vacuum gave the diacyl chloride (mp 95–99 °C), which was dissolved in benzene (15 mL). This solution was then gradually added to a stirred slurry of aluminum chloride (435 mg, 0.33 mmol) in benzene (30 mL) at 5 °C. The reaction mixture was stirred at room temperature (~25 °C) for 3 h and worked up by pouring over crushed ice and extraction with benzene. Removal of the solvent under vacuum gave 520 mg (74%) of **11**, mp 241 °C (mixture melting point), after recrystallization from a mixture (1:1) of methylene dichloride and petroleum ether.

Preparation of 12 from 15. Treatment of **15** (500 mg, 0.15 mmol) with thionyl chloride (175 mg, 0.15 mmol) as in the earlier case gave the corresponding acyl chloride (mp 83–85 °C), which was subsequently treated with aluminum chloride in benzene to give 446 mg (78%) of **12**, mp 203 °C (mixture melting point), after recrystallization from a mixture (1:1) of benzene and petroleum ether.

Laser Flash Photolysis. Pulse excitation was carried out at 337.1 nm (2–3 mJ, ~8 ns), employing a UV 400 Molectron nitrogen laser. The transient phenomena were observed in 3 × 7 mm quartz cells by using a kinetic spectrometer, described elsewhere.[46] The solvents employed were benzene and methanol, and unless oxygen effects were meant to be studied, the solutions were deoxygenated by purging with argon or nitrogen. In the experiments where a large number of laser shots were necessary, e.g., for wavelength-by-wavelength measurements of transient absorption spectra, a flow system was used in which the solution for photolysis was allowed to drain from a reservoir through the cell.

Acknowledgment. We thank the Department of Science and Technology, Government of India, Indian Institute of Technology, Kanpur, and the Office of Basic Energy Sciences of the US Department of Energy for financial support of this work.

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Pseudomonic Acid C from L-Lyxose

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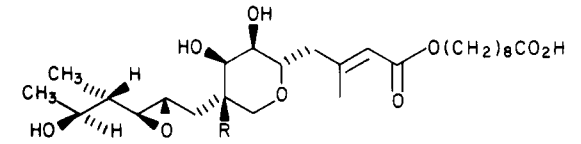
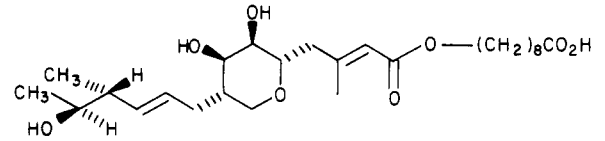
Full details of the total synthesis of pseudomonic acid C from L-lyxose are described. Key features of the approach involve free-radical allylation for stereoselective C–C bond formation at C_4 of lyxose, Frater alkylation to generate correct stereochemistry at C_{12} and C_{13}, and stereoselective intramolecular Michael addition to establish the correct stereochemistry of the "anomeric" appendage.

The pseudomonic acids are a relatively small group of antibiotics of unusual structure. Representative examples of these materials include pseudomonic acid A (**1**), pseudomonic acid B (**2**), and pseudomonic acid C (**3**). Since



pseudomonic acid A, R = H
pseudomonic acid B, R = OH



pseudomonic acid C

the isolation and structure elucidation of pseudomonic acid A,[1,2] numerous papers[3–10] have appeared describing the elucidation of structure, including absolute configuration, of these antibiotics as well as the chemistry associated with them. Studies on the mode of action of these materials have also been reported.[11–13] Finally, these antibiotics, particularly pseudomonic acid C,[7,8] have been the target of rather intensive investigation with respect to chemical synthesis. The first total synthesis of *d,l*-pseudomonic acid C was recorded by Kozikowski, Schmiesing, and Sorgi.[14] Much more recently, a synthesis of the naturally occurring (+)-enantiomer was achieved with D-glucose as the source of carbons 9–14.[15] In addition to these efforts, Snider has succeeded in a very efficient construction of the key Kozikowski intermediate **17**, leading to a formal synthesis of pseudomonic acids A and C. Numerous other approaches have also been recorded,[17–20] as has the conversion of pseudomonic acid C to pseudomonic acid A.[21] We detail herein our own efforts in this area which have led to the total synthesis of (+)-pseudomonic acid C.

Synthetic Approach. From a consideration of the structure of pseudomonic acid C, two possible disconnections are immediately apparent, namely those at the C_2–C_3

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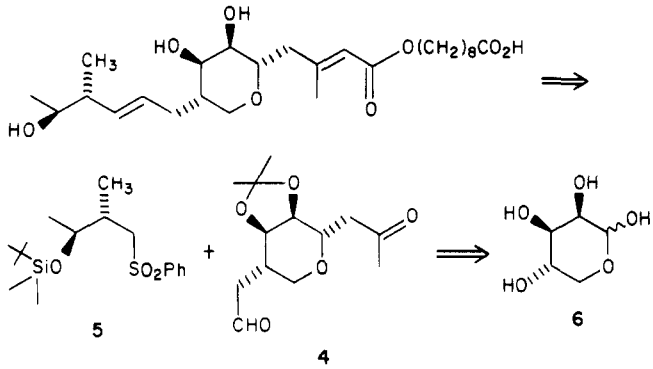
and C_{10}–C_{11} unsaturations. In fact, the viability of establishing the E unsaturation at C_2–C_3 via an Emmons reaction had already been demonstrated by the Beecham group,[6] and subsequently used in the total synthesis by Kozikowski, Schmiesing, and Sorgi.[14] No satisfactory method for a connective approach to the C_{10}–C_{11} trans olefin, however, was known. Application of the Salmond Wittig procedure[22] in the Kozikowski synthesis was found to lead to a 1:1 mixture of cis and trans olefins. Since it appeared most expedient, in terms of relating absolute chirality at C_{12} and C_{13} to chirality at C_5–C_8 in the pyran nucleus of pseudomonic acid C, to proceed via a connective construction of the C_{10}–C_{11} unsaturation, an efficient procedure for accomplishing such a coupling reaction was needed. We decided to investigate the reductive elimination of a β-hydroxy sulfone derivative in this context, since such reductive eliminations generally lead to the production of trans olefinic products.[24] Thus the synthetic problem can be reduced to the synthesis of keto aldehyde 4, or some protected equivalent, and a sulfone such as 5.



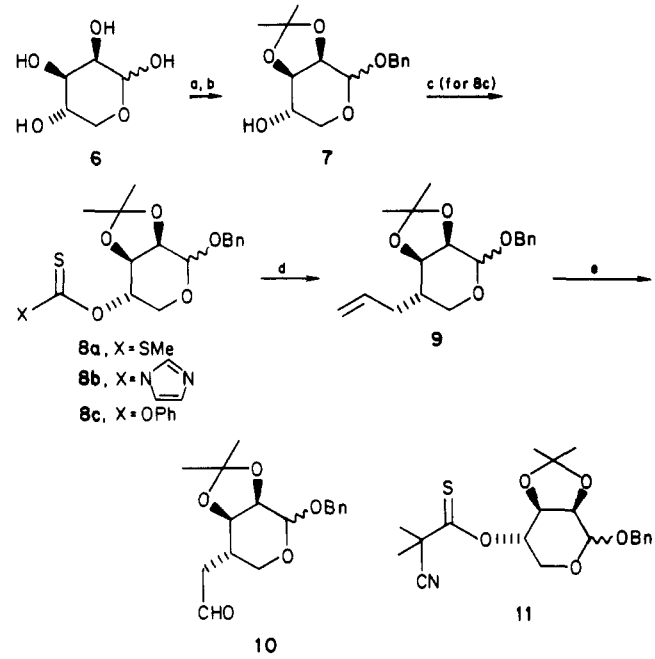
Key to the strategy detailed herein is the recognition of the structure of 4 as that of a highly modified L-lyxose (6), a commercially available sugar. We anticipated that incorporation of a latent acetaldehyde unit at C_4 (lyxose numbering) could be accomplished by free-radical allylation with allyltri-*n*-butylstannane.[25] Similarly, incorporation of a latent acetone moiety at C-1 (lyxose numbering) could be envisioned via the same procedure with either allyl or methallyltri-*n*-butylstannane. Moreover, opportunities for a "two electron" version of the same basic bond construction at this position were presented by the presence of the anomeric center.

Our first task was thus to differentiate the C_2, C_3 hydroxyls of lyxose from the C_1, C_4 pair, and also to differentiate C_1 and C_4 from each other. Moreover, it was necessary to build in sufficient steric bias on the β face of the molecule that free radical C–C bond formation would be expected to occur preferentially from the α face. At this point, the question of timing (i.e., which appendage to incorporate first) appeared open, although a natural choice evolved rapidly as discussed below.

Results

The Pyran Nucleus and C_9–C_{14} Appendage. A very direct approach to the above hydroxyl differentiation problem would be simple acetonide formation utilizing the

Scheme I[a]



[a] Reagents: (a) $PhCH_2OH$, *p*-TsOH; (b) $(MeO)_2C(CH_3)_2$, *p*-TsOH; (c) MeLi; PhOCSCl; (d) $CH_2{=}CHCH_2SnBu_3$, *hν*; (e) OsO_4, $NaIO_4$.

C_2 and C_3 hydroxyls of lyxose. Unfortunately, lyxose is known to form acetonide derivatives from its furanose form,[26] which necessitated glycoside formation prior to this operation. Reaction of L-lyxose with benzyl alcohol (taken as solvent) in the presence of *p*-toluenesulfonic acid (*p*-TsOH) yielded, after appropriate workup, the desired *O*-benzylglycoside as a mixture of anomers. Treatment of this material with dimethoxypropane and *p*-TsOH in acetone then gave the desired acetonide 7[27] in 85% overall yield from L-lyxose.

