1 = J_2 = 9.2 Hz, 1 H), 5.57 (d, J = 8.0 Hz, 1 H), 7.21–7.42 (comp m, 10 H); high-resolution mass spectrum (CI, NH_3) m/z 895.3832 [$(M + H)^+$, calcd for $C_{47}H_{59}O_{17}$ 895.3752].

Mitsunobu Coupling of 52 and Benzoic Acid. To a solution of lactol **52** (36 mg, 0.058 mmol) in THF (1.0 mL) at room temperature under argon were added benzoic acid (15 mg, 1.5 equiv), triphenylphosphine (23 mg, 1.5 equiv), and diethyl azodicarboxylate (0.014 mL, 1.5 equiv). After 1 h, the solvent was removed in vacuo, and the product was purified by flash chromatography, with ethyl acetate–hexane (1:3) as eluant, to give 41 mg (95% yield) of **67** as a white crystalline solid: mp 166–167 °C; $[\alpha]^{22}_D$ −11.5° (c 0.59, $CHCl_3$); IR ($CHCl_3$) 3020 (m), 2980 (w), 2920 (w), 2850 (w), 1745 (s), 1600 (w), 1490 (w), 1450 (m), 1370 (m), 1260 (m), 1230 (s), 1170 (m), 1060 (s), 900 (w), 705 (m), 690 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.02 (d, J = 6.3 Hz, 3 H), 1.21 (d, J = 6.3 Hz, 3 H), 1.87 (s, 3 H), 1.93 (s, 3 H), 1.95 (s, 3 H), 3.18 (m, 1 H), 3.55 (dd, J_1 = J_2 = 9.3 Hz, 1 H), 3.67 (m, 1 H), 3.71 (dd, J_1 = J_2 = 9.3 Hz, 1 H), 4.01 (dd, J = 9.3 and 8.1 Hz, 1 H), 4.52 (d, J = 2.6 Hz, 2 H), 4.60 (d, J = 9.4 Hz, 1 H), 4.72–5.03 (comp m, 5 H), 5.85 (d, J = 8.1 Hz, 1 H), 7.17–7.40 (comp m, 10 H), 7.47 (t, J = 6.5 Hz, 2 H), 7.61 (t, J = 6.5, 1 H), 8.15 (dd, J = 6.5 and 1.0 Hz, 2 H); high-resolution

mass spectrum (CI, NH_3) m/z 721.2870 [$(M + H)^+$, calcd for $C_{39}H_{45}O_{13}$ 721.2860].

Mitsunobu Coupling of 68 and Cyclohexanecarboxylic Acid. Under argon, a solution of triphenylphosphine (31 mg, 1.5 equiv) and diisopropyl azodicarboxylate (0.023 mL, 1.5 equiv) in THF (0.2 mL) was cooled to −50 °C, and lactol **68** (50 mg, 0.079 mmol) and cyclohexanecarboxylic acid (12 mg, 1.2 equiv) were added. Over a period of 2 h the mixture was warmed to room temperature. Following concentration in vacuo, the product was purified by flash chromatography, with ethyl acetate–hexane (1:1) as eluant, to give 49.6 mg (85% yield) of **69** as an oil: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.23–2.22 (comp m, 12 H), 1.99 (s, 3 H), 2.01 (s, 3 H), 2.02 (s, 3 H), 2.02 (s, 3 H), 2.07 (s, 3 H), 2.11 (s, 3 H), 2.12 (s, 3 H), 2.35 (m, 1 H), 3.69 (m, 1 H), 3.88 (dd, J = 9.0 and 8.0 Hz, 1 H), 4.06 (br d, J = 11.7 Hz, 2 H), 4.31 (m, 2 H), 4.66 (d, J = 8.1 Hz, 1 H), 4.90 (dd, $J_1 = J_2$ = 9.1 Hz, 1 H), 5.01 (td, J = 9.6 and 2.1 Hz, 1 H), 5.13 (dd, $J_1 = J_2$ = 9.3 Hz, 1 H), 5.23 (dd, $J_1 = J_2$ = 9.3 Hz, 1 H), 5.64 (d, J = 8.0 Hz, 1 H). Anal. Calcd for $C_{33}H_{46}O_{19}$: C, 53.06; H, 6.21. Found: C, 53.02; H, 6.28.

Mitsunobu Coupling of 70 and Cyclohexanecarboxylic Acid. A solution of triphenylphosphine (40 mg, 1.5 equiv) and diisopropyl azodicarboxylate (0.03 mL, 1.5 equiv) in THF (0.2 mL) was cooled to −50 °C under argon, and lactol **70** (62 mg, 0.099 mmol) and cyclohexanecarboxylic acid (26 mg, 2 equiv) were added. The reaction mixture was warmed to room temperature for 2 h and then concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (1:4) as eluant, gave 46.4 mg (64% yield) of **71** as an oil: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.22 (d, superimposed on m, J = 6.1 Hz, 3 H), 1.26 (d, superimposed on m, J = 6.2 Hz, 3 H), 1.21–1.28 (m, 3 H), 1.33–1.79 (comp m, 7 H), 1.96 (m, 1 H), 1.99 (s, 3 H), 2.03 (s, 3 H), 2.34 (m, 1 H), 3.58–3.73 (m, 2 H), 3.89 (dd, J = 9.3 and 8.1 Hz, 1 H), 3.89–4.12 (m, 5 H), 4.66–4.92 (comp m, 4 H), 5.16 (dd, $J_1 = J_2$ = 9.5 Hz, 1 H), 5.25 (dd, $J_1 = J_2$ = 9.4 Hz, 1 H), 5.61 (d, J = 8.1 Hz, 1 H).

Mitsunobu Coupling of 72 and Benzoic Acid. Under argon, a solution of triphenylphosphine (180 mg, 1.5 equiv) and diisopropyl azodicarboxylate (0.14 mL, 1.5 equiv) in THF (2.0 mL) was cooled to −50 °C, followed by addition of lactol **72** (25 mg, 0.463 mmol) and benzoic acid (73 mg, 1.3 equiv). The reaction mixture was warmed to room temperature for 2 h, the solvent was removed in vacuo, and the product was purified by flash chromatography, with ethyl acetate–hexane (1:5) as eluant, to give 160 mg (54% yield) of glycosyl esters **73** as an oil. The anomer ratio was determined to be 4:1 (β:α) by ^{1}H NMR: ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.64–4.14 (comp m, 6 H), 4.45–5.02 (comp m, 8 H), 5.89, 6.61 (diastereomers, dd, d, J = 5.6 and 2.1 Hz, J = 3.5 Hz, 1 H), 7.14–7.63 (comp m, 23 H), 8.07 (m, 2 H); high-resolution mass spectrum (CI, NH_3) m/z 662.3132 [$(M + NH_4)^+$, calcd for $C_{41}H_{44}NO_7$ 662.3118].

