Approach to the Synthesis of the Acyltetramic Acid Antibiotic Bu-2313

Thesis by

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To my father

ACKNOWLEDGEMENTS

I wish to thank Dr. Robert E. Ireland for his support and patience during this work. I would like to thank the Ireland group, particularly Mike Smith, Pat Dussault and Paul Brown, for their assistance. Special thanks go to Prof. Peter Dervan for his interest in my progress. I would like to thank Brian Masek, Doug Meinhart and Eric Anslyn for help rendered. I would like to thank The Honor Society Phi Kappa Phi, the ARCS Foundation and the California Institute of Technology for financial support. Most importantly I would like to acknowledge the help of my family.

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FAUST. Habe nun, ach! Philosophie,
Juristerei und Medizin
Und, leider! auch Theologie
Durchaus studiert, mit heissem Bemuehn.
Da steh ich nun, ich armer Tor!
Und bin so klug, als wie zuvor;

Bilde mir nicht ein, was Rechts zu wissen,
Bilde mir nicht ein, ich koennte was lehren,
Die Menschen zu bessern und zu bekehren.

Goethe

3-Acyltetramic Acid Antibiotics. 3. An approach to the Synthesis of Bu-2313[1]

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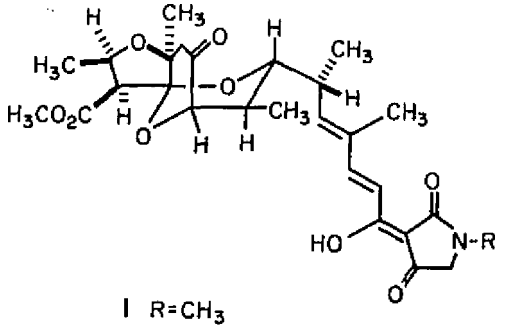
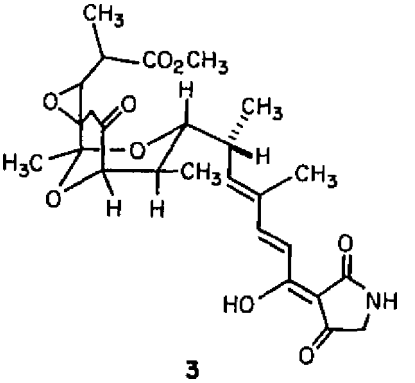
Abstract: An approach to the synthesis of the bicyclononane portion of the 3-acyltetramic acid antibiotic Bu-2313 is presented. The highly unstable α-ketoaldehyde obtained by Swern oxidation of the diol **30** was allowed to condense with the unreactive α-ketophosphoranylidene **18** affording the enedione **31**. The silyl ether was cleaved and the hydroxyl caused to add to the enedione in a five-exo fashion to form the tetrahydrofuran. The combination of functional groups necessary for ketal formation was investigated showing that the system does not form the desired ketal in most circumstances (Table I). Given the correct functional group array, it was shown that the ketalization is more favorable with the stereochemistry of the natural product.

Members of the acyl tetramic acid class of compounds, Bu-2313 A (1),[3] Bu-2313 B (2),[3] nocamycin (3),[4,5] tirandamycin (4)[6] and streptolydigin (5)[7] have



1 R=CH_3
2 R=H



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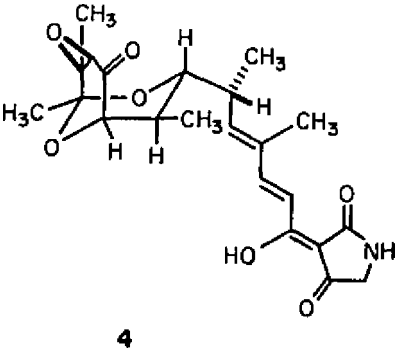

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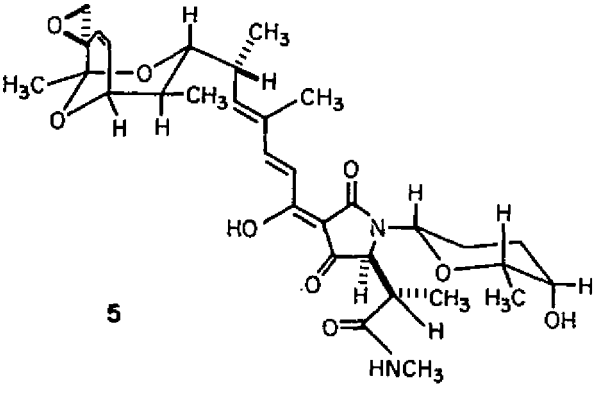

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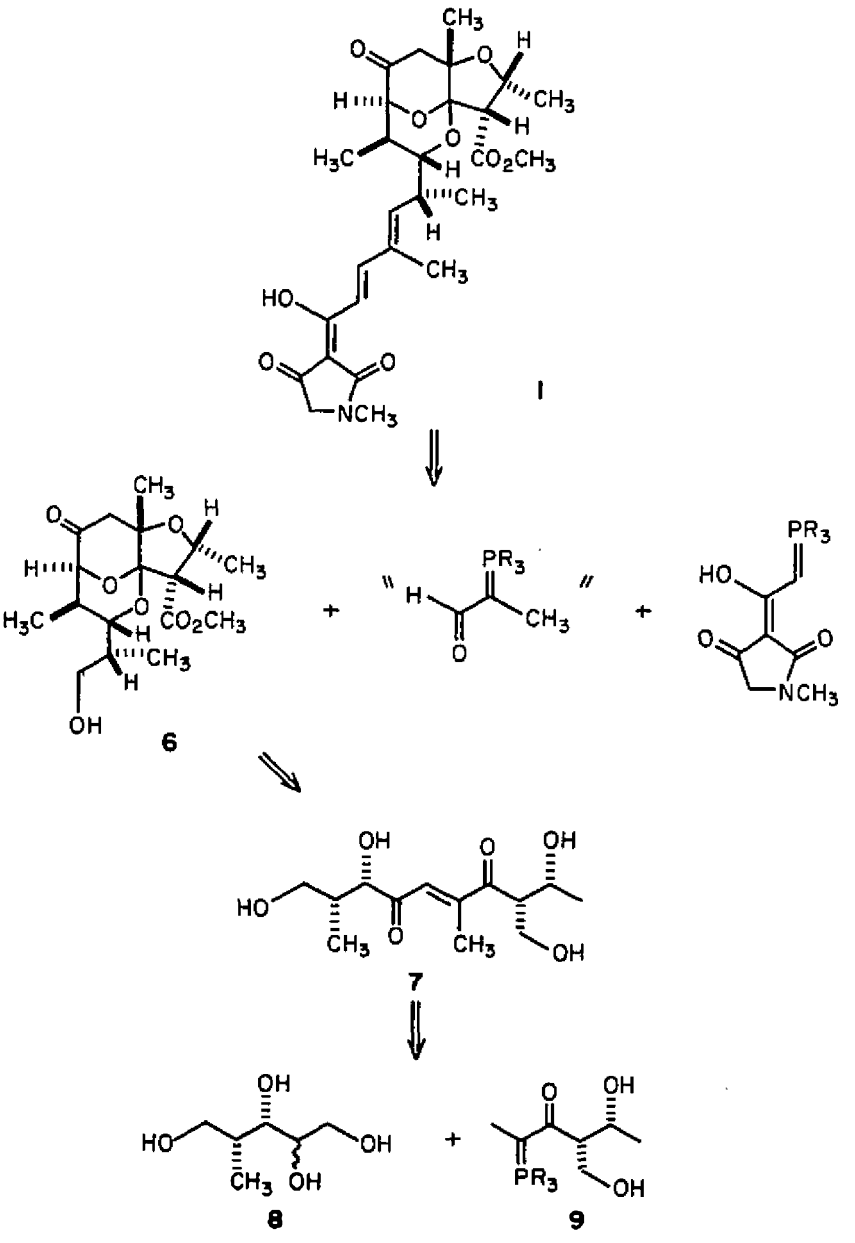
aroused interest because of their significant biological activities and complex structures. Both streptolydigin and tirandamycin have been shown to inhibit RNA polymerase[8] and the process of oxidative phosphorylation.[9] The mode of action for Bu-2313 has

not been determined but is presumably similar to that of tirandamycin and streptolydigin. These compounds differ from the simpler tetramic acids structurally and biologically.[10] Synthetic routes to these antibiotics are of interest because of both their structural complexity and the potential value of structure-activity studies with analogues. The first two phases of this effort, syntheses of tirandamycic acid[11] and streptolic acid[12] have been reported. Several other efforts directed at tirandamycin have been reported,[13] a number of which have culminated in successful total syntheses. As a continuation of the program in these laboratories we have undertaken a synthesis of Bu-2313.