Incorporation of an allyl unit at C_4 was now possible by using the free-radical methodology reported earlier.[25] Stereochemical control in this instance was envisioned to result from approach of allyltri-*n*-butylstannane to the less hindered convex face of a C_4 free radical derived from 7, leading to the desired α allyl derivative. Although attempts to convert 7 to the corresponding bromide or phenylselenide proved fruitless, various thioacyl derivatives (8a–c) proved readily accessible. Of these, the best allylation results were obtained with 8c, which gave 9 in 80–93% yield upon reaction with 2.0 equiv of allyltri-*n*-butylstannane in toluene at ambient temperature, with photochemical (λ >300 nm) initiation. Chemical initiation with AIBN proved less satisfactory, particularly with 8b, where substantial amounts of 11 were formed. This product presumably arises from addition of the 2-cyanopropyl radical to carbon, rather than sulfur, of the thioacylimidazoyl moiety, followed by scission of the imidazole moiety.

Since allyl derivative 9, by oxidative cleavage of the sole unsaturation, is a functional equivalent of the desired aldehyde for the condensation process (note 4 above), attention was now turned to construction of the requisite sulfone (5) for the condensation process. The relative and absolute stereochemistry for the fragment containing C_{12} and C_{13} was readily established by alkylation of the dianion

(22) For a preliminary account of this work note: Keck, G. E.; Kachensky, D. F.; Enholm, E. J. *J. Org. Chem.* **1984**, *49*, 1462.
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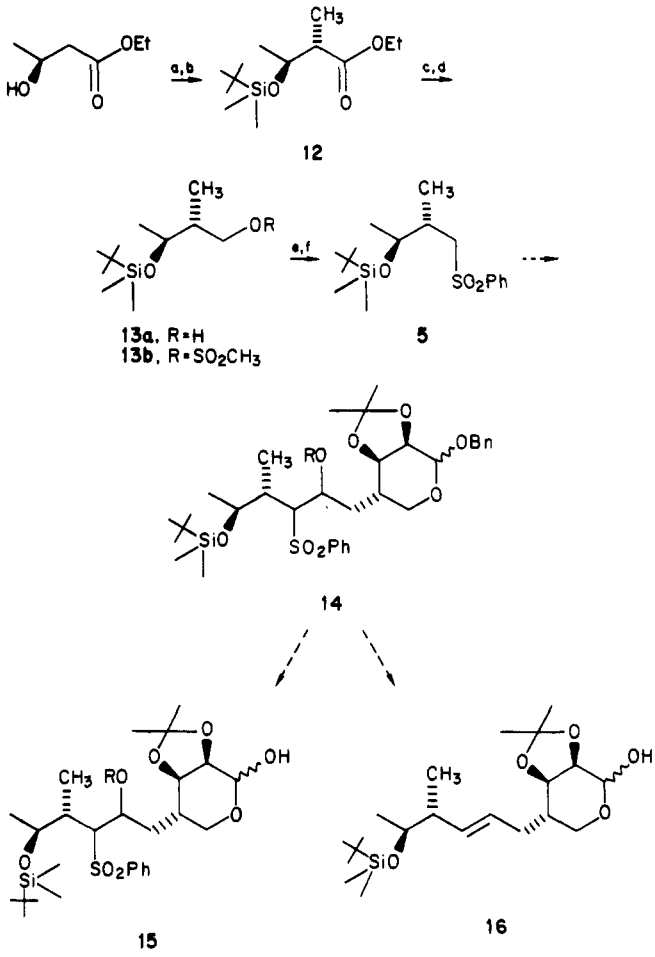
Scheme II[a]



[a] Reagents: (a) LDA; MeI; (b) *t*-BuSi(Me)$_2$Cl, imidazole; (c) (*i*-Bu)$_2$AlH; (d) MsCl, pyr; (e) KSPh; (f) *m*-CPBA.

obtained from (*S*)-(+)-methyl 3-hydroxybutanoate[28] with methyl iodide according to the general protocol of Frater.[29] The desired 2(*S*),3(*R*) isomer was obtained, along with its C-2 epimer, in a ratio of 96:4 (as determined by VPC analysis) in 85% isolated yield. After protection of the hydroxyl substituent by reaction with *tert*-butyldimethylsilyl chloride under standard[30] conditions, reduction of the ester moiety with 2.2 equiv of diisobutylaluminum hydride very cleanly afforded alcohol **13a**, which was easily converted to the corresponding mesylate (**13b**) by exposure to methanesulfonyl chloride in pyridine.

Attempts to construct sulfone **5** directly from this material, via displacement with sodium benzenesulfinate, were unsuccessful even under forcing (DMF, reflux) conditions, presumably due to steric hindrance imposed by branching at both the α and β carbons. However, displacement with sodium thiophenoxide in THF at 23 °C proceeded very smoothly. Oxidation with *m*-chloroperbenzoic acid in methylene chloride at room temperature then afforded **5** in 90% overall yield from the Frater alkylation product. The stage was thus set for the coupling of sulfone **5** with the aldehyde **10** to afford, after reductive elimination, intermediate **14**, from which pseudomonic acid C should be readily accessible after a second free-radical C–C bond-forming reaction to incorporate an acetonyl function at carbon 1 (lyxose numbering).

At this point, however, several important questions arose, in particular, the issue of timing regarding the crucial stages of the route and the stereochemistry associated with the introduction of the allyl appendage. With regard to the latter issue, evidence was accumulated that intermediate **9** was, for all practical purposes, at least, stereochemically homogeneous at the C_4 position (lyxose numbering). Thus, only two compounds were detectable by VPC and HPLC analysis, as well as by ^{1}H NMR, which we attributed to the presumably inconsequential anomeric mixture at C_1.

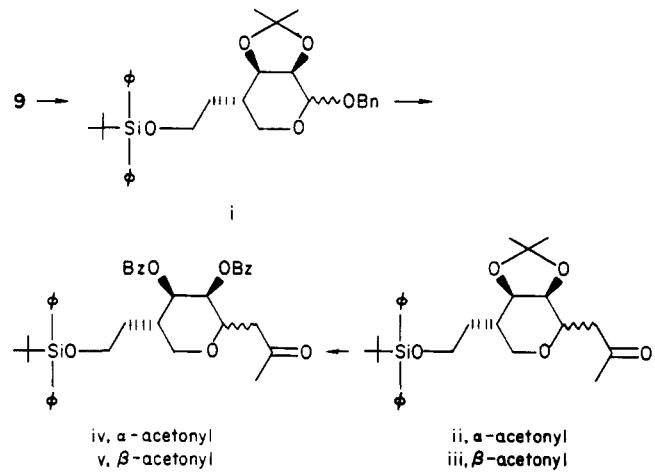
Separation of these materials provided the two anomers in pure form. The higher R_f material was isolated as a low melting crystalline solid, while the lower R_f anomer was obtained as an oil. ^{1}H and ^{13}C NMR spectroscopy of these materials clearly revealed their homogeneity. Finally, in order to confirm unambiguously the stereochemistry of this key intermediate, the mixture of anomers was converted to an intermediate thoroughly characterized in the Kozikowski total synthesis.[14,31]

Model Studies on the Coupling–Reductive Elimination Sequence. Prior to embarking on the final steps necessary to establish the "lower appendage" of pseudomonic acid C, we deemed it prudent to investigate the viability and stereoselectivity of the sulfone coupling sequence as a route to the desired trans olefin. Moreover, such model studies promised to shed light on the possibilities for "timing" in the total synthesis effort, that is, identification of the stages at which introduction of the upper appendage could realistically be pursued.

It was found that condensation of sulfone **5** with cyclohexane carboxaldehyde or propanal could be readily accomplished, in high yield, by reaction of the lithiated sulfone (prepared by reaction with 1.1 equiv of LDA, 0 °C, 15 min) with the aldehyde in THF at −20 °C. Moreover, various derivatives of the resulting β-hydroxy sulfone suitable for the reductive elimination step were also readily

(28) Available from Aldrich Chemical Co.
(29) Frater, G. *Helv. Chim. Acta* **1979**, 2825, 2829.
(30) Corey, E. J.; Vankateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.

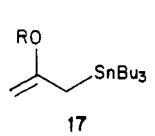
(31) In this process, the anomeric stereocenter is lost, and hence *both* anomers funnel to the same intermediate. The allyl compound **9** was subjected to oxidative olefin cleavage (OsO_4, $NaIO_4$), sodium borohydride reduction, and silylation with *tert*-butyldiphenylsilyl chloride, to yield i.



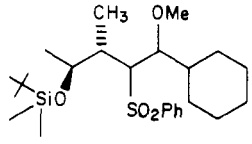
Removal of the benzylglycoside via lithium–ammonia reduction was followed by Wittig reaction with acetylmethylenetriphenylphosphorane to give a mixture of ketones ii and iii. Removal of the acetonide moiety from the major ketone (ii) (pTsOH, MeOH, 23 °C) and benzoylation of the resulting diol then gave iv, which exhibited a high field (300 MHz) NMR spectrum essentially identical with that reported by Kozikowski. The only differences observed were that some resonances reported as multiplets at 270 MHz were resolved and interpretable at 300 MHz. All reported coupling constants, including those used to differentiate iv and v, were in full agreement.

prepared: treatment of the reaction mixture with methyl iodide and dilution with HMPA smoothly afforded the β-methoxy derivatives; additionally, mesylation could be accomplished either in situ or as a separate step (methanesulfonyl choride, pyr, 0 °C) after isolation of the β-hydroxy sulfone. The reductive elimination process also proved, as expected, to be stereoselective for production of the trans olefin. Thus reduction with either 6% sodium amalgam in ethanol at 60 °C, in the presence of disodium hydrogen phosphate or with lithium in liquid ammonia–THF at −78 °C (in the absence of a proton source) gave trans/cis olefin mixtures with a trans/cis ratio ranging from 5–13/1, depending upon the substrate, reduction method, and precise experimental conditions. With these findings in hand, the stage was nearly set for completing the introduction of the lower arm; however, the question of timing remained. Two rather different scenarios could be envisioned for the remainder of the route, namely, (a) sulfone condensation and hydroxyl protection, followed by hydrogenolysis of the benzyl glycoside, to afford **15**, and (b) sulfone condensation and hydroxyl activation, followed by lithium–ammonia reduction, to afford **16**.