Mitsunobu Coupling of 74 and Benzoic Acid. A solution of triphenylphosphine (1 g, 1.3 equiv) and diisopropyl azodicarboxylate (0.74 mL, 1.3 equiv) in THF (7.0 mL) was cooled to −50 °C under argon, and lactol **74** (1 g, 2.87 mmol) and benzoic acid (460 mg, 1.5 equiv) were added. The reaction mixture was warmed to room temperature for 2 h and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (1:3) as eluant, furnished 660 mg (51% yield) of glycosyl esters **75** as an oil. The anomer ratio was determined to be 4:1 (β:α) by ^{1}H NMR: ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.04 (s, 3 H), 2.08 (s, 3 H), 2.10 (s, 3 H), 2.22, 2.28 (diastereomers, s, s, 3 H), 3.90–4.39 (m, 3 H), 5.24 (dd, J = 9.9 and 3.3 Hz, 1 H) 5.36 (dd, $J_1 = J_2$ = 9.6 Hz, 1 H), 5.47, 5.63 (diastereomers, m, 1 H), 6.12, 6.36 (diastereomers, d, d, J = 0.93 Hz, J = 1.4 Hz, 1 H), 7.41–7.36 (comp m, 3 H), 7.96, 8.08 (diastereomers, d, d, J = 7.3 Hz, J = 7.1 Hz, 2 H); high-resolution mass spectrum (CI, NH_3) m/z 470.1715 [$(M + NH_4)^+$, calcd for $C_{21}H_{28}NO_{11}$ 470.1662].

Mitsunobu Coupling of 76 and Cyclohexanecarboxylic Acid. Under argon, a solution of triphenylphosphine (400 mg, 1.5 equiv) and diisopropyl azodicarboxylate (0.3 mL, 1.5 equiv) in THF (5.0 mL) was cooled to −40 °C, followed by addition of lactol **76** (650 mg, 1.02 mmol) and cyclohexanecarboxylic acid (170 mg, 1.3 equiv). The mixture was warmed to room temperature for 12 h and then concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (2:3) as eluant, gave 480 mg (63% yield) of glycosyl esters **77** as an oil. The anomer ratio was determined to be 4.5:1 (β:α) by ^{1}H NMR: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.17–2.40 (comp m, 11 H), 1.97 (s, 3 H), 2.02 (s, 3 H), 2.05 (s, 3 H), 2.06 (s, 3 H), 2.07 (s, 3 H), 2.12 (s, 3 H), 2.16 (s, 3 H), 3.73–3.91 (m, 3 H), 3.97–4.18 (m, 3 H), 4.43–4.52 (m, 2 H), 4.92–5.35 (comp m, 4 H), 5.25, 5.46 (diastereomers, dd, dd, $J_1 = J_2$ = 9.0 Hz, $J_1 = J_2$ = 9.7 Hz, 1 H), 5.67, 6.27 (diastereomers, d, d, J = 8.2 Hz, J = 3.7 Hz, 1 H). Anal. Calcd for $C_{33}H_{46}O_{19}$: C, 53.06; H, 6.21. Found: C, 52.91; H, 6.18.

Mitsunobu Coupling of 78 and Benzoic Acid. A solution of triphenylphosphine (1.0 g, 1.5 equiv) and diisopropyl azodicarboxylate (0.74 mL, 1.5 equiv) in THF (6.0 mL) was cooled to −50 °C under argon, and lactol **76** (1 g, 2.87 mmol) and benzoic acid (460 mg, 1.3 equiv) were added. The reaction mixture was warmed to room temperature for 12 h and then concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (1:4) as eluant, gave 1.04 g (80% yield) of glycosyl esters **79** as an oil. The anomer ratio was determined to be 4:1 (β:α) by ^{1}H NMR: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.94, 1.97 (diastereomers, s, s, 3 H), 1.99 (s, 3 H), 2.00 (s, 3 H), 2.02 (s, 3 H), 3.88–4.32 (comp m, 3 H), 5.11–6.55 (comp m, 4 H), 7.27–7.60 (comp m, 3 H), 7.97–8.06 (m, 2 H); high-resolution mass spectrum (CI, NH_3) m/z 470.1693 [$(M + NH_4)^+$, calcd for $C_{21}H_{28}NO_{11}$ 470.1662]. Anal. Calcd for $C_{21}H_{24}O_{11}$: C, 55.74; H, 5.35. Found: C, 55.84; H, 5.40.

Mitsunobu Coupling of 52 and 80. To a solution of lactol **52** (35 mg, 0.086 mmol) in THF (0.73 mL) at room temperature under argon were added aglycon acid **80** (25 mg, 1.5 equiv), triphenylphosphine (23 mg, 1.5 equiv), and diethyl azodicarboxylate (0.014 mL, 1.5 equiv). After 1 h, the mixture was concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (7:13) as eluant, gave 45 mg (90% yield) of **57β** as a thick oil.

Mitsunobu Coupling of 66 and 80. To a solution of lactol 66 (22 mg, 0.045 mmol) in THF (1.0 mL) at room temperature under argon were added aglycon acid **80** (16 mg, 1.2 equiv), triphenylphosphine (9 mg, 1.2 equiv), and diisopropyl azodicarboxylate (0.011 mL, 1.3 equiv). After 30 min, the mixture was concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (2:3, then 1:1, then 3:2) as eluant, furnished 14 mg (40% yield) of the glycosyl esters (**81β**:**81α**) and 7 mg (32% yield) of recovered 66, all as oils.

Acetylation of 81β and 81α. Under argon, a solution of triols **81β** and **81α** (14 mg, 0.018 mmol) and DMAP (catalytic amount) in methylene chloride (1.0 mL) at room temperature was treated with triethylamine (10 μL, excess) and acetic anhydride (10 μL). The reaction mixture was stirred for 3 h and then concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (3:7) as eluant, afforded 4.3 mg (26% yield) of the less polar **57α** and 8.7 mg (53% yield) of **57β**, both as oils.

Enol Ether 82α. A solution of disaccharide **53α** (210 mg, 0.320 mmol) and 10% Pd/C (catalytic amount) in methanol (12 mL) was heated to reflux for 3.5 h. After cooling to room temperature, the mixture was filtered through a Celite pad. Following concentration in vacuo, the product was purified by flash chromatography, with ethyl acetate–hexane (1:3) as eluant, to provide 172 mg (82% yield) of **82α** as a solid, determined to be a 4:1 mixture of *Z*:*E* isomers by ^{1}H NMR: mp 145–150 °C; IR ($CHCl_3$) 3010 (m), 2980 (m), 2940 (m), 2860 (m), 1750 (s), 1675 (m), 1495 (w), 1450 (m), 1375 (m), 1230 (s), 1175 (m), 1120 (m), 1070 (s), 1050 (s), 970 (m), 695 (m) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.12 (d, J = 6.4 Hz, 3 H), 1.20 (d, J = 6.5 Hz, 3 H), 1.57, 1.67 (diastereomers, dd, dd, J = 6.7 and 1.0 Hz, J = 6.7 and 1.2 Hz, 3 H), 1.78, 1.81 (diastereomers, s, s, 3 H), 1.88, 1.92 (diastereomers, s, s, 3 H), 2.01 (s, 3 H), 3.45 (m, 1 H), 3.63 (dd, J = 9.4 and 3.5 Hz, 1 H), 3.73 (dd, J = 9.4 and 3.5 Hz, 1 H), 3.84 (m, 1 H), 3.91 (dd, $J_1 = J_2$ = 9.4 Hz, 1 H), 4.50–4.87 (comp m, 7 H), 4.92 (dd, $J_1 = J_2$ = 9.4 Hz, 1 H), 5.02–5.24 (m, 2 H), 6.05, 6.15 (diastereomers, dd, dd, J = 10.8 and 1.2 Hz, J = 13.3 and 1.0 Hz, 1 H), 7.13–7.47 (comp m, 10 H). Anal. Calcd for $C_{35}H_{44}O_{16}$: C, 64.01; H, 6.75. Found: C, 64.23; H, 6.82.