The synthetic approach we envisioned (Scheme I) was designed to utilize the chemistry developed in our previous efforts.[11,12] However, it was clear that a significant digression would be neccesary because formation of the tetrahydrofuran fused to the 2,9-bicyclononane in Bu-2313 was not compatible with the established strategy. We therefore proposed to apply the combination Swern oxidation-Wittig condensation procedure recently reported from these laboratories[14] to form an enedione (7) which could be cyclized to form the tetrahydrofuran. We anticipated that the chain could then be extended and the ketal formed, at which point the precedented route would be joined. Our efforts to

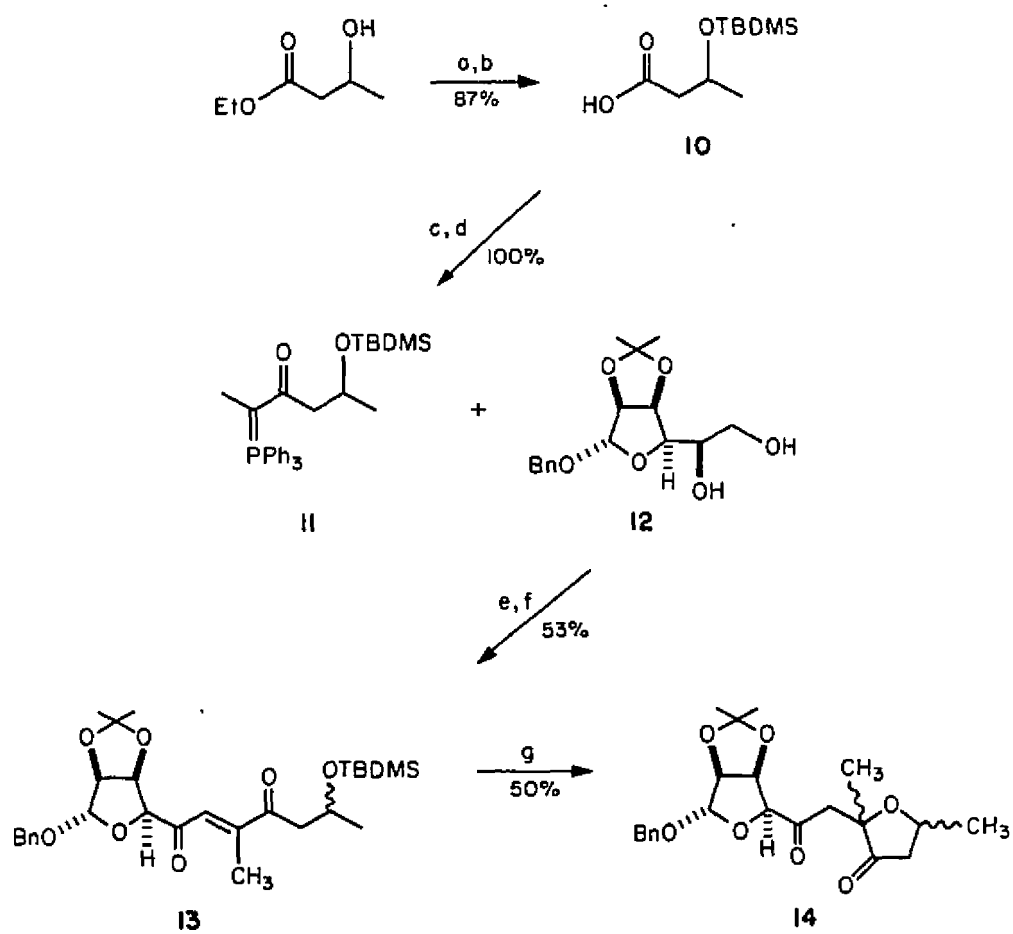
Scheme I Retrosynthetic Analysis for Bu-2313



prove the viability of this approach are the subject of this report.

The greatest concerns we had for the synthesis were whether reaction conditions could be found under which a stabilized Wittig reagent (**9**) would condense with the proposed α-ketoaldehyde (from **8**) and whether the resultant enedione would cyclize to form the furan. In order to allay these concerns, a model Wittig reagent was synthesized (Scheme II). Treatment of the acid **10** with oxalyl chloride and catalytic N,N-dimethylformamide formed the acid chloride. Addition of the crude reaction mixture to 3 equivalents of salt free ethyl Wittig reagent afforded, after aqueous workup, the desired stabilized Wittig reagent **11**.[15] Similar compounds have been shown[16] to condense very slowly with unhindered aldehydes at elevated temperatures and not at all with ketones. Fortunately, the high reactivity of the α-ketoaldehyde formed by Swern oxidation of the diol **12**[17] allowed the condensation with **11** to proceed at a reasonable rate at $0^{o}C$ to afford the enedione **13** as a mixture of diastereomers. Assignment of the indicated stereochemistry was based upon the ^{1}H NMR and UV spectra.[18] It had been hoped that the alkoxide formed by removal of the tert-butyldimethylsilyl (TBDMS) group under standard conditions (tetra-n-butylammonium fluoride in THF) would spontaneously add to the enedione

Scheme II Wittig Reaction with an ∝-Keto Aldehyde and Closure[a]



[a](a) TBSCl, imidazole, DMF; (b) 1N NaOH, MeOH (c) $(COCl)_2$, DMF, benzene; (d) ethyl triphenylphosphoranylidene, benzene; (e) 12: $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2; (f) 11, CH_2Cl_2; (g) $LiBF_4$, TsOH, CH_2Cl_2, acetone.

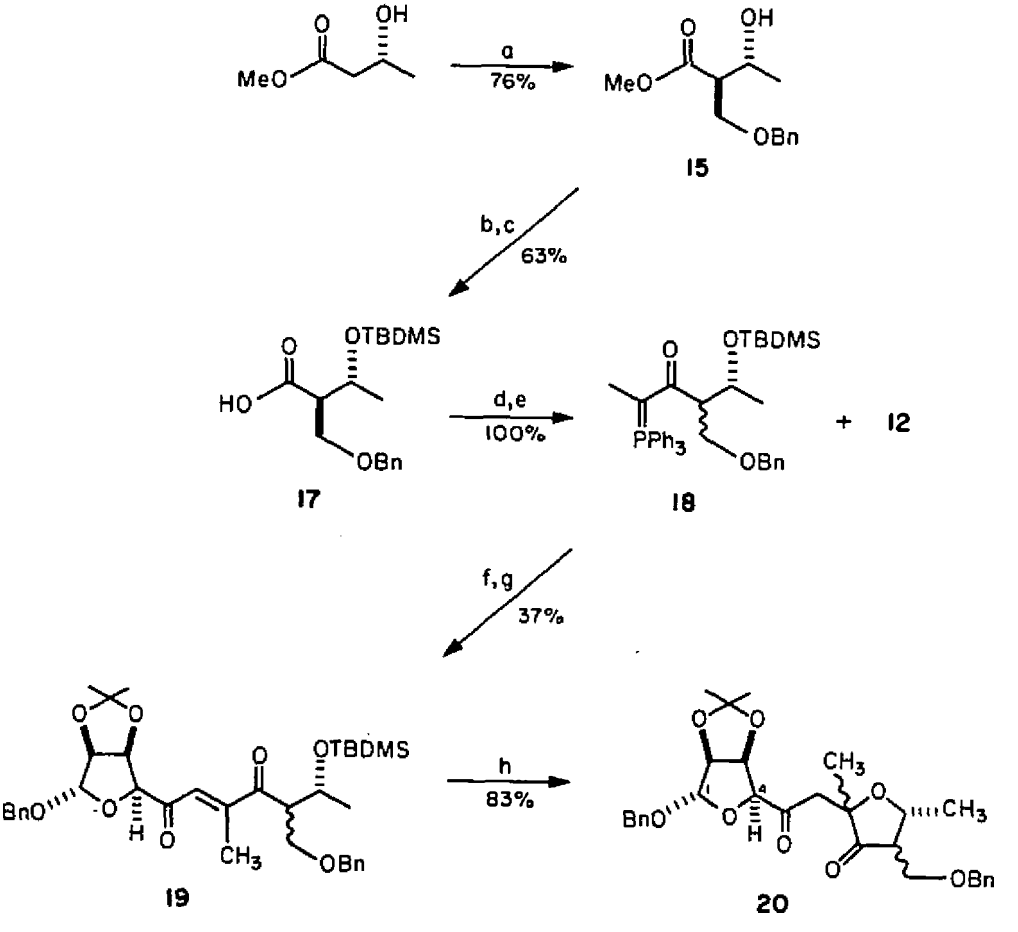
to form the desired tetrahydrofuran. Unfortunately this did not occur. A detailed investigation of this reaction provided conditions that produced the tetrahydrofuran in moderate yield. The stereochemical