In the first instance, elaboration of the "upper" appendage could be expected to proceed without incident, by a sequence involving free-radical reaction with methallyltri-*n*-butylstannane, oxidative cleavage, and finally, reductive elimination to generate the C_{10}–C_{11} trans olefin. In this case, the worst possible synthetic situation would involve merely reoxidation of an alcohol produced by ketone reduction during the reductive elimination step. In the second case, however, introduction of the requisite acetyl function at C_1 (lyxose numbering) via the free-radical methodology previously discussed would be a much more demanding proposition, relying upon either a selective oxidative operation on the "upper" unsaturation, in the presence of the C_{10}–C_{11} unsaturation (Wacker oxidation or oxidative cleavage, depending on whether allyl or methallyl were introduced) or on the development of an acetonyl equivalent which could be introduced and exposed without the necessity for an oxidative step, such as reagent **17**. The opportunities offered by the former approach seemed much more secure and thus the viability of the requisite hydrogenolysis was investigated by using a simple "zero order" model: the hydrogenolysis of simple benzyl ethers in the presence of substrate **18** derived from the model condensations of sulfone **15**. It was found that reductive cleavage of the benzyl function could be accomplished without incident. The final operations necessary for the construction of the "lower arm" were then initiated.



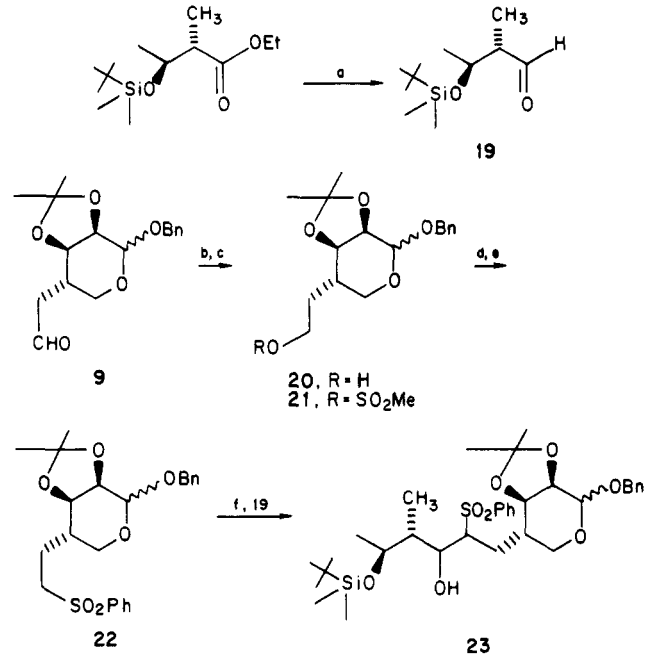
17



18

Construction of the Lower Appendage. The initial task to be accomplished in this endeavor, armed with the information gleaned from various model studies as discussed above, was the seemingly trivial condensation of sulfone **5** with aldehyde **10**, readily accessible via oxidative cleavage of olefin **9** with $OsO_4/NaIO_4$. However, despite extensive experimental investigation, this condensation could not be accomplished in anything approaching satisfactory yield; under most conditions, starting materials were recovered. We reasoned that this failure could result from a cumulative electron-withdrawing effect by the three remote oxygens present in **9**, leading perhaps to enolization

Scheme III[a]



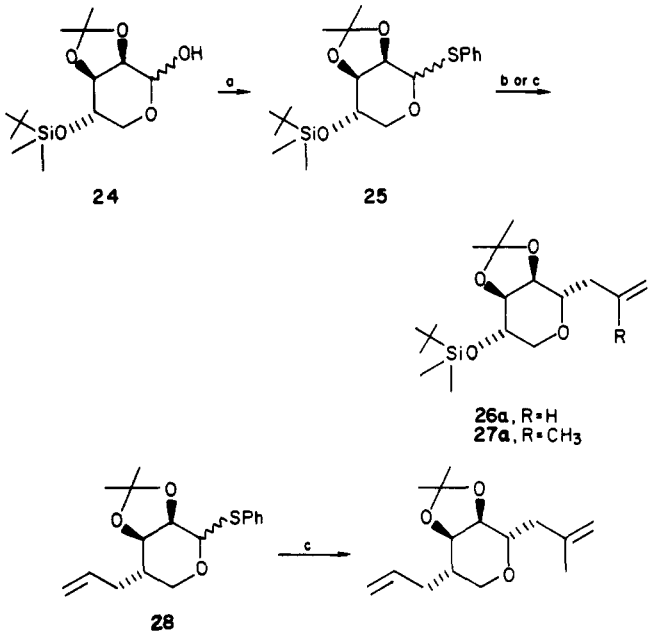
[a] Reagents: (a) $(i\text{-Bu})_2AlH$; (b) $NaBH_4$; (c) MsCl, pyr; (d) KSPh; (e) CH_3CO_3H; (f) $LiN(TMS)_2$.

of the aldehyde by the lithiated sulfone rather than the desired addition reaction. We were thus led to examine an approach in which the roles of nucleophilic and electrophilic partners were reversed. To this end, ester **12**, comprising the C_{11}–C_{14} segment of pseudomonic acid C, was reduced (1.0 equiv of $(i\text{-Bu})_2AlH$, CH_2Cl_2, −78 °C) to give aldehyde **19**, and aldehyde **9** was converted to sulfone **22** by a process paralleling that previously described: (a) $NaBH_4$/EtOH to yield alcohol **20**; (b) MsCl–pyr to give mesylate **21**; (c) NaSPh in DMF (d) CH_3CO_3H in CH_2Cl_2 buffered with $NaHCO_3$.

To our delight, condensation of sulfone **22** with aldehyde **9** proceeded smoothly in accord with our earlier model work, to afford **23**. However, a major complication was now encountered, in that hydrogenolysis of the benzylglycoside could not be accomplished, even with moderate pressures (ca. 100 psi) of hydrogen, in the absence of strong acid catalysis, which resulted in destruction of the compound. With respect to timing, this appeared to leave us only option (b) presented previously; sulfone condensation, hydroxyl activation, and lithium–ammonia reduction, to yield **16**, followed by incorporation of a latent acetyl fragment, as previously discussed and with the potential problems previously described. We were not at all enamored with the prospect of a selective oxidative cleavage step at this stage, particularly since no reasonable model studies could be conducted; all relevant experiments would require a rather advanced intermediate, such as **16**. Although there was reasonable prospect that a reagent such as **17** could prove accessible, the potential intermediacy of **16** posed another important question, namely the compatibility of the C_{10}–C_{11} unsaturation (pseudomonic acid numbering) with a C–C bond-forming process proceeding via a carbon centered radical at the anomeric center. These considerations, and the question of stereochemistry of free-radical C–C bond formation at C_1, led us to investigate the viability of such a sequence in two model systems before studying the chemistry associated with the construction and reactivity of materials such as **16**.

Model Studies on "One Electron" Routes to the Incorporation of the "Upper" Appendage. We began

Scheme IV[a]



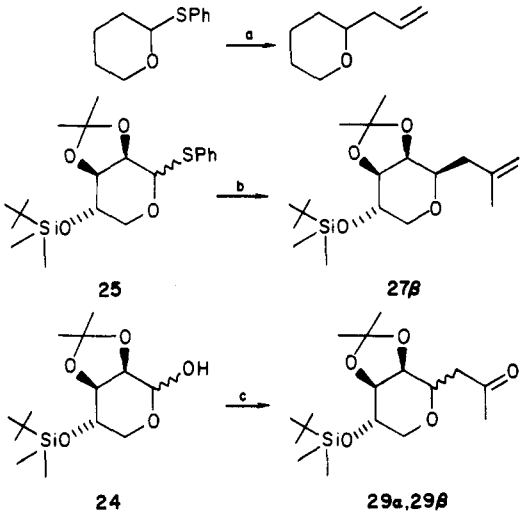
[a] Reagents: (a) PhSSPh, $P(n\text{-}Bu)_3$; (b) $CH_2{=}CHCH_2SnBu_3$, $h\nu$; (c) $CH_2{=}CH(CH_3)CH_2SnBu_3$, $h\nu$.

by investigating the stereoselectivity of free-radical C–C bond-forming reactions at C_1 in a simple, readily available, lyxose derivative, **24**. Parallel investigations had revealed that anomerically substituted chlorides, thioacylimidazoles, or phenyl thiocarbonates were unsuitable substrates (in this system) for "one-electron" allylation due to hydrolytic instability and accompanying purification difficulties. However, we were pleased and somewhat surprised[32] to find that phenyl thioglycosides are excellent substrates for our free-radical allylation reaction with photochemical initiation. Thus, the lyxose derived substrate **25** reacted with allyl or methallyltri-*n*-butylstannane to yield **26** or **27** with ca. 95:5 selectivity for formation of the α anomer, consistent with steric approach control to the less hindered (convex) face of an intermediate radical.

