Total Synthesis of Tricolorin A

Daniel P. Larson and Clayton H. Heathcock*

Department of Chemistry, University of California, Berkeley, California 94720

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Tricolorin A (**1**) is a novel tetrasaccharide macrolactone that is a natural herbicide. In this paper is reported a total synthesis of **1**. Coupling of hydroxy ester **18** with D-fucosyl trichloroacetimidate **23** gave fucoside **24**. Removal of the C-2 pivaloyl group of **24** followed by coupling with D-glucosyl trichloroacetimidate **29** resulted in isolation of disaccharide **30**. Saponification of the ester groups of **30** and subsequent selective macrolactonization of the acid diol **31** by the Yonemitsu protocol gave only the desired lactone **32**. The key step in the assembly of disaccharide glycosyl trichloroacetimidate **52** was coupling L-rhamnoside **47** with L-rhamnosyl trichloroacetimidate **43**. Attempts to couple lactone disaccharide **32** with disaccharide **52** were unsuccessful. Using an alternate plan for assembly of the tetrasaccharide, reaction of disaccharide glycosyl trichloroacetimidate **58** with disaccharide **37** gave tetrasaccharide **59**. Diester lactone **63** was generated by selective macrolactonization of tetrasaccharide acid triol **60**, again using the Yonemitsu protocol, followed by addition of the chiral side chain acid to the reaction vessel. Synthetic tricolorin A (**1**) was obtained by deprotection of **63**. Starting from fucose, glucose, rhamnose, and (*S*)-1-octyn-3-ol, the synthesis required 39 steps overall. The longest linear sequence was 14 steps, with an overall yield for this longest linear sequence of 6%.

Farmers in the southeastern intertropical Mexican state of Morelos use *Ipomoea tricolor* as a cover crop during the fallow period in sugar cane fields. An ability to control weed growth prompted investigation of the compounds responsible for the biological activity of this plant. Pereda-Miranda and co-workers[1] reported the isolation of tricolorin A (**1**) from *Ipomoea tricolor* in 1993. This unusual tetrasaccharide macrolactone demonstrated significant cytotoxic activity against cultured P-388 and human breast cancer cells. We chose tricolorin A as a synthetic target because of the unique challenge in forming the macrolactone in this molecule.

The goal of this project was not necessarily to develop new synthetic methodology for the synthesis of carbohydrates but rather to apply the known chemistry in as efficient manner as possible. Our plan that would accomplish this goal can best be described by retrosynthetic analysis of the target molecule. A key disconnection is the glycosidic linkage between the glucose and rhamnose rings. This bond would be formed by coupling a rhamnose-rhamnose disaccharide glycosyl donor **3** with a lactone disaccharide glycosyl acceptor **2** (Scheme 1). An important feature of this assembly strategy is that upon coupling of the two fragments the entire skeleton of tricolorin A would be intact. This strategy would give a maximally convergent synthesis. Retrosynthesis of the lactone disaccharide fragment **2** illustrates how we planned to use the intrinsic difference in reactivities of the hydroxyl groups of the molecule to selectively form some of the carbon−oxygen bonds. Macrolactonization would occur on an acid diol substrate **4**. We believed lactonization would selectively occur at the C-3 glucose hydroxyl group due to the steric impediment that the large substituent at the anomeric position of the glucose ring would present at the C-2 hydroxyl group. By using the intrinsic difference in reactivities of these hydroxyl groups, we could minimize the number of different types of protecting groups used in the synthesis. Using fewer types of protecting groups would result in a reduction of protecting and deprotecting steps.

Our initial task in the project was to develop an efficient synthesis of the hydroxy ester portion of the molecule with a high degree of enantiomeric purity. Starting from 1-decyne, deprotonation of the akyne followed by addition of hexanal gave the racemic propargylic alcohol **6** (Scheme 2). Moffat-Swern oxidation of the propargylic alcohol to the corresponding acetylenic ketone **7** and chiral reduction with NB-Enantrane[2] gave an optically active alcohol **8**. Derivatization of the alcohol as the Mosher ester[3] revealed that the compound had a modest enantiomeric purity (81% ee). The remaining steps of the side chain synthesis were investigated using the less precious racemic material. Isomerization of the propargylic alcohol **6** with $KNH(CH_2)_3NH_2$ (KAPA)[4] gave the terminal alkyne **9** in good yield. Refunctionalization of the alkyne to the ester was a multistep procedure. Deprotonation with base followed by addition of TMSCl gave the bis-silyl compound **10**. Hydroboration with $(C_6H_{11})_2BH$ followed by oxidation of the alkylborane resulted in isolation of the acid **11**.[5] Finally, the desired methyl ester **12** was obtained by Fisher esterification of **11**.

Although multigram quantities of material could be moved through this synthesis, which could give enantiomerically enriched hydroxy ester in 37% overall yield, the approach had two major flaws. First, the enantiomeric purity of material generated from this synthesis would not be sufficient for our needs. Additionally, oxidative cleavage of the alkyne was unnecessarily labor intensive and clumsy. Thus, we sought to develop an improved synthesis of the hydroxy ester.

⊗ Abstract published in *Advance ACS Abstracts,* November 15, 1997.

(1) Pereda-Miranda, R.; Mata, R.; Anaya, A. L.; Wickramaratne, D. B. M.; Pezzuto, J. M.; Kinghorn, A. D. *J. Nat. Prod.* **1993**, *56*, 571.

(2) NB-Enantrane is the reaction product of 9-borabicyclo[3.3.1]-nonane (9-BBN) and (1*R*)-(−)-nopol benzyl ether. Midland, M.; Kazubski, A. *J. Org. Chem.* **1982**, *47*, 2814. The reagent is commercially available from the Aldrich Chemical Co., Inc.

(3) Dale, J.; Dull, D.; Mosher, H. *J. Org. Chem.* **1969**, *34*, 2543.

(4) (a) Brown, C. A.; Yamashita, A. *J. Am. Chem. Soc.* **1975**, *97*, 891. (b) Midland, M. M.; Halterman, R. L.; Brown, C. A.; Yamaichi, A. *Tetrahedron Lett.* **1981**, *22*, 4171.

(5) Zweifel, G.; Backlund, S. *J. Am. Chem. Soc.* **1977**, *99*, 3184.

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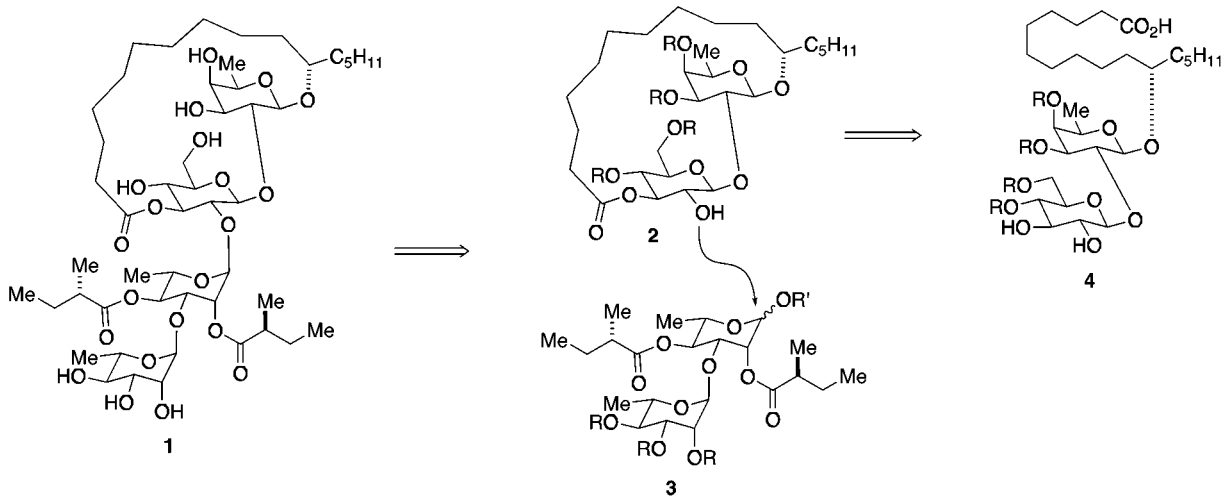
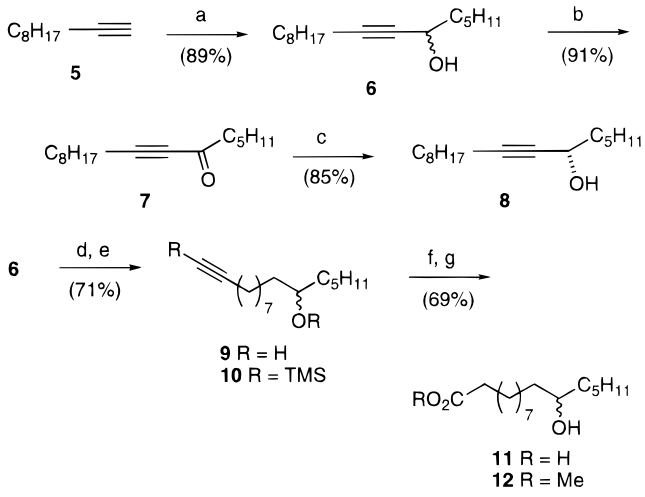
Scheme 1

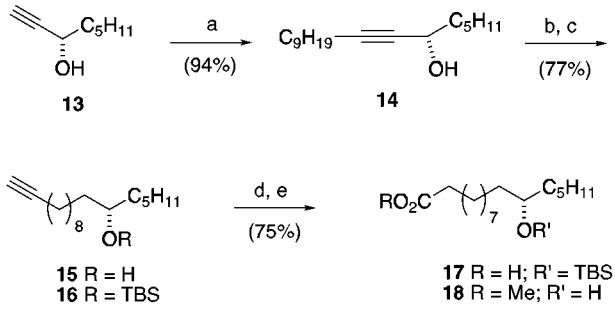


Scheme 2[a]



[a] Key: (a) (i) *n*-BuLi; (ii) hexanal; (b) $(COCl)_2$, DMSO, Et_3N; (c) NB-Enantrane; (d) KAPA; (e) (i) *n*-BuLi; (ii) Me_3SiCl; (f) (i) $(C_6H_{11})_2BH$; (ii) H_2O_2, NaOH; (g) MeOH, H_2SO_4.

Scheme 3[a]



[a] Key: (a) (i) $LiNH_2$, NH_3, −33 °C; (ii) $C_9H_{19}I$, THF, −33 → 25 °C; (b) KAPA, THF; (c) TBSCl, imidazole, DMF; (d) $KMnO_4$, HOAC, H_2O, pentane; (e) MeOH, H_2SO_4.

Our second generation hydroxy ester synthesis (Scheme 3) began with the (*S*)-propargylic alcohol **13**, which was obtained by resolution of the corresponding racemate.[6] Deprotonation of compound **13** with $LiNH_2$ followed by addition of excess 1-iodononane gave only the C-alkylated product **14** in 94% yield. Terminal alkyne **15** was produced in 79% yield by isomerization of the propargylic alcohol with KAPA. Protection of the alcohol with *tert*-butyldimethylsilyl chloride, followed by oxidative cleavage of the alkyne to the corresponding acid,[7] and subsequent Fisher esterification gave the methyl ester. Additionally, the acidic esterification reaction conditions conveniently cleaved the TBS ether to give the desired hydroxy ester **18**. The second generation synthesis gave the hydroxy ester in 56% yield over five steps, and the product had a very high degree of enantiomeric purity.

The next task was to synthesize glucose and fucose glycosyl donors and assemble the aliphatic glycoside of the fucosyl-glucose unit. We initially investigated use of the sulfoxide glycosylation method[8] to assemble these fragments but found the glycosyl trichloroacetimidate method[9] to be more successful in forming the glycosidic linkages that we desired in high yield. As shown in Scheme 4, the fucose trichloroacetimidate donor synthesis began with the known benzyl α-D-fucopyranoside (**19**).[10] Selective protection of the C-3 and C-4 hydroxyl groups as the acetonide followed by protection of the C-2 hydroxyl group as the pivaloyl ester gave the fully protected intermediate **21**. The anomeric position was then unmasked by catalytic hydrogenation of the benzyl ether. Activation of the fucose derivative for glycoside formation was achieved by treatment with Cl_3CCN and Cs_2CO_3[11] to furnish trichloroacetimidate **23**. Coupling of hydroxy ester **18** and the crude trichloroacetimidate occurred smoothly in CH_2Cl_2 with catalytic TMSOTf to give **24**, having the desired β-glycosidic linkage, in 79% yield. We found that use of a pivaloyl protecting group at the C-2 position of the fucose donor resulted in a cleaner coupling reaction. Use of the acetyl-protected analogue resulted in significant acyl transfer to the acceptor hydroxyl group. The C-2 hydroxyl group was exposed by cleavage of the pivaloyl ester with NaOMe in a MeOH/MeOAc cosolvent to give coupling partner **25**. A large excess of NaOMe was employed in this reaction to allow the reaction to proceed at a practical rate. We found that use of MeOAc in this step greatly minimized saponification of the

(6) Hashimoto, S.; Kase, S.; Suzuki, A.; Yanagiya, Y.; Ikegami, S. *Synth. Commun.* **1991**, *21*, 833.

(7) Krapcho, A. P.; Larson, J. R.; Eldridge, J. M. *J. Org. Chem.* **1977**, *42*, 3749.

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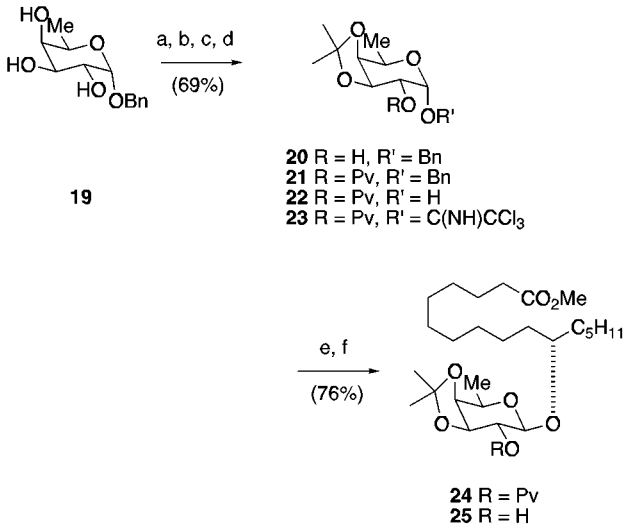
(9) Schmidt, R. R. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 212.

(10) Heyns, K.; Baron, A. L.; Paulsen, H. *Chem. Ber.* **1964**, *97*, 921.

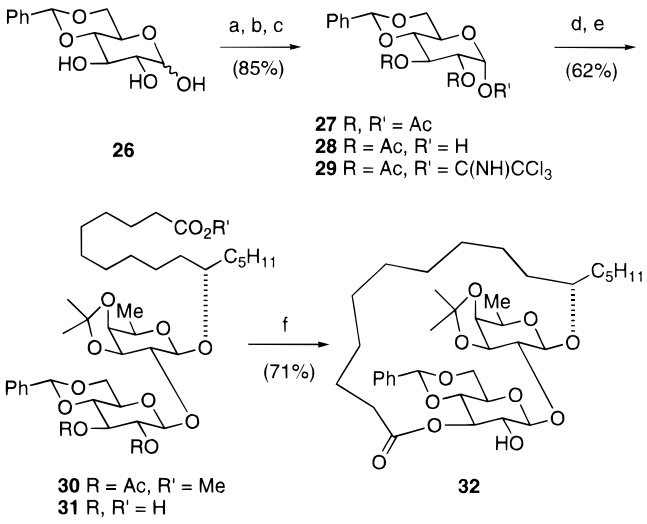
(11) Urban, F. J.; Moore, B. S.; Breitenbach, R. *Tetrahedron Lett.* **1990**, *31*, 4421.

Scheme 4[a]



[a] Key: (a) 2,2-dimethoxypropane, *p*-TsOH; (b) *t*-BuCOCl, pyridine, DMAP, 70 °C; (c) 50 psi H_2, $Pd(OH)_2$, EtOAc; (d) Cl_3CCN, Cs_2CO_3, CH_2Cl_2; (e) (i) **18**; (ii) TMSOTf, CH_2Cl_2; (f) NaOMe, MeOH, MeOAc.