Enol Ether 82β. A solution of disaccharide **53β** (450 mg, 0.686 mmol) and 10% Pd/C (catalytic amount) in methanol (17 mL) was heated to reflux for 4 h. After cooling to room temperature, the mixture was filtered through a Celite pad, and the filtrate was concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (1:3) as eluant, gave 327 mg (73% yield) of **82β** as a solid and 111 mg (12% yield) of **52**. Enol ester **82β** was obtained as a 4:1 mixture of *Z*/*E* isomers.

82β: mp 158–164 °C; IR ($CHCl_3$) 3015 (m), 3010 (m), 2950 (m), 2880 (m), 1745 (s), 1675 (m), 1495 (w), 1455 (w), 1375 (m), 1230 (s), 1170 (m), 1075 (s), 910 (w), 695 (m) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.21 (d, J = 6.7 Hz, 6 H), 1.58, 1.67 (diastereomers, dd, dd, J = 6.7 and 1.2 Hz, J = 6.7 and 1.0 Hz, 3 H), 1.74, 1.80 (diastereomers, s, s, 3 H), 1.85, 1.90 (diastereomers, s, s, 3 H), 2.03 (s, 3 H), 3.31–3.50 (m, 2 H), 3.61 (q, J = 9.2 Hz, 2 H), 3.78 (dd, J = 9.2 and 8.4 Hz, 1 H), 4.47–4.63 (comp m, 4 H), 4.67 (d, J = 9.5 Hz, 1 H), 4.72–4.85 (m, 3 H), 4.90 (dd, $J_1 = J_2$ = 9.5 Hz, 1 H), 5.10 (dd, $J_1 = J_2$ = 9.4 Hz, 1 H), 6.15, 6.20 (diastereomers, dd, dd, J = 11.9 and 1.2 Hz, J = 15.3 and 1.0 Hz, 1 H), 7.20–7.42 (comp m, 10 H). Anal. Calcd for $C_{35}H_{44}O_{16}$: C, 64.01; H, 6.75. Found: C, 64.23; H, 6.73.

Triethylsilyl Ether 83α. A solution of disaccharide **82α** (374 mg, 0.0570 mmol) in methanol (15 mL) and THF (2.0 mL) at room temperature was treated with potassium carbonate (23 mg, catalytic amount). After 23 h, the mixture was concentrated in vacuo. The residue was then dissolved at room temperature in DMF (10 mL) containing DMAP (catalytic amount) and triethylchlorosilane–triethylamine (1:1, 1.0 mL). The resultant mixture was stirred for 12 h, diluted with ether, washed twice with saturated $NaHCO_3$, washed with 10% $CuSO_4$

and brine, and dried over $MgSO_4$. After concentration in vacuo, the product was purified by flash chromatography, with ethyl acetate–hexane (1:24) as eluant, to give 473 mg (95% yield) of **83α** as an oil: IR ($CHCl_3$) 3010 (m), 2950 (m), 2910 (m), 2875 (m), 1670 (m), 1460 (m), 1450 (m), 1360 (m), 1225 (m), 1110 (m), 1100 (m), 975 (s), 905 (m), 845 (m), 715 (m), 660 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.45–0.72 (comp m, 18 H), 0.81–0.97 (comp m, 27 H), 1.23 (d, J = 6.4 Hz, 3 H), 1.27 (d, J = 6.5 Hz, 3 H), 1.66 (dd, J = 6.8 and 1.6 Hz, 3 H), 3.05 (dd, $J_1 = J_2$ = 8.6 Hz, 1 H), 3.18–3.37 (m, 3 H), 3.48 (dd, J = 8.1 and 7.7 Hz, 1 H), 3.71–3.91 (m, 3 H), 4.51 (dd, $J_1 = J_2$ = 8.1 Hz, 1 H), 4.57 (d, J = 7.7 Hz, 1 H), 4.61–4.73 (m, 2 H), 4.91 (d, J = 11.6 Hz, 1 H), 4.97 (d, J = 3.4 Hz, 1 H), 5.11 (d, J = 10.9 Hz, 1 H), 6.12, 6.18 (diastereomers, dd, dd, J = 6.4 and 1.6 Hz, J = 12.5 and 1.6 Hz, 1 H), 7.20–7.51 (comp m, 10 H); high-resolution mass spectrum (CI, isobutane) m/z 815.4727 [$(M - C_3H_5O)^+$, calcd for $C_{44}H_{75}O_8Si_3$ 815.4470]. Anal. Calcd for $C_{47}H_{80}O_9Si_3$: C, 64.63; H, 9.23. Found: C, 64.33; H, 9.39.

Triethylsilyl Ether 83β. A solution of **82β** (300 mg, 0.457 mmol) in methanol (15 mL) and THF (3.0 mL) at room temperature was treated with potassium carbonate (20 mg, catalytic amount). After 23 h, the mixture was concentrated in vacuo, and the residue was dissolved at room temperature in DMF (10 mL) containing DMAP (catalytic amount) and triethylchlorosilane–triethylamine (1:1, 1.0 mL). The reaction mixture was stirred for 12 h, diluted with ether, washed twice with saturated $NaHCO_3$, washed with 10% $CuSO_4$ and brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (3:97) as eluant, furnished 332 mg (83% yield) of **83β** as an oil. The enol ether was determined to be exclusively *Z* by ^1H NMR: IR ($CHCl_3$) 3010 (m), 2950 (s), 2910 (m), 2875 (s), 1670 (m), 1495 (w), 1455 (m), 1410 (w), 1355 (m), 1235 (m), 1160 (m), 1100 (s), 1075 (s), 1005 (s), 820 (m), 795 (m), 715 (m), 690 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.45–0.75 (comp m, 18 H), 0.81–1.01 (comp m, 27 H), 1.23 (d, J = 6.7 Hz, 3 H), 1.30 (d, J = 6.5 Hz, 3 H), 1.65 (dd, J = 6.8 and 1.5 Hz, 3 H), 3.05 (dd, $J_1 = J_2$ = 8.7 Hz, 1 H), 3.15 (m, 1 H), 3.26 (dd, $J_1 = J_2$ = 8.7 Hz, 1 H), 3.35–3.55 (comp m, 5 H), 3.94 (dd, $J_1 = J_2$ = 7.7 Hz, 1 H), 4.49–4.61 (comp m, 4 H), 4.78 (ABq, J_{AB} = 11.1 Hz, $\Delta\nu_{AB}$ = 72 Hz, 2 H), 6.14 (dd, J = 6.2 and 1.7 Hz, 1 H), 7.20–7.40 (comp m, 10 H); high-resolution mass spectrum (CI, isobutane), m/z 815.4768 [$(M - C_3H_5O)^+$, calcd for $C_{44}H_{75}O_8Si_3$ 815.4470]. Anal. Calcd for $C_{47}H_{80}O_9Si_3$: C, 64.63; H, 9.23. Found: C, 64.25; H, 9.30.