At this point, we turned our attention to free-radical C–C bond formation utilizing intermediate **28**, since this material possessed the potentially complicating feature of an olefinic unit suitably disposed to intervene in such a free-radical C–C bond construction via intramolecular cyclization processes.[33] Exposure of the phenyl thioglycoside **28** to the previously mentioned conditions resulted in no more than trace amounts of the desired product; instead, a major product was isolated, which, although not fully characterized, exhibited the following features: (a) the presence of the acetonide moiety of **28**; (b) a total absence of the vinyl group present in **28**; (c) incorporation of a methallyl unit and loss of the phenylthio moiety.

These observations strongly suggested that attempted bimolecular free-radical C–C bond constructions at C-1

Scheme V[a]



[a] Reagents: (a) $CH_2{=}CHCH_2SnBu_3$, Bu_3SnOTf; (b) $CH_2{=}C(CH_3)CH_2SnBu_3$, Bu_3SnOTf; (c) $(Ph)_3P{=}CHCOCH_3$.

with substrates derived from lactol **16** (regardless of the nature of the stannyl reagent) would provide fruitless, or, minimally, inefficient due to competing intramolecular cyclization processes. We were thus led to turn our attention to alternative "two electron" stratagems for C–C bond formation at the anomeric center.

"Two Electron" Approaches for Incorporation of the Upper Appendage. During the course of our studies, several reports had appeared dealing with the synthesis of C-allyl glycosides by the Lewis acid catalyzed reaction of an appropriate anomerically substituted sugar derivative, generally an acyl derivative of some sort, with allyltrimethylsilane.[35] We had independently investigated the use of similar reactions for the incorporation of allyl units in substrates such as **24**, but with little success. In our hands, loss of various protecting groups invariably occurred. However, it occurred to us that a phenylthioglycoside such as **25** should serve as a substrate in such "two electron" processes via chemospecific activation of sulfur by reaction with some electrophilic species. Tri-*n*-butylstannyl triflate seemed an ideal choice in this context, since the high Sn–S bond strength should ensure chemospecificity, and if allyltri-*n*-butylstannane were employed as the carbon nucleophile, only catalytic amounts of the stannyl triflate should be required. Finally, the use of such a stannyl triflate for activation of sulfur would be compatible with the presence of the allylstannane, which itself reacts rapidly with some other obvious choices for the sulfur activating reagent, e.g., *N*-bromosuccinimide.[36]

Thus we were very pleased to find that this premise could be reduced to practice quite easily. Exposure of 2-phenylthiopyran to 2.0 equiv of allyltri-*n*-butylstannane in the presence of 0.2 equiv of tri-*n*-butylstannyl triflate[37]

(32) Hanessian, S.; Lavellee, P. *Can. J. Chem.* **1975**, *53*, 2975.

(33) Previous work in our laboratories had revealed phenylthio derivatives to be unreactive under conditions which led to high yields of allylated products with the corresponding bromides or phenyl selenides. The lack of reactivity of such materials in tin hydride reduction has also been noted: Powell, D. W.; Vedejs, E. *J. Am. Chem. Soc.* **1982**, *104*, 2046.

(34) For excellent recent reviews of such reactions, note: (a) Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073. (b) Beckwith, A. L. J.; Ingold, K. U. In "Rearrangements in Ground and Excited States"; de Mayo, P., Ed.; Academic Press: New York, 1980; Vol. 1, p 161. (c) Surzur, J. M. In "Reactive Intermediates"; Abramovitch, A. A., Ed.; Plenum Press: New York, 1981; Vol. 2, Chapter 3.

(35) (a) Kozikowski, A. P.; Sorgi, K. L. *Tetrahedron Lett.* **1982**, *23*, 2281. (b) Lewis, M. D.; Cha, J. K; Kishi; Y. *J. Am. Chem. Soc.* **1982**, *104*, 4976. (c) Kozikowski, A. P.; Sorgi, K. L.; Wang, B. C.; Zhang-bao, X. *Tetrahedron Lett.* **1983**, *24*, 1563.

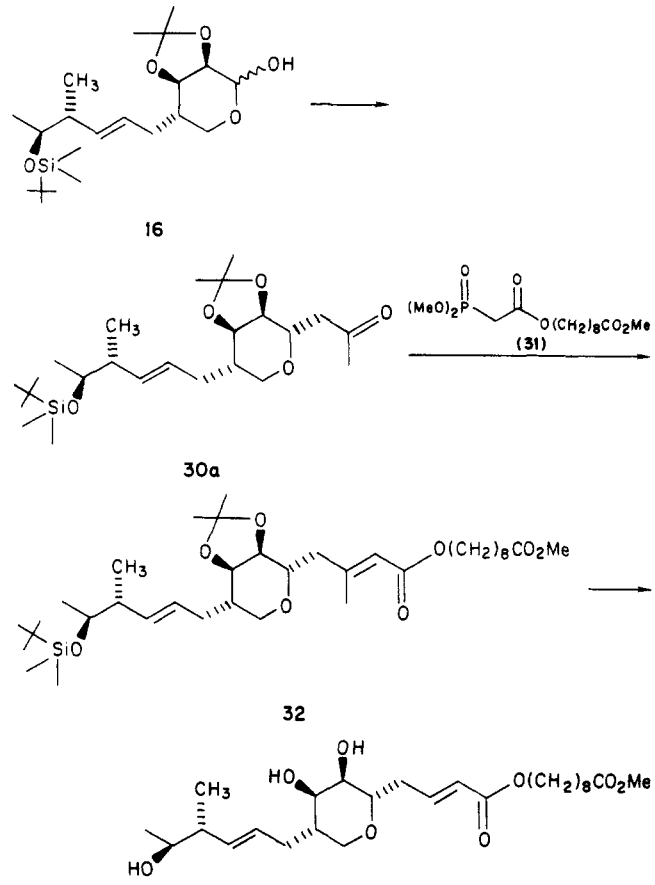
(36) For the preparation of glycosides from phenyl thioglycosides with NBS and an alcohol, note: Nicolau, K. C.; Seitz, S. P.; Paphatzis, D. P. *J. Am. Chem. Soc.* **1983**, *105*, 2430.

(37) (a) This material was prepared by reaction of tri-*n*-butyltin chloride with triflic acid. Note: Schmeisser, M.; Sartari, P.; Lippsmeir, B. *Chem. Ber.* **1973**, *103*, 868. (b) For a similar C-glycosidation using pyridyl thioglycosides, silver triflate, and various carbon nucleophiles, see: Williams, R. M.; Stewart, A. O. *Tetrahedron Lett.* **1983**, *24*, 2715.

in toluene resulted in complete consumption of starting material and quantitative conversion to 2-allylpyran within 10 min at room temperature. As expected, the more highly oxygenated derivatives such as **25** required more forcing conditions. Reaction of **25** with methallyltri-*n*-butylstannane as carbon nucleophile required heating at 90 °C for 2.5 h for complete consumption of starting material and gave a VPC separable mixture of α- and β-methallyl glycosides **27**α and **27**β in 85% yield. We were surprised to find that in this case, however, the β anomer was produced with extremely high (99:1) stereoselectivity. Although this was an intriguing and potentially useful observation, it did nothing to advance the problem at hand, since, of course, the α stereochemistry at C_1 (lyxose numbering) was required. Thus, although two new protocols for the formation of C-allyl glycosides from readily available phenylthioglycosides were now in hand, neither was of utility in the present context.

We thus decided to examine the Wittig–Michael process previously used in the Kozikowski total synthesis. As originally employed, this process yielded the α and β acetonyl compounds in a ratio of 2.5:1.[14] However, the conditions utilized (CH_3CN, 170 °C) seemed less than ideal for obtention of good stereocontrol. In fact, reaction of the model compound **24** with excess acetylmethylenetriphenylphosphorane in CH_3CN at 70 °C, followed by treatment of the crude product with potassium carbonate in methanol at 0 °C, gave ketones **29**α and **29**β in a ratio of 6:1. In parallel fashion, lactol **16**, prepared via mesylation of **23** followed by reduction with lithium in liquid ammonia, yielded a 5:1 mixture of α and β ketones from which the α derivative **30a** could be separated by chromatography over silica gel.

The final chain extension operation had previously been accomplished via a four-step sequence: Emmons reaction with (methyldimethylphosphono)acetate, ester hydrolysis, alkylation of the resulting acid salt with methyl 9-iodononanoate, and ester hydrolysis.[14g] We chose a more convergent process by reaction of ketone **30**α with Emmons reagent **31**. This material proved readily accessible from methyl 9-hydroxynonanoate[38] via esterification with bromoacetic acid using the general procedure of Steglich,[39] followed by Arbuzov reaction with trimethyl phosphite. The Emmons reaction of this material proceeded smoothly to give a ca. 4:1 mixture of *E* and *Z* unsaturated esters, from which the *E* isomer (**32**) was obtained in 75% isolated yield. This material proved chromatographically and spectroscopically indistinguishable with material prepared from authentic methyl pseudomonate C. Particularly compelling evidence of correct gross structure and stereochemistry was obtained from the high-field ^{13}C NMR spectra, which were superimposable. Removal of the silyl and acetonide protecting groups (80% acetic acid)[5] afforded methyl pseudomonate C, which was again chromatographically and spectroscopically identical with naturally derived material. Finally, selective methyl ester hydrolysis as previously described[6] yields the title compound.