outcome of this reaction was not rigorously determined since racemic material was used to form the model Wittig reagent. However, the reaction appeared to yield a mixture of four compounds suggesting a non-specific addition to the olefin. Successful formation of the tetrahydrofuran by this sequence of reactions was an encouraging result. The apparent lack of stereoselectivity in the addition reaction was disturbing, but further study of this issue was deferred until we began working with chiral materials.

Analysis[19] of the retrosynthetic intermediate **6** suggested that the thermodynamically most favorable stereochemistry of both the methyl ester and quaternary methyl centers was that of the natural product. We therefore predicted that these centers could be equilibrated to the desired configuration once the ketal had been formed. Thus, the main criterion for a chiral starting material for the Wittig reagent was the stereochemistry at the secondary hydroxyl in **9**. For ease of compound identification, a single stereoisomer would be advantageous. A suitable candidate was methyl-(R)-3-hydroxybutyrate available in high enantiomeric excess[22] by depolymerization of the biopolymer poly-(R)-3-hydroxybutyrate. Alkylation of the dianions of β-hydroxyesters has been shown[23] to yield products of high diastereomeric excess with predictable

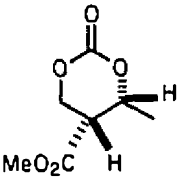
stereochemistry. In this case, alkylation of the dianion with benzyloxymethylchloride[24] (BOMCl) afforded the benzyl ether **15** (Scheme III) and the alternate diastereomer in a ratio of greater than 90:10 (capillary

Scheme III Synthesis of the Chiral ∝-Keto Phosphoranylidene[a]



[a](a) LDA, THF; BOMCl, THF; (b) TBSCl, imidazole, DMF; (c) 1N LiOH, MeOH; (d) $(COCl)_2$, DMF, benzene; (e) ethyl triphenylphosphoranylidene, benzene; (f) **12**: $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2; (g) **18**, CH_2Cl_2; (h) $LiBF_4$, TsOH, CH_2Cl_2, acetone.

gas chromatography). The percent conversion in this reaction was always low (ca. 50%). Attempts to improve the efficency by addition of excess BOMCl or by prolongation of the reaction time resulted in a lower yield of product. The product stereochemistry was proven through removal of the benzyl ether and formation of the cyclic carbonate **16**. The ^1H NMR spectrum of this



16

rigid derivative was indicative of the assigned structure.

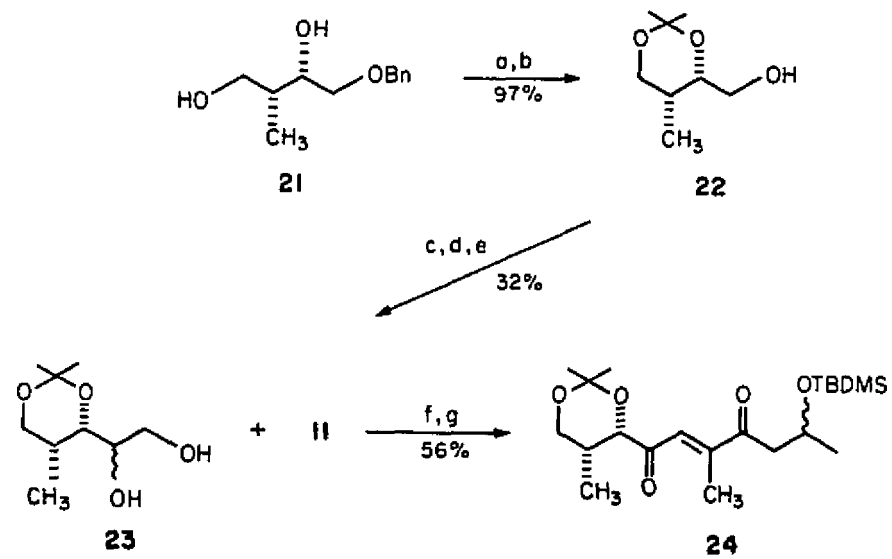
Protection of the secondary alcohol **15** as the silyl ether proceeded in high yield. Basic hydrolysis of the methyl ester was sluggish and was complicated by the production of two side products. These products arose from β-elimination of the benzyl ether and from epimerization of the α-center. Fortunately both by-products could be separated from the desired acid **17** by careful chromatography. Formation of the Wittig reagent under the conditions used previously afforded the desired material along with large amounts of β-elimination product. Attempted application of the

thiopyridyl ester method of Overman[25] resulted in a higher percentage of β-elimination. Careful formation and workup of the acid chloride derived from the acid **17** followed by treatment with slightly less than 2 equivalents of salt free ethyl Wittig reagent afforded the chiral stabilized Wittig reagent **18**. Although the spectral evidence was inconclusive, it appeared that the stereochemistry at the center α to the ketone had been compromised during this reaction. Application of the Swern-Wittig procedure afforded the enedione **19** as an inseparable mixture of two compounds. Conversion of this mixture to the tetrahydrofuran proceeded under the previously optimized conditions to afford **20** in 83% yield. The 400 MHz ^{1}H NMR spectrum of **20** showed it to be a mixture of two compounds. The diastereomeric centers responsible for the mixture could not be clearly deduced at this point. However, it was obvious from the presence of a 'W' coupling[26] between the C2 and C4 protons (**20**) in the 400 MHz ^{1}H NMR spectrum that the mixture was not a result of epimerization of the C4 center. This was a critical result because the configuration at that center determines the stereochemistry of the ketal formed later in the synthesis.

Attention was then turned to the retrosynthetic target **8** (Scheme I). Protection of the known[27] diol **21**

(Scheme IV) as the acetonide and reductive removal of the benzyl ether afforded the alcohol **22.** The aldehyde obtained by oxidation of this alcohol proved to be unstable even to a simple aqueous workup. However, addition of 3 equivalents of benzyloxymethyllithium[28] to the crude Swern oxidation reaction mixture at -78°C afforded, after aqueous workup, the desired benzyl ether in 50% yield as a 91:9 mixture of diastereomers. The absolute stereochemistry was not determined because the new center would be destroyed in the imminent oxidation.

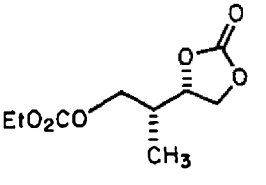
Scheme IV Synthesis of a Protected 8 and Enedione Formation[a]



[a](a) TsOH, DMP, acetone; (b) Li, NH_3, THF; (c) $(COCl)_2$, DMSO, Et_3N, THF; (d) $BnOCH_2Li$, THF; (e) Li, NH_3, THF; (f) 23: $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2; (g) 11, CH_2Cl_2.

The benzyl ether was removed to afford the diol **23** which was submitted to the Swern-Wittig procedure as before to afford the enedione **24.** Attempted furan formation under the established conditions did not lead to the desired product, but to loss of the acetonide and formation of several undesired products. Attempts to find milder conditions to effect the cyclization were unsuccessful.