Formation Ester (+)-84α. A solution of enol ether **83α** (155 mg, 0.177 mmol) in methylene chloride (10 mL) was cooled to −78 °C, and ozone was bubbled into the solution. When the solution turned blue, triphenylphosphine (93 mg) was added, and the resultant mixture was warmed to room temperature and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (3:93) as eluant, gave 137 mg (90% yield) of **84α** as an oil: $[\alpha]^{22}_D$ +36.8° (*c* 5.52, $CHCl_3$); IR ($CHCl_3$) 3020 (m), 3000 (m), 2960 (s), 2910 (s), 2880 (s), 1740 (s), 1495 (w), 1460 (m), 1455 (m), 1415 (m), 1380 (m), 1365 (m), 1235 (m), 1170 (s), 1120 (s), 1080 (s), 1010 (s), 895 (m), 840 (m), 800 (m), 715 (m), 690 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.45–0.71 (comp m, 18 H), 0.82–1.00 (comp m, 27 H), 1.22 (d, J = 6.7 Hz, 3 H), 1.25 (d, J = 6.6 Hz, 3 H), 3.05 (dd, $J_1 = J_2$ = 8.7 Hz, 1 H), 3.17–3.45 (comp m, 4 H), 3.76 (dd, $J_1 = J_2$ = 8.7 Hz, 1 H), 3.81 (m, 1 H), 3.99 (dd, J = 8.7 and 3.9 Hz, 1 H), 4.54 (d, J = 8.7 Hz, 1 H), 4.78 (ABq, J_{AB} = 12.5 Hz, $\Delta\nu_{AB}$ = 42.5 Hz, 2 H), 4.91 (ABq, J_{AB} = 12.5 Hz, $\Delta\nu_{AB}$ = 97.5 Hz, 2 H), 5.12 (d, J = 3.9 Hz, 1 H), 7.18–7.48 (comp m, 10 H), 8.15 (s, 1 H); high-resolution mass spectrum (CI, isobutane) m/z 831.4351 [$(M - C_2H_5)^+$, calcd for $C_{43}H_{71}O_{10}Si_3$ 831.4355]. Anal. Calcd for $C_{45}H_{76}O_{10}Si_3$: C, 62.75; H, 8.89. Found: C, 62.97; H, 8.90.

Formate Ester (+)-84β. A solution of enol ether **83β** (200 mg, 0.229 mmol) in methylene chloride (20 mL) was cooled to −78 °C, and ozone was bubbled into the solution. When the solution turned blue, triphenylphosphine (120 mg) was added, and the resultant mixture was warmed to room temperature. The mixture was concentrated in vacuo, and the product was purified by flash chromatography, with ethyl acetate–hexane (3:93) as eluant, to give 129 mg (66% yield) of **84β** as an oil: $[\alpha]^{22}_D$ +27.5° (*c* 3.8, $CHCl_3$); IR ($CHCl_3$) 3030 (w), 3000 (m), 2960 (s), 2910 (s), 2880 (s), 1740 (s), 1495 (m), 1455 (m), 1410 (m), 1340 (m), 1270 (s), 1080 (s), 1005 (s), 970 (m), 895 (w), 820 (m), 800 (m), 715 (m), 690 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.45–0.70 (comp m, 18 H), 0.81–1.03 (comp m, 27 H), 1.22 (d, J = 6.7 Hz, 3 H), 1.30 (d, J = 6.7 Hz, 3 H), 2.97 (dd, $J_1 = J_2$ = 9.1 Hz, 1 H), 3.13 (m, 1 H), 3.23 (dd, $J_1 = J_2$ = 9.1 Hz, 1 H), 3.37–3.60 (comp m, 4 H), 3.95 (dd, $J_1 = J_2$ = 9.1 Hz, 1 H), 4.55 (d, J = 9.1 Hz, 1 H), 4.76 (ABq, J_{AB} = 12.5 Hz, $\Delta\nu_{AB}$ = 57.7 Hz, 2 H), 4.90 (ABq, J_{AB} = 11.0 Hz, $\Delta\nu_{AB}$ = 55 Hz, 2 H), 5.71 (d, J = 9.1 Hz, 1 H), 7.21–7.43 (comp m, 10 H), 8.10 (s, 1 H); high-resolution mass spectrum (EI, isobutane) m/z 831.4351 [$(M - C_2H_5)^+$, calcd for $C_{43}H_{71}O_{10}Si_3$ 831.4355].

Diol (+)-85α. A mixture of 10% Pd/C (30 mg) and ethyl acetate (4.0 mL) was flushed with hydrogen at room temperature, and a solution of **84α** (52 mg, 0.060 mmol) in ethyl acetate (freshly distilled, 8.0 mL) was introduced dropwise. The reaction mixture was stirred under a hydrogen atmosphere (maintained with a balloon) until TLC analysis showed complete consumption of starting material. The flask was then flushed with air, and the mixture was filtered through a Celite plug. After concentration in vacuo, the product was purified by flash chromatography, with ethyl acetate–hexane (1:19) as eluant, to afford 31.3 mg (77% yield) of **85α** as an oil: $[\alpha]^{22}_D$ +44.2° (*c* 3.13, $CHCl_3$); IR ($CHCl_3$) 3600 (w), 2950 (s), 2920 (s), 2870 (s), 1735 (s), 1460 (m), 1410 (w), 1380 (m), 1240 (m), 1110 (s), 1080 (s), 1005 (s), 895 (m), 840 (m), 800 (w), 680 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.55–0.77 (comp m, 18 H), 0.88–1.09 (comp m, 27 H), 1.22 (d, J = 6.0 Hz, 3 H), 1.24 (d, J = 6.0 Hz, 3 H), 2.05 (d, J = 2.4 Hz, 1 H), 2.67 (d, J = 2.4 Hz, 1 H), 3.12–3.38 (comp m, 5 H), 3.61 (dd, J = 9.6 and 3.6 Hz, 1 H), 3.75 (m, 1 H), 3.86 (ddd, J = 9.6, 9.6 and 2.4 Hz, 1 H), 4.45 (d, J = 9.6 Hz, 1 H), 6.19 (d, J = 3.6 Hz, 1 H), 8.12 (s, 1 H); high-resolution mass spectrum (CI, isobutane) m/z 605.3369 {[$M - (C_2H_5 + HO_2CH)$]$^+$, calcd for $C_{28}H_{57}O_8Si_3$ 605.3369}.

Diol (+)-85β. A mixture of 10% Pd/C (20 mg) and ethyl acetate (4.0 mL) was flushed with hydrogen at room temperature and a solution of **84β** (30 mg, 0.035 mmol) in ethyl acetate (freshly distilled, 4.0 mL) was introduced dropwise. The reaction mixture was stirred under a hydrogen atmosphere (maintained with a balloon) until TLC analysis showed the complete consumption of starting material. The flask was then flushed with air, and the mixture was filtered through a Celite plug and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (1:19) as eluant, gave 21 mg (88% yield) of **85β** as an oil: $[\alpha]^{22}_D$ +13.6° (*c* 2.15, $CHCl_3$); IR ($CHCl_3$) 3600 (w), 3550–3320 (w), 2960 (s), 2910 (s), 2880 (s), 1740 (s), 1460 (m), 1410 (m), 1380 (m), 1240 (m), 1150 (s), 1080 (s), 1005 (s), 830 (m), 795 (m), 715 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.61–0.78 (comp m, 18 H), 0.89–1.04 (comp m, 27 H), 1.23 (d, J = 6.0 Hz, 3 H), 1.29 (d, J = 6.0 Hz, 3 H), 2.03 (d, J = 3.0 Hz, 1 H), 3.13–3.62 (comp m, 9 H), 4.49 (d, J = 7.3 Hz, 1 H), 5.64 (d, J = 7.3 Hz, 1 H), 8.06 (s, 1 H); high-resolution mass spectrum (CI, isobutane) m/z 605.3364 {[$M - (C_2H_5 + HO_2CH)$]$^+$, calcd for $C_{28}H_{57}O_8Si_3$ 605.3361}. Anal. Calcd for $C_{31}H_{64}O_{10}Si_3$: C, 54.67; H, 9.47. Found: C, 54.43; H, 9.52.