Scheme 5[a]

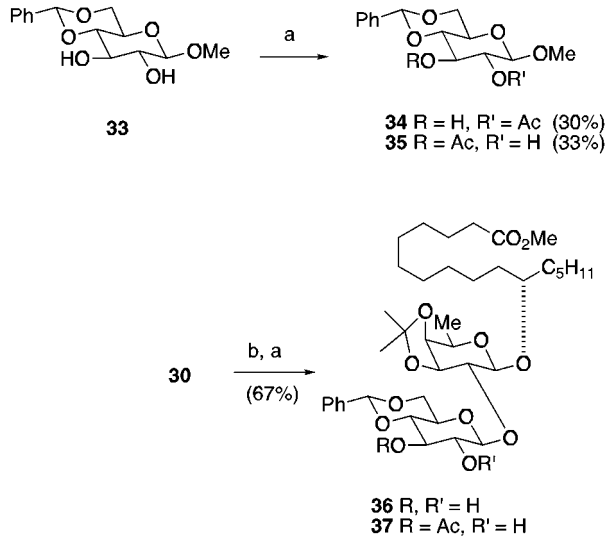


[a] Key: (a) Ac_2O, Et_3N, DMAP, CH_2Cl_2; (b) (i) $BnNH_2$, THF; (ii) 1 N HCl; (c) Cl_3CCN, Cs_2CO_3, CH_2Cl_2; (d) (i) **25**; (ii) AgOTf, CH_2Cl_2; (e) LiOH, THF, H_2O; (f) 2,4,6-trichlorobenzoyl chloride, Et_3N, DMAP, benzene.

methyl ester functionality in the molecule by a minor amount of hydroxide present in the NaOMe reaction solution.

The glucose unit preparation began by protection of the known glucopyranose **26**[12] to form the triacetyl compound **27** (Scheme 5). Formation of the amino glycoside by treatment with $BnNH_2$ followed by selective hydrolysis with dilute aqueous acid[13] furnished pyranose **28** in 87% yield. Formation of the corresponding trichloroacetimidate by treatment with Cl_3CCN and Cs_2CO_3 gave glycosyl donor **29**. Treatment of alcohol **25** with the crude trichloroacetimidate and anhydrous AgOTf[14] in

Scheme 6[a]



[a] Key: (a) Ac_2O (1 equiv), Et_3N, DMAP, CH_2Cl_2; (b) NaOMe, MeOH, MeOAc.

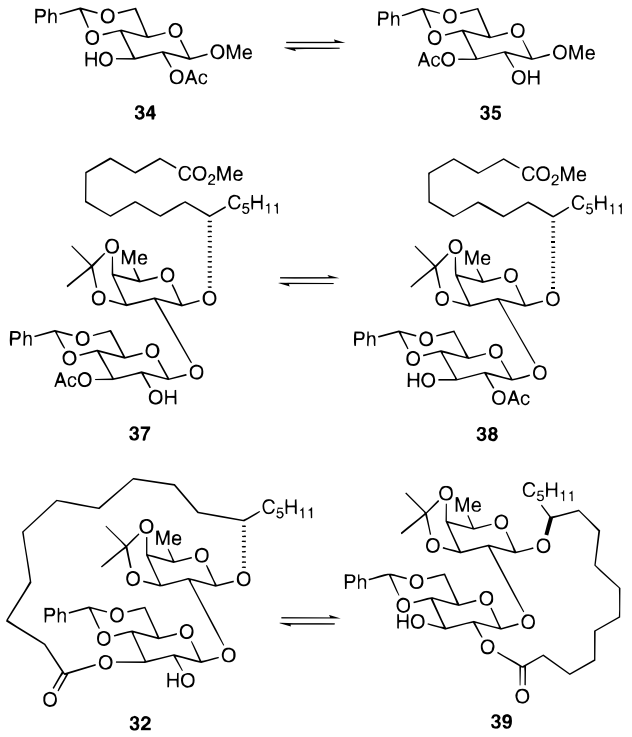
CH_2Cl_2 gave the β-disaccharide **30** in 84% yield. Simultaneous saponification of the three ester groups in disaccharide **30** with LiOH provided the macrolactonization precursor **31**. Following the Yonemitsu protocol,[15] the dihydroxy acid lactonized at the C-3 hydroxyl position of the glucose ring with a high degree of selectivity over the C-2 position to give the target lactone **32** in 71% yield.

Although we expected the macrolactonization reaction to be selective, we were intrigued by the extremely high degree of selectivity of this reaction and were curious about whether the selectivity was due to something intrinsic to the macrolactonization or common to other acylations of this substrate type. Also, we wondered if this was a kinetic or a thermodynamic result. To address the question of the selectivity of intermolecular acylations, the acylation of a simple glucose derivative was first investigated to provide a basis of comparison. Reaction of diol **33** with 1 equiv of acetic anhydride resulted in isolation of C-2 and C-3 monoacetate compounds (**34** and **35**) in a ratio of about 1:1 (Scheme 6). Conversely, when diol **36** was treated with 1 equiv of acetic anhydride, the C-3 monoacetate **37** was formed in 80% yield. Only a trace of another compound, presumed to be the C-2 monoacetate, was observed to be present in the ^1H NMR spectrum of the crude reaction product. Thus, the C-3 glucose hydroxyl group of the disaccharide diol was found to be much more reactive than the C-2 hydroxyl group in an intermolecular acylation as well as in the previously discussed intramolecular acylation. It is likely that the steric bulk of the glucose anomeric substituent is responsible for the regioselectivity observed in acylation of **36** and in the intramolecular acylation observed in **31**.

To address the equilibration characteristics of the reaction substrate, we first examined equilibration of the simple glucose monosacccharide monoacetates **34** and **35**. To simulate the acylation reaction conditions, each of the C-2 and C-3 monoacetates was treated with triethylammonimum acetate and DMAP in methylene chloride. Neither compound equilibrated to an observable extent

(12) Wood, H. B., Jr.; Diehl, H. W.; Fletcher, H. G., Jr. *J. Am. Chem. Soc.* **1957**, *79*, 1986.
(13) (a) Sim, M. M.; Kondo, H.; Wong, C.-H. *J. Am. Chem. Soc.* **1993**, *115*, 2260. (b) Helferich, B.; Portz, W. *Chem. Ber.* **1953**, *86*, 604.
(14) Douglas, S. P.; Whitfield, D. M.; Krepinsky, J. J. *J. Carbohydr. Chem.* **1993**, *12*, 131.
(15) (a) Evans, D. A., Ng, H. P.; Rieger, D. L. *J. Am. Chem. Soc.* **1993**, *115*, 11446. (b) Hikota, M.; Sakurai, Y.; Horita, K.; Yonemitsu, O. *Tetrahedron Lett.* **1990**, *31*, 6367.

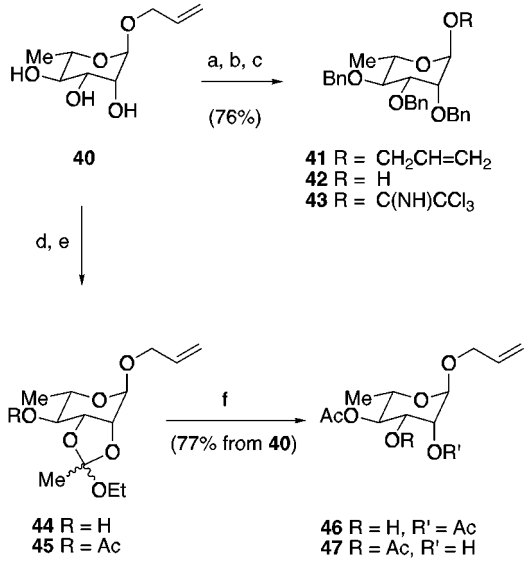
Scheme 7



under these conditions after 48 h. In contrast, the C-2 monoacetate **34** rapidly equilibrated to a 1:1.3 ratio of **34** and **35** when reacted with a catalytic amount of NaH (Scheme 7). Reaction of the C-3 monoacetate **35** with catalytic NaH resulted in generation of a similar ratio of monoacetates. Disaccharide monoacetate **37** behaved in the same manner, equilibrating to a 1.3:1 ratio of C-3 monoacetate **37** and a new compound when treated with catalytic NaH. Although the new compound was chromatographically inseparable from isomer **37**, the ^{1}H NMR spectrum of the mixture was consistent with the new compound being the C-2 monoacetate **38**. When macrolactone **32** was subjected to the equilibration conditions, a 5.8:1 ratio of **32** and a new compound resulted. Again, the new compound could not be cleanly isolated, but the ^{1}H NMR spectrum of the impure material was consistent with the major component being the C-2 isomer **39**. Thus, the observed acylation selectivity appears to be kinetic. Interestingly though, even under thermodynamic conditions, the desired C-3 macrolactone is favored substantially.

With a good route to **32** in hand, we turned our attention to the rhamnose disaccharide glycosyl donor. Since the trichloroacetimidate glycosylation method had worked so well in the assembly of the glycosidic linkages in the lactone disaccharide subunit, we decided to employ this method in the formation of the remaining glycosidic linkages in the natural product. The rhamnose donor synthesis began from the known allyl rhamnoside **40** (Scheme 8).[16] Benzylation of the hydroxyl groups, followed by isomerization of the allyl group with *t*-BuOK and DMSO and acid hydrolysis of the resulting enol ether, gave the tribenzylrhamnose **42** in high yield.[17] Formation of the corresponding trichloroacetimidate by

Scheme 8[a]



[a] Key: (a) BnBr, Bu_4NI, NaH, DMF; (b) (i) *t*-BuOK, DMSO, 100 °C; (ii) 1 N HCl, acetone, reflux; (c) Cl_3CCN, Cs_2CO_3, CH_2Cl_2; (d) $(EtO)_3CMe$, *p*-TsOH, CH_2Cl_2; (e) Ac_2O, Et_3N, DMAP, CH_2Cl_2; (f) HOAc, H_2O.

treatment with Cl_3CCN and Cs_2CO_3 gave glycosyl donor **43**. For synthesis of the rhamnose acceptor, **40** was transformed into the 2,3 ortho ester by reaction with triethyl orthoacetate and catylatic acid. The acid-labile ortho ester was immediately subjected to standard acylation conditions to give the fully protected rhamnoside **45**. Brief exposure of the ortho ester to aqueous acetic acid resulted in transformation to a 7:1 mixture of 2,4-acetyl (**46**) and 3,4-acetyl (**47**) derivatives.[18] Although the isomers were not separable by chromatography, recrystallization two times resulted in isolation of pure **46**. The overall yield of **46** by this sequence was 77%, based on compound **40**.

In the coupling of the two rhamnose sugars, we were concerned that the Lewis acidic reaction conditions might catalyze acetyl migration between the cis-oriented C-2 and C-3 positions of the acceptor **46**. Addition of either BF_3 etherate or TMSOTf to a solution of donor **43** and acceptor **46** failed to give the desired disaccharide coupling product. Instead, a small amount of a C1−O−C1 glycosyl acetal dimer of **43** and good recovery of the acceptor resulted. Although we were disappointed that coupling failed, we were pleased that the anticipated problem with acetyl migration did not manifest itself. The dimerization of the donor was a strong indication of its unstable nature. We hypothesize that during the workup of the trichloroacetimidate formation reaction a small amount of the trichloroacetimidate decomposes back to the reducing sugar **42**. When this mixture is activated with the Lewis acid, the donor rapidly reacts with the reducing sugar and also decomposes before it can couple with the relatively unreactive acceptor. To minimize the exposure of the donor to the Lewis acidic reaction solution, a solution of donor **43** was slowly added by syringe pump to a solution of the acceptor **46** and Lewis acid. Thus, the ratio of acceptor to activated donor in the reaction solution would be relatively high, which

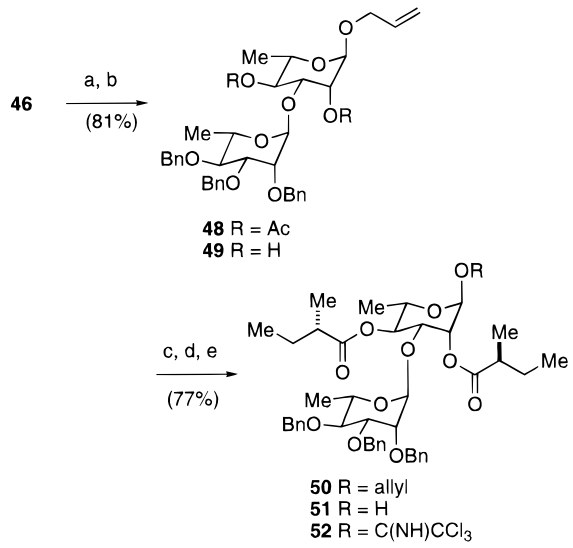
(16) Aspinall, G.; Crane, A.; Gammon, D.; Ibrahim, I.; Khare, N.; Chatterjee, D.; Rivoire, B.; Brennan, P. *Carbohydr. Res.* **1991**, *216*, 337.

(17) (a) Gigg, J.; Gigg, R. *J. Chem. Soc.* **1966**, 82. (b) Gigg, R.; Warren, C. *J. Chem. Soc.* **1965**, 2205.

(18) (a) Garegg, P.; Hultberg, H. *Carbohydr. Res.* **1979**, *72*, 276. (b) Lemieux, R.; Driguez, H. *J. Am. Chem. Soc.* **1975**, *97*, 4069.

(19) Schmidt, R.; Toepfer, A. *Tetrahedron Lett.* **1991**, *32*, 3353.

Scheme 9[a]



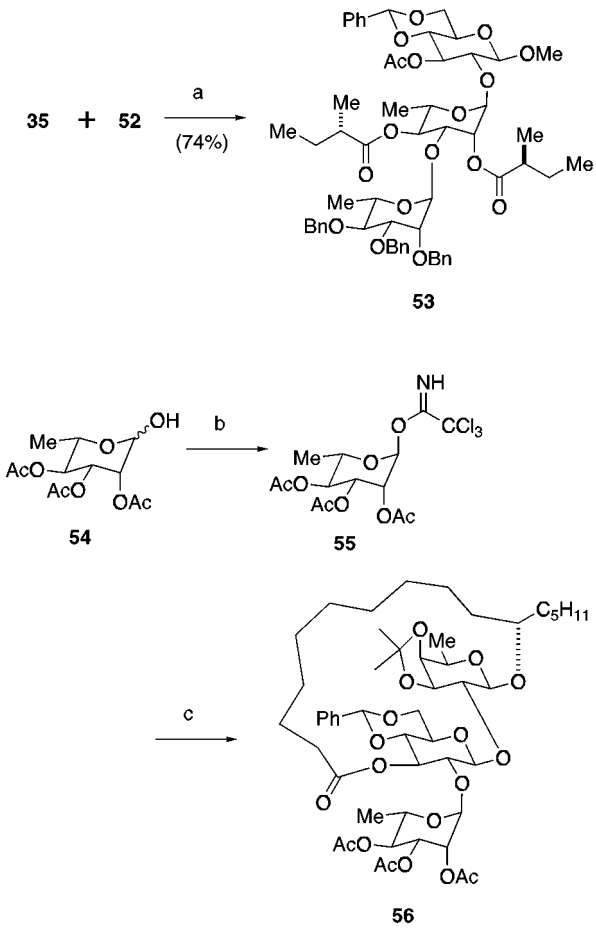
[a] Key: (a) (i) $BF_3{\cdot}Et_2O$, CH_2Cl_2; (ii) **43**, CH_2Cl_2; (b) NaOMe, MeOH; (c) (*S*)-2-methylbutyric acid, DCC, DMAP, CH_2Cl_2; (d) (i) $(Ph_3P)_3RhCl$, EtOH, H_2O, reflux; (ii) HgO, $HgCl_2$, acetone, H_2O; (e) Cl_3CCN, Cs_2CO_3, CH_2Cl_2.

would favor the cross-coupling reaction.[19] By employing this strategy, the desired disaccharide **48** was obtained in 91% yield (Scheme 9). The synthesis of the disaccharide donor was continued by removing the acetate groups and installing the chiral side chains. The anomeric position was unmasked by isomerization of the allyl group with Wilkinson's catalyst and cleavage of the resulting enol ether with HgO and $HgCl_2$. The resulting lactol was converted to the corresponding glycosyl trichloroacetimidate **52**.

With both disaccharides in hand, the final task was to couple the fully elaborated disaccharide donor **52** with the lactone disaccharide acceptor **32**. Unfortunately, this coupling failed. We investigated many reaction conditions using either AgOTf or TMSOTf as a catalyst. In retrospect, it is not especially surprising that this reaction was unsuccessful, as both the glycosyl donor and acceptor are sterically congested at their respective reaction sites. Donor **52** is probably deactivated by the α-branched ester adjacent to the anomeric position, and acceptor **32** may be hindered by the bulky anomeric substituent and the macrolactone at the sites adjacent to the C-2 hydroxyl group. To test this theory, two model couplings were performed. In the first of these test reactions, donor **52** was coupled to the less sterically hindered glucoside **35**, giving trisaccharide **53** in good yield (Scheme 10). Additionally, macrolactone **32** was successfully coupled with a simplified rhamnose donor **55**, providing a compound that was spectroscopically consistent with trisaccharide **56** in good yield.

On the basis of the foregoing model studies, our synthetic approach to tricolorin A was modified to permit coupling of less congested donor and acceptor disaccharides. To this end, allyl glycoside **48** was isomerized by a newly developed rhodium catalyst, formed by reaction of $(Ph_3P)_3RhCl$ and *n*-butyllithium (Scheme 11).[20] Cleavage of the enol ether was effected by HgO and $HgCl_2$, and the lactol was converted to the trichloroacetimidate **58**. Reaction of donor **58** with monoacetate **37** (see Scheme 6) in the presence of TMSOTf gave the tetrasaccharide **59** in 75% yield. In preparation for macrolactonization, the four ester groups were saponified to give the acid triol **60**.