To avoid this acidic cleavage of the protecting group the diol **21** was instead protected as the bis ethyl carbonate. Unfortunately this dicarbonate spontaneously cyclized to the cyclic carbonate **25** upon cleavage of the benzyl ether. Formation of the cyclic carbonate of **21** followed by removal of the benzyl ether likewise afforded the migrated carbonate **26.** At this point it



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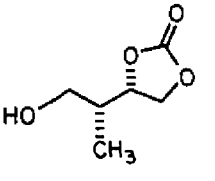

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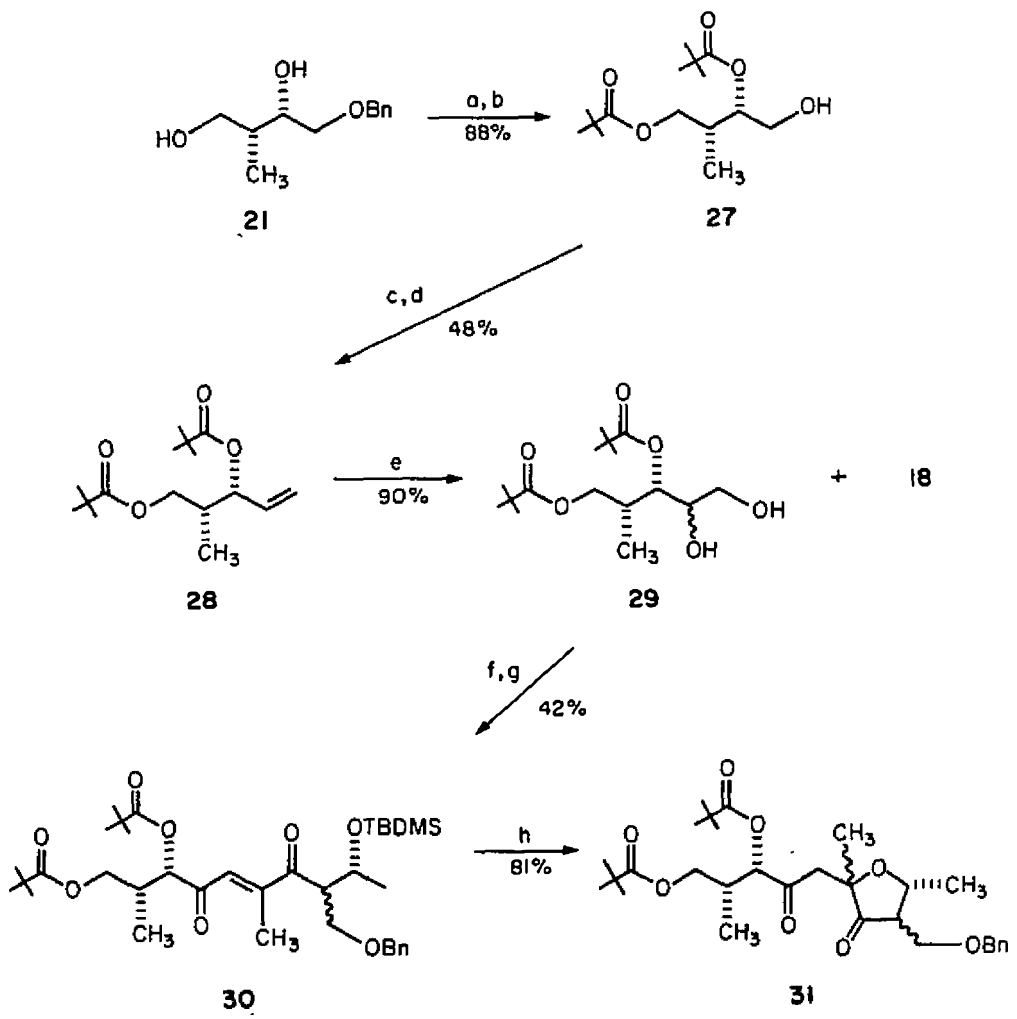
was determined that a protecting group with greater stability would be necessary. Pivaloate esters were chosen because of acid stability and low migratory aptitude. Cleavage was a concern, however, it was anticipated that treatment with ammonia or, at worst, a

sequence involving ketalization of the ketones, hydride reduction and deketalization would remove the pivaloates without otherwise affecting the molecule. Protection of the diol **21** as the bis-pivaloate ester and hydrogenolysis of the benzyl ether afforded the alcohol **27** (Scheme V). Oxidation to the aldehyde proceeded smoothly. Addition of benzyloxymethyllithium was predicted to result in a mixture of compounds. An alternative strategy for this homologation would be to convert the aldehyde into the analagous olefin and then hydroxylate. Addition of a methyl Wittig reagent to the aldehyde afforded, at best, very low yields of the olefin. Olefination using Tebbe's reagent[29] afforded the desired compound **28** in 48% unoptimized yield from the alcohol **27**.

The diol **29**, obtained from the olefin by catalytic osmium tetroxide hydroxylation,[30] was submitted to the Swern-Wittig procedure as before but only gave a 10-15% yield of the desired enedione. Also obtained were the ketoalcohol resulting from partial oxidation of **29**, large amounts of polymeric material (apparently from the α-ketoaldehyde) and unreacted Wittig reagent. The yield was improved to 42% by allowing the activated dimethylsulfoxide to react with the diol at -30°C in order to facilitate the oxidation and maintaining that temperature throughout the reaction to minimize

Scheme V Synthesis of an Acid Stable Protected 8 and Closure[a]

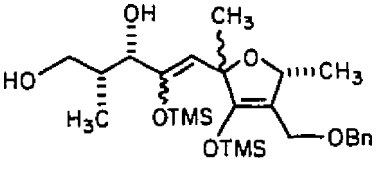


[a](a) pivaloyl chloride, DMAP, pyridine, CH_2Cl_2; (b) H_2, 10% Pd/C, EtOH; (c) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2; (d) Tebbe's reagent, pyridine, benzene; (e) OsO_4, NMO, acetone, H_2O; (f) **29**: $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2; (g) **18**, CH_2Cl_2; (h) $LiBF_4$, TsOH, CH_2Cl_2, acetone.

polymerization. It was also shown at this time that an excess of the Wittig reagent was not necessary. As before, two diastereomers were obtained which were separated with difficulty. Their respective ^1H NMR spectra showed definitively that the stereochemistry of the α-center in the Wittig reagent **18** had indeed been scrambled. Because the separation of these two compounds was extremely tedious and because it was planned that this center would shortly be equilibrated to the thermodynamically most favorable configuration, the diastereomers were carried on as a mixture. Closure to the tetrahydrofuran by the usual method proceeded in good yield affording what appeared to be two compounds, thus suggesting that some selectivity had occured in the cyclization.

Attempted removal of the pivaloate esters using refluxing ammonia,[31] refluxing methylamine or THF saturated with ammonia returned starting material. Aqueous methylamine opened the tetrahydrofuran ring. Hydroxylamine and hydrazine hydrate produced none of the desired product. Attempted transesterifications[32] also failed. Thwarted along this approach we attempted to form the bis-ketal of **31** using several sets of standard conditions.[33] Only one method met with even partial success. A mono-dithiolane could be formed but this approach was abandoned because of poor yield (40%) and,

more significantly, because of the lack of utility of a mono-ketal. It was found that both ketones could be protected as the trimethylsilyl (TMS) enol ethers[34] and then the pivaloates removed reductively to afford **32**.