Experimental Section

General Methods. Melting points were recorded on a Meltemp apparatus and are uncorrected. Infrared spectra were recorded on a Beckman Acculab 3 IR spectrometer. ^1H NMR spectra were recorded at 90 MHz with a Varian EM-390 or at 300 MHz with a Varian SC-300. ^{13}C NMR were recorded at 20 MHz with a Varian FT-80 or at 75 MHz with a Varian SC-300. Chemical shifts are in parts per million downfield from internal Me_4Si; coupling constants are given in hertz. Solvents and reagents were purified as follows: ether, toluene, and tetrahydrofuran by distillation from benzophenone ketyl under argon; hexanes and ethyl acetate by distillation; HMPA, toluene, methylene chloride, pyridine, and diisopropylamine by distillation from calcium hydride. Mass spectra were recorded on a Varian Mat 112s, Varian MA7-731, or a VG Micromass 7070 in the electron impact or chemical ionization (CI) mode with the indicated reagent gas, or by fast atom bombardment (FAB). Elemental analyses were performed by Galbraith Laboratories. All yields reported are isolated yields of material judged homogeneous by thin-layer chromatography and NMR spectroscopy and, for crystalline solids, material having the indicated melting point. Thin-layer chromatography was performed on Merck 0.25-mm glass silica gel plates; visualization of developed plates was by fluorescence quenching and staining with phosphomolybdic acid. Column chromatography was performed by using Merck or Davison silica gel 60 (60–240 mesh). MPLC refers to medium-pressure liquid chromatography over Merck silica gel 60 (230–400 mesh) with an FMI lab pump operated at 60–100 psi, Altex columns, and a UV detector and fraction collector.

1-*O*-Benzyl-L-lyxose. A solution of L-lyxose (10.30 g, 0.0686 mol) in 30 mL of benzyl alcohol containing 0.10 g of *p*-toluenesulfonic acid was heated at 60 °C for 48 h. Benzene (3 mL) was added and ca. 10 mL of volatiles were removed in vacuo (0.25 mm, 45 °C) to yield a semisolid white mass, which was suspended in 2:1 hexanes–dichloromethane and filtered. The crystals were washed with ether and the filtrate was concentrated and resubjected to the treatment above to yield a total of 13.30 g (81%) of colorless crystals as a mixture of anomers, R_f 0.13 (5% MeOH–$CHCl_3$). For analytical purposes, a sample of 0.50 g of this material was dissolved in 3 mL of hot acetone and kept at 0 °C overnight to afford 0.16 g of a single anomer as colorless needles: mp 141–143 °C; $[\alpha]^{25}_D$ –84.1 (*c* 0.0135, methanol); 300 MHz ^1H NMR ($(CD_3)_2CO$) δ 7.39 (m, 5 H), 4.79 (d, J = 3.1, 1 H), 4.62 (center of AB q, J = 12.4, 2 H), 3.88 (d of d, J = 4.7, 14.0 Hz, 1 H), 3.82 (m, 2 H), 3.72 (m, 1 H), 3.68 (d of d, J = 4.7, 10.9,

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(39) Steglich, W.; Neises, B. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 522.

1 H), 3.52 (d of d, J = 9.3, 0.9, 1 H), 3.08 (m, 1 H), 2.87 (m, 1 H); 75 MHz ^{13}C NMR (CD_3OD) δ 139.4, 129.8, 129.4, 129.1, 101.4, 73.0, 72.0, 70.4, 68.7, 64.4; IR (KBr pellet) 3350, 2929 (s), 1460, 1375, 1060, 740, 700 cm^{-1}; mass spectrum (CI isobutane), 241.1 (M + 1, 1), 205 (34), 133 (M - OCH_2Ph, 100), 92 (30), 91 (100), 73 (25), 57.1 (100).

1-*O*-Benzyl-2,3-isopropylidene-D-lyxose (7). To a stirred suspension of an anomeric mixture of 1-*O*-benzyl-L-lyxose (11.54 g, 0.048 mol) in 160 mL of acetone was added 20 mL of dimethoxypropane and 0.20 g of *p*-toluenesulfonic acid. After 12 h at room temperature 140 mL of 1:1 hexanes–diethyl ether was added, and the solution was washed once with aqueous sodium bicarbonate solution and twice with water and concentrated in vacuo. The resulting material was chromatographed over silica gel to yield 12.08 g (90%) of a colorless oil as a mixture of anomers, R_f 0.38, 0.37 (35% THF–hexanes).

An analytical sample of the higher R_f anomer was obtained by using the same procedure with the mp 141–143 °C anomer of 1-*O*-benzyl-L-lyxose described above: mp 63–66 °C; $[\alpha]^{25}_D$ –74.7 (*c* 0.0311, CH_2Cl_2); 300 MHz ^{1}H NMR ($CDCl_3$) δ 7.32 (m, 5 H), 4.84 (d, J = 2.8, 1 H), 4.68 (center of AB q, J = 11.4, 2 H), 4.18 (m, 2 H), 3.76 (m, 3 H), 3.56 (m, 1 H), 1.46 (s, 3 H), 1.34 (s, 3 H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 137.2, 128.8, 128.5, 128.3, 109.7, 97.7, 77.1, 74.8, 69.7, 67.6, 62.9, 27.7, 25.9; IR (KBr pellet) 3420 (s), 2923 (s), 1450, 1375, 1240, 1220, 1070 (vs), 910, 860, 740, 700 cm^{-1}; mass spectrum (CI isobutane), 281.1 (M + 1, 0.6), 205 (15), 173 (100), 131 (23), 91 (56). Anal. ($C_{15}H_{20}O_5$) C, H.

Preparation of Thionocarbonate 8c. A solution of alcohol **7** (12.90 g, 0.0460 mol) in 100 mL of THF was cooled to –78 °C, and 1.4 M MeLi in ether (36.1 mL, 0.0500 mol) was added dropwise over a 15-min period. After stirring for 15 min at –78 °C phenyl chlorothionocarbonate (7.64 mL, 0.055 mol) was added dropwise by syringe over a 10-min period. The resulting solution was allowed to warm to room temperature over 45 min, then water (70 mL) was added and the aqueous layer was extracted with ether (3 × 50 mL). The combined organic layers were dried and concentrated to an oil which was chromatographed over silica gel (30% ether–hexanes) to yield 17.1 g (90%) of a thick straw colored oil as a mixture of anomers, R_f 0.54, 0.65 (35% THF–hexanes), higher R_f anomer (isolated by chromatography over silica gel): 90 MHz ^{1}H NMR ($CDCl_3$) δ 7.30 (m, 10 H), 5.50 (m, 1 H), 4.95 (d, J = 3, 1 H), 4.50 (center of AB q, J = 12, 2 H), 4.45 (m, 1 H), 4.20 (d of d, J = 3, 6, 1 H), 3.90 (m, 2 H), 1.45 (s, 3 H), 1.30 (s, 3 H). Lower R_f anomer (isolated by chromatography over silica gel): 90 MHz ^{1}H NMR ($CDCl_3$) δ 7.30 (m, 10 H), 6.75 (m, 1 H), 4.70 (center of AB q, J = 12.0, 2 H), 6.75 (d, J = 4.5, 1 H), 4.40 (m, 1 H), 3.95 (d of d, J = 4.5, 6.0, 1 H), 3.75 (m, 2 H), 3.40 (d of d, J = 7.0, 13.5, 1 H), 1.40 (s, 3 H), 1.30 (s, 3 H); IR (neat) 3030–3060, 2760–2980, 1600 (s), 1200, 860, 770, 750, 690 cm^{-1}; mass spectrum (CI isobutane) 417.2 (M + 1, 2.5), 309 (M - OCH_2Ph, 36), 231 (36), 126 (41), 107 (25), 91 (100).

Preparation of Allyl Adduct 9. Thionocarbonate **8c** (11.16 g, 26.8 mmol) was placed in Hanovia photolysis apparatus along with 17.68 g (53.6 mmol) of allyltributylstannane and 54 mL of toluene. After thoroughly degassing the solution with argon, it was irradiated for 65 h at 23 °C with a 450-W Hanovia lamp with Pyrex filter. Solvents were removed in vacuo and the crude product was chromatographed over silica gel (5% ether hexanes) to yield a total of 6.25 g (80%) of a colorless oil: R_f 0.36, 0.29 (20% ether–hexanes); higher R_f anomer (isolated by chromatography over silica gel) mp 43–44 °C; $[\alpha]^{25}_D$ –70.3 (*c* 0.0774, CH_2Cl_2); 300 MHz ^{1}H NMR ($CDCl_3$) δ 7.32 (m, 5 H), 5.74 (m, 1 H), 5.00 (m, 2 H), 4.86 (d, J = 2.1, 1 H), 4.61 (center of AB q, J = 12.0, 2 H), 3.95 (m, 2 H), 3.58 (d of d, J = 3.8, 12.0, 1 H), 3.48 (d of d, J = 8.8, 12.0, 1 H), 2.33 (m, 1 H), 1.95 (m, 2 H), 1.44 (s, 3 H), 1.32 (s, 3 H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 137.6, 136.0, 128.7, 128.4, 128.1, 117.2, 109.0, 98.2, 76.1, 74.2, 69.3, 61.4, 38.1, 34.1, 28.2, 26.5. Lower R_f anomer (isolated by chromatography over silica gel): 300 MHz ^{1}H NMR ($CDCl_3$) δ 7.36 (m, 5 H), 5.78 (m, 1 H), 5.06 (m, 2 H), 4.72 (center of AB q, J = 11.8, 2 H), 4.48 (d, J = 5.7, 1 H), 4.31 (d of d, J = 3.2, 6.3, 1 H), 3.96 (d of d, J = 6.1, 11.6, 1 H), 3.74 (d of d, J = 6.1, 11.6, 1 H), 3.45 (m, 1 H), 2.18 (m, 1 H), 2.02 (m, 2 H), 1.36 (s, 3 H), 1.32 (s, 3 H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 137.9, 135.7, 128.7, 128.5, 128.3, 117.1, 109.4, 100.1, 75.7, 74.0, 70.1, 64.3, 35.7, 32.3, 27.5, 25.7; IR (neat) 3020, 3060 (ws), 2920, 1640, 1375, 1080, 735, 700 cm^{-1}; mass spectrum (CI isobutane) 305 (M + 1, 5), 197 (M - OCH_2Ph, 100), 139 (47), 91 (56); exact mass calcd for $C_{18}H_{24}O_4$ 304.1674, found 304.1656. Anal. ($C_{18}H_{24}O_4$) C, H.