Scheme 10[a]



[a] Key: (a) TMSOTf, CH_2Cl_2; (b) Cl_3CCN, Cs_2CO_3, CH_2Cl_2; (c) (i) **32**; (ii) TMSOTf, CH_2Cl_2.

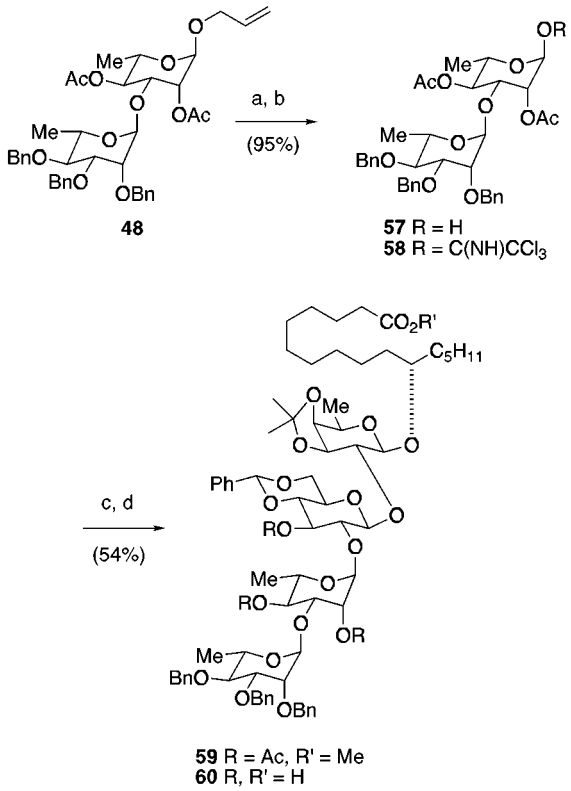
Macrolactonization with DCC, DMAP, and DMAP−TFA as activating agents in refluxing $CHCl_3$[21] resulted in formation of the desired C-3 glucose lactone **61**, accompanied by a compound spectroscopically consistent with C-2 rhamnose lactone **62**, each in about 25% yield. However, use of the Yonemitsu lactonization protocol gave varying ratios of **61** and **62**, depending on the reaction conditions (Scheme 12). A reaction time of 16 h gave the best yield of 61% for the desired lactone **61**, with only about 1−2% of the isomeric lactone **62**. Shorter reaction times led to incomplete reaction, and longer reaction times led to lower yields of the desired lactone **61** and slightly higher yields of **62**, accompanied by general decomposition. We believe that the desired lactone is a kinetic reaction product and that the isomeric lactone **62** results from subsequent acyl migration. However, we were not able to validate this hypothesis experimentally. Attempts to equilibrate either **61** or **62** by treatment with 2,4,6-trichlorobenzoyl chloride, Et_3N, and DMAP or catalytic NaH were inconclusive. Only decomposition products were observed to result from these reactions.

Acylation of **61** with (*S*)-2-methylbutyric acid, DCC, and DMAP resulted in smooth installation of the two chiral side chains. Since the lactonization employed a

(20) Boons, G.-J.; Burton, A.; Isles, S. *Chem. Commun.* **1996**, 141.

(21) Boden, E.; Keck, G. *J. Org. Chem.* **1985**, *50*, 2394.

Scheme 11[a]



[a] Key: (a) (i) $(Ph_3P)_3RhCl$, *n*-BuLi, THF, reflux; (ii) HgO, $HgCl_2$, acetone, H_2O; (b) Cl_3CCN, Cs_2CO_3, CH_2Cl_2; (c) (i) **37**; (ii) TMSOTf, CH_2Cl_2; (d) LiOH, THF, H_2O.

vast excess of activating agent, we thought that these two steps could be successfully combined into a one-pot procedure. This tandem process turned out to work very well. After the lactonization had proceeded for 16 h, excess (*S*)-2-methylbutyric acid was introduced. After an additional 2.5 h, the reaction mixture was worked up in the normal manner to afford the fully elaborated tetrasaccharide **63** in 61% yield. Global deprotection was accomplished by catalytic hydrogenation under acidic conditions to give tricolorin A (**1**) in good yield. The synthetic material was found to be identical in all respects (^{13}C NMR, ^1H NMR, mp, and TLC mobility) with an authentic sample provided by Dr. Pereda-Miranda.

In summary, we have developed an efficient synthesis of the natural product tricolorin A. Starting from fucose, glucose, rhamnose, and (*S*)-1-octyn-3-ol, the synthesis required 39 steps overall. The longest linear sequence was 14 steps, with an overall yield for this longest linear sequence of 6%.

Experimental Section

General Methods. Unless otherwise noted, starting materials were obtained from commercial suppliers and used as received. All reactions were carried out under an argon atmosphere, unless otherwise stated. Tetrahydrofuran (THF) was distilled under nitrogen from sodium/benzophenone immediately prior to use. Benzene, CH_2Cl_2, and Et_3N were distilled under nitrogen from CaH_2 immediately prior to use. Silica gel chromatography was performed according to the method of Still.[22] All melting points are uncorrected. Coupling constants (*J*) are reported in Hz.

(6*S*)-6-Hydroxy-7-heptadecyne (14). Approximately 50 mL of NH_3 was condensed into a three-necked round-bottomed flask fitted with a dry ice condenser. Upon addition of approximately 5 mg of lithium to the refluxing NH_3, the reaction solution became dark blue. Addition of 10 mg of $Fe(NO_3)_3 \cdot 9H_2O$ resulted in a sudden change of the reaction solution to brownish gray after 2−3 min. Lithium (total of 190 mg, 27.4 mmol) was then added in several portions, and the solution was stirred until the brownish gray color persisted. (3*S*)-1-Octyn-3-ol (1.00 mL, 6.85 mmol) was added dropwise, and the resulting grayish suspension was stirred for 20 min. 1-Iodononane (4.06 mL, 20.6 mmol) in 30 mL of THF was added dropwise, and the reaction mixture was stirred at NH_3 reflux temperature for 30 min. The reaction mixture was warmed to room temperature over 90 min and then stirred for 90 min. After careful addition of 10 mL of H_2O, the reaction mixture was diluted with 1:1 EtOAc/hexanes and washed with 1 N HCl, saturated $NaHCO_3$, 10% $Na_2S_2O_3$, and brine. The organic layer was dried over Na_2SO_4, concentrated, and purified by chromatography on silica gel with 510% EtOAc in hexanes as eluent to give 1.62 g (94%) of a clear, colorless oil: ^1H NMR ($CDCl_3$, 400 MHz) δ 0.86−0.91 (m, 6H), 1.03−1.75 (m, 22H), 2.19 (dt, 2H, J = 1.9, 7.1), 4.34 (tt, 1H, J = 1.9, 6.6); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.0, 14.1, 18.7, 22.6, 22.7, 24.9, 28.7, 28.8, 29.1, 29.3, 29.5, 31.5, 31.9, 38.2, 62.8, 81.3, 85.5; IR (thin film) 3349 cm^{-1}; $[\alpha]_D$ −1 (c = 0.68, CH_2Cl_2). Anal. Calcd for $C_{17}H_{32}O$: C, 80.89; H, 12.78. Found: C, 80.76; H, 12.87.

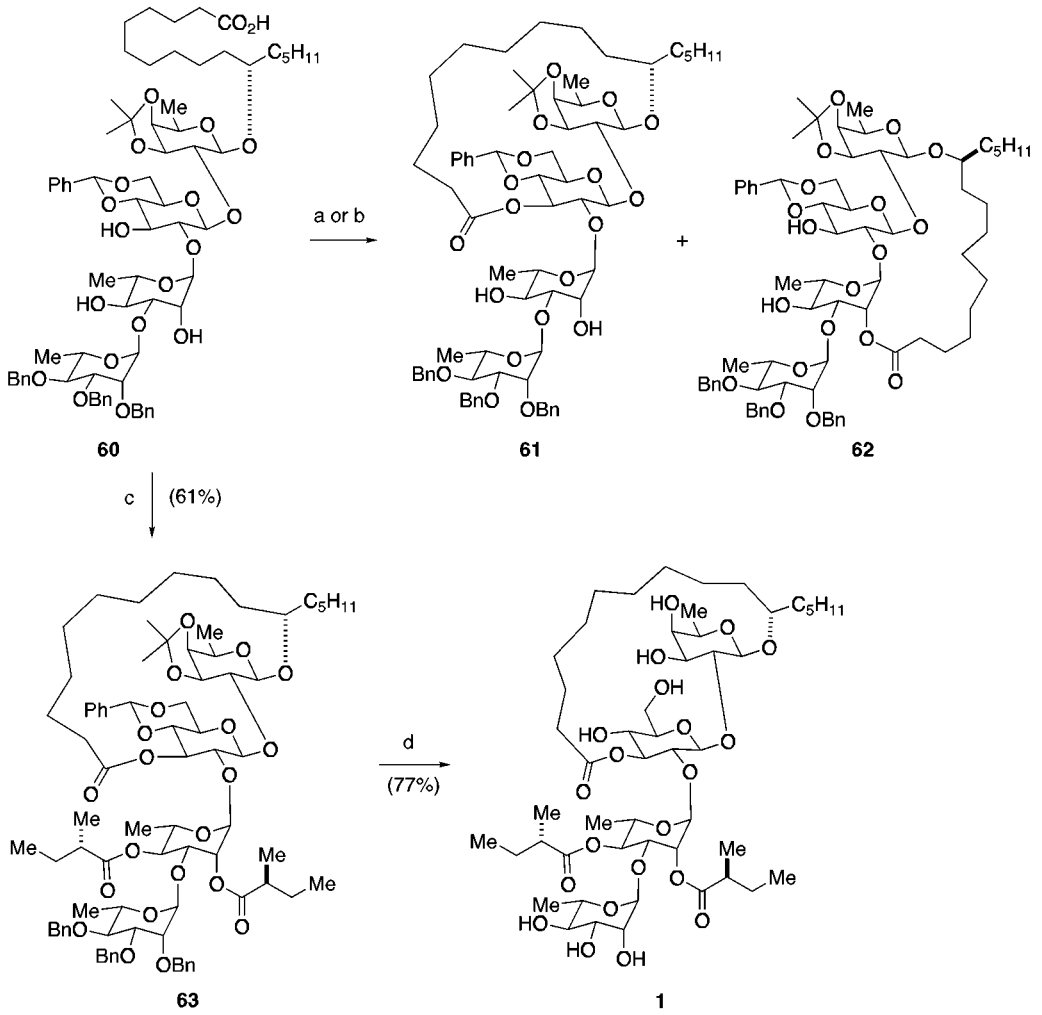
(12*S*)-12-Hydroxy-1-heptadecyne (15). A dry flask was charged with 3.51 g (30.7 mmol) of a 35% (weight) oil dispersion of KH that was rinsed with pentane. The last of the pentane was removed under a stream of argon. 1,3-Diaminopropane (16.7 mL, 200 mmol) was added dropwise and stirred for 90 min to give a homogeneous brown solution. Propargylic alcohol **14** (1.50 g, 5.94 mmol) in 8 mL of THF was added dropwise and stirred for 90 min. The viscous reddish brown mixture was quenched with 10 mL of H_2O and extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, concentrated, and purified by chromatography on silica gel with 58% EtOAc in hexanes as eluent to give 1.18 g (79%) of a white solid: mp 37−38 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.88 (t, 3H, J = 6.9), 1.28−1.55 (m, 24H), 1.92 (t, 1H, J = 2.6), 2.17 (dt, 2H, J = 2.6, 7.1), 3.57 (br m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.0, 18.4, 22.6, 25.3, 25.6, 28.5, 28.7, 29.0, 29.4, 29.5, 29.7, 31.9, 37.4, 37.4, 68.0, 72.0, 84.7; IR (KBr) 3308, 3233, 2143 cm^{-1}; $[\alpha]_D$ +0.8 (c = 0.37, CH_2Cl_2). Anal. Calcd for $C_{17}H_{32}O$: C, 80.89; H, 12.78. Found: C, 81.20; H, 12.77.

(12*S*)-12-[(*tert*-Butyldimethylsilyl)oxy]-1-heptadecyne (16). A solution of alcohol **15** (1.12 g, 4.44 mmol), *tert*-butyldimethylsilyl chloride (1.00 g, 6.66 mmol), and imidazole (605 mg, 8.88 mmol) in 3 mL of DMF was stirred overnight at room temperature. The reaction solution was diluted with 75 mL of Et_2O and washed with H_2O, 1 N HCl, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$, concentrated, and purified by chromatography on silica gel with 05% EtOAc in hexanes as eluent to give 1.59 g (98%) of a clear, colorless oil: ^1H NMR ($CDCl_3$, 400 MHz) δ 0.03 (s, 6H), 0.87−0.90 (m, 12H), 1.27−1.40 (m, 22H), 1.52 (m, 2H), 1.93 (t, 1H, J = 2.7), 2.18 (dt, 2H, J = 2.7, 7.1), 3.61 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ −4.4, 14.1, 18.2, 18.4, 22.7, 25.0, 25.3, 25.9, 28.5, 28.8, 29.1, 29.4, 29.6, 29.8, 32.1, 37.1, 37.1, 68.0, 72.4, 84.7; IR (thin film) 3314, 2136, 1057 cm^{-1}; $[\alpha]_D$ −0.05 (c = 5.60, CH_2Cl_2). Anal. Calcd for $C_{23}H_{46}OSi$: C, 75.33; H, 12.64. Found: C, 75.31; H, 12.84.

(11*S*)-11-[(*tert*-Butyldimethylsilyl)oxy]hexadecanoic Acid (17). A solution of $KMnO_4$ (3.08 g, 19.5 mmol) in 20 mL of H_2O was cooled in an ice bath. In one portion a solution of alkyne **16** (1.43 g, 3.90 mmol), 6 mL of HOAc, and 5 drops of Aliquat 336 in 15 mL of pentane was added. Without replenishing the ice in the cooling bath, the reaction mixture was stirred for 24 h. After cooling in an ice bath, 5 g of Na_2SO_3 and 10 mL of 6 N HCl were carefully added to the viscous black reaction mixture. After the mixture was stirred for 10 min, a white precipitate formed as the reaction mixture became colorless. The reaction mixture was diluted with 50 mL of H_2O and extracted with hexanes. The combined organic layers were dried over Na_2SO_4 and concentrated to give 1.46

(22) Still, W. C.; Kahn, M., Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

Scheme 12[a]



[a] Key: (a) DCC, DMAP, DMAP·TFA, $CHCl_3$, reflux (28% for **61**, 24% for **62**); (b) 2,4,6-trichlorobenzoyl chloride, Et_3N, DMAP, benzene (61% for **61**); (c) (i) 2,4,6-trichlorobenzoyl chloride, Et_3N, DMAP, benzene; (ii) (*S*)-2-methylbutyric acid; (d) $Pd(OH)_2$, H_2, HCl, MeOH.

g of slightly yellowish oil. The product was used in the following step without further purification.

Methyl (11*S*)-11-Hydroxyhexadecanoate (18). A solution of crude acid **17** (1.46 g) and 0.5 mL of H_2SO_4 in 50 mL MeOH was heated at reflux for 2 h. After the solution was cooled to room temperature, 1 g of $NaHCO_3$ was added in small portions. The resulting slurry was concentrated, diluted with 75 mL of H_2O, and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, concentrated, and purified by chromatography on silica gel with 5 → 20% EtOAc in hexanes as eluent to give 835 mg (75%) of a white solid: mp 44−45 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.88 (t, 3H, J = 6.8), 1.27−1.47 (m, 22H), 1.60 (br m, 2H), 2.29 (t, 2H, J = 7.6), 3.56 (br m, 1H), 3.65 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.0, 22.6, 24.9, 25.3, 25.6, 29.1, 29.2, 29.3, 29.5, 29.6, 31.9, 34.1, 37.4, 37.4, 51.4, 72.0, 174.3; IR (KBr) 3343, 1746, 1175 cm^{-1}; $[\alpha]_D$ +0.8 (c = 0.51, CH_2Cl_2). Anal. Calcd for $C_{17}H_{34}O_3$: C, 71.28; H, 11.96. Found: C, 71.51; H, 12.05.