Diacetate (+)-86α. To a solution of diol **85α** (60 mg, 0.088 mmol) and 4-pyrrolidinopyridine (catalytic amount) in triethylamine (freshly distilled, 1.5 mL) at room temperature was added acetic anhydride (5 drops, excess). After 5 h, the mixture was diluted with ether, filtered through a Celite pad, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (1:39, then 3:47) as eluant, furnished 69 mg (100% yield) of **86α** as an oil: $[\alpha]^{22}_D$ +32.2° (*c* 1.4, $CHCl_3$); IR ($CHCl_3$) 3010 (w), 2975 (s), 2925 (s), 2895 (s), 1750 (s), 1465 (m), 1421 (m), 1375 (m), 1245 (s), 1180 (s), 1130–1090 (s), 1075 (s), 1020 (s), 915 (w), 890 (w), 850 (m), 805 (s), 720 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.48–0.72 (comp m, 18 H), 0.81–1.03 (comp m, 27 H), 1.25 (d, J = 6.4 Hz, 6 H), 2.10 (s, 3 H), 2.13 (s, 3 H), 3.27–3.51 (comp m, 4 H), 3.79–3.91 (m, 2 H), 4.32 (d, J = 8.6 Hz, 1 H), 4.88 (dd, $J_1 = J_2$ = 8.9 Hz, 1 H), 5.37 (dd, J = 8.9 and 8.6 Hz, 1 H), 6.20 (d, J = 3.9 Hz, 1 H), 8.09 (s, 1 H); high-resolution mass spectrum (CI, isobutane) m/z 735.3627 {[$M - (C_2H_5 + HO_2CH)$]$^+$, calcd for $C_{32}H_{61}O_{10}Si_3$ 735.3627}.

Diacetate (+)-86β. A solution of diol **85β** (83 mg, 0.122 mmol) and 4-pyrrolidinopyridine (catalytic amount) in triethylamine (freshly distilled, 2.0 mL) at room temperature was treated with acetic anhydride (10 drops, excess). After 4.5 h, the mixture was diluted with ether and filtered through a Celite pad. Following concentration in vacuo, purification by flash chromatography, with ethyl acetate–hexane (1:19) as eluant, afforded 90 mg (96% yield) of **86β** as an oil: IR ($CHCl_3$) 2960 (s), 2930 (s), 2880 (s), 1750 (s), 1460 (m), 1365 (m), 1215–1260 (s, br), 1160–1175 (m, br), 1060–1120 (s, br), 1000–1020 (m, br) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.50–0.71 (comp m, 18 H), 0.89–1.01 (comp m, 27 H), 1.26 (d, J = 6.5 Hz, 3 H), 1.32 (d, J = 6.0 Hz, 3 H), 2.11 (s, 3 H), 2.14 (s, 3 H), 3.31–3.38 (m, 3 H), 3.45 (dd, $J_1 = J_2$ = 9.3 Hz, 1 H), 3.61 (m, 1 H), 3.84 (dd, J = 9.0 and 10.0 Hz, 1 H), 4.39 (d, J = 7.5 Hz, 1 H), 4.90 (dd, $J_1 = J_2$ = 9.1 Hz, 1 H), 5.12 (dd, $J_1 = J_2$ = 9.1 Hz, 1 H), 5.72 (d, J = 8.5 Hz, 1 H), 8.08 (s, 1 H).

Lactol 87. To a solution of diacetate **86α** (60 mg, 0.079 mmol) in methanol (1.0 mL) at room temperature was added a "puff" of triethylamine through a pipet. After stirring for 23 h at room temperature, the reaction mixture was concentrated in vacuo to give 59 mg (100% yield) of **87** as an oil. The anomer ratio was determined to be 2:1 (α:β) by ^1H NMR. Diacetate **86β** was analogously converted to **87** (quantitative): IR ($CHCl_3$) 3600–3300 (w), 2955 (s), 2880 (s), 1745 (s), 1460 (m), 1410 (m), 1365 (m), 1240 (s), 1160 (m), 1110–1070 (s), 1005 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.50–0.75 (m, 18 H), 0.87–1.07 (m, 27 H), 1.27, 1.31 (diastereomers, d, d, J = 6.6 Hz, J = 6.5 Hz, 6

H), 2.10, 2.15 (diastereomers, s, s, 6 H), 2.85 (br s, 1 H), 3.52 (m, 4 H), 3.92 (dd, J = 10.0 and 3.6 Hz, 1 H), 4.02 (dq, J = 10.0 and 6.6 Hz, 1 H), 4.30, 4.37 (diastereomers, d, d, J = 7.5 Hz, J = 7.5 Hz, 1 H), 4.55–4.61, 5.21 (diastereomers, m, br s, 1 H), 4.91, 4.92 (diastereomers, dd, dd, $J_1 = J_2$ = 8.9 Hz, $J_1 = J_2$ = 8.9 Hz, 1 H), 5.11, 5.35 (diastereomers, dd, dd, $J_1 = J_2$ = 8.6 Hz, $J_1 = J_2$ = 9.3 Hz, 1 H); high-resolution mass spectrum (CI, isobutane) m/z 707.3677 [$(M - C_2H_5)^+$, calcd for $C_{32}H_{63}O_{11}Si_3$ 707.3678]. Anal. Calcd for $C_{34}H_{68}O_{11}Si_3$: C, 55.39; H, 9.29. Found: C, 55.26; H, 9.46.

Glycosyl Esters (+)-88β and (+)-88α. A mixture of lactol **87** (40 mg, 0.054 mmol), triphenylphosphine (22 mg, 0.084 mmol, 1.54 equiv), and aglycon acid **80** (31 mg, 0.105 mmol, 1.94 equiv) was dried in a desiccator over P_2O_5 at high vacuum (0.2 mmHg) for 12 h. Under argon, the mixture was dissolved in THF (0.25 mL) at room temperature, and diisopropyl azodicarboxylate (16 μL, 0.077 mmol, 1.42 equiv) was added. After 3 h, additional triphenylphosphine (11 mg, 0.77 equiv) and DIAD (8 μL, 0.71 equiv) were added, and the resultant solution was stirred for 24 h. Concentration in vacuo and flash chromatography, with ethyl acetate–hexane (7:93, then 17:83) as eluant, provided 30 mg (55% yield) of **88β** and **88α** and 17 mg of recovered **87**. The anomer ratio was determined to be 2:1 (β:α) by ^{1}H NMR. The glycosyl esters were then separated by HPLC [ethyl acetate–hexane (22:3)]. The yield based on recovered lactol was 94%.

88β: $[\alpha]^{22}_D$ +31.0° (c 1.0, $CHCl_3$); IR ($CHCl_3$) 3010 (m), 2985 (s), 2920 (s), 2895 (s), 1755 (s), 1740 (s), 1465 (m), 1385 (m), 1240 (s), 1170 (m), 1090 (s), 1010 (m), 805 (m), 720 (m) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.51–0.72 (comp m, 18 H), 0.85–1.04 (comp m, 30 H), 1.21–1.42 (comp m, 8 H), 1.55–1.71 (m, 1 H), 1.84 (ddd, J = 15.5, 14.0, and 4.0 Hz, 1 H), 2.00–2.19 (m, 2 H), 2.10 (s, superimposed on m, 3 H), 2.13 (s, superimposed on m, 3 H), 2.25–2.50 (m, 3 H), 2.52–2.72 (m, 2 H), 3.06 (ABq, J_{AB} = 5.1 Hz, $\Delta\nu_{AB}$ = 22.7 Hz, 2 H), 3.24 (q, J = 7.5 Hz, 2 H), 3.31–3.45 (m, 2 H), 3.57 (m, 1 H), 3.67–3.92 (m, 3 H), 4.34 (d, superimposed on m, J = 7.7 Hz, 1 H), 4.39 (m, 1 H), 4.88 (dd, $J_1 = J_2$ = 9.1 Hz, 1 H), 5.10 (dd, $J_1 = J_2$ = 9.2 Hz, 1 H), 5.63 (d, J = 7.7 Hz, 1 H); high-resolution mass spectrum (CI, isobutane) m/z 985.4836 [$(M - C_2H_5)^+$, calcd for $C_{47}H_{81}O_{16}Si_3$ 985.4832]. Anal. Calcd for $C_{49}H_{86}O_{16}Si_3$: C, 57.95; H, 8.54. Found: C, 57.59; H, 8.52.