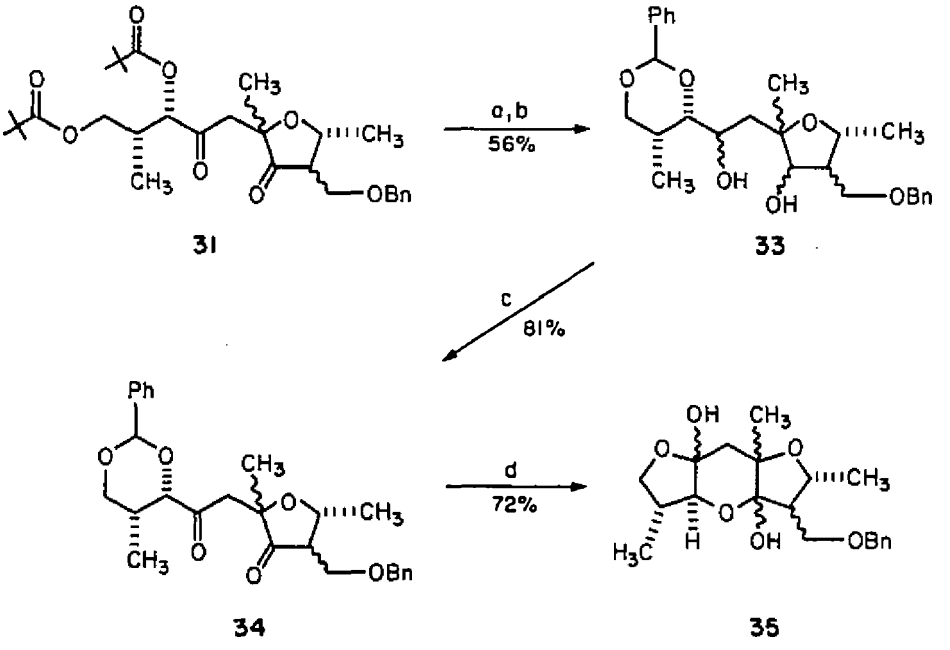


32

However, the silyl enol ethers could not be cleaved without entering several undesired reaction manifolds. Therefore, this reaction sequence was not explored further. Discouraged by these results, we conceded that any effort to complete the synthesis would require an alternate hydroxyl protecting group. However, we decided to proceed with the material in hand in order to probe the conditions necessary for the ketal formation and to determine whether the equilibration to the desired stereochemistry could be executed.

Reduction of **31** (Scheme VI) with lithium tetrahydridoaluminate followed by treatment with benzaldehyde and catalytic acid[35] afforded **33**. Naturally, the intermediate tetra-ol and the acetal **33** as well as similar intermediates throughout the

Scheme VI Deprotection of 31 by Reduction–Protection–Oxidation[a]



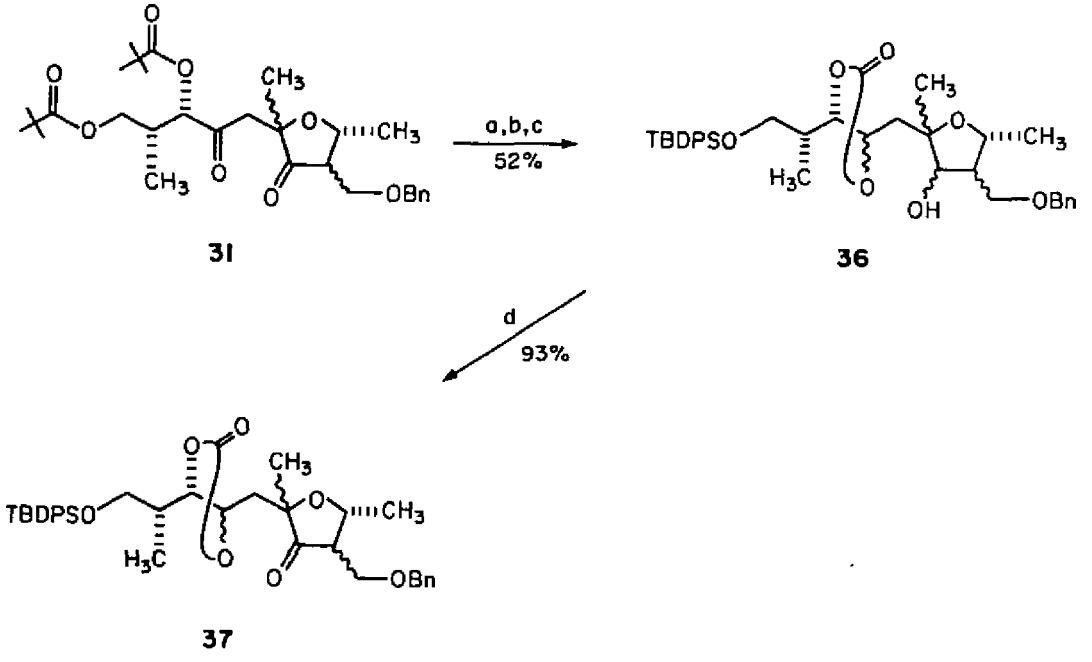
[a](a) LAH, THF; (b) PhCHO, TsOH, benzene; (c) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2; (d) 10% HCl, THF.

remainder of this effort were complex mixtures of diastereomers. The complete stereochemical identities of these mixtures were not elucidated fully. However, the alcohol resulting from reduction of the ring ketone possessed a syn relationship to the neighboring benzyloxymethyl substituent and at no time did there appear to be more than four compounds in any of the

product mixtures. Because these compounds were mixtures, identification was a significant problem and a greater reliance was necessarily placed both on conversion of the intermediate products to more easily identifiable species and on combustion analysis. Because of these difficulties the structure of **33** was not firmly established until after Swern oxidation to the diketone **34**. The benzylidene acetal was surprisingly stable to attempted acidic hydrolysis but succumbed to 10% HCl. Not surprisingly, the product recovered from the hydrolysis was not the diol or the desired ketal, but the bis hemi-ketal **35**. However, it was very disappointing to find that this hemi-ketal could not be dehydrated to the desired ketal.

A solution to this complication was sought in differentiating the ketones so that only the tetrahydrofuran ketone would be available for ketalization. Accordingly, the diketone **31** was exhaustively reduced as before, the primary alcohol was protected as the tert-butyldiphenysilyl (TBDPS) ether[36] and the 1,2 diol was protected as the cyclic carbonate to afford the alcohol **36** (Scheme VII) which was easily oxidized to the ketone **37**. However, even under the mildly basic conditions necessary to remove the carbonate, the benzyl ether was partially eliminated and several unidentified products were produced rather than

Scheme VII Differentiation of the Ketones in 31[a]

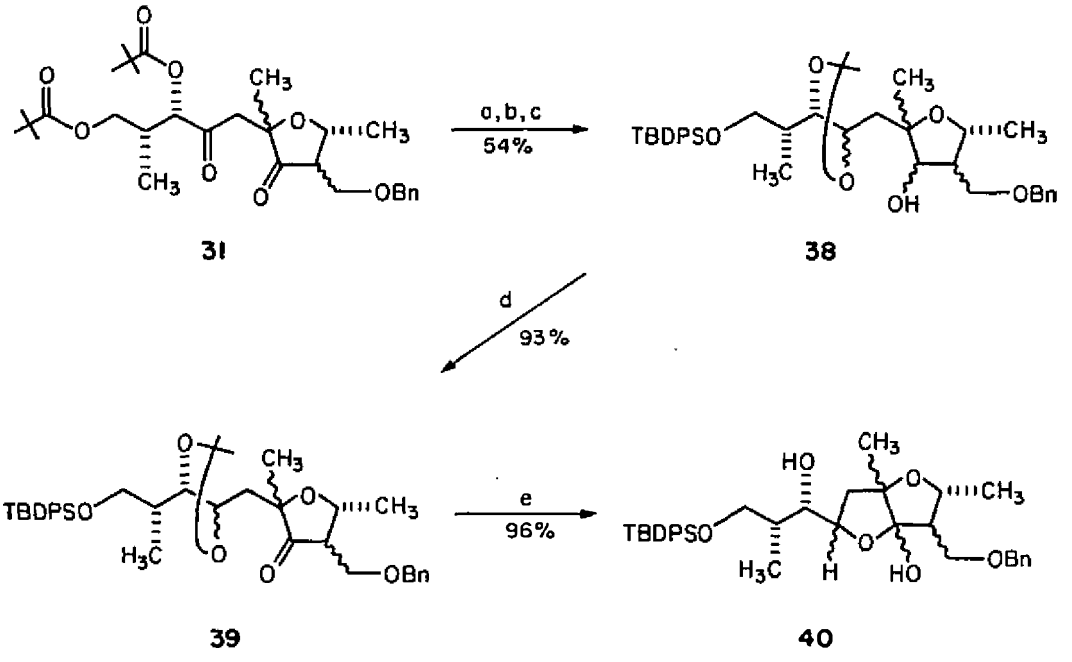


31 36 37

[a](a) LAH, THF; (b) TBDPSCl, DMAP, CH_2Cl_2; (c) $COCl_2$, benzene, pyridine; (d) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2.

the desired material. To circumvent this problem, the 1,2 diol was protected as the acetonide **38** (Scheme VIII) and the remaining free alcohol was converted to the ketone. Cleavage of the acetonide **39** afforded the five membered hemi-ketal **40**. The ring size was suggested by the ^1H NMR and verified by Swern oxidation of **40** to the corresponding ketone in which the carbonyl position could be determined unambiguously by ^1H NMR.