Preparation of Alcohol 20. A solution of allyl adduct **9** (2.54 g, 8.35 mmol) in 45 mL of 30% aqueous THF was cooled to 0 °C. Sodium metaperiodate (3.57 g, 16.70 mmol) was added followed by 0.25 mL of OsO_4 solution (1 M in THF). After 2 h the mixture was warmed to 23 °C, an additional 0.25 mL of OsO_4 solution was added, and stirring was continued for an additional hour. The mixture was diluted with 75 mL of water and extracted with ether (4 × 50 mL). The organic phase was concentrated and the crude product was used immediately in the next step without purification: ^{1}H NMR ($CDCl_3$) δ 10.15 (s, 1 H), 7.50–7.70 (s, 5 H), 5.15 (d, J = 8, 1 H), 4.80 (m, 4 H), 4.15 (br s, 1 H), 3.70 (m, 1 H), 2.35 (m, 2 H), 1.05–1.65 (m, 6 H); IR (neat) 3020–3080, 2920 (s), 2720 (w), 1722 (s), 1375, 1080, 700; mass spectrum (CI, methane), no M + 1 observed, 216 (31), 215 (P, M - CH_2Ph), 199 (P, M - OCH_2Ph), 141 (34), 91 (25), 57 (100).

A solution of the crude aldehyde **10** in 60 mL of absolute ethanol was cooled to 0 °C, $NaBH_4$ (0.48 g, 12.5 mmol) was added, and after 1 h the solution was warmed to 23 °C. After 1 h at 23 °C, 50 mL of water was added and the aqueous layer was extracted with 70% ether–hexanes. Solvents were removed under reduced pressure and the residue was chromatographed over silica gel to yield 2.19 g (85%) of the alcohol as a mixture of anomers: R_f 0.33, 0.22 (5% MeOH–$CHCl_3$); higher R_f anomer (isolated by chromatography over silica gel) $[\alpha]^{25}_D$ –70.6; (*c* 0.0378, CH_2Cl_2); 300 MHz ^{1}H NMR ($CDCl_3$) δ 7.35 (m, 5 H), 5.05 (s, 1 H), 4.64 (center of AB q, J = 11.8, 2 H), 4.04 (m, 2 H), 3.75 (m, 3 H), 3.52 (m, 2 H), 1.97 (m, 1 H), 1.51 (m, 2 H), 1.52 (s, 3 H), 1.35 (s, 3 H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 137.5, 128.9, 128.5, 128.3, 109.3, 97.1, 76.8, 73.9, 69.3, 61.5, 61.2, 37.3, 33.7, 28.2, 26.4; IR (neat), 3420, 3020–3060 (br), 2920, 1450, 1375, 1220, 1060, 860, 735, 700 cm^{-1}; mass spectrum (CI isobutane), 309 (M + 1, 3), 201 (M - OCH_2Ph, 75), 183 (31), 143 (85), 113 (45), 91 (100). Anal. ($C_{17}H_{24}O_5$) C, H. Lower R_f isomer (isolated by chromatography over silica gel): 90 MHz ^{1}H NMR δ 7.30 (s, 5 H), 4.70 (center of AB q, J = 12, 2 H), 4.40 (m, 2 H), 3.95 (m, 2 H), 3.60 (m, 3 H) 2.30 (bm, 1 H), 1.60 (m, 3 H), 1.35 (m, 6 H).

Preparation of Mesylate 21. To a solution of alcohol **20** (650 mg, 2.11 mmol) in 30 mL of pyridine at 0 °C was added 0.40 mL of methanesulfonyl chloride dropwise over 10 min and the mixture was then allowed to warm to 23 °C. After 12 h, sufficient ice was added to double the volume and the aqueous layer was extracted with ether (3 × 70 mL). Solvents were removed under reduced pressure and the crude product was chromatographed over silica to yield 730 mg (90%) of a thick oil as a mixture of anomers: R_f 0.51, 0.40 (1% MeOH–$CHCl_3$); higher R_f isomer (isolated by chromatography over silica gel); 90 MHz ^{1}H NMR ($CDCl_3$) δ 7.31 (s, 5 H), 4.93 (d, J = 1.5, 1 H), 4.55 (center of AB q, J = 12, 2 H), 4.25 (m, 1 H), 3.50 (m, 4 H), 2.95 (s, 3 H), 1.80 (m, 3 H), 1.48 (s, 3 H), 1.33 (s, 3 H); IR (neat) 3020–3060 (s), 2930, 1355, 1175, 1070, 740, 700 cm^{-1}; 20 MHz ^{13}C NMR ($(CD_3)_2CO$) δ 129.0, 128.8, 128.4, 109.3, 98.5, 77.1, 74.7, 69.6, 69.3, 61.4, 37.2, 36.3, 30.5, 28.5, 26.7; mass spectrum (CI methane), no M + 1 observed, 291 (M - OMs, 2.0), 95 (56), 91 (100), 78.9 (28.1), 74 (73).

Preparation of Sulfone 22. To a stirring solution of potassium thiophenoxide (prepared from 0.133 g (1.20 mmol) of potassium *tert*-butoxide and 0.110 g (1.20 mmol) of thiophenol) in 2 mL of DMF at 0 °C was added 0.210 g (0.55 mmol) of mesylate **21** in 3 mL of DMF. The mixture was allowed to warm to 23 °C over 1 h, during which time additional small portions of DMF were added as the mixture thickened. After TLC analysis showed complete reaction, 50 mL of ice water was added and the mixture was extracted with ether (3 × 50 mL). The organic phase was dried and concentrated in vacuo to yield a thick oil used without purification in the subsequent step.

To a solution of the crude sulfide in 5 mL of chloroform, maintained at 0 °C, was added 1.5 g of $NaHCO_3$ and 0.5 mL of 40% peracetic acid. After 5 h the solution was warmed to 23 °C. After 5 h at 23 °C, water (50 mL) was added and the mixture was extracted with ether (3 × 50 mL). The organic phase was dried, concentrated in vacuo, and chromatographed over silica gel to yield 0.230 g (98%) of a thick, colorless oil; R_f 0.28, 0.32 (35% THF–hexanes); physical data for faster R_f isomer: colorless crystalline plates from 75% ether–hexanes, mp 94.5–95.5 °C; $[\alpha]^{25}_D$

−34.4 (c 0.0445, CH_2Cl_2); 300 MHz ^1H NMR ($(CD_3)_2CO$) δ 7.97 (m, 2 H), 7.73 (m, 3 H), 7.38 (m, 5 H) 4.94 (d, J = 1.9, 1 H), 4.62 (center of AB q, J = 11.8, 2 H), 3.96 (m, 2 H), 3.56 (d of d, J = 4.8, 11.8, 1 H), 3.46 (m, 1 H), 3.40 (m, 2 H), 1.72 (m, 3 H), 1.39 (s, 3 H), 1.26 (s, 3 H); 75 MHz ^{13}C NMR ($(CD_3)_2CO$) δ 141.0, 139.1, 134.9, 130.6, 129.5, 129.2, 129.1, 128.8, 109.7, 98.7, 77.3, 74.9, 69.8, 61.4, 54.5, 38.4, 28.5, 26.7, 24.3; IR 3020–3060, 2940 (s), 1450, 1375, 1305, 1150, 1070, 740, 700 cm^{-1}; mass spectrum (CI isobutane) 433 (M + 1, 1.1), 325 (M − OCH_2Ph, 23) 295 (23), 267 (100), 91 (83). Anal. ($C_{23}H_{28}O_6S$) C, H.