88a: $[\alpha]^{22}_D$ +71.0° (c 1.4, $CHCl_3$); IR ($CHCl_3$) 3010 (m), 2960 (s), 2940 (s), 2910 (m), 2880 (s), 1750 (s), 1740 (s), 1460 (m), 1450 (m), 1415 (m), 1380 (m), 1365 (m), 1240 (s), 1165 (m), 1115 (s), 1090 (s), 1070 (s), 1010 (m), 970 (m), 798 (m), 715 (m) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.42–0.71 (comp m, 18 H), 0.82–1.03 (comp m, 30 H), 1.24 (d, superimposed on m, J = 6.0 Hz, 6 H), 1.20–1.51 (m, 2 H), 1.64–1.88 (m, 2 H), 2.00–2.19 (m, 2 H), 2.09 (s, superimposed on m, 3 H), 2.13 (s, superimposed on m, 3 H), 2.32 (m, 2 H), 2.41 (d, J = 6.6 Hz, 1 H), 2.46–2.72 (m, 2 H), 3.07 (ABq, J_{AB} = 5.1 Hz, $\Delta\nu_{AB}$ = 18.0 Hz, 2 H), 3.23–3.44 (comp m, 4 H), 3.70–3.92 (comp m, 4 H), 4.29 (d, J = 7.6 Hz, 1 H), 4.39 (m, 1 H), 4.89 (dd, $J_1 = J_2$ = 8.9 Hz, 1 H), 5.31 (dd, $J_1 = J_2$ = 9.5 Hz, 1 H), 6.11 (d, J = 3.8 Hz, 1 H); high-resolution mass spectrum (CI, isobutane) m/z 985.4836 [$(M - C_2H_5)^+$, calcd for $C_{47}H_{81}O_{16}Si_3$ 985.4832].

Reduction of Ketone 88β. A solution of **88β** (10 mg, 0.0099 mmol) in methanol (1.0 mL) and THF (2 drops) was cooled to −20 °C, and sodium borohydride (4 mg, 10 equiv) was added. After 5 min, the reaction mixture was diluted with ether, quenched with saturated NH_4Cl, and extracted three times with ether. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (3:17, then 2:3) as eluant, gave 8.6 mg (86% yield) of the less polar axial alcohol **89** and 1.3 mg (13% yield) of the more polar equatorial alcohol **90**, both as oils.

89: $[\alpha]^{22}_D$ +39.3° (c, 0.7, $CHCl_3$); IR ($CHCl_3$) 3570 (w), 3010 (m), 2980 (s), 2895 (s), 1755 (s), 1460 (m), 1420 (m), 1380–1370 (m), 1240 (s), 1165 (m), 1110 (s), 1085 (s), 1010 (s), 950 (m), 800 (m), 720 (m) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.50–0.72 (comp m, 18 H), 0.81–1.08 (comp m, 30 H), 1.21–1.50 (comp m, 8 H), 1.57–1.67 (m, 2 H), 1.70–2.20 (comp m, 5 H), 2.12 (s, superimposed on m, 3 H), 2.15 (s, superimposed on m, 3 H), 2.30 (m, 1 H), 2.68 (m, 1 H), 2.96 (s, 2 H), 3.11 (d, J = 10.3 Hz, 1 H), 3.25 (q, J = 9.1 Hz, 2 H), 3.32–3.48 (m, 3 H), 3.60 (m, 1 H), 3.72 (dd, $J_1 = J_2$ = 11.8 Hz, 1 H), 3.81 (m, 2 H), 4.37 (d, J = 7.6 Hz, 1 H), 4.47 (m, 1 H), 4.90 (dd, $J_1 = J_2$ = 9.2 Hz, 1 H), 5.12 (dd, $J_1 = J_2$ = 9.2 Hz, 1 H), 5.65 (d, J = 7.8 Hz, 1 H); high-resolution mass spectrum (CI, isobutane) m/z 987.4993 [$(M - C_2H_5)^+$, calcd for $C_{47}H_{83}O_{16}Si_3$ 987.4989].

90: $[\alpha]^{22}_D$ +21.3° (c 0.13, $CHCl_3$); IR ($CHCl_3$) 3600–3500 (w), 3010 (m), 2980 (s), 2965 (s), 2880 (m), 1750 (s), 1460 (m), 1375 (m), 1230 (s), 1165 (m), 1080 (s), 800 (m), 715 (m), 660 (m) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.50–0.73 (comp m, 18 H), 0.80–1.08 (comp m, 30 H), 1.15–1.41 (comp m, 8 H), 1.51–1.72 (m, 2 H), 1.89 (m, 1 H), 1.98–2.10 (comp m, 6 H), 2.11 (s, superimposed on m, 3 H), 2.14 (s, superimposed on m, 3 H), 2.35 (m, 1 H), 2.95 (q, J = 4.6 Hz, 2 H), 3.25 (q, J = 8.6 Hz, 2 H), 3.30–3.68 (comp m, 6 H), 3.81 (dd, J = 9.5 and 8.0 Hz, 1 H), 4.38 (d, superimposed on m, J = 8.0 Hz, 1 H), 4.38 (m, 1 H), 4.89 (dd, $J_1 = J_2$ = 8.0 Hz, 1 H), 5.13 (dd, $J_1 = J_2$ = 8.1 Hz, 1 H), 5.66 (d, J = 7.9 Hz, 1 H).

Cinnamate (+)-91. Under argon, a solution of alcohol **89** (8.0 mg, 0.0079 mmol) in pyridine (0.3 mL) and triethylamine (0.3 mL) at room temperature was treated with 4-pyrrolidinopyridine (catalytic amount) and *trans*-cinnamoyl chloride (10 mg, excess). After 24 h, the reaction mixture was diluted with ether, washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (1:9, then 3:17) as eluant, afforded 8.4 mg (93% yield) of **91** as a white crystalline solid: mp 169–170 °C; $[\alpha]^{22}_D$ +9.3° (c 1.0, $CHCl_3$); IR ($CHCl_3$) 3010 (m), 2960 (s), 2880 (s), 1750 (s), 1700 (s), 1650 (w), 1450 (m), 1370 (m), 1310 (m), 1240 (s), 1170 (m), 1080 (s), 1050 (s), 1010 (m), 800 (m), 720 (m) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.48–0.71 (comp m, 18 H), 0.71–1.08 (comp m, 30 H), 1.22 (d, J = 6.5 Hz, 6 H), 1.27 (m, 3 H), 1.65 (m, 1 H), 1.82–2.07 (comp m, 4 H), 2.08 (s, 3 H), 2.10 (s, 3 H), 2.17–2.32 (m, 2 H), 2.60 (m, 1 H), 2.95 (ABq, J_{AB} = 5.0 Hz, $\Delta\nu_{AB}$ = 0.2, 2 H), 3.18–3.57 (comp m, 6 H), 3.72 (dd, J = 9.5 and 7.8 Hz, 1 H), 3.98 (dd, $J_1 = J_2$ = 11.4 Hz, 1 H), 4.29 (d, J = 7.6 Hz, 1 H), 4.43 (m, 1 H), 4.89 (dd, $J_1 = J_2$ = 9.1 Hz, 1 H), 5.08 (dd, $J_1 = J_2$ = 9.3 Hz, 1 H), 5.17 (m, 1 H), 5.56 (d, J = 7.8 Hz, 1 H), 6.46 (d, J = 16.0 Hz, 1 H), 7.38 (m, 3 H), 7.55 (m, 2 H), 7.77 (d, J = 16.0 Hz, 1 H); high-resolution mass spectrum (CI, isobutane) m/z 1117.5416 [$(M - C_2H_5)^+$, calcd for $C_{56}H_{89}O_{17}Si_3$ 1117.5408]. Anal. Calcd for $C_{58}H_{94}O_{17}Si_3$: C, 60.70; H, 8.26. Found: C, 60.75; H, 8.33.