Scheme VIII Alternative Differentiation of the Ketones in 31[a]

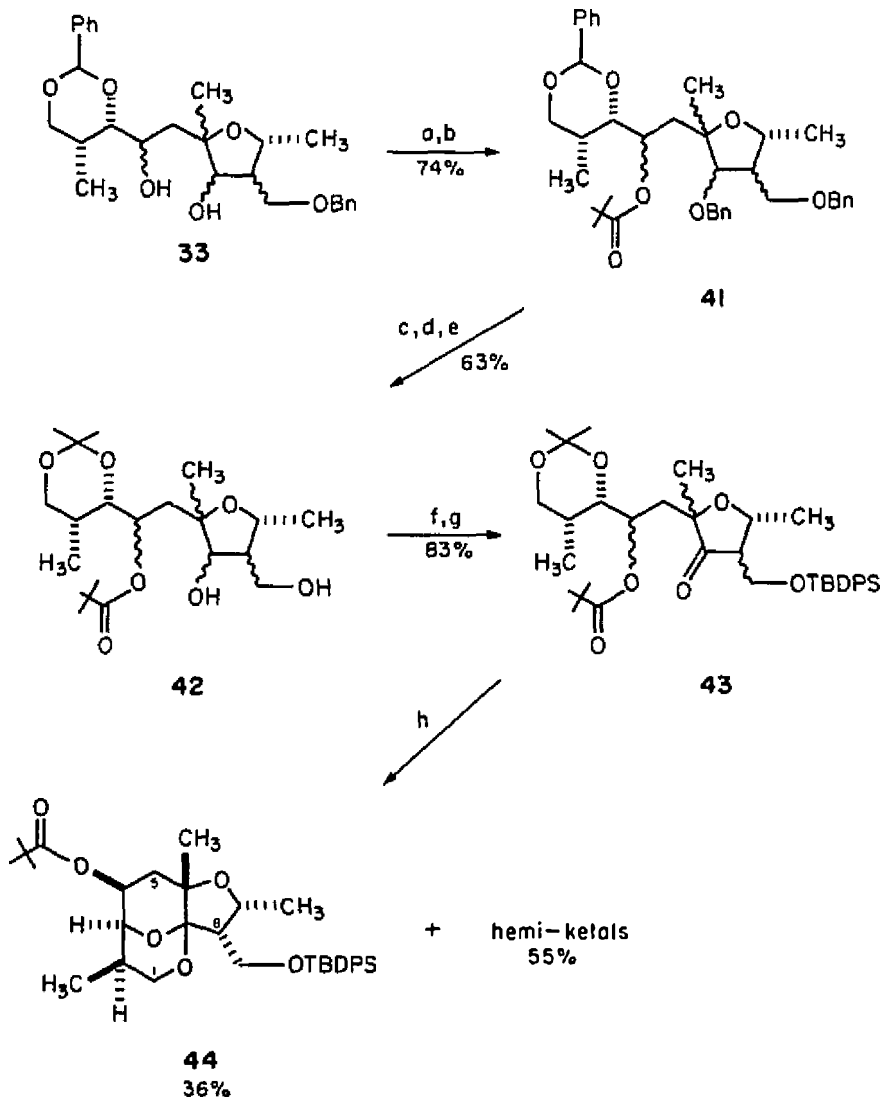


[a](a) LAH, THF; (b) TBDPSCl, DMAP, CH_2Cl_2; (c) TsOH, acetone; (d) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2; (e) 10% HCl, MeOH.

At this point it became obvious that the only way to form the ketal would be to deprotect the 1,3 diol in the presence of the tetrahydrofuran ketone with the acyclic ketone protected. The realization of this turned out to be somewhat tedious in practice. Compound **33** (Scheme IX) already had the 1,3 diol protected and if one of the remaining secondary alcohols could be selectively protected then the necessary differentiation

would be accomplished. Several different protections were attempted but only a benzyl group was incorporated selectively using a modification of the procedure of Paulsen.[37] The location of the benzyl group in this product was not obvious but oxidation to the ketone left no question that the tetrahydrofuran alcohol had been protected. That the tetrahydrofuran alcohol rather than the acyclic alcohol was protected was actually the less desirable result as it required substitution of an alternate protecting group for the benzylidene acetal because the 1,3 diol needed to remain protected while the benzyl ethers were cleaved. The remaining secondary alcohol was initially protected as the trimethylsilyloxymethyl (SEM)[38] or methoxymethyl (MOM)[39] ethers, but these groups were abandoned when they were found to hydrolyze at a rate similar to the benzylidene acetal. This alcohol was finally protected as the pivaloate ester (**41**). This protecting group was chosen for the stability that had made it problematic earlier. Cleavage of the benzylidene acetal proceeded at a reasonable rate with 3:1 THF/10% aqueous HCl only at 50°C, conditions that are unusually vigorous.[40] Formation of the acetonide and hydrogenolysis of the benzyl ethers afforded the diol **42**. Attempts to oxidize **42** to the keto-acid failed. In the case of Jones oxidation several highly non-polar products were

Scheme IX Ketal Formation[a]



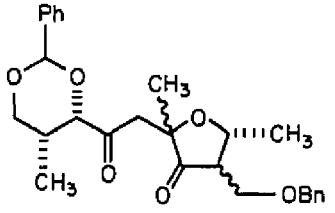
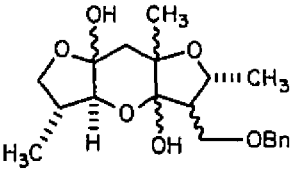
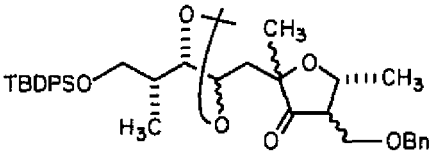
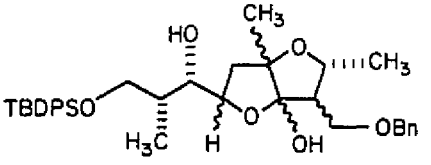
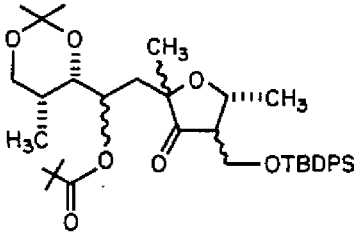
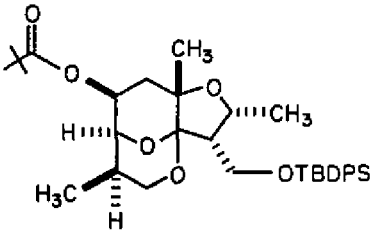
[a](a) BaO, $Ba(OH)_2$, BnBr, DMF; (b) pivaloyl chloride, DMAP, CH_2Cl_2; (c) 10% HCl, THF; (d) TsOH, DMP, acetone; (e) H_2, 10% Pd/C, HOAc, EtOAc; (f) TBDPSCl, DMAP, CH_2Cl_2; (g) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2; (h) 10% HCl, THF.

recovered which appeared to have resulted from spontaneous decarboxylation[41] of the desired product. Swern oxidation did not provide the desired keto-aldehyde but rather an extremely complex mixture from which no identifiable products could be recovered. Therefore the primary alcohol was selectively protected as the TBDPS ether[36] and the resultant mono-alcohol was oxidized to afford the desired tetrahydrofuran ketone with the acyclic ketone still blocked. Acidic hydrolysis of the acetonide[42] provided a single ketal as the major product along with three hemi-ketals, none of which could be dehydrated to a ketal[43].