Preparation of Ester 12. **12** was prepared according to the method of Frater.[29] A solution of ethyl (*S*)-(+)-3-hydroxybutyrate (1.00 g, 7.7 mmol) in 5 mL of THF was added dropwise within 2 min to a stirred, hexane-free solution of lithium diisopropylamide (23.1 mmol) in 10 mL of THF at −78 °C. After 20 min, methyl iodide (10.92 g, 77 mmol) was added via syringe and the mixture was allowed to warm slowly to room temperature with the dissipation of the cold bath. The reaction mixture was then quenched with 1 M HCL solution to neutral pH and extracted with ether. The combined ether extracts were washed with brine, dried, and concentrated in vacuo affording the crude methylated hydroxy ester as an oil which was immediately silylated as follows. To a solution of the hydroxy ester in 5 mL of anhydrous DMF was added imidazole (786 mg, 11.6 mmol) followed by *tert*-butyldimethylchlorosilane (1.74 g, 11.6 mmol). After 18 h at 23 °C the solution was diluted with ether and washed with small portions of water. The organic phase was dried and concentrated yielding 1.8 g (90%) of the desired compound as a clear oil which by VPC analysis (5% OV-1 on Variport 30, 6′ × 2 mm; 110°) consisted of 93% threo isomer: $[\alpha]^{25}_D$ +28.3 (c 0.102, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 4.15 (q, J = 7, 2 H), 4.12 (q, J = 7.5, 1 H), 2.50 (p, J = 7.5, 1 H), 1.21 (t, J = 7, 3 H), 1.18 (d, J = 7, 3 H), 1.15 (d, J = 7, 3 H), 0.87 (s, 9 H), 0.07 (s, 3 H), 0.03 (s, 3 H); IR (neat) 3000–2860 cm^{-1} (b), 1732 (s), 1252 (s), 1180 (s), 840 (m), 810 (w), 775 (m); ^{13}C NMR ($CDCl_3$) 175.0 (s), 76.2 (d), 66.1 (t), 54.2 (d), 31.7 (q), 26.5 (q), 23.9 (s), 20.2 (q), 18.6 (q), 1.7 (q), 0.9 (q); mass spectrum (EI) 258 (13.4), 245 (4.6), 244 (6.7), 204 (23.4), 203 (100.00), 175 (19.7), 159 (14.2), 103 (13.4), 75.0 (71.5). Anal. ($C_{13}H_{28}O_3Si$) C, H.

Preparation of Aldehyde 19. Diisobutylaluminum hydride (4.66 mL of 1.25 M in toluene, 5.83 mmol) was slowly added dropwise to a solution of ester **12** (1.52 g, 5.83 mmol) in 30 mL of methylene chloride at −78 °C under argon. After 1 h at the same temperature, TLC analysis indicated consumption of the starting ester and the formation of a new material with R_f 0.53 (10% THF–hexanes). The mixture was quenched by addition of 10 mL of anhydrous methanol at −78 °C and poured into 200 mL of saturated aqueous Rochelle salt solution. The clear organic phase was removed after 2 h, dried, and concentrated in vacuo to afford the crude product which was purified by rapid chromatography over silica gel. Elution with hexanes afforded a clear, homogeneous oil (0.99 g, 87%): $[\alpha]^{25}_D$ +28.9° (c 0.097, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 9.8 (d, J = 3, 1 H), 4.5 (p, J = 6, 1 H), 2.35 (m, 1 H), 1.2 (d, J = 7, 3 H), 1.05 (d, J = 7, 3 H), 0.85 (s, 9 H), 0.05 (s, 6 H); IR (neat) 1715 (s), 1410 (s), 1220 (s), 1000 (w), 740 (w); ^{13}C NMR ($CDCl_3$) 177.0, 74.0, 57.8, 29.9, 25.9, 22.2, 14.8, 0.00, −0.8; mass spectrum (CI, methane) 233 [M·H^+·CH_4] (17.3), 217 [M·H^+] (21.0), 201 (34.7), 160 (37.1), 159 (100.0), 115 (19.6), 57 (11.1), 29 (24.7).

Preparation of Lactol 16. A solution of sulfone **20** (0.3709 g, 0.85 mmol) in 7.8 mL of THF was added dropwise to a solution of lithiohexamethyldisilazane (prepared from hexamethyldisilane (0.22 g, 1.39 mmol) and *n*-butyllithium (0.69 mL of 1.6 M solution in hexane, 1.11 mmol) in 10 mL of THF at 0 °C. After the addition, the solution was maintained at 0 °C for 15 min, whereupon aldehyde **19** (0.28 g, 1.28 mmol) was added as a THF solution (2 mL) within 30 s. TLC analysis (5 min) indicated consumption of the starting sulfone and the production of two faster running materials with R_f 0.46, 0.39 (35% THF–hexanes).

The solution was diluted with aqueous NH_4Cl solution and extracted with ether, and the combined extracts were dried and concentrated in vacuo to a colorless oil which was taken up in pyridine (14 mL) and treated with methanesulfonyl chloride (0.98 g, 8.5 mmol) at 25 °C. After 3 h, TLC analysis showed the formation of two more polar products with R_f 0.37, 0.28 (35% THF–hexanes) and consumption of the starting alcohols. The crude mesylate was diluted with ethyl acetate, washed with water, concentrated in vacuo, and azeotroped with toluene. The residue was dissolved in THF (18 mL) and ca. 30 mL of ammonia was added at −78 °C. Lithium was added in small portions until the blue color persisted for 1 min, at which time excess lithium was destroyed via the dropwise addition of ethylene dibromide in THF, followed by the addition of solid ammonium chloride. After evaporation of ammonia and addition of water, the mixture was extracted exhaustively with methylene chloride, dried, concentrated in vacuo, and chromatographed over silica gel. Elution with 2.5% THF–hexanes afforded 125 mg (0.31 mmol, 37% from **21**) of two less polar materials, R_f 0.43, 0.23 (35% THF–hexanes), identified as an anomeric mixture of the title compound. Physical data for higher R_f anomer: $[\alpha]^{25}_D$ +4.9 (c 0.0231, CH_2Cl_2); 300 MHz ^1H NMR ($CDCl_3$) δ 5.4 (m, 2 H), 5.15 (d, J = 3.5, 1 H), 4.15–3.6 (m, 6 H), 2.25–1.85 (m, 4 H), 1.55 (s, 3 H), 1.45 (s, 3 H), 1.15 (d, J = 6, 3 H), 1.05 (d, J = 6, 3 H), 0.87 (s, 9 H), 0.05 (s, 6 H); 75 MHz ^{13}C NMR ($CDCl_3$) 135.8, 127.1, 109.1, 95.1, 76.2, 75.0, 72.0, 62.4, 44.3, 39.1, 38.0, 33.2, 28.2, 25.9, 20.6, 17.3, 16.0, −4.4, −4.9; IR (neat) 3650–3190 (b), 2957–2857 (s), 1372 (s), 1250 (s), 1219 (m), 836 (m), 775 (m); mass spectrum (+)-FAB (Xe°), m/z 493 [M·gly·H^+], 401 [M·H^+], 383 [M·H^+ − H_2O], 334, 339, 326, 269, 251, 212, 186; (+)-FAB exact mass calcd for ($C_{21}H_{40}O_5Si$) 401.27231, found 401.27193.

Preparation of Ketone 30. To an oven-dried vial with stir bar was added the lactol **16** (10.0 mg, 0.025 mmol) and acetonylmethylenetriphenylphosphorane (39.7 mg, 0.12 mmol) followed by 0.20 mL of 1,2-dichloroethane. The vial was sealed and heated at 75 °C for 48 h. TLC analysis indicated the formation of a less polar spot with R_f 0.65 and a more polar spot with R_f 0.24 relative to the starting lactol (35% THF–hexanes). The reaction mixture was diluted with 2 mL of anhydrous methanol and potassium carbonate (ca. 50 mg) was added as the solid. The mixture was stirred at room temperature for 1 h whereupon TLC analysis revealed consumption of the material with R_f 0.24 and enhancement of the product at R_f 0.65 (35% THF–hexanes). The reaction mixture was filtered through a Celite pad and concentrated in vacuo, and the residue was chromatographed over silica gel, eluting with 5% THF–hexanes, to provide 7 mg (0.016 mmol) of product as a clear oil: $[\alpha]^{25}_D$ +2.05 (c 0.0031, CH_2Cl_2); 300 MHz ^1H NMR ($CDCl_3$ partial) δ 5.8 (m, 2 H), 4.48 (m, 1 H), 4.08 (m, 2 H), 3.15 (m, 1 H), 2.55 (s, 3 H), 2.52 (m, 4 H), 1.86 (s, 3 H), 1.70 (s, 3 H), 1.61 (s, 3 H), 1.42 (dd, J = 6.7, 6.3, 1 H), 1.38 (d, J = 6.3, 3 H), 1.32 (d, J = 6.7, 3 H), 1.24 (s, 9 H), 0.39 (s, 6 H); IR (neat) 3025 cm^{-1} (s), 2860 (s), 1740 (s), 1370 (s), 1250 (m), 1060 (s), 840 (s), 775 (s); mass spectrum (+)-FAB (Xe°), m/z 511 [M·gly_2·H^+], 419 [M·gly·H^+], 327 [M·H^+], 309, 278, 259, 185, 186, 167, 93. Anal. No parent ion could be observed for this intermediate even with fast atom bombardment (FAB). However, a parent ion could be observed after desilylation with tetra-*N*-butylammonium fluoride. (+)-FAB exact mass calcd for $C_{18}H_{30}O_5$ 327.1714, found 327.1700.

Methyl 9-Hydroxynonanoate. To a solution of methyl semiazelaaldehyde[38] (6.9 g, 37 mmol) in 200 mL of absolute ethanol at 0 °C was added $NaBH_4$ (2.8 g, 74 mmol) in small portions as the solid. Immediately after addition (15 min), TLC analysis indicated complete consumption of starting aldehyde and the appearance of a more polar spot with R_f 0.43 (35% THF–hexanes). The reaction was quenched with NH_4Cl solution, adjusted to pH 7, and extracted with methylene chloride. The combined extracts were dried and concentrated in vacuo to yield the crude alcohol which was then chromatographed over silica gel with 10% EtOAc–hexanes to yield 6.75 g (97%) of a colorless oil: 90 MHz ^1H NMR ($CDCl_3$) δ 3.70 (s, 3 H), 3.65 (t, J = 6.0, 2 H), 2.60 (s, 1 H), 2.35 (t, J = 6.0, 2 H), 1.95–1.2 (m, 12 H); IR (neat) 3630–3150 (b), 2990–2860 (m), 1735 (s), 1440 (s), 1200 (s); ^{13}C NMR ($CDCl_3$) 174.4 (s), 62.7 (t), 51.4 (q), 34.1 (t), 32.7 (t), 29.4 (t), 29.3 (t), 29.1 (t), 25.8 (t), 25.0 (t) mass spectrum (EI) m/z 158 (23.7), 152 (9.2), 138 (41.9), 127 (9.7), 106 (20.9), 96 (26.3), 72 (100.0), 71 (63.2), 56 (52.3), 39 (69.7), 29 (42.1).