Benzyl 3,4-*O*-Isopropylidene-α-D-fucopyranoside (20). Benzyl fucoside **19** (3.07 g, 12.1 mmol) and *p*-TsOH·H_2O (228 mg, 1.2 mmol) were combined with 25 mL of reagent grade acetone and 25 mL of 2,2-dimethoxypropane. After the reaction solution stirred for 19 h, 1 mL of Et_3N was added and the reaction solution was concentrated. The oily residue was purified by chromatography on silica gel with 20 → 40% EtOAc in hexanes as eluent to give 3.08 g (87%) of a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.31 (d, 3H, J = 6.7), 1.35 (s, 3H), 1.51 (s, 3H), 3.82 (dd, 1H, J = 4.0, 6.4), 4.06 (dd, 1H, J = 2.3, 6.1), 4.16 (dq, 1H, J = 2.2, 6.7), 4.23 (t, 1H, J = 6.3), 4.57 (d, 1H, J = 11.8), 4.79 (d, 1H, J = 11.8), 4.94 (d, 1H, J = 3.9), 7.30−7.39 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.2, 25.9, 27.7, 64.1, 69.3, 69.7, 75.6, 76.1, 96.9, 109.2, 127.9, 128.5, 128.5, 137.2; IR (thin film) 3466, 1071 cm^{-1}; $[\alpha]_D$ +140 (c = 0.56, CH_2Cl_2). Anal. Calcd for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53. Found: C, 65.10; H, 7.69.

Benzyl 3,4-*O*-Isopropylidene-2-*O*-pivaloyl-α-D-fucopyranoside (21). A solution of benzyl fucoside **20** (3.08 g, 10.5 mmol) and pivaloyl chloride (6.47 mL, 52.5 mmol) in 50 mL of pyridine was stirred at 70 °C for 18 h. The reaction solution was then diluted with 200 mL of Et_2O and washed with 1 N HCl, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$, concentrated, and purified by chromatography on silica gel with 10 → 20% EtOAc in hexanes as eluent to give 3.81 g (96%) of a clear, colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.20 (s, 9H), 1.35 (s, 3H), 1.36 (d, 3H, J = 6.7), 1.52 (s, 3H), 4.08 (dd, 1H, J = 2.5, 5.4), 4.17 (dq, 1H, J = 2.4, 6.6), 4.36 (dd, 1H, J = 5.4, 8.0), 4.49 (d, 1H, J = 12.2), 4.69 (d, 1H, J = 12.2), 4.91 (dd, 1H, J = 3.7, 8.0), 4.97 (d, 1H, J = 3.7), 7.28−7.35 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.3, 26.4, 27.1, 28.0, 38.8, 63.5, 69.5, 71.4, 73.6, 76.1, 95.5, 109.3, 127.7, 127.8, 128.4, 137.3, 178.0; IR (thin film) 1732 cm^{-1}; $[\alpha]_D$ +165 (c = 1.18, CH_2Cl_2). Anal. Calcd for $C_{21}H_{30}O_6$: C, 66.65; H, 7.99. Found: C, 66.77; H, 8.01.

3,4-*O*-Isopropylidene-2-*O*-pivaloyl-α-D-fucopyranose (22). In a Parr hydrogenation bottle, benzyl fucoside **21** (3.54 g, 9.35 mmol) and 1.0 g of $Pd(OH)_2$ were combined with 50 mL of EtOAc. The bottle was then evacuated and back-filled with H_2 three times. The reaction mixture was shaken under 50 psi of H_2 for 5 days and filtered through a pad of Celite and the pad washed with MeOH. The combined filtrate was concentrated and purified by chromatography on silica gel with 20 → 30% EtOAc in hexanes as eluent to give 2.26 g (84%) of

a white solid: mp 140.5−141.5 °C; α:β ($CDCl_3$) = 1:1; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.22 (s, 4.5H), 1.23 (s, 4.5H), 1.33−1.34 (m, 4.5H), 1.41 (d, 1.5H, *J* = 6.6), 1.50 (s, 1.5H), 1.53 (s, 1.5H), 3.91 (dq, 0.5H, *J* = 2.1, 6.6), 4.04 (dd, 0.5H, *J* = 2.1, 5.6), 4.07 (dd, 0.5H, *J* = 2.3, 5.7), 4.21 (dd, 0.5H, *J* = 5.6, 7.1), 4.34−4.37 (m, 1H), 4.53 (d, 0.5H, *J* = 7.4), 4.79 (t, 0.5H, *J* = 7.4), 4.91 (dd, 0.5H, *J* = 3.6, 7.2), 5.28 (d, 0.5H, *J* = 3.6); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.4, 16.5, 26.1, 26.1, 27.0, 27.1, 27.6, 27.7, 38.8, 38.9, 63.7, 68.9, 71.0, 73.1, 75.0, 75.8, 76.0, 76.2, 90.1, 95.3, 109.4, 110.1, 178.0, 179.5; IR (KBr) 3448, 1731 cm^{-1}; $[\alpha]_D$ +67.4 (*c* = 1.29, CH_2Cl_2). Anal. Calcd for $C_{14}H_{24}O_6$: C, 58.32; H, 8.39. Found: C, 58.50; H, 8.53.

3,4-*O*-Isopropylidene-2-*O*-pivaloyl-α-D-fucopyranose 1-Trichloroacetimidate (23). A slurry of fucopyranose **22** (672 mg, 2.33 mmol), Cl_3CCN (467 μL, 4.66 mmol), and Cs_2CO_3 (75 mg, 0.23 mmol) in 3 mL of CH_2Cl_2 was stirred for 12 h. The reaction mixture was filtered through a short pad of silica gel, and the pad was washed with 250 mL of 30% EtOAc in hexanes. The combined filtrate was concentrated to give 1.05 g of slightly yellowish oil. The product was immediately used in the following step without further purification.

Methyl (11*S*)-11-[(3,4-*O*-Isopropylidene-2-*O*-pivaloyl-β-D-fucopyranosyl)oxy]hexadecanoate (24). The crude tricholoracetimidate **23** (1.05 g) and alcohol **18** (500 mg, 1.75 mmol) were combined in a flask and concentrated from freshly distilled benzene. The resulting residue was dissolved in 900 μL of CH_2Cl_2, and 940 μL of 0.05 M TMSOTf in CH_2Cl_2 was added over 25 min. After the reaction mixture was stirred for an additional 30 min, 10 mL of saturated $NaHCO_3$ was added with vigorous stirring. Following extraction with CH_2Cl_2, the combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by chromatography on silica gel with 10% EtOAc in hexanes as eluent to give 768 mg (79%) of a clear, colorless oil: ^1H NMR (C_6D_6, 400 MHz) δ 0.89 (t, 3H, *J* = 7.0), 1.20−1.68 (m, 42H), 2.12 (t, 2H, *J* = 7.4), 3.35 (s, 3H), 3.38 (m, 1H), 3.57 (dd, 1H, *J* = 2.1, 5.3), 3.68 (m, 1H), 3.96 (m, 1H), 4.33 (d, 1H, *J* = 8.3), 5.41 (t, 1H, *J* = 8.0); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.1, 16.6, 22.6, 24.6, 24.9, 25.3, 26.5, 27.2, 27.7, 29.1, 29.2, 29.4, 29.5, 29.9, 31.9, 33.9, 34.1, 34.5, 38.7, 51.4, 68.7, 73.2, 76.6, 76.7, 79.2, 99.4, 110.0, 174.3, 176.9; IR (thin film) 1740 cm^{-1}; $[\alpha]_D$ +9.0 (*c* = 0.87, CH_2Cl_2). Anal. Calcd for $C_{31}H_{56}O_8$: C, 66.87; H, 10.14. Found: C, 66.75; H, 10.01.

Methyl (11*S*)-11-[(3,4-*O*-Isopropylidene-β-D-fucopyranosyl)oxy]hexadecanoate (25). To fucopyranoside **24** (704 mg, 1.27 mmol) were added 5 mL of MeOAc and 5 mL of 10% NaOMe in MeOH sequentially. A white crystalline precipitate was observed in the reaction mixture after stirring for 10 h. The mixture was diluted with 50 mL of saturated $NaHCO_3$ and extracted with CH_2Cl_2 (2 × 50 mL). The combined organic extracts were dried over Na_2SO_4, concentrated, and purified by chromatography on silica gel with 20 → 30% EtOAc in hexanes as eluent to give 574 mg (96%) of a clear, colorless oil: ^1H NMR (C_6D_6, 400 MHz) δ 0.90 (t, 3H, *J* = 7.0), 1.20−1.72 (m, 33H), 2.12 (t, 2H, *J* = 7.4), 2.36 (br s, 1H), 3.33 (dq, 1H, *J* = 2.2, 6.6), 3.36 (s, 3H), 3.54 (dd, 1H, *J* = 2.2, 5.5), 3.69 (m, 1H), 3.76 (tt, 1H, *J* = 2.4, 7.9), 4.01 (dd, 1H, *J* = 5.5, 7.3), 4.12 (d, 1H, *J* = 8.2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.0, 16.6, 22.5, 24.7, 24.9, 25.1, 26.3, 28.2, 29.0, 29.1, 29.3, 29.4, 29.7, 31.8, 33.9, 34.0, 34.7, 51.4, 69.0, 73.7, 76.4, 78.8, 79.8, 101.3, 109.7, 174.2; IR (thin film) 3497, 1740 cm^{-1}; $[\alpha]_D$ +6.1 (*c* = 0.84, CH_2Cl_2). Anal. Calcd for $C_{26}H_{48}O_7$: C, 66.07; H, 10.24. Found: C, 65.93; H, 10.14.

Acetyl 1,2,3-Tri-*O*-acetyl-4,6-*O*-benzylidene-α−D-glucopyranose (27). A solution of glucopyranose **26** (3.25 g, 12.1 mmol) in 100 mL of CH_2Cl_2 was cooled in an ice bath and treated with Et_3N (15.2 mL, 109 mmol), Ac_2O (7.32 mL, 72.6 mmol), and DMAP (148 mg, 1.21 mmol). The cooling bath was removed, and the reaction solution was stirred overnight. The reaction solution was diluted with 150 mL of CH_2Cl_2 and washed with 1 N HCl, saturated $NaHCO_3$, and H_2O. The organic layer was dried over Na_2SO_4, concentrated, and purified by chromatography on silica gel with 40 → 60% EtOAc in hexanes as eluent to give 4.61 g (96%) of a white amorphous solid: α:β = 2:3; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.04 (s, 1.2H), 2.05 (s, 1.8H), 2.06 (s, 1.8H), 2.08 (s, 1.2H), 2.11 (s, 1.8H), 3.64−3.80 (m, 2.6H), 4.04 (dt, 0.4H, *J* = 4.9, 9.9), 4.32 (dd, 0.4H, *J* = 4.9, 10.4), 4.39 (dd, 0.6H, *J* = 4.6, 10.3), 5.10−5.14 (m, 1H), 5.37 (t, 0.6H, *J* = 9.3), 5.51 (s, 0.6H), 5.52 (s, 0.4H), 5.59 (t, 0.4H, *J* = 9.9), 5.79 (d, 0.6H, *J* = 8.2), 6.31 (d, 0.4H, *J* = 3.8), 7.35−7.45 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.4, 20.5, 20.7, 20.8, 64.9, 67.0, 68.2, 68.5, 68.7, 69.8, 71.2, 71.7, 78.0, 78.6, 89.6, 92.2, 101.6, 126.1, 126.1, 128.2, 129.1, 129.2, 136.6, 136.7, 168.8, 169.0, 169.5, 169.9; IR (KBr) 1750 cm^{-1}; $[\alpha]_D$ +4.3 (*c* = 0.69, CH_2Cl_2). Anal. Calcd for $C_{19}H_{22}O_9$: C, 57.87; H, 5.62. Found: C, 57.68; H, 5.80.

2,3-Di-*O*-acetyl-4,6-*O*-benzylidene-D-glucopyranose (28). A solution of triacetate **27** (2.00 g, 5.07 mmol) and $BnNH_2$ (831 μL, 7.61 mmol) in 10 mL of THF was stirred for 14 h. After addition of 4 mL of 1 N HCl, the reaction mixture was stirred for 1 h. The reaction mixture was diluted with 50 mL of 1 N HCl and extracted with CH_2Cl_2 (3 × 50 mL). The combined extracts were dried over Na_2SO_4, concentrated, and purified by chromatography on silica gel with 30 → 50% EtOAc in hexanes as eluent to give 1.57 g (88%) of a white amorphous solid: α:β ($CDCl_3$) = 1:1; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.06 (s, 1.5H), 2.06 (s, 1.5H), 2.09 (s, 3H), 3.55 (dt, 0.5H, *J* = 5.0, 9.7), 3.61−3.86 (m, 2.5H), 4.17 (dt, 0.5H, *J* = 4.9, 9.9), 4.29 (dd, 0.5H, *J* = 4.9, 10.2), 4.36 (dd, 0.5H, *J* = 4.9, 10.5), 4.79 (d, 0.5H, *J* = 7.9), 4.88−4.92 (m, 1H), 5.34 (t, 0.5H, *J* = 9.5), 5.41 (d, 0.5H, *J* = 3.7), 5.49 (s, 0.5H), 5.50 (s, 0.5H), 5.62 (t, 0.5H, *J* = 9.8), 7.34−7.45 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.7, 20.8, 62.3, 66.5, 68.4, 68.8, 68.8, 71.3, 71.9, 74.1, 78.4, 79.1, 90.9, 95.8, 101.4, 101.5, 126.1, 126.1, 128.2, 128.9, 129.0, 129.1, 129.7, 136.6, 136.8, 170.1, 170.5, 170.9; IR (KBr) 3461, 1745 cm^{-1}; $[\alpha]_D$ −8.4 (*c* = 0.87, CH_2Cl_2). Anal. Calcd for $C_{17}H_{20}O_8$: C, 57.95; H, 5.72. Found: C, 57.72; H, 6.00.

2,3-Di-*O*-acetyl-4,6-*O*-benzylidene-α-D-glucopyranose 1-Trichloroacetimidate (29). A slurry of glucopyranose **28** (817 mg, 2.32 mmol), Cl_3CCN (465 μL, 4.64 mmol), and Cs_2CO_3 (75 mg, 0.23 mmol) in 4 mL of CH_2Cl_2 was stirred for 12 h. The reaction mixture was filtered through a short pad of silica gel, and the pad was washed with 250 mL of 40% EtOAc in hexanes. The combined filtrate was concentrated to give 1.16 g of slightly yellowish oil. The product was immediately used in the following step without further purification.

Methyl (11*S*)-11-[[(2,3-Di-*O*-acetyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-(1→2)-3,4-*O*-isopropylidene-β-D-fucopyranosyl]oxy]hexadecanoate (30). The crude tricholoracetimidate **29** (1.16 g) and alcohol **25** (556 mg, 1.18 mmol) were combined in a flask and concentrated from freshly distilled benzene. To the resulting residue were added anhydrous AgOTf (596 mg, 2.32 mmol) and 3 mL of CH_2Cl_2. The reaction flask was covered with aluminum foil, and the reaction mixture was stirred for 40 h. The reaction mixture was filtered though a pad of Celite, washing with EtOAc, and the combined filtrate concentrated. Purification by chromatography on silica gel with 20 → 30% EtOAc in hexanes as eluent gave 795 mg (84%) of a clear, colorless oil that contained a minor impurity: ^1H NMR (C_6D_6, 400 MHz) δ 0.89 (t, 3H, *J* = 7.1), 1.22−1.73 (m, 36H), 1.88 (s, 3H), 2.13 (t, 2H, *J* = 7.5), 3.27 (dq, 1H, *J* = 2.0, 6.6), 3.34 (s, 3H), 3.34−3.41 (m, 1H), 3.54 (dd, 1H, *J* = 2.0, 5.2), 3.59 (t, 1H, *J* = 10.2), 3.68 (t, 1H, *J* = 9.5), 3.72 (br m, 1H), 3.96−4.02 (m, 2H), 4.23 (dd, 1H, *J* = 5.0, 10.3), 4.28 (d, 1H, *J* = 7.6), 5.13 (d, 1H, *J* = 7.5), 5.31 (s, 1H), 5.43 (dd, 1H, *J* = 7.5, 8.7), 5.62 (dd, 1H, *J* = 8.4, 9.5), 7.04−7.15 (m, 3H), 7.55 (d, 2H, *J* = 7.0); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.1, 16.6, 20.8, 20.8, 22.6, 24.7, 24.9, 25.1, 26.3, 27.9, 29.1, 29.3, 29.5, 29.7, 29.9, 31.9, 33.8, 34.1, 34.6, 51.4, 66.3, 68.5, 68.8, 72.0, 72.9, 76.4, 78.3, 79.2, 79.6, 80.5, 100.1, 100.7, 101.4, 109.6, 126.1, 128.2, 129.1, 136.9, 169.6, 170.1, 174.2; IR (thin film) 1755, 1740 cm^{-1}. Attempts to further purify this compound for microanalysis were unsuccessful.