(+)-Phyllanthoside (1). Trisilyl ether **91** (8.0 mg, 0.0070 mmol) was dissolved in HOAc–H_2O–THF (6:3:1, 0.5 mL) at room temperature. The reaction mixture was stirred at room temperature for 21 h (monitoring by TLC analysis) and then concentrated in vacuo by using a bulb-to-bulb distillation apparatus. Flash chromatography, with methanol–chloroform (1:19) as eluant, gave 6.0 mg (100% yield) of phyllanthoside (**1**) as a white solid: mp 125–127 °C; $[\alpha]^{22}_D$ +19.5° (c 0.6, $CHCl_3$); IR ($CHCl_3$) 3600–3300 (m), 3020 (m), 3010 (m), 2940 (m), 2880 (m), 1745 (s), 1740 (s), 1705 (s), 1640 (m), 1450 (m), 1375 (m), 1310 (s), 1280 (s), 1255 (s), 1170 (s), 1120 (s), 1080 (s), 1050 (s), 1030 (s), 960 (m), 905 (m), 860 (w) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.84 (d, J = 6.9 Hz, 3 H), 1.24 (d, J = 5.9 Hz, 3 H), 1.29 (d, J = 6.1 Hz, 3 H), 1.67–2.25 (comp m, 12 H), 2.17 (s, superimposed on m, 6 H), 2.40 (m, 1 H), 2.52 (m, 1 H), 2.95 (ABq, J_{AB} = 4.8 Hz, $\Delta\nu_{AB}$ = 3.3 Hz, 2 H), 3.06–3.21 (m, 4 H), 3.29 (dd, J = 9.7 and 7.9 Hz, 1 H), 3.45 (m, 2 H), 3.98 (dd, $J_1 = J_2$ = 11.5 Hz, 1 H), 4.01 (d, J = 7.9 Hz, 1 H), 4.45 (m, 1 H), 4.81 (dd, $J_1 = J_2$ = 9.1 Hz, 1 H), 4.89 (dd, $J_1 = J_2$ = 9.4 Hz, 1 H), 5.12 (m, 1 H), 5.48 (d, J = 8.1 Hz, 1 H), 6.62 (d, J = 16.0 Hz, 1 H), 7.43 (m, 3 H), 7.63 (m, 2 H), 7.79 (d, J = 16.0 Hz, 1 H); high-resolution mass spectrum (CI, NH_3) m/z 805.3295 [$(M + H)^+$, calcd for $C_{40}H_{53}O_{17}$ 805.3283]. Anal. Calcd for $C_{40}H_{52}O_{17}$: C, 59.69; H, 6.51. Found: C, 59.61; H, 6.64.

Reduction of Ketone 88α. A solution of **88α** (6 mg, 0.0059 mmol) in methanol (2.0 mL) and THF (2 drops) was cooled to −20 °C and sodium borohydride (5 mg) was added. After 5 min, the reaction mixture was diluted with ether, quenched with saturated NH_4Cl, and extracted three times with ether. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (3:17) as eluant, gave 5.0 mg (83% yield) of axial alcohol **92** as an oil: $[\alpha]^{22}_D$ +82.4° (c 1.0, $CHCl_3$); IR ($CHCl_3$) 3550 (w), 3010 (m), 2970 (s), 2890 (s), 1750 (s), 1465 (m), 1415 (w), 1370 (m), 1240 (s), 1220 (s), 1160 (m), 1125 (s), 1070 (s), 1010 (s), 950 (m), 920 (m), 800 (m), 720 (m) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.50–0.72 (comp m, 18 H), 0.73–1.02 (comp m, 30 H), 1.13–1.32 (comp m, 8 H), 1.41 (m, 1 H), 1.52–1.78 (m, 2 H), 1.79–1.95 (m, 2 H), 1.96–2.12 (m, 2 H), 2.08 (s, superimposed on m, 3 H), 2.12 (s, superimposed on m, 3 H), 2.32 (m, 1 H), 2.67 (m, 1 H), 2.93 (s, 2 H), 2.98 (d, J = 7.5 Hz, 1 H), 3.25–3.42 (comp m, 4 H), 3.67–3.87 (comp m, 5 H), 4.29 (d, J = 7.5 Hz, 1 H), 4.46 (m, 1 H), 4.89 (dd, $J_1 = J_2$ = 9.0 Hz, 1 H), 5.31 (dd, J = 10.3 and 9.2 Hz, 1 H), 6.13 (d, J = 3.8 Hz, 1 H); high-resolution mass spectrum (CI, isobutane) m/z 987.4993 [$(M - C_2H_5)^+$, calcd for $C_{47}H_{83}O_{16}Si_3$ 987.4989].

Cinnamate (+)-93. Under argon, a solution of alcohol **92** (8.0 mg, 0.0079 mmol) and 4-pyrrolidinopyridine (catalytic amount) in pyridine (0.3 mL) and triethylamine (0.3 mL) was treated with *trans*-cinnamoyl chloride (10 mg, excess). After 20 h at room temperature, the reaction mixture was diluted with ether, washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography, with ethyl acetate–hexane (1:9, then 3:17) as eluant, afforded 8.2 mg (91% yield) of **93** as an oil: $[\alpha]^{22}_D$ +31.3° (c 0.82, $CHCl_3$); IR ($CHCl_3$) 3010 (m), 2960 (s), 2940 (s), 2880 (m), 1755 (s), 1705 (m), 1450 (w), 1365 (w), 1240 (s), 1120 (s), 1085 (s), 1075 (s), 1010 (s), 845 (m), 715 (m) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.45–0.70 (comp m,

18 H), 0.72-1.03 (comp m, 30 H), 1.21 (d, J = 6.9 Hz, 3 H), 1.25 (d, J = 5.9 Hz, 3 H), 1.30-1.48 (m, 2 H), 1.61-1.73 (m, 2 H), 1.82-2.20 (comp m, 4 H), 2.06 (s, 3 H), 2.09 (s, 3 H), 2.39 (m, 1 H), 2.66 (m, 1 H), 2.95 (ABq, J_{AB} = 5.5 Hz, $\Delta\nu_{AB}$ = 3.6 Hz, 2 H), 3.00 (m, 1 H), 3.08 (dd, J = 9.9 and 8.1 Hz, 1 H), 3.23 (dd, $J_1 = J_2$ = 9.3 Hz, 1 H), 3.30-3.45 (m, 2 H), 3.49 (q, J = 8.0 Hz, 1 H). 3.67 (m, 1 H), 3.80 (dd, J = 10.0 and 3.9 Hz, 1 H). 3.98 (dd, $J_1 = J_2$ = 9.9 Hz, 1 H), 4.26 (d, J = 7.6 Hz, 1 H), 4.48 (m, 1 H), 4.83 (dd, $J_1 = J_2$ = 8.1 Hz, 1 H), 5.21 (m, 1 H), 5.27 (dd, J = 9.9 and 8.1 Hz, 1 H), 6.03 (d, J = 3.9 Hz, 1 H), 6.45 (d, J = 16.0 Hz, 1 H), 7.39 (m, 3 H), 7.55 (m, 2 H), 7.78 (d, J = 16.0 Hz, 1 H); high-resolution mass spectrum (CI, isobutane) m/z 1117.5417 [$(M - C_2H_5)^+$, calcd for $C_{56}H_{89}O_{17}Si_3$ 1117.5408].