Preparation of phosphonate 31 was accomplished according to the general procedure of Steglich. (Diethylphosphono)acetic acid (2.20 g, 11.2 mmol) was combined with methyl 9-hydroxynonanoate (2.11 g, 11.2 mmol) and DMAP (0.14 g, 1.1 mmol) under argon. The mixture was diluted with 50 mL of anhydrous methylene chloride and then cooled to 0 °C. Dicyclohexyl-

carbodiimide (2.43 g, 11.3 mmol) was then added as the solid and the mixture was stirred for an additional 10 min at 0 °C and warmed to room temperature. After 20 min, TLC analysis revealed total consumption of the starting alcohol and the presence of a more polar material with R_f 0.35 (35% THF–hexanes). The reaction mixture was filtered, concentrated in vacuo, and chromatographed over silica gel to afford 3.65 g (89%) of a colorless product: 300 MHz ^{1}H NMR ($CDCl_3$) δ 4.1 (m, 6 H), 3.65 (s, 3 H), 2.95 (d, J = 21, 2 H), 2.75 (t, J = 7.4, 2 H), 1.8–0.95 (m, 18 H); IR (neat) 3025–2840 cm^{-1} (s), 1735 (s), 1270 (s), 1120 (m), 1025 (m), 970 (m); ^{13}C NMR ($CDCl_3$) 172.6 (s), 164.7 (s), 164.4 (s), 64.2 (t), 61.6 (t), 61.2 (t), 50.1 (q), 36.4 (t), 32.7 (t), 29.7 (t), 27.9 (t), 27.4 (t), 24.6 (t), 23.8 (t), 15.4 (q), 15.1 (q); mass spectrum (EI), m/z 366 (4.4), 335 (2.9), 293 (9.7), 225 (11.5), 197 (100.0), 183 (32.1), 179 (13.3), 151 (44.4), 123 (4.1). Anal. ($C_{16}H_{31}O_7P$) C, H.

Methyl 6,7-*O*-Isopropylidene-13-(*tert*-butyldimethylsiloxy)pseudomonate C. To an oven-dried vial with stir bar was added phosphonate **31** (24.6 mg, 0.067 mmol) in 0.25 mL of dioxane under argon. A dioxane solution of lithiohexamethyldisilazane (0.047 mL of 0.94 M, 0.045 mmol) was added slowly dropwise at 25 °C. The clear homogeneous solution was stirred for 5 min and then treated dropwise with a dioxane solution of the ketone **30** (0.0721 mL of 0.062 M, 0.002 g, 0.0045 mmol) via syringe. After 12 h at 25 °C, TLC analysis (3 elutions in 10% THF–hexanes) clearly revealed the consumption of starting ketone and the presence of a less polar material with R_f 0.55. The mixture was diluted with water, extracted with methylene chloride, and chromatographed over silica gel. Elution with 2.5% THF–hexanes afforded a clear oil which was rechromatographed via HPLC (SI-5 analytical silica gel with 4% THF–hexanes). The material thus obtained (0.002 g, 0.0031 mmol, 75%) was identical with the title compound obtained from degradation of methyl (+)-pseudomonate A via TLC, HPLC, 300 MHz ^{1}H NMR, and 75 MHz ^{13}C NMR: $[\alpha]^{25}_D$ –9.0° (c 0.0067, CH_2Cl_2); 300 MHz ^{1}H NMR ($CDCl_3$ partial) δ 6.12 (s, 1 H), 5.79 (m, 2 H), 4.49 (dd, J = 5.2, 1.9, 2 H), 4.43 (t, J = 6.7, 2 H), 4.04 (m, 1 H), 4.03 (s, 3 H), 3.78 (m, 1 H), 2.91 (d, J = 2.3, 1 H), 2.84 (d, J = 1.6, 1 H), 2.67 (t, J = 7.5, 2 H), 2.56 (s, 3 H), 2.53 (m, 2 H), 2.34 (m, 1 H), 1.97 (m, 1 H), 1.95 (m, 1 H), 1.71 (s, 3 H), 1.67 (m, 15 H), 1.62 (s, 3 H), 1.39 (d, J = 6, 3 H), 1.32 (d, J = 6.9, 3 H), 1.24 (s, 9 H), 0.40 (s, 6 H) ; 75 MHz ^{13}C NMR ($CDCl_3$) 174.6, 167.1, 156.7, 135.8, 127.3, 117.7, 108.7, 77.2, 76.4, 75.3, 74.1, 71.7, 66.7, 63.7, 51.3, 44.1, 43.9, 36.6, 33.9, 31.7, 29.5, 29.1, 28.9, 28.5, 28.2, 26.1, 25.7, 24.7, 22.5, 20.4, 18.8, 15.7, –4.7, –5.1; IR (neat) 3025 cm^{-1} (s), 2860 (m), 1735 (s), 1710 (s), 1650 (w), 1455 (w), 1370 (m), 1220 (s), 1150 (s), 1060 (s), 960 (w), 835 (s), 775 (s); mass spectrum (+)-FAB (Xe°), m/z 745 [M·gly·H$^+$], 653 [M·H$^+$], 595, 549, 521, 425, 352, 334, 302, 255, 242, 155, 93; (+)-FAB exact mass calcd for ($C_{36}H_{69}O_8Si$) 653.4448, found 653.4453.

(+)-Methyl Pseudomonate C. Into an oven-dried 1.0-mL vial with stir bar was introduced methyl 6,7-*O*-isopropylidene-13-(*tert*-butyldimethylsilyl)pseudomonate C (0.0021 g, 0.0032 mmol) in 50 μL of THF, followed by 0.3 mL of 80% acetic acid. The solution was stirred at 25 °C for 36 h after which time analytical TLC revealed total consumption of starting material and the formation of a more polar UV active substance having R_f 0.59 (15% MeOH–$CHCl_3$). The reaction mixture was concentrated in vacuo and azeotroped with toluene. The material thus obtained was filtered through a silica gel plug with 2% MeOH–$CHCl_3$ to provide 0.0015 g (0.0030 mmol, 93%) of (+)-methyl pseudomonate C that was identical in every respect with naturally derived (+)-methyl pseudomonate C: $[\alpha]^{25}_D$ +3.0° (c 0.005, CH_2Cl_2); 300 MHz ^{1}H NMR ($CHCl_3$) δ 5.77 (s, 1 H), 5.45 (m, 2 H), 4.07 (t, J = 6.6, 2 H), 3.78 (m, 3 H), 3.67 (s, 3 H), 3.55 (m, 3 H), 2.59 (d, J = 2.6, 1 H), 2.30 (t, J = 7.4, 2 H), 2.2 (d, J = 1.1, 3 H), 2.08 (m, 4 H), 1.85 (m, 1 H), 1.63 (m, 2 H), 1.31 (m, 13 H), 1.16 (d, J = 6.2, 3 H), 0.99 (d, J = 6.8, 3 H); 75 MHz ^{13}C NMR ($CHCl_3$) δ 174.9, 167.3, 157.3, 134.9, 129.9, 117.9, 77.5, 74.9, 71.4, 70.6, 69.1, 65.0, 64.0, 51.7, 45.0, 43.3, 42.1, 34.2, 32.4, 29.2, 29.1, 28.8, 26.0, 25.0, 20.4, 19.2, 16.7; mass spectrum (+)-FAB (Xe°), NaCl doped, m/z 521 [M·Na$^+$], 499 [M·H$^+$], 476, 312, 293, 275, 212, 208, 193, 185; (+)-FAB exact mass calcd for $C_{27}H_{47}O_8$ 499.32708, found 499.32603.

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Registry No. β-L-**6** (1-*O*-benzylated), 89726-80-7; α-L-**6** (1-*O*-benzylated), 89726-77-2; β-L-**7**, 89726-78-3; α-L-**7**, 89726-65-8; α-L-**8c**, 89726-66-9; β-L-**8g**, 89726-79-4; β-L-**9**, 89824-50-0; α-L-**9**, 89824-47-5; β-L-**10**, 89824-51-1; α-L-**10**, 89726-67-0; β-L-**10**-ol, 89824-52-2; α-L-**10**-ol, 89726-69-2; **12**, 85576-58-5; β-L-**16**, 89824-48-6; α-L-**16**, 89726-73-8; **19**, 85576-60-9; β-L-**21**, 97997-35-8; α-L-**21**, 98049-13-9; β-L-**22**, 89824-53-3; α-L-**22**, 89726-70-5; **30**, 89726-74-9; **31**, 92516-83-1; **32**, 89726-76-1; phenyl chlorothiocarbamate, 1005-56-7; ethyl (*S*)-(+)-3-hydroxybutyrate, 56816-01-4; acetonylmethylenetriphenylphosphorane, 97997-36-9; methyl 9-hydroxynonanoate, 34957-73-8; methyl semiazelaaldehyde, 1931-63-1; (diethylphosphono)acetic accid, 3095-95-2; (+)-methyl pseudomonate C, 97997-37-0; L-lyxose, 1949-78-6; benzyl alcohol, 100-51-6; allyltributylstannane, 24850-33-7; potassium thiophenoxide, 3111-52-2; methyl iodide, 74-88-4.