It was with great satisfaction that we discovered upon extensive ^{1}H NMR investigation that this ketal had the stereochemistry of the natural product at all the established stereocenters. The key evidence came in the form of nuclear Overhauser effect experiments which verified that the C2 and C6 methyl groups as well as the C8 proton (**44**) were all on one 'face' of the molecule (see experimental section). The exclusive formation of the 'natural' ketal partially[44] verified our prediction that this configuration would be energetically the most favorable.

Contrasting the facile nature of this ketalization with the failures of the previously attempted ketalizations (Table I) leads us to a conclusion about

Table I Summary of Ketal Formation Attempts

Starting Material	Product
 **34**	 **35**
 **39**	 **40**
 **43**	 **44**

conditions necessary to form such ketals. Apparently, when this system is given a choice of several possible modes of ketalization or hemi-ketalization, it does not adopt the mode of the natural product. This implies that in the biosynthesis of this class of compounds

nature cannot form the ketal in solution from an otherwise intact product but that either the second ketone is not present (even as an alcohol) during ketalization or that the closure is enzymatically controlled. These results also show that although our synthetic approach must be altered to accomodate differentiation of the two ketones more easily, the synthetic concept laid out here can provide access to the Bu-2313 skeleton.

Experimental Section

Proton nuclear magnetic resonance spectra were recorded with a Varian EM-390 spectrometer at 90 MHz unless otherwise specified. 400 MHz refers to a spectrum recorded with a Jeol JNM-GX400 and 200 MHz refers to a spectrum recorded with a Varian XL-200. Data are reported as follows: chemical shift in parts per million downfield from tetramethylsilane (multiplicity, integrated relative intensity, assignment, coupling constants). Optical rotations were measured with a Jasco DIP-181 polarimeter in a 1 dm cell of 1 mL capacity; chloroform for these measurements was filtered through activity III alumina immediately prior to use. Infrared spectra were recorded with a Perkin-Elmer 1310 spectrometer. Ultra-violet spectra were recorded with a Beckman 25 spectrometer. Capillary gas chromatography was performed with a Hewlett Packard 5890A gas chromatograph on columns from J & W Scientific using prescribed flow conditions. Data is reported as follows: (column, temperature program) retention times, ratio.

Reaction solvents and liquid reagents were purified by distillation or dried over appropriate agents prior to use. Reactions were run under an atmosphere of argon

which had been dried by passage through a drying tower filled with anhydrous $CaSO_4$. Reaction flasks were flame dried when possible and always purged with argon and evacuated under high vacuum several times using a manifold system. Syringes and reaction flasks were dried at least 12 h in an oven (120-140°C) and cooled in a desiccator over anhydrous $CaSO_4$ prior to use. Elemental analyses were performed by Spang Microanalytical Laboratory, Star Route 1, Box 142, Eagle Harbor, MI 49951. High Resolution Mass Spectra were performed by the Midwest Center for Mass Spectrometry, University of Nebraska, Lincoln, NE 68588-0362 or the University of California at Riverside Mass Spectrometry Lab.

Ethyl 3-O-(tert-butyldimethylsiloxy)-butyrate. To a stirred solution of 2.50 g (18.9 mmol) of ethyl 3-hydroxybutyrate in 50 mL of N,N-dimethylformamide were added 3.60 g (23.9 mmol) of tert-butylchlorodimethylsilane and 3.4 g (49.9 mmol) of imidazole. After 8 h, the reaction mixture was diluted with 200 mL of ether and 50 mL of 5% aqueous HCl. The phases were separated and the organic phase was extracted with 50 mL of water,then 50 mL of saturated aqueous $NaHCO_3$. The organic phase was dried ($MgSO_4$) then the solvent was removed under reduced pressure to

yield 4.66 g (100%) of the desired silyl ether as a colorless oil: R_f= 0.56 (1:1 petroleum ether/ether); IR ($CHCl_3$) 2940, 2880, 2850, 1770, 1450, 1380, 1300, 1180, 1130, 1080, 1030, 1000, 830 cm^{-1}; ^1H NMR ($CDCl_3$) δ0.05 (s, 6H, $(CH_3)_2Si$), 0.82 (s, 9H, $(CH_3)_3C$), 1.18 (d, 3H, CH_3C, J= 6 Hz), 1.21 (t, 3H, CH_3CH_2, J= 7 Hz), 2.38 (2d, 2H, $CH_2C=O$, J= 6Hz), 4.10 (q, 2H, CH_2O, J= 7Hz), 4.20 (sextet, 1H, HCO, J= 6Hz).

3-O-(tert-butyldimethylsiloxy)-butyric acid (10). To a stirred solution of 4.0 g (16.3 mmol) of the above ester in 150 mL of methanol were added 60 mL of 1N aqueous NaOH. After 20 h, the reaction mixture was diluted with 100 mL of ether and the phases were separated. The aqueous phase was acidified to pH 2 and extracted with three portions of 200 mL of ether. The combined organics were dried ($MgSO_4$) and concentrated under reduced pressure to afford 3.1 g (87.1%) of the acid **10** as a colorless oil: R_f= 0.47 (1:1 petroleum ether/ether); IR ($CHCl_3$) 3300-2400 (br), 1710, 1460, 1410, 1380, 1300, 1250, 1135, 1090, 1005, 835 cm^{-1}; ^1H NMR ($CDCl_3$) δ0.08 (s, 6H, $(CH_3)_2Si$), 0.85 (s, 9H, $(CH_3)_3C$), 1.18 (d, 3H, CH_3C, J= 6Hz), 2.48 (d, 2H, CH_2, J= 6Hz), 4.28 (sextet, 1H, HCO, J= 6Hz), 8.7 (br s, 1H, COOH). To a small portion of the product in ether was added excess ethereal diazomethane. After 15 min, the

solvent was removed under reduced pressure. The residue was chromatographed on silica gel with 98:2 petroleum ether/ether to afford an analytically pure sample of the methyl ester of **10**: R_f= 0.30 (95:5 petroleum ether/ether); IR ($CHCl_3$) 2945, 2925, 2885, 2850, 1725, 1460, 1435, 1375, 1300, 1250, 1180, 1130, 1085, 1005, 835 cm^{-1}; ^1H NMR ($CDCL_3$) δ0.00, 0.02 (2s, 6H, $(CH_3)_2Si$), 0.83 (s, 9H, $(CH_3)_3C$), 1.15 (d, 3H, CH_3C, J= 6Hz), 2.38 (d, 2H, CH_2, J= 6Hz), 3.70 (s, 3H, CH_3O), 4.22 (sextet, 1H, HCO, J= 6Hz). Analysis calculated for $C_{11}H_{24}O_3Si$: C, 56.85; H, 10.41. Found: C, 56.87; H, 10.31.

5-(tert-butyldimethylsiloxy)-2-(triphenylphosphoranylidene)-3-hexanone (11). To a stirred solution of 1.8 g (8.24 mmol) of the acid **10** in 25 mL of benzene were added 50 μL (0.65 mmol) of N,N-dimethylformamide, then 0.74 mL (8.48 mmol) of oxalyl chloride. After 1 h, the reaction mixture was added via cannula over 6 min to the supernatant centrifugate of 9.2 g (24.8 mmol) of ethyltriphenylphosphonium bromide and 10.3 mL of 2.4 M n-butyllithium in hexanes in 105 mL of benzene at 80°C. After 10 min, the reaction mixture was allowed to cool to room temperature and was diluted with 300 mL of ether and 75 mL of 10% aqueous K_2CO_3. The phases were separated and the aqueous phase was extracted with 100 mL of ether. The combined organics

were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was diluted with 300 mL of ether and then extracted with two portions of 75 mL of 10% aqueous K_2CO_3. The organic phase was dried ($MgSO_4$) and the solvent removed under reduced pressure to afford 4.1 g (100%) of the α-ketophosphoranylidene **11** as a red oil: IR ($CHCl_3$) 3030, 2955, 2930, 2850, 1720, 1500, 1435, 1380, 1255, 1170, 1110, 1100, 990, 840, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ0.05 (s, 6H, $(CH_3)_2Si$), 0.80 (s, 9H, $(CH_3)_3C$), 1.18 (d, 3H, CH_3C, J= 6Hz), 1.58 (d, 3H, $CH_3C=P$, J= 18Hz), 2.46 (d, 2H, CH_2, J= 6Hz), 4.1-4.2 (m, 1H, HCO), 7.2-7.9 (m, 15H, PhH).