(11*S*)-11-[[(4,6-*O*-Benzylidene-β-D-glucopyranosyl)-(1→2)-3,4-*O*-isopropylidene-β-D-fucopyranosyl]oxy]hexadecanoic Acid (31). To a solution of triester **30** (400 mg, 0.496 mmol) in 4.5 mL of THF was added 1.5 mL of 3.3 M LiOH. The reaction solution was stirred for 15 h, acidified with 25 mL of 1 N HCl, and extracted with CH_2Cl_2. The combined extracts were dried over Na_2SO_4, concentrated, and purified by chromatography on silica gel with 5 → 10% MeOH in CH_2Cl_2 as eluent to give 258 mg (74%) of a clear, colorless, sticky solid:

^{1}H NMR (C_6D_6, 400 MHz) δ 0.90 (t, 3H, J = 6.9), 1.22−1.76 (m, 33H), 2.15 (t, 2H, J = 6.4), 3.31 (dq, 1H, J = 2.0, 6.5), 3.39 (dt, 1H, J = 4.7, 9.6), 3.47−3.53 (m, 2H), 3.60 (t, 1H, J = 10.1), 3.73−3.88 (m, 3H), 4.04 (t, 1H, J = 7.5), 4.12 (dd, 1H, J = 5.6, 7.0), 4.27 (dd, 1H, J = 4.9, 10.3), 4.32 (d, 1H, J = 7.9), 4.95 (d, 1H, J = 7.5), 5.33 (s, 1H), 7.11−7.21 (m, 3H), 7.60 (d, 2H, J = 7.1); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.0, 16.5, 22.6, 24.5, 24.6, 25.0, 26.1, 27.8, 28.9, 29.1, 29.3, 29.4, 29.9, 31.9, 33.6, 33.9, 34.4, 66.9, 68.5, 68.7, 72.6, 75.8, 76.5, 78.6, 79.8, 80.6, 80.8, 100.3, 101.9, 104.1, 110.2, 126.3, 128.2, 129.2, 137.0, 178.8; IR (thin film) 3426, 1708 cm^{-1}; $[\alpha]_D$ −5.8 (c = 1.70, CH_2Cl_2). Anal. Calcd for $C_{38}H_{60}O_{12}$: C, 64.39; H, 8.53. Found: C, 64.43; H, 8.58.

(11*S*)-11-[[(4,6-*O*-Benzylidene-*β*-D-glucopyranosyl)-(1→2)-3,4-*O*-isopropylidene-*β*-D-fucopyranosyl]oxy]hexadecanoic Acid 3_{glu}-Lactone (32). To a solution of acid **31** (50 mg, 0.0706 mmol) in 375 mL of benzene were added Et_3N (591 μL, 4.24 mmol) and 2,4,6-trichlorobenzoyl chloride (440 μL, 2.82 mmol). DMAP (172 mg, 1.41 mmol) was added to the reaction mixture in two portions, 1 h apart. After being stirred for 18 h, the milky white reaction mixture was washed with 100 mL of H_2O and separated. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, concentrated, and purified by chromatography on silica gel with 20 → 30% EtOAc in hexanes as eluent to give 35 mg (71%) of a white solid: mp 186.5−188.5 °C; ^{1}H NMR (C_6D_6, 400 MHz) δ 0.88 (t, 3H, J = 7.0), 1.26−1.78 (m, 32H), 1.99 (m, 1H), 2.12 (m, 1H), 2.22 (m, 1H), 2.89 (d, 1H, J = 4.2), 3.35−3.43 (m, 3H), 3.53−3.55 (m, 2H), 3.62, (t, 1H, J = 9.2), 3.83 (dt, 1H, J = 3.5, 8.3), 4.01 (t, 1H, J = 5.7), 4.11 (dd, 1H, J = dd, 1H, J = 3.9, 9.3), 4.19−4.26 (m, 2H), 5.12 (d, 1H, J = 7.6), 5.22 (s, 1H), 5.44 (t, 1H, J = 9.1), 7.04−7.15 (m, 3H), 7.51 (d, 2H, J = 6.8); ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 13.5, 16.1, 22.3, 24.9, 24.9, 25.5, 25.9, 26.7, 27.4, 28.1, 28.2, 29.2, 30.3, 31.6, 34.7, 35.5, 35.7, 65.8, 68.3, 68.4, 73.7, 74.5, 74.8, 76.5, 78.0, 79.0, 82.0, 98.4, 101.4, 101.7, 109.4, 126.0, 127.9, 128.8, 137.0, 173.7; IR (KBr) 3597, 1736 cm^{-1}; $[\alpha]_D$ −28.1 (c = 0.48, CH_2Cl_2). Anal. Calcd for $C_{38}H_{58}O_{11}$: C, 66.06; H, 8.46. Found: C, 66.19; H, 8.59.

Methyl 2-*O*-Acetyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (34) and Methyl 3-*O*-Acetyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (35). To a solution of methyl 4,6-*O*-benzylidene-*β*-D-glucopyranoside (400 mg, 1.42 mmol) in 15 mL of CH_2Cl_2 was added Et_3N (396 μL, 2.84 mmol), Ac_2O (143 μL, 1.42 mmol), and DMAP (17 mg, 0.14 mmol). After being stirred for 2 days, the reaction solution was diluted with 50 mL of CH_2Cl_2 and washed with 1 N HCl and saturated $NaHCO_3$. The organic layer was dried over Na_2SO_4, concentrated, and purified by chromatography on silica gel with 30 → 50% EtOAc in hexanes as eluent to give 137 mg (30%) of a less polar compound and 152 mg (33%) of a more polar compound. Less polar compound: white solid; mp 162−164 °C; ^{1}H NMR (C_6D_6, 400 MHz) δ 1.73 (s, 3H), 2.15 (d, 1H, J = 4.3), 3.05 (dt, 1H, J = 4.8, 9.5), 3.12 (t, 1H, J = 9.2), 3.20 (s, 3H), 3.42 (t, 1H, J = 10.1), 3.69 (dt, 1H, J = 4.2, 9.2), 4.09 (dd, 1H, J = 10.3, 4.9), 4.11 (d, 1H, J = 7.9), 5.15 (s, 1H), 5.25 (dd, 1H, J = 9.3, 8.0), 7.10−7.35 (m, 3H), 7.57 (d, 2H, J = 6.9); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.9, 57.0, 66.1, 68.5, 72.1, 73.9, 80.8, 101.7, 102.1, 126.2, 128.3, 129.2, 136.9, 170.3; IR (CH_2Cl_2 solution) 3584, 3048, 2988, 1749 cm^{-1}; $[\alpha]_D$ −77.7 (c = 1.72, CH_2Cl_2). Anal. Calcd for $C_{16}H_{20}O_7$: C, 59.25; H, 6.22. Found: C, 59.55; H, 6.57. More polar compound: white solid; mp 146−147 °C; ^{1}H NMR (C_6D_6, 400 MHz) δ 1.70 (s, 3H), 2.37 (d, 1H, J = 3.6), 3.17 (m, 1H), 3.18 (s, 3H), 3.41 (t, 1H, J = 9.6), 3.42 (t, 1H, J = 10.2), 3.59 (ddd, 1H, J = 9.3, 7.6, 3.5), 3.93 (d, 1H, J = 7.6), 4.08 (dd, 1H, J = 10.3, 5.0), 5.18 (s, 1H), 5.49 (t, 1H, J = 9.5), 7.04−7.15 (m, 3H), 7.58−7.60 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.9, 57.6, 66.4, 68.6, 73.4, 73.6, 78.5, 101.4, 104.5, 126.1, 128.2, 129.0, 136.9, 171.0; IR (CH_2Cl_2 solution) 3588, 3057, 1742 cm^{-1}; $[\alpha]_D$ −42.0 (c = 3.86, CH_2Cl_2). Anal. Calcd for $C_{16}H_{20}O_7$: C, 59.25; H, 6.22. Found: C, 59.13; H, 6.34.

Methyl (11*S*)-11-[[(4,6-*O*-Benzylidene-*β*-D-glucopyranosyl)-(1→2)-3,4-*O*-isopropylidene-*β*-D-fucopyranosyl]oxy]-hexadecanoate (36). To diacetate **30** (740 mg, 0.918 mmol) were added, 5 mL of MeOAc and 15 drops of 25% NaOMe in MeOH sequentially. A white crystalline precipitate was observed in the reaction mixture after stirring for 2 h. The mixture was diluted with 50 mL of saturated $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4, concentrated, and purified by chromatography on silica gel with 40 → 50% EtOAc in hexanes as eluent to give 558 mg (84%) of a clear, colorless oil: ^{1}H NMR (C_6D_6, 500 MHz) δ 0.90 (t, 3H, J = 7.0), 1.20−1.76 (m, 33H), 2.13 (t, 2H, J = 7.4), 3.29 (dq, 1H, J = 2.1, 6.5), 3.36 (s, 3H), 3.39 (dt, 1H, J = 4.9, 9.6), 3.48−3.52 (m, 2H), 3.61 (t, 1H, J = 10.2), 3.72−3.75 (m, 2H), 3.82 (t, 1H, J = 8.9), 3.98 (t, 1H, J = 7.6), 4.06 (dd, 1H, J = 7.1, 5.6), 4.29−4.32 (m, 2H), 4.86 (d, 1H, J = 7.6), 5.32 (s, 1H), 7.10−7.19 (m, 3H), 7.59 (d, 2H, J = 7.1); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.0, 16.4, 22.5, 24.4, 24.8, 24.9, 26.1, 27.7, 29.0, 29.1, 29.3, 29.5, 29.8, 31.8, 33.6, 34.0, 34.3, 51.3, 66.9, 68.4, 68.7, 72.5, 75.8, 76.4, 78.5, 79.7, 80.6, 80.9, 100.2, 101.8, 104.3, 110.2, 126.2, 128.2, 129.1, 137.0, 174.2; IR (thin film) 3472, 1739 cm^{-1}; $[\alpha]_D$ −3.19 (c = 5.01 CH_2Cl_2). Anal. Calcd for $C_{39}H_{62}O_{12}$: C, 64.80; H, 8.64. Found: C, 64.62; H, 8.83.

Methyl (11*S*)-11-[[(3-*O*-Acetyl-4,6-*O*-benzylidene-*β*-D-glucopyranosyl)-(1→2)-3,4-*O*-isopropylidene-*β*-D-fucopyranosyl]oxy]hexadecanoate (37). To a solution of diol **36** (265 mg, 0.367 mmol) in 10 mL of CH_2Cl_2 were added Et_3N (102 μL, 0.734 mmol), Ac_2O (37 μL, 0.37 mmol), and DMAP (5 mg, 0.04 mmol). After being stirred for 50 min, the reaction solution was diluted with 10 mL of CH_2Cl_2 and washed with 1 N HCl and saturated $NaHCO_3$. The organic layer was dried over Na_2SO_4, concentrated, and purified by chromatography on silica gel with 20 → 40% EtOAc in hexanes as eluent to give 224 mg (80%) of a clear oil: ^{1}H NMR (C_6D_6, 400 MHz) δ 0.91 (t, 3H, J = 7.0), 1.16−1.75 (m, 36H), 2.12 (t, 2H, J = 7.4), 3.25 (br q, 1H), 3.35 (s, 3H), 3.35 (br m, 1H), 3.48 (dd, 1H, J = 5.2, 1.9), 3.54−3.61 (m, 2H), 3.71 (br m, 1H), 3.78 (d, 1H, J = 2.6), 3.88 (br t, 1H, J = 9.6), 3.92−4.01 (m, 2H), 4.24−4.30 (m, 2H), 4.82 (d, 1H, J = 7.6), 5.28 (s, 1H), 5.61 (t, 1H, J = 9.5), 7.04−7.45 (m, 3H), 7.58 (d, 2H, J = 7.2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.0, 16.4, 20.9, 22.5, 24.3, 24.8, 24.9, 26.1, 27.8, 29.0, 29.1, 29.3, 29.4, 29.8, 31.8, 33.5, 33.9, 34.3, 51.3, 66.8, 68.4, 68.6, 72.7, 74.1, 76.4, 78.5, 78.7, 79.3, 80.9, 99.9, 101.3, 104.3, 110.1, 126.0, 128.1, 128.9, 136.9, 170.2, 174.1; IR (CH_2Cl_2 solution) 3477, 1740 cm^{-1}; $[\alpha]_D$ −2.5 (c = 2.59, CH_2Cl_2). Anal. Calcd for $C_{41}H_{64}O_{13}$: C, 64.38; H, 8.43. Found: C, 64.51; H, 8.63.

Equilibration of Methyl 2-*O*-Acetyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (34). A solution of 2-acetyl compound **34** (25 mg, 0.77 mmol) and 1 mg of 60% NaH in mineral oil in 3 mL of THF was stirred for 15 min. The reaction was quenched with 5 mL of H_2O and extracted with CH_2Cl_2 (2 × 10 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated. ^{1}H NMR of the crude reaction mixture shows a 1.3:1 ratio of the 3-acetyl compound to the 2-acetyl compound.

Equilibration of Methyl 3-*O*-Acetyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (35). A solution of 3-acetyl compound **35** (25 mg, 0.77 mmol) and 1 mg of 60% NaH in mineral oil in 3 mL of THF was stirred for 15 min. The reaction was quenched with 5 mL of H_2O and extracted with CH_2Cl_2 (2 × 10 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated. ^{1}H NMR of the crude reaction mixture shows a 1.2:1 ratio of the 3-acetyl compound to the 2-acetyl compound.

Equilibration of Methyl (11*S*)-11-[[(3-*O*-Acetyl-4,6-*O*-benzylidene-*β*-D-glucopyranosyl)-(1→2)-3,4-*O*-isopropylidene-*β*-D-fucopyranosyl]oxy]hexadecanoate (37). A solution of 3-acetyl compound **37** (10 mg, 0.013 mmol) and 1 mg of 60% NaH in mineral oil in 2 mL of THF was stirred for 15−120 min. The reaction was quenched with 5 mL of H_2O and extracted with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4 and concentrated. ^{1}H NMR of the crude reaction mixture shows a 1.3:1 ratio of the 3-acetyl compound **37** to a new compound: ^{1}H NMR (C_6D_6, 500 MHz) δ 0.88−0.92 (3.00H), 1.16−1.73 (m, 33.00H), 1.73 (s, 1.68H), 1.88 (s, 1.32H), 2.11−2.15 (m, 2.00H), 2.45 (d, 0.44H, J = 4.0), 3.25−3.40 (m, 4.56H), 3.45−3.49 (m, 1.00H), 3.54−3.65 (m, 2.00H), 3.71−3.74 (m, 1.56H), 3.80 (dt, 0.44H, J = 3.6, 8.9),

3.87 (m, 0.56H), 3.93 (t, 0.56H, $J = 7.6$), 3.97−4.03 (m, 1.32H), 4.24−4.29 (m, 2.00H), 4.81 (d, 0.56H, $J = 7.6$), 5.07 (d, 0.44H, $J = 7.5$), 5.28 (s, 0.56H), 5.32−5.36 (m, 0.88H), 5.61 (t, 0.56H, $J = 9.5$), 7.05−7.19 (m, 3.00H), 7.57−7.59 (m, 2.00H). The compounds were chromatographically inseparable.

Equilibration of (11*S*)-11-[[(4,6-*O*-Benzylidene-β-D-glucopyranosyl)-(1→2)-3,4-*O*-isopropylidene-β-D-fucopyranosyl]oxy]hexadecanoic Acid 3_{glu}-Lactone (32). A solution of lactone **32** (5 mg, 7 mmol) and 1 mg of 60% NaH in mineral oil in 1 mL of THF was stirred for 7−30 min. The reaction was quenched with 5 mL of H_2O and extracted with CH_2Cl_2 (2 × 10 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated. ^1H NMR of the crude reaction mixture shows a 5.8:1 ratio of the lactone **32** to a new compound. An attempt to isolate the new compound by purification of the crude reaction mixture with 10% EtOAc in toluene as eluent gave ∼0.5 mg of an impure, colorless oil. Major component: ^1H NMR (C_6D_6, 500 MHz) δ 0.86 (t, 3H, $J = 7.1$), 1.24−1.83 (m, 33H), 2.17−2.29 (m, 3H), 3.18 (t, 1H, $J = 9.2$), 3.36−3.40 (m, 2H), 3.46 (t, 1H, $J = 10.1$), 3.53 (dd, 1H, $J = 5.4, 2.1$), 3.72 (br m, 1H), 3.79 (br t, 1H), 4.02 (dd, 1H, $J = 6.9, 5.5$), 4.14 (dd, 1H, $J = 10.2, 4.7$), 4.27 (dd, 1H, $J = 8.2, 7.1$), 4.33 (d, 1H, $J = 8.3$), 5.18 (s, 1H), 5.34−5.38 (m, 2H), 7.08−7.19 (m, 3H), 7.51 (d, 2H, $J = 7.0$).