(+)-α-Phyllanthoside (1α). Trisilyl ether **93** (5.0 mg, 0.0044 mmol) was dissolved in AcOH-H_2O-THF (6:3:1; 1.0 mL) at room temperature. After 23 h. the mixture was concentrated in vacuo by using a bulb-to-bulb distillation apparatus. Flash chromatography, with menthanol-chloroform (1:24) as eluant, gave 3.3 mg (94% yield) of α-phyllanthoside (**1α**): $[\alpha]^{22}_D$ +68.7° (c 0.6, $CHCl_3$); IR ($CHCl_3$) 3600-3300 (m), 3020 (m), 2950 (m), 1745 (s), 1710 (s), 1640 (m), 1450 (m), 1375 (m), 1310 (m). 1240 (s), 1170 (s), 1120 (s), 1075 (s), 1050 (s), 1010 (s), 945 (w), 795 (w) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.88 (d, J = 6.9 Hz, 3 H), 1.25 (dd, $J_1 = J_2$ = 5.9 Hz, 6 H), 1.30-1.48 (m, 2 H), 1.61-1.72 (m, 2 H), 1.77-2.10 (comp m, 8 H), 2.16 (s, 3 H), 2.18 (s, 3 H). 2.25 (m, 1 H), 2.64 (m, 1 H), 2.97 (s, 2 H), 3.16 (dd, $J_1 = J_2$ = 9.2 Hz, 1 H). 3.27-3.38 (m, 3 H), 3.43 (dd, J = 9.3 and 4.2 Hz, 1 H), 3.67 (m, 1 H). 3.79 (dd, J = 10.0 and 3.9 Hz, 1 H), 3.99 (dd, $J_1 = J_2$ = 11.5 Hz, 1 H), 4.31 (d, J = 7.7 Hz, 1 H), 4.46 (m, 1 H), 4.76 (dd, $J_1 = J_2$ = 9.4 Hz, 1 H), 5.15 (m, 1 H), 5.18 (dd, $J_1 = J_2$ = 9.7 Hz, 1 H), 6.14 (d, J = 3.8 Hz, 1 H), 6.52 (d, J = 16.0 Hz. 1 H), 7.39 (m, 3 H), 7.56 (m, 2 H), 7.78 (d, J = 16.0 Hz, 1 H). Anal. Calcd for $C_{40}H_{52}O_{17}$: C, 59.69; H. 6.51. Found: C, 59.73; H, 6.71.

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Phyllanthoside-Phyllanthostatin Synthetic Studies. 9. Total Syntheses of (-)-Phyllanthostatin 1, (+)-Phyllanthostatin 2, and (+)-Phyllanthostatin 3

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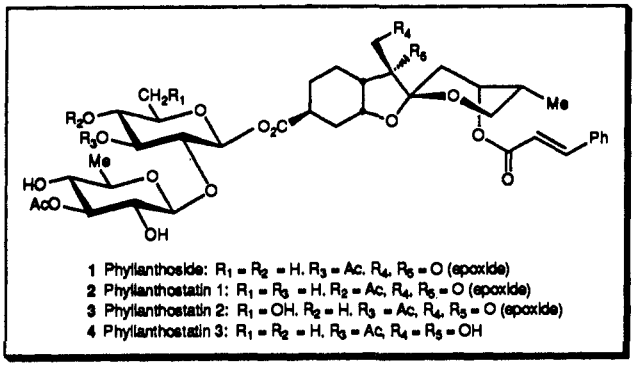
Abstract: Phyllanthostatins 1, 2, and 3 (**2-4**) have been synthesized for the first time. The unusual **1'→2β** glycosidic linkages of the disaccharide moieties were constructed via anchimerically-assisted Koenigs-Knorr reactions. The novel β-glycosyl esters were then generated through Mitsunobu coupling of suitably protected disaccharides with fully endowed aglycon carboxylic acids. For phyllanthostatins 1 and 2, the use of chloroacetate esters for disaccharide hydroxyl protection was explored. This tactic afforded a crystalline α-lactol precursor of **2**, which in turn furnished the requisite β-glycosyl ester exclusively. However, inefficient dechloroacetylation with hydrazine dithiocarbonate gave **2** and **3** in low yield. Triethylsilyl ether protection was uneventfully employed in the synthesis of phyllanthostatin 3 (**4**). Finally, a more convergent endgame for phyllanthoside (**1**) further exploited the aglycon precursor of **2** and **3**.

In the preceding paper in this issue we described the first (and, to date, the only) total synthesis of (+)-phyllanthoside (**1**), a novel bisabolane glycoside isolated by Kupchan in 1977 from the roots of the Central American tree *Phyllanthus acuminatus* Vahl.[1,2] Pettit reported the complete structures of **1** and of the closely related phyllanthostatins (**2-4**) in 1982.[3] The unusually selective cytotoxic properties and highly challenging architecture have established these glycosides as important targets for total synthesis.[4]

In this full account, we describe the completion of the first total syntheses of phyllanthostatins 1-3 (**2-4**) as well as a new endgame for phyllanthoside (**1**). These efforts comprise a second-generation approach to the phyllanthoside-phyllanthostatin antitumor glycosides, wherein we attempted to capitalize on the strengths of our initial strategy while addressing its shortcomings.[5]



1 Phyllanthoside: $R_1 = R_2 = H$, $R_3 = Ac$, $R_4, R_5 = O$ (epoxide)
2 Phyllanthostatin 1: $R_1 = R_3 = H$, $R_2 = Ac$, $R_4, R_5 = O$ (epoxide)
3 Phyllanthostatin 2: $R_1 = OH$, $R_2 = H$, $R_3 = Ac$, $R_4, R_5 = O$ (epoxide)
4 Phyllanthostatin 3: $R_1 = R_2 = H$, $R_3 = Ac$, $R_4 = R_5 = OH$

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(4) Phyllanthoside (**1**) and phyllanthostatin 1 (**2**) are in phase 1 clinical trials under the auspices of the NCI-EORTC. Both compounds inhibit human breast cancer cell lines, with ED50s (μg/mL) against P388 of 0.27 and 0.19, respectively. Against P388 in vivo, the respective T/C values are 152% and 162-190% at doses of 6.68 and 4-16 mg/kg. Personal communication from Dr. Charles K. Grieshaber, Chief, Toxicology Branch, Developmental Therapeutics Program, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892. Also, see: Powis, G.; Moore, D. J. *J. Chromatogr.* **1985**, *342*, 129.

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