Allyl 2,3,4-Tri-*O*-benzyl-α-L-rhamnopyranoside (41). A solution of 2.77 g of allyl rhanmopyranoside **40** in 50 mL of DMF was cooled in an ice bath. To the solution were added NaH (3.26 g of 60% oil dispersion, 81.6 mmol), Bu_4NI (1.51 g, 4.1 mmol), and BnBr (9.71 mL, 81.6 mmol). The cooling bath was removed, and the reaction solution was stirred overnight. After addition of 10 mL of MeOH, the solution was stirred for 2 h. The reaction solution was diluted with 100 mL of Et_2O and washed with H_2O, 10% $Na_2S_2O_3$, and brine. The organic layer was dried over $MgSO_4$, concentrated, and purified by chromatography on silica gel with 5 → 10% EtOAc in hexanes as eluent to give 5.90 g (92%) of a clear oil: ^1H NMR ($CDCl_3$, 400 MHz) δ 1.46 (d, 3H, $J = 6.1$), 3.76 (t, 1H, $J = 9.3$), 3.84 (dq, 1H, $J = 9.5, 6.1$), 3.92 (dd, 1H, $J = 3.1, 1.9$), 3.98−4.03 (m, 2H), 4.22 (ddt, 1H, $J = 13.0, 5.0, 1.6$), 4.73 (br s, 2H), 4.75 (d, 1H, $J = 10.9$), 4.83 (d, 1H, $J = 12.5$), 4.87 (d, 1H, $J = 12.5$), 4.92 (d, 1H, $J = 1.7$), 5.07 (d, 1H, $J = 10.8$), 5.24 (dd, 1H, $J = 10.5, 1.6$), 5.31 (dd, 1H, $J = 17.2, 1.6$), 5.92 (m, 1H), 7.35−7.49 (m, 15H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.9, 67.5, 68.0, 72.0, 72.7, 74.8, 75.2, 80.1, 80.4, 97.0, 116.9, 127.4, 127.5, 127.5, 127.8, 127.9, 128.2, 133.7, 138.2, 138.5, 138.5; IR (thin film) 3030 cm^{-1}; $[\alpha]_D$ −15.1 ($c = 2.01$, CH_2Cl_2). Anal. Calcd for $C_{30}H_{34}O_5$: C, 75.92; H, 7.22. Found: C, 75.67; H, 7.27.

2,3,4-Tri-*O*-benzyl-α-L-rhamnopyranose (42). A solution of rhamnoside **41** (1.08 g, 2.28 mmol) and *t*-BuOK (256 mg, 2.28 mmol) in 5 mL of DMSO was heated at 100 °C for 15 min. After cooling, the reaction solution was diluted with 50 mL of Et_2O, washed with H_2O, and concentrated. The residue was dissolved in a solution of 10 mL of reagent grade acetone and 2 mL of 1 N HCl. The reaction solution was heated at reflux for 30 min, cooled, neutralized with $NaHCO_3$, and concentrated to approximately 3 mL. After dilution with 25 mL of H_2O, the reaction solution was extracted with CH_2Cl_2 (3 × 25 mL). The combined organic extracts were dried over Na_2SO_4, concentrated, and purified by chromatography on silica gel with 30% EtOAc in hexanes as eluent to give 825 mg (83%) of a white solid. A portion of this solid was recrystallized from Et_2O/hexanes to give white crystals: mp 88−89 °C (lit.[23] mp 89−90 °C).

Allyl 2,4-Di-*O*-acetyl-α-L-rhamnopyranoside (46). To a solution of allyl rhanmopyranoside **40** (407 mg, 1.99 mmol) in 5 mL of CH_2Cl_2 were added triethyl orthoacetate (3.01 mL, 16.4 mmol) and *p*-TsOH·H_2O (38 mg, 0.20 mmol). The reaction solution was stirred at room temperature overnight. After addition of 0.5 mL of Et_3N, the reaction solution was concentrated under high vacuum to give a slightly yellowish viscous oil.

After the oil was dissolved in 4 mL of CH_2Cl_2, Ac_2O (401 μL, 3.98 mmol), Et_3N (832 μL, 5.97 mmol), and DMAP (24 mg, 0.20 mmol) were added. The reaction solution was stirred for 1 h. The reaction solution was then diluted with 50 mL of CH_2Cl_2 and washed with saturated $NaHCO_3$ and H_2O. The organic layer was dried over Na_2SO_4 and concentrated to give a slightly yellowish oil.

To the oil was added 7 mL of 20% H_2O in HOAc while the reaction flask was vigorously stirred. After 10 min, the reaction solution was carefully poured into 100 mL of saturated $NaHCO_3$. The resulting mixture was extracted with CH_2Cl_2, and the combined organic layers were dried over Na_2SO_4, concentrated, and purified by chromatography on silica gel with 35 → 40% EtOAc in hexanes as eluent to give 536 mg of a white solid (by ^1H NMR, a 7:1 ratio of 2,4:2,3 acetyl isomers.) After two recrystallizations from 15% EtOAc in hexanes (7 mL/g), 441 mg (77%) of a isomerically pure white solid was isolated: mp 101−102 °C; ^1H NMR (C_6D_6, 400 MHz) δ 1.18 (d, 3H, $J = 6.3$), 1.62 (s, 3H), 1.70 (s, 3H), 2.48 (d, 1H, $J = 8.1$), 3.66 (ddt, 1H, $J = 13.0, 5.8, 1.4$), 3.83 (dq, 1H, $J = 9.8, 6.3$), 3.90 (ddt, 1H, $J = 13.1, 5.1, 1.5$), 4.20 (ddd, 1H, $J = 9.8, 8.1, 3.6$), 4.89 (d, 1H, $J = 1.4$), 4.97 (dq, 1H, $J = 10.4, 1.5$), 5.12 (dq, 1H, $J = 17.2, 1.6$), 5.25 (t, 1H, $J = 9.8$), 5.34 (dd, 1H, $J = 3.6, 1.6$), 5.61−5.71 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.2, 20.8, 65.9, 68.1, 72.6, 74.5, 96.3, 117.5, 133.3, 170.5, 171.2; IR (thin film) 3436, 1737 cm^{-1}; $[\alpha]_D$ −46.7 ($c = 2.89$, CH_2Cl_2). Anal. Calcd for $C_{13}H_{20}O_7$: C, 54.16; H, 6.99. Found: C, 54.21; H, 7.04.

2,3,4-Tri-*O*-benzyl-α-L-rhamnopyranose 1-Trichloroacetimidate (43). A slurry of rhamnopyranose **42** (2.22 g, 5.10 mmol), Cl_3CCN (1.02 mL, 10.2 mmol), and Cs_2CO_3 (220 mg, 0.675 mmol) in 20 mL of CH_2Cl_2 was stirred for 3.5 h. The reaction mixture was filtered through a short pad of silica gel, and the pad was washed with 250 mL of 1:49:50 Et_3N:EtOAc:hexanes. The combined filtrate was concentrated to give 2.93 g of slightly yellowish oil. The product was immediately used in the following step without further purification.

Allyl (2,3,4-Tri-*O*-benzyl-α-L-rhamnopyranosyl)-(1→3)-2,4-di-*O*-acetyl-α-L-rhamnopyranoside (48). The crude tricholoracetimidate **43** (2.93 g) and alcohol **46** (960 mg, 3.33 mmol) were each concentrated from freshly distilled benzene in separate flasks. Alcohol **46** was dissolved in 1.0 mL of CH_2Cl_2, 4.0 mL of 17 mM $BF_3{\cdot}Et_2O$ in CH_2Cl_2 was added, and the reaction solution was stirred for 5 min. The tricholoracetimidate **43** in 7 mL of CH_2Cl_2 was added to the reaction solution over 100 min. After the reaction mixture was stirred for an additional 20 min, 10 mL of saturated $NaHCO_3$ was added with vigorous stirring. Following extraction with CH_2Cl_2, the combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by chromatography on silica gel with 10 → 20% EtOAc in hexanes as eluent to give 2.18 g (93%) of a clear oil: ^1H NMR (C_6D_6, 500 MHz) δ 1.23 (d, 3H, $J = 6.3$), 1.43 (d, 3H, $J = 6.2$), 1.62 (s, 3H), 1.65 (s, 3H), 3.70 (ddt, 1H, $J = 12.9, 5.9, 1.4$), 3.81−3.85 (m, 2H), 3.88 (m, 1H), 3.93 (ddt, 1H, $J = 12.9, 5.3, 1.5$), 4.05 (m, 1H), 4.07 (dd, 1H, $J = 8.8, 3.0$), 4.32 (dd, 1H, $J = 9.9, 3.5$), 4.48−4.55 (m, 3H), 4.60−4.66 (m, 2H), 4.87 (d, 1H, $J = 11.4$), 4.94 (d, 1H, $J = 1.7$), 4.97 (dq, 1H, $J = 10.4, 1.4$), 5.09 (d, 1H, $J = 2.1$), 5.14 (dq, 1H, $J = 17.2, 1.6$), 5.50 (t, 1H, $J = 9.9$), 5.63 (dd, 1H, $J = 3.4, 1.8$), 5.67 (m, 1H), 7.04−7.18 (m, 9H), 7.25 (d, 2H, $J = 7.1$), 7.30 (d, 2H, $J = 7.1$), 7.34 (d, 2H, $J = 7.2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.3, 17.8, 20.6, 20.9, 66.3, 68.3, 68.9, 71.9, 72.3, 72.6, 72.7, 74.7, 74.7, 75.2, 79.5, 80.2, 96.3, 100.5, 117.6, 127.4, 127.4, 127.5, 127.6, 127.6, 127.7, 127.7, 128.2, 128.3, 128.3, 133.3, 138.2, 138.5, 138.6, 169.6, 170.2; IR (thin film) 1746 cm^{-1}; $[\alpha]_D$ −31.9 ($c = 3.27$, CH_2Cl_2). Anal. Calcd for $C_{40}H_{48}O_{11}$: C, 68.17; H, 6.86. Found: C, 67.96; H, 6.84.

Allyl (2,3,4-Tri-*O*-benzyl-α-L-rhamnopyranosyl)-(1→3)-α-L-rhamnopyranoside (49). A solution of rhamnopyranoside **48** (956 mg, 1.36 mmol), 10 mL of MeOH, and 1 mL of 25% NaOMe in MeOH was stirred overnight. The solution was diluted with 50 mL of saturated $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4, concentrated, and purified by chromatography on silica gel with 30 → 40% EtOAc in hexanes as eluent to give 732 mg (87%) of a white solid: mp 105−106 °C; ^1H NMR (C_6D_6, 400 MHz) δ 1.32 (d, 3H, $J = 6.2$), 1.36 (d, 3H, $J = 6.2$), 1.44

(23) Rathore, H.; From, A.; Ahmed, K.; Fullerton, D. *J. Med. Chem.* **1986**, *29*, 1945.

(d, 1H, J = 4.6), 1.95 (d, 1H, J = 4.0), 3.57 (dt, 1H, J = 4.5, 9.4), 3.70−3.76 (m, 2H), 3.82−3.87 (m, 2H), 3.93−4.03 (m, 3H), 4.07−4.14 (m, 2H), 4.47−4.54 (m, 3H), 4.56−4.63 (m, 2H), 4.79 (d, 1H, J = 1.4), 4.93 (d, 1H, J = 11.3), 4.97 (dq, 1H, J = 10.4, 1.6), 5.13 (dq, 1H, J = 17.2, 1.7), 5.26 (d, 1H, J = 2.0), 6.08 (m, 1H), 7.07−7.40 (m, 15H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.5, 18.1, 67.8, 67.9, 69.1, 70.6, 72.1, 72.4, 72.7, 75.0, 75.1, 79.0, 79.7, 80.3, 98.5, 99.7, 117.4, 127.7, 127.7, 127.8, 128.0, 128.4, 128.4, 128.4, 133.7, 138.0, 138.3, 138.3; IR (thin film) 3465, 3031 cm^{-1}; $[\alpha]_D$ −50 (c = 0.44, CH_2Cl_2). Anal. Calcd for $C_{36}H_{44}O_9$: C, 69.66; H, 7.14. Found: C, 69.49; H, 7.31.

Allyl (2,3,4-Tri-*O*-benzyl-α-L-rhamnopyranosyl)-(1→3)-2,4-di-*O*-[(2*S*)-2-methylbutyryl]-α-L-rhamnopyranoside (50). A solution of diol **49** (1.07 g, 1.72 mmol), (2*S*)-2-methylbutyric acid (749 μL, 6.88 mmol), DCC (1.42 g, 6.88 mmol), and DMAP (86 mg, 0.70 mmol) in 10 mL of CH_2Cl_2 was stirred overnight. To the reaction solution was added 1 mL of MeOH, followed 10 min later by 50 mL of hexanes. The mixture was filtered through a small plug of Celite, concentrated, and purified by chromatography on silica gel with 5 → 10% EtOAc in hexanes as eluent to give 1.25 g (92%) of a clear oil: ^{1}H NMR (C_6D_6, 400 MHz) δ 0.77 (t, 3H, J = 7.4), 0.88 (t, 3H, J = 7.4), 1.00 (d, 3H, J = 7.0), 1.08 (d, 3H, J = 7.0), 1.25 (m, 1H), 1.28 (d, 3H, J = 6.3), 1.37 (m, 1H), 1.45 (d, 3H, J = 6.2), 1.65 (m, 1H), 1.79 (m, 1H), 2.16 (m, 1H), 2.31 (m, 1H), 3.71 (dd, 1H, J = 12.8, 6.0), 3.85 (t, 1H, J = 9.3), 3.83−3.93 (m, 3H), 4.03 (m, 1H), 4.11 (dd, 1H, J = 9.2, 2.9), 4.42 (dd, 1H, J = 9.9, 3.3), 4.48 (d, 1H, J = 11.5), 4.58 (br m, 2H), 4.68 (d, 1H, J = 12.3), 4.76 (d, 1H, J = 12.3), 4.90 (d, 1H, J = 11.4), 4.96 (dd, 1H, J = 10.4, 1.4), 5.02 (d, 1H, J = 1.5), 5.12−5.17 (m, 2H), 5.58 (t, 1H, J = 9.9), 5.65−5.74 (m, 2H), 7.05−7.20 (m, 9H), 7.25 (d, 2H, J = 7.0), 7.33 (d, 2H, J = 7.2), 7.40 (d, 2H, J = 7.1); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 11.7, 11.8, 16.6, 16.7, 17.6, 17.8, 26.3, 26.5, 41.0, 41.1, 66.7, 68.4, 68.9, 71.8, 72.2, 72.3, 72.8, 74.6, 75.1, 75.6, 80.0, 80.1, 96.3, 100.8, 117.5, 127.2, 127.4, 127.4, 127.5, 128.1, 128.3, 128.3, 133.5, 138.4, 138.5, 138.9, 175.3, 175.9; IR (thin film) 1741 cm^{-1}; $[\alpha]_D$ −10.6 (c = 1.27, CH_2Cl_2). Anal. Calcd for $C_{46}H_{60}O_{11}$: C, 70.03; H, 7.66. Found: C, 70.33; H, 7.91.

(2,3,4-Tri-*O*-benzyl-α-L-rhamnopyranosyl)-(1→3)-2,4-di-*O*-[(2*S*)-2-methylbutyryl]-α-L-rhamnopyranose (51). A solution of allyl rhamnoside **50** (1.25 g, 1.58 mmol) and $(Ph_3P)_3$-RhCl (880 mg, 0.951 mmol) in 20 mL of 10% H_2O in EtOH was heated at reflux overnight. After cooling, the reaction mixture was concentrated and dissolved in 50 mL of 10% H_2O in acetone, and $HgCl_2$ (1.0 g, 3.7 mmol) and HgO (1.0 g,4.6 mmol) were added. The reaction mixture was stirred for 2 h, filtered through a plug of Celite, and concentrated. The residue was purified by chromatography on silica gel with 20 → 30% EtOAc in hexanes as eluent to give 994 mg (84%) of a clear oil: ^{1}H NMR (C_6C_6, 400 MHz) δ 0.76 (t, 3H, J = 7.4), 0.87 (t, 3H, J = 7.4), 0.99 (d, 3H, J = 6.9), 1.08 (d, 3H, J = 7.0), 1.24 (m, 1H), 1.28 (d, 3H, J = 6.2), 1.36 (m, 1H), 1.45 (d, 3H, J = 6.1), 1.63 (m, 1H), 1.77 (m, 1H), 2.14 (m, 1H), 2.31 (m, 1H), 2.31 (d, 1H, J = 4.3), 3.84 (t, 1H, J = 9.3), 3.93−4.10 (m, 4H), 4.38 (dd, 1H, J = 9.9, 3.0), 4.49 (d, 1H, J = 11.5), 4.57 (br s, 2H), 4.67 (d, 1H, J = 12.2), 4.76 (d, 1H, J = 12.3), 4.90 (d, 1H, J = 11.4), 5.08 (br d, 1H, J = 3.9), 5.13 (br s, 1H), 5.52 (t, 1H, J = 9.9), 5.54 (br s, 1H), 7.05−7.19 (m, 9H), 7.25 (d, 2H, J = 7.5), 7.32 (d, 2H, J = 7.6), 7.40 (d, 2H, J = 7.6); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 11.5, 11.6, 16.4, 16.5, 17.5, 17.6, 26.2, 26.4, 40.9, 41.0, 66.2, 68.7, 72.2, 72.3, 72.4, 72.6, 74.5, 74.7, 75.3, 79.8, 79.9, 91.2, 100.5, 127.1, 127.3, 127.3, 127.4, 127.9, 128.1, 138.0, 138.2, 138.6, 175.3, 176.1; IR (thin film) 3423, 1738 cm^{-1}; $[\alpha]_D$ +4.43 (c = 12.29, CH_2Cl_2). Anal. Calcd for $C_{43}H_{56}O_{11}$: C, 68.96; H, 7.54. Found: C, 69.04; H, 7.68.

(2,3,4-Tri-O-benzyl-α-L-rhamnopyranosyl)-(1→3)-2,4-di-*O*-[(2*S*)-2-methylbutyryl]-α-L-rhamnopyranose 1-Trichloroacetimidate (52). A slurry of rhamnopyranose **51** (78 mg, 0.10 mmol), Cl_3CCN (30 μL, 0.30 mmol), and Cs_2CO_3 (20 mg, 0.061 mmol) in 2 mL of CH_2Cl_2 was stirred for 9 h. The reaction mixture was filtered through a short pad of silica gel, and the pad was washed with 75 mL of 50% EtOAc in hexanes. The combined filtrate was concentrated to give 90 mg of slightly yellowish oil. The product was immediately used in the following step without further purification.

Methyl (2,3,4-Tri-*O*-benzyl-α-L-rhamnopyranosyl)-(1→3)-(2,4-di-*O*-[(2*S*)-2-methylbutyryl]-α-L-rhamnopyranosyl)-(1→2)-3-*O*-acetyl-4,6-*O*-benzylidene-β-D-glucopyranoside (53). The crude tricholoracetimidate **52** (90 mg) and alcohol **35** (20 mg, 0.062 mmol) were combined in a flask and concentrated from freshly distilled benzene. The resulting residue was dissolved in 400 μL of CH_2Cl_2, and 100 μL of 0.01 M TMSOTf in CH_2Cl_2 was added over 35 min. After the reaction mixture was stirred for an additional 25 min, 5 mL of saturated $NaHCO_3$ was added with vigorous stirring. Following extraction with CH_2Cl_2, the combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by chromatography on silica gel with 20% EtOAc in hexanes as eluent to give 48 mg (74%) of a clear, colorless oil: ^{1}H NMR (C_6D_6, 500 MHz) δ 0.79 (t, 3H, J = 7.4), 0.86 (t, 3H, J = 7.4), 1.04 (d, 3H, J = 7.0), 1.06 (d, 3H, J = 7.0), 1.27−1.39 (m, 2H), 1.42 (d, 3H, J = 6.3), 1.56 (d, 3H, J = 6.2), 1.65−1.77 (m, 2H), 2.19 (s, 3H), 2.21−2.19 (m, 2H), 3.12 (dt, 1H, J = 4.8, 9.6), 3.23 (s, 3H), 3.29 (t, 1H, J = 9.7), 3.40 (t, 1H, J = 10.2), 3.70 (dd, 1H, J = 9.3, 7.7), 3.85 (t, 1H, J = 9.3), 3.94−4.01 (m, 3H), 4.06−4.10 (m, 2H), 4.37 (m, 1H), 4.48 (d, 1H, J = 11.1), 4.50 (dd, 1H, J = 10.0, 3.2), 4.56 (d, 1H, J = 11.7), 4.70 (d, 1H, J = 12.3), 4.78 (d, 1H, J = 12.3), 4.88 (d, 1H, J = 11.4), 5.17 (s, 1H), 5.27 (d, 1H, J = 1.7), 5.30 (d, 1H, J = 1.7), 5.50 (dd, 1H, J = 3.1, 2.0), 5.61−5.68 (m, 2H), 7.05−7.19 (m, 12H), 7.24 (d, 2H, J = 7.2), 7.33 (d, 2H, J = 7.0), 7.40 (d, 2H, J = 7.1), 7.59 (d, 2H, J = 7.2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 11.7, 11.8, 16.5, 16.7, 17.2, 17.6, 20.8, 26.4, 26.5, 41.0, 41.2, 57.1, 66.3, 67.0, 68.6, 68.9, 71.9, 72.0, 72.3, 72.8, 72.9, 74.7, 75.0, 75.7, 78.5, 78.9, 80.1, 80.1, 98.3, 100.8, 101.3, 103.2, 126.1, 127.2, 127.4, 127.4, 127.5, 128.1, 128.2, 128.3, 128.3, 129.0, 136.9, 138.5, 138.5, 138.9, 170.1, 175.3, 175.7; IR (thin film) 1738 cm^{-1}; $[\alpha]_D$ −17.7 (c = 2.00, CH_2Cl_2). Anal. Calcd for $C_{59}H_{74}O_{17}$: C, 67.16; H, 7.07. Found: C, 66.82; H, 7.23.

2,3,4-Tri-*O*-acetyl-L-rhamnopyranose (54). A solution of D-rhamnose·H_2O (500 mg, 2.74 mmol) in 25 mL of CH_2Cl_2 was cooled in an ice bath. The solution was treated with Et_3N (3.44 mL, 24.7 mmol), Ac_2O (1.66 mL, 16.4 mmol), and DMAP (37 mg, 0.30 mmol). The cooling bath was removed, and the reaction solution was stirred overnight. The reaction solution was diluted with 25 mL of CH_2Cl_2 and washed with 1 N HCl, saturated $NaHCO_3$, and H_2O. The organic layer was dried over Na_2SO_4 and concentrated to yield a slightly yellow oil.

A solution of the oil and $BnNH_2$ (449 μL, 4.11 mmol) in 15 mL of THF was stirred for 12 h. After addition of 5 mL of 1 N HCl, the reaction mixture was stirred for 30 min. The reaction mixture was diluted with 50 mL of 1 N HCl and extracted with CH_2Cl_2. The combined extracts were dried over Na_2SO_4, concentrated, and purified by chromatography on silica gel with 40% EtOAc in hexanes as eluent to give 629 mg (79%) of a white amorphous solid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.15 (d, 3H, J = 6.1), 1.94 (s, 3H), 2.00 (s, 3H), 2.10 (s, 3H), 4.09 (m, 1H), 4.22 (d, 1H, J = 3.8), 5.00 (t, 1H, J = 10.0), 5.09 (br s, 1H), 5.19 (br s, 1H), 5.30 (dd, 1H, J = 10.0, 2.7); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.3, 20.6, 20.7, 20.8, 66.1, 68.8, 70.4, 71.1, 91.8, 170.2, 170.2, 170.4. The preceding spectral data was consistent with that prevously reported for this compound.[24]

(2,3,4-Tri-*O*-acetyl-α-L-rhamnopyranose 1-Trichloroacetimidate (55). A slurry of rhamnopyranose **54** (21 mg, 0.072 mmol), Cl3CCN (15 mL, 0.15 mmol), and Cs_2CO_3 (15 mg, 0.046 mmol) in 1 mL of CH_2Cl_2 was stirred for 2.5 h. The reaction mixture was filtered through a short pad of silica gel, and the pad was washed with 75 mL of 50% EtOAc in hexanes. The combined filtrate was concentrated to give 30 mg of slightly yellowish oil. The product was immediately used in the following step without further purification.

(11*S*)-11-[[(2,3,4-Tri-*O*-acetyl-α-L-rhamnopyranosyl)-(1→2)-(4,6-*O*-benzylidene-β-D-glucopyranosyl)-(1→2)-3,4-*O*-isopropylidene-β-D-fucopyranosyl]oxy]hexadecanoic Acid 3_{glu}-Lactone (56). The crude tricholoracetimidate **55** (30 mg) and alcohol **32** (25 mg, 0.036 mmol) were combined in a flask and concentrated from freshly distilled benzene. The

(24) Bashir, N.; Phythian, S., Reason, A., Roberts, S. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2203.

resulting residue was dissolved in 200 μL of CH_2Cl_2, and 220 μL of 0.01 M TMSOTf in CH_2Cl_2 was added over 30 min. After the reaction mixture was stirred for an additional 30 min, 5 mL of saturated $NaHCO_3$ was added with vigorous stirring. Following extraction with CH_2Cl_2, the combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by chromatography on silica gel with 10% EtOAc in toluene as eluent. Isolation of two middle chromatography fractions gave 10 mg of a clear, colorless oil that contained a major component and minor impurities: ^{1}H NMR (C_6D_6, 500 MHz) δ 0.87 (t, 3H, *J* = 7.0), 1.12−1.88 (m, 45H), 2.34 (m, 1H), 2.79 (m, 1H), 3.19 (dq, 1H *J* = 2.1, 6.6), 3.25 (dt, 1H, *J* = 5.0, 9.7), 3.43 (t, 1H, *J* = 10.3), 3.56−3.57 (m, 2H), 3.80 (t, 1H, *J* = 9.6), 4.06−4.09 (m, 2H), 4.19−4.25 (m, 2H), 4.44 (m, 1H), 4.51 (dd, 1H, *J* = 7.0, 5.5), 5.27 (s, 1H), 5.29 (d, 1H, *J* = 6.9), 5.60 (d, 1H, *J* = 1.7), 5.63 (t, 1H, *J* = 9.9), 5.70−5.75 (m, 2H), 5.81 (dd, 1H, *J* = 3.1, 2.0), 7.04−7.19 (m, 3H), 7.56 (d, 2H, *J* = 7.1); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.1, 16.7, 17.2, 20.7, 20.9, 20.9, 22.6, 24.1, 25.2, 25.2, 26.5, 26.9, 27.6, 27.7, 27.9, 29.1, 30.2, 31.9, 34.1, 34.6, 35.3, 65.0, 67.0, 68.8, 68.9, 69.0, 69.8, 70.9, 73.3, 75.0, 77.9, 79.5, 80.8, 81.2, 97.3, 97.9, 101.0, 101.3, 109.7, 126.2, 128.2, 128.6, 137.2, 169.6, 169.7, 170.1, 172.3; IR (thin film) 1752 cm^{-1}. Attempts to further purify this compound were unsuccessful.

(2,3,4-Tri-*O*-benzyl-α-L-rhamnopyranosyl)-(1→3)-2,4-di-*O*-acetyl-α-L-rhamnopyranose (57). To a degassed solution of $(Ph_3P)_3RhCl$ (49 mg, 0.053 mmol) in 5 mL of THF was added 35 μL of 2.31 M *n*-BuLi in hexane. After stirring for 10 min, the reaction solution was added to a degassed solution of allyl rhamnoside **48** (372 mg, 0.528 mmol) in 10 mL of THF. The reaction solution was heated at reflux for 15 min, cooled, and concentrated. The residue was dissolved in 10 mL of 10% H_2O in acetone, and $HgCl_2$ (300 mg, 1.10 mmol) and HgO (300 mg, 1.39 mmol) were added. The reaction mixture was stirred for 2 h, filtered through a plug of Celite, and concentrated. The residue was purified by chromatography on silica gel with 30 → 40% EtOAc in hexanes as eluent to give 334 mg (95%) of a clear oil: ^{1}H NMR (C_6C_6, 400 MHz) δ 1.24 (d, 3H, *J* = 6.2), 1.43 (d, 3H, *J* = 6.2), 1.60 (s, 3H), 1.64 (s, 3H), 2.07 (d, 1H, *J* = 4.2), 3.81−3.85 (m, 2H), 3.97−4.08 (m, 3H), 4.30 (dd, 1H, *J* = 9.9, 3.4), 4.46−4.55 (m, 3H), 4.62 (br s, 2H), 4.87 (d, 1H, *J* = 11.4), 5.01 (br m, 1H), 5.08 (br s, 1H), 5.46 (t, 1H, *J* = 9.9), 5.51 (br m, 1H), 7.05−7.18 (m, 9H), 7.25 (d, 2H *J* = 7.5), 7.30 (d, 2H, *J* = 7.6), 7.34 (d, 2H, *J* = 7.5); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.4, 17.7, 20.6, 20.9, 66.1, 68.8, 72.3, 72.4, 72.6, 72.8, 74.3, 74.7, 75.0, 79.5, 80.1, 91.4, 100.3, 127.4, 127.6, 127.6, 127.7, 127.8, 128.2, 128.3, 128.3, 138.0, 138.3, 138.4, 169.8, 170.5; IR (thin film) 3416, 1746 cm^{-1}; $[\alpha]_D$ −9.74 (*c* = 2.33, CH_2Cl_2). Anal. Calcd for $C_{37}H_{44}O_{11}$: C, 66.85; H, 6.67. Found: C, 66.56; H, 6.74.

(2,3,4-Tri-*O*-benzyl-α-L-rhamnopyranosyl)-(1→3)-2,4-di-*O*-acetyl-α-L-rhamnopyranose 1-Trichloroacetimidate (58). A slurry of rhamnopyranose **57** (153 mg, 0.230 mmol), Cl_3CCN (46 μL, 0.46 mmol), and Cs_2CO_3 (8 mg, 0.023 mmol) in 1 mL of CH_2Cl_2 was stirred for 11 h. The reaction mixture was filtered through a short pad of silica gel, and the pad was washed with 100 mL of 50% EtOAc in hexanes. The combined filtrate was concentrated to give 181 mg of slightly yellowish oil. The product was immediately used in the following step without further purification.

Methyl (11*S*)-11-[[(2,3,4-Tri-*O*-benzyl-α-L-rhamnopyranosyl)-(1→3)-(2,4-di-*O*-acetyl-α-L-rhamnopyranosyl)-(1→2)-(3-*O*-acetyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-(1→2)-3,4-*O*-isopropylidene-β-D-fucopyranosyl]oxy]-hexadecanoate (59). The crude tricholoracetimidate **58** (181 mg) and alcohol **37** (117 mg, 0.153 mmol) were combined in a flask and concentrated from freshly distilled benzene. The resulting residue was dissolved in 400 μL of CH_2Cl_2, and 225 μL of 0.02 M TMSOTf in CH_2Cl_2 was added over 45 min. After the reaction mixture was stirred for an additional 15 min, 10 mL of saturated $NaHCO_3$ was added with vigorous stirring. Following extraction with CH_2Cl_2, the combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by chromatography on silica gel with 20 → 30% EtOAc in hexanes as eluent to give 162 mg (75%) of a sticky white solid: ^{1}H NMR (C_6D_6, 500 MHz) δ 0.89 (t, 3H, *J* = 7.0), 1.25−1.75 (m, 45H), 2.13 (t, 1H, *J* = 7.4), 2.16 (s, 3H), 3.32 (m, 1H), 3.34 (s, 3H), 3.45 (dq, 1H, *J* = 1.9, 6.5), 3.53 (t, 1H, *J* = 10.2), 3.59 (t, 1H, *J* = 9.6), 3.70 (dd, 1H, *J* = 5.7, 1.9), 3.73 (br m, 1H), 3.81−3.89 (m, 3H), 4.00 (m, 1H), 4.10 (dd, 1H, *J* = 8.9, 2.9), 4.14 (dd, 1H, *J* = 10.4, 4.9), 4.19 (t, 1H, *J* = 7.1), 4.38−4.58 (m, 7H), 4.69 (br s, 2H), 4.89 (d, 1H, *J* = 11.3), 5.16 (d, 1H, *J* = 7.4), 5.26 (d, 1H, *J* = 1.8), 5.32 (s, 1H), 5.43 (d, 1H, *J* = 1.7), 5.49 (dd, 1H, *J* = 3.0, 2.1), 5.56 (t, 1H, *J* = 9.9), 5.66 (t, 1H, *J* = 9.2), 7.04−7.19 (m, 12H), 7.25 (d, 2H, *J* = 7.1), 7.30 (d, 2H, *J* = 7.2), 7.39 (d, 2H, *J* = 7.3), 7.55 (d, 2H, *J* = 7.2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.0, 16.6, 17.5, 17.8, 20.6, 20.9, 20.9, 22.6, 24.7, 24.9, 25.1, 26.3, 27.7, 29.1, 29.3, 29.5, 29.7, 29.9, 31.9, 34.0, 34.0, 34.7, 51.3, 65.8, 66.8, 68.4, 68.8, 68.9, 71.9, 72.3, 72.3, 72.5, 73.2, 74.8, 75.0, 75.1, 76.4, 76.7, 78.4, 79.2, 79.6, 80.2, 80.4, 98.1, 99.6, 100.3, 100.4, 101.3, 109.7, 126.1, 127.4, 127.6, 127.8, 128.1, 128.2, 128.3, 128.3, 128.9, 137.0, 138.2, 138.5, 138.6, 169.5, 170.0, 170.3, 174.1; IR (thin film) 1745 cm^{-1}; $[\alpha]_D$ −25.6 (*c* = 1.70, CH_2Cl_2). Anal. Calcd for $C_{78}H_{106}O_{23}$: C, 66.36; H, 7.57. Found: C, 66.00; H, 7.77.

(11*S*)-11-[[(2,3,4-Tri-*O*-benzyl-α-L-rhamnopyranosyl)-(1→3)-(α-L-rhamnopyranosyl)-(1→2)-(4,6-*O*-benzylidene-β-D-glucopyranosyl)-(1→2)-3,4-*O*-isopropylidene-β-D-fucopyranosyl]oxy]hexadecanoic Acid (60). To a solution of tetraester **59** (80 mg, 0.057 mmol) in 5 mL of THF was added 2 mL of 0.3 M LiOH. The reaction solution was stirred for 16 h, acidified with 25 mL of 1 N HCl, and extracted with CH_2Cl_2. The combined extracts were dried over Na_2SO_4, concentrated, and purified by chromatography on silica gel with 60% EtOAc in hexanes as eluent to give 52 mg (72%) of a sticky white solid: ^{1}H NMR (C_6D_6, 400 MHz) δ 0.90 (t, 3H, *J* = 7.0), 1.26−1.78 (m, 39H), 2.16 (t, 2H, *J* = 7.0), 3.32 (dt, 1H, *J* = 4.7, 9.4), 3.45 (t, 1H, *J* = 9.2), 3.49−3.51 (m, 2H), 3.75−3.80 (m, 3H), 3.84−3.92 (m, 3H), 4.07 (br s, 1H), 4.15−4.33 (m, 5H), 4.39 (dd, 1H, *J* = 9.4, 6.3), 4.47−4.51 (m, 4H), 4.59−4.75 (m, 4H), 4.89 (d, 1H, *J* = 11.2), 5.15 (d, 1H, *J* = 7.4), 5.29 (s, 1H), 5.53 (br s, 1H), 5.70 (br s, 1H), 7.08 (m, 12H), 7.27 (d, 2H, *J* = 7.1), 7.40 (d, 2H, *J* = 7.4), 7.43 (d, 2H, *J* = 7.4), 7.56 (d, 2H, *J* = 7.2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.1, 16.6, 17.6, 18.0, 22.6, 24.6, 24.8, 25.1, 26.2, 27.6, 28.8, 29.1, 29.3, 29.6, 29.8, 31.9, 33.8, 33.9, 34.8, 65.7, 68.1, 68.2, 68.7, 68.8, 70.4, 72.2, 72.4, 72.6, 74.4, 75.1, 75.3, 76.3, 77.9, 78.5, 78.7, 79.1, 79.9, 80.5, 80.8, 99.6, 100.4, 100.7, 101.7, 109.8, 126.2, 127.6, 127.7, 127.7, 127.8, 128.1, 128.2, 128.3, 129.1, 137.1, 138.1, 138.1, 138.4, 178.1; IR (thin film) 3458, 1712 cm^{-1}; $[\alpha]_D$ −37 (*c* = 0.67, CH_2Cl_2). Anal. Calcd for $C_{71}H_{98}O_{20}$: C, 67.07; H, 7.77. Found: C, 66.69; H, 7.90.

DMAP·TFA. A solution of DMAP (1.00 g, 8.19 mmol) in 20 mL of THF was cooled in an ice bath. Trifluoroacetic acid (631 μL, 8.19 mmol) was added to the solution. Without replenishing the cooling bath, the reaction solution was stirred overnight. The heterogeneous reaction solution was then filtered, and the solid was washed with Et_2O and dried under vacuum to give 1.81 g of white crystals.

(11*S*)-11-[[(2,3,4-Tri-*O*-benzyl-α-L-rhamnopyranosyl)-(1→3)-(α-L-rhamnopyranosyl)-(1→2)-(4,6-*O*-benzylidene-β-D-glucopyranosyl)-(1→2)-3,4-*O*-isopropylidene-β-D-fucopyranosyl]oxy]hexadecanoic Acid 2_{rha}-Lactone (62) and (11*S*)-11-[[(2,3,4-Tri-*O*-benzyl-α-L-rhamnopyranosyl)-(1→3)-(α-L-rhamnopyranosyl)-(1→2)-(4,6-*O*-benzylidene-β-D-glucopyranosyl)-(1→2)-3,4-*O*-isopropylidene-β-D-fucopyranosyl]oxy]hexadecanoic Acid 3_{glu}-Lactone (61). DMAP (14 mg, 0.11 mmol) and DMAP·TFA (23 mg, 0.097 mmol) were combined and azeotroped from benzene. To the dried reagents was added DCC (20 mg, 0.097 mmol) and 25 mL of EtOH-free $CHCl_3$. The reaction solution was then heated to reflux. Triol **60** (25 mg, 0.020 mmol) was azeotroped from benzene, dissolved in 7 mL of EtOH-free $CHCl_3$, and added to the reaction solution over 20 h. After addition was complete, the reaction solution was heated at reflux for 1 h, cooled, and concentrated to ∼2 mL. The solution was diluted with 25 mL of Et_2O, filtered, and concentrated. The residue was purified by chromatography on silica gel with 5 → 20% EtOAc in toluene as eluent to give 6 mg (24%) of a slightly impure, less polar compound and 7 mg (28%) of a more polar compound. Less polar compound: white solid; ^{1}H NMR (C_6D_6, 500 MHz) δ 0.87 (t, 3H, *J* = 7.1), 1.15−1.80 (m, 39H), 2.13 (br

s, 1H), 2.20 (m, 1H), 2.31 (m, 1H), 2.46 (br s, 1H), 3.18−2.26 (m, 2H), 3.34−3.40 (m, 2H), 3.43 (dd, 1H, J = 5.1, 2.0), 3.62 (dt, 1H, J = 3.2, 8.7), 3.68 (dd, 1H, J = 8.6, 7.6), 3.77−3.78 (m, 2H), 3.85 (t, 1H, J = 9.1), 3.92 (t, 1H, J = 9.5), 4.05−4.13 (m, 3H), 4.22 (dd, 1H, J = 9.5, 3.2), 4.25−4.36 (m, 3H), 4.41 (d, 1H, J = 7.9), 4.48 (d, 1H, J = 11.8), 4.52 (d, 1H, J = 11.3), 4.56 (d, 1H, J = 11.8), 4.57 (d, 1H, J = 12.1), 4.67 (br s, 1H), 4.90 (d, 1H, J = 11.3), 5.13 (s, 1H), 5.18 (d, 1H, J = 2.0), 5.27 (d, 1H, J = 7.5), 5.40 (br s, 1H), 5.85 (dd, 1H, J = 3.9, 1.9), 7.08−7.20 (m, 12H), 7.30−7.31 (m, 4H), 7.41 (d, 2H, J = 7.5), 7.51 (d, 2H, J = 7.2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.1, 16.7, 18.0, 18.1, 22.6, 25.2, 25.5, 26.6, 27.8, 28.8, 29.2, 29.4, 29.7, 30.5, 31.9, 34.0, 34.6, 35.1, 65.8, 68.2, 68.4, 68.8, 69.1, 71.8, 72.0, 72.5, 72.6, 74.4, 74.5, 75.1, 75.5, 76.8, 78.4, 79.2, 80.2, 80.4, 80.4, 80.6, 84.4, 98.1, 99.7, 100.1, 100.8, 101.6, 109.7, 126.2, 127.7, 127.7, 127.8, 127.9, 128.0, 128.3, 128.3, 128.3, 128.4, 128.6, 129.0, 137.2, 138.1, 138.5, 138.5, 173.3; IR (CH_2Cl_2 solution) 3585, 1734 cm^{-1}. Attempts to further purify this compound were unsuccessful. More polar compound: clear oil; ^{1}H NMR (C_6D_6, 500 MHz) δ 0.88 (t, 3H, J = 7.1), 1.26−1.91 (m, 39H), 2.07 (br s, 1H), 2.21 (m, 1H), 2.28 (m, 1H), 3.28−3.34 (m, 2H), 3.49 (t, 1H, J = 10.2), 3.57 (br m, 1H), 3.61 (dd, 1H, J = 5.3, 2.1), 3.69 (br t, 1H, J = 9.1), 3.84−3.88 (m, 3H), 4.00−4.04 (m, 2H), 4.08−4.13 (m, 2H), 4.16 (dd, 1H, J = 9.5, 3.0), 4.19−4.25 (m, 3H), 4.34 (br s, 1H), 4.50−4.53 (m, 4H), 4.70 (br s, 1H), 4.95 (d, 1H, J = 11.4), 5.31 (s, 1H), 5.36 (d, 1H, J = 6.5), 5.44 (d, 1H, J = 2.0), 5.50 (br s, 1H), 5.61 (dd, 1H, J = 9.5, 7.2), 7.05−7.23 (m, 12H), 7.30−7.33 (m, 4H), 7.47 (d, 2H, J = 7.5), 7.54 (d, 2H, J = 7.1); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.1, 16.7, 17.4, 18.2, 22.6, 24.3, 25.2, 25.3, 26.5, 27.1, 27.7, 27.9, 27.9, 29.1, 30.2, 31.9, 34.5, 34.7, 35.4, 65.0, 68.7, 68.7, 68.9, 69.2, 70.6, 71.9, 72.3, 72.4, 74.1, 75.0, 75.1, 75.1, 77.2, 77.8, 78.9, 79.4, 79.8, 80.2, 80.8, 81.4, 98.2, 99.2, 99.2, 101.2, 101.2, 109.6, 126.1, 127.7, 127.7, 127.8, 127.9, 128.0, 128.2, 128.3, 128.4, 129.0, 137.2, 138.1, 138.4, 138.4, 172.3; IR (CH_2Cl_2 solution) 3480, 1738 cm^{-1}; $[\alpha]_D$ −31 (c = 0.74, CH_2Cl_2). Anal. Calcd for $C_{71}H_{96}O_{19}$: C, 68.03; H, 7.72. Found: C, 67.73; H, 7.70.

(11*S*)-11-[[(2,3,4-Tri-*O*-benzyl-α-L-rhamnopyranosyl)-(1→3)-(α-L-rhamnopyranosyl)-(1→2)-(4,6-*O*-benzylidene-*β*-D-glucopyranosyl)-(1→2)-3,4-*O*-isopropylidene-*β*-D-fucopyranosyl]oxy]hexadecanoic Acid 3_{glu}-Lactone (61). To a solution of acid **60** (51 mg, 0.041 mmol) in 225 mL of benzene were added Et_3N (341 μL, 2.45 mmol) and 2,4,6-trichlorobenzoyl chloride (256 μL, 1.64 mmol). DMAP (100 mg, 0.819 mmol) was added to the reaction mixture in two portions, 1 h apart. After being stirred for 15 h, the milky white reaction mixture was washed with 100 mL of H_2O and separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 75 mL). The combined organic layers were dried over Na_2SO_4, concentrated, and purified by chromatography on silica gel with 20% EtOAc in toluene as eluent to give 31 mg (61%) of a clear oil. The isolated product was spectroscopically identical with the more polar product obtained from the alternative macrolactonization.

(11*S*)-11-[(2,3,4-Tri-*O*-benzyl-α-L-rhamnopyranosyl)-(1→3)-[2,4-di-*O*-[(2*S*)-2-methylbutyryl]-α-L-rhamnopyranosyl]-(1→2)-[(4,6-*O*-benzylidene-*β*-D-glucopyranosyl)-(1→2)-3,4-*O*-isopropylidene-*β*-D-fucopyranosyl]-oxy]hexadecanoic Acid 3_{glu}-Lactone (63). To a solution of acid **60** (25 mg, 0.020 mmol) in 100 mL of benzene were added Et_3N (164 μL, 1.18 mmol) and 2,4,6-trichlorobenzoyl chloride (123 μL, 0.788 mmol). DMAP (48 mg, 0.39 mmol) was added to the reaction mixture in two portions, 1 h apart. After the solution was stirred for 15 h, (2*S*)-2-methylbutyric acid (43 μL, 0.39 mmol) was added and the reaction solution was stirred for 2.5 h. The milky white reaction mixture was then washed with 50 mL of H_2O and separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over Na_2SO_4, concentrated, and purified by chromatography on silica gel with 3% EtOAc in toluene as eluent to give 17 mg (61%) of a slightly impure, clear oil: ^{1}H NMR (C_6D_6, 500 MHz) δ 0.80 (t, 3H, J = 7.4), 0.85−0.92 (m, 6H), 1.04−1.87 (m, 49H), 2.23−2.28 (m, 2H), 2.58 (m, 1H), 3.16 (dt, 1H, J = 5.0, 9.8), 3.32 (dq, 1H, J = 2.1, 6.6), 3.39 (t, 1H, J = 10.2), 3.58−3.60 (m, 2H), 3.77 (t, 1H, J = 9.6), 3.91 (t, 1H, J = 9.4), 4.03−4.07 (m, 4H), 4.17 (dd, 1H, J = 9.3, 3.0), 4.21−4.26 (m, 2H), 4.45 (m, 1H), 4.54−4.61 (m, 4H), 4.66 (m, 1H), 4.86 (d, 1H, J = 12.6), 4.89 (d, 1H, J = 12.5), 4.97 (d, 1H, J = 11.4), 5.24 (s, 1H), 5.26 (d, 1H, J = 7.0), 5.52 (d, 1H, J = 1.7), 5.54 (d, 1H, J = 1.9), 5.64−5.69 (m, 3H), 7.05−7.23 (m, 12H), 7.28 (d, 2H, J = 7.9), 7.36 (d, 2H, J = 7.1), 7.51−7.55 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 11.7, 11.8, 14.1, 16.7, 16.8, 16.8, 17.4, 17.8, 22.6, 24.0, 25.1, 25.2, 26.4, 26.5, 26.6, 26.9, 27.7, 27.8, 27.9, 29.2, 30.4, 31.9, 34.3, 34.8, 35.3, 41.2, 41.3, 65.2, 67.3, 68.7, 68.8, 68.9, 71.7, 72.0, 72.2, 72.3, 73.5, 74.7, 74.9, 75.0, 75.7, 76.7, 78.2, 79.2, 80.0, 80.2, 80.7, 82.1, 96.3, 98.0, 100.5, 101.3, 101.5, 109.7, 126.1, 127.2, 127.4, 127.5, 127.5, 127.6, 128.1, 128.2, 128.3, 128.3, 128.6, 129.0, 137.1, 138.3, 138.5, 139.0, 172.3, 175.2, 175.4; IR (thin film) 1741 cm^{-1}. Attempts to further purify this compound were unsuccessful.

Tricolorin A. To a solution of compound **63** (18 mg, 0.013 mmol) in 1 mL of MeOH was added 0.5 mL of 11% HCl in MeOH and 10 mg of $Pd(OH)_2$ on activated charcoal. The reaction flask was evacuated and back-filled with H_2 three times. The reaction solution was stirred overnight under the pressure of a balloon filled with H_2. The reaction solution was basified with 1 mL of Et_3N and filtered through a small plug of Celite. The Celite plug was washed with MeOH and the combined filtrate and washes were concentrated and purified by chromatography on silica gel with 10:10:1 acetone−$CHCl_3$−MeOH as eluent to give 10 mg (77%) of a white solid: mp 117−119 °C. ^{1}H NMR (C_5D_5N, 400 MHz) δ 0.79−0.84 (m, 6H), 0.90 (t, 3H, J = 7.4), 1.08−1.89 (m, 43H), 2.27−2.47 (m, 3H), 2.99 (br dd, 1H), 3.45 (br dt, 1H), 3.80−3.82 (m, 2H), 3.88 (dd, 1H, J = 11.7, 2.7), 4.01 (br d, 1H, J = 3.2), 4.08−4.14 (m, 2H), 4.20−4.23 (m, 3H), 4.34 (t, 1H, J = 9.5), 4.40 (br m, 1H), 4.50 (dd, 1H, J = 3.3, 1.5), 4.64 (d, 1H, J = 7.8), 4.71 (dd, 1H, J = 9.3, 7.9), 4.77 (dd, 1H, J = 9.9, 3.2), 4.92 (dq, 1H, J = 9.9, 6.2), 5.49 (br s, 1H), 5.54 (br s, 1H), 5.69 (t, 1H, J = 9.7), 5.75−5.82 (m, 3H); ^{13}C NMR (C_5D_5N, 100 MHz) δ 11.9, 14.3, 17.0, 17.1, 17.4, 18.4, 18.6, 22.9, 23.8, 24.9, 25.7, 26.7, 26.9, 27.1, 28.0, 28.4, 29.6, 31.8, 32.2, 34.5, 35.2, 41.5, 41.6, 61.3, 67.3, 69.6, 70.6, 71.4, 72.4, 72.6, 72.9, 73.3, 73.4, 73.5, 74.8, 76.0, 76.3, 79.1, 80.7, 80.9, 98.4, 99.9, 103.2, 104.7, 172.4, 173.4, 175.7, 175.8; IR (CH_2Cl_2 solution) 3444, 1735 cm^{-1}; $[\alpha]_D$ −24 (c = 0.30, MeOH). Anal. Calcd for $C_{50}H_{86}O_{21}$: C, 58.69; H, 8.47. Found: C, 58.84; H, 8.57. This compound was spectroscopically identical with a sample of authentic tricolorin A.

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Supporting Information Available: Experimental procedures for the preparation of compounds **6**−**12** (Scheme 2), ^{1}H NMR spectra of compounds **30**, **32**, **37**, **39**, **56**, **61**−**63**, and **1** (both synthetic and authentic natural product), and ^{13}C NMR spectra of **1** (15 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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