(10ξ)-Benzyl-(E)-10-O-(tert-butyldimethylsilyl)-6,7,9,11-tetradeoxy-2,3-O-isopropylidene-7-methyl-α-D-lyxo-undec-6-enofuranosido-5,8-diulose (13). To a stirred solution of 0.60 mL (6.91 mmol) of oxalyl chloride in 6 mL of dichloromethane at -78°C was added a solution of 0.58 mL (8.16 mmol) of dimethylsulfoxide in 3 mL of dichloromethane. After 12 min, a solution of 597.3 mg (3.14 mmol) of the diol **12** in 8.0 mL of dichloromethane was added to the reaction mixture over 3.5 min. After 15 min, 2.19 mL (15.70 mmol) of triethylamine was added and after 15 min at -78°C, a solution of 3.0720 g (6.26 mmol) of the α-ketophosphoranylidene **11** in 14 mL of dichloromethane was

added over 5 min. The reaction mixture was allowed to warm to 0°C. After 45 min, the reaction mixture was diluted with 200 mL of ether and 50 mL of saturated aqueous NaCl. The phases were separated and the organic phase was dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue chromatographed on 60 g of silica gel with 9:1 petroleum ether/ether to afford 860.2 mg (52.7%) of the desired enedione **13** as a colorless oil: R_f= 0.57 (1:1 petroleum ether/ether); evaporative distillation 195°C (0.05 mm Hg); IR ($CHCl_3$) 3030, 2950, 2930, 2850, 1780, 1685, 1610, 1460, 1380, 1255, 1090, 1035, 1000, 840 cm^{-1}; UV (methanol) λ_{max}= 247nm ϵ= 13,000; ^1H NMR ($CDCl_3$) δ0.01, 0.01 (2s, 6H, $(CH_3)_2Si$), 0.82 (s, 9H, $(CH_3)_3C$), 1.16 (d, 3H, CH_3COSi, J= 6Hz), 1.20, 1.32 (2s, 6H, $(CH_3)_2C$), 2.14 (s, 3H, $CH_3C=C$), 2.6-2.7 (m, 2H, $CH_2C=O$), 4.4-4.7 (m, 5H, HCO, CH_2Ph), 4.98 (2d, 1H, CHC=O, J= 5Hz, J'= 4.5Hz), 5.20 (s, 1H, CHOBn), 7.10 (s, 1H, HC=C), 7.26 (s, 5H, PhH). Analysis calculated for $C_{28}H_{42}O_7Si$: C, 64.83; H, 8.16. Found: C, 64.84; H, 8.02.

(7,10ξ)-7,10-Anhydro-benzyl-6,9,11-trideoxy-2,3-O-isopropylidene-7-C-methyl-α-D-lyxo-undecafuranosido-5,8-diulose (14). To a stirred solution of 76.5 mg (0.15 mmol) of the enedione **13** in 2.6 mL of 1:1 acetone/dichloromethane were added 110 mg (1.17 mmol) of

lithium tetrafluoroborate and 55 mg (0.29 mmol) of p-toluenesulfonic acid. After 3.5 h, the reaction was diluted with 2 mL of carbon tetrachloride and directly chromatographed on 10 g of silica gel with 4:1 petroleum ether/ether to afford 29.7 mg (49.8%) of the furanone **14** as a colorless oil: R_f= 0.35 (1:1 petroleum ether/ether); evaporative distillation 180-185°C (0.05 mm Hg); IR ($CHCl_3$) 2920, 2850, 1755, 1725, 1455, 1385, 1080, 1030, 970, 870 cm^{-1}; ^1H NMR ($CDCl_3$) 400 MHz δ1.24, 125, 126, 1.27 (4s, 6H, $(CH_3)_2C$), 1.32-1.40 (m, 3H, CH_3CO), 1.39, 1.41 (2s, 3H, $CH_3CC=O$), 2.2-3.4 (m, 4H, $CH_2C=O$), 4.32-4.34 (m, 1H, $CHCH_3$), 4.45-4.67 (m, 4H, CH_2O, OCHCHO), 4.98-5.02 (m, 1H, CHC=O), 5.20 (d, 1H, CHOBn, J= 6Hz), 7.24-7.33 (m 5H, PhH). Analysis calculated for $C_{22}H_{28}O_7$: C, 65.33; H, 6.98. Found: C, 65.38; H, 6.82.

(2R, 3R)-Methyl-2-[(benzyloxy)methyl]-3-hydroxy-butyrate (15). To a stirred solution of 11.8 mL (84.4 mmol) of di-iso-propylamine and 41.0 mL of 2.06 M n-butyllithium in 160 mL of tetrahydrofuran at -78°C was added a solution of 3.99 g (33.8 mmol) of Methyl (R)-3-hydroxybutyrate in 80 mL of tetrahydrofuran over 6 min. After 55 min, a solution of 5.2 mL (37.4 mmol) of benzylchloromethyl ether in 36 mL of tetrahydrofuran was added to the reaction mixture over 3 min. The reaction

mixture was allowed to warm to 0°C. After 4 h, 100 mL of saturated aqueous NH_4Cl were added followed by 400 mL of ether and 50 mL of water. The phases were separated and the aqueous phase was extracted with 400 mL of ether. The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was flash chromatographed on silica gel using 3:2 petroleum ether/ether to afford 3.3984 g (42.2%) of the benzyl ether **15** then 1.78 g of starting material (76.2% based on unrecovered starting material). The product was a colorless oil: R_f= 0.38 (ether); evaporative distillation 95-100°C (0.008 mm Hg); $[\alpha]^{21}_D$= -8.0° (c 1.00, $CHCl_3$); IR ($CHCl_3$) 3530, 3010, 2950, 2920, 2870, 1730, 1455, 1440, 1370, 1270, 1225, 1180, 1100, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.22 (d, 3H, CH_3C, J= 6.5Hz), 2.75 (q, 1H, CHC=O, J= 6Hz), 2.81 (br s, 1H, OH), 3.74 (s, 3H, CH_3OC=O), 3.76 (abx, 1H, HC<u>H</u>O, J= 9.4Hz, 6.0Hz), 3.77 (abx, 1H, HC<u>H</u>O, J= 9.4Hz, 6.0Hz), 4.13 (dq, 1H, CHOSi, J= 6.0Hz, 6.5Hz), 4.51 (ab, 1H, HC<u>H</u>Ph, J=11.6Hz), 4.52 (ab, 1H, HC<u>H</u>Ph, J=11.6Hz), 7.25-7.4 (m, 5H, PhH); Cap GC (DB1701, 120°C 2 min, 10°C/min to 180°C) major= 12.13 min; minor= 12.31 min; ratio= 14.0:1. Analysis calculated for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.52; H, 7.67.

(2<u>R</u>, 3<u>R</u>)-2-Carbomethoxy-butan-1,3-diol cyclic carbonate

(16). To a stirred solution of a small portion of the benzyl ether **15** in ethyl acetate was added a small amount of 10% palladium on carbon. The reaction mixture was stirred under a hydrogen atmosphere for 24 h. The catalyst was removed by filtration and the solvent was removed under reduced pressure. To the residue dissolved in 1 mL of benzene were added 0.5 mL of pyridine, then 4 mL of a solution of phosgene in benzene. After 1 h, the reaction mixture was diluted with 85 mL of ether and 15 mL of 10% aqueous HCl. The phases were separated and the organic phase was dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was chromatographed on 1 g of silica gel with ether to afford the carbonate **16** as a colorless oil: R_f= 0.14 (ether); ^1H NMR ($CDCl_3$) 400MHz δ1.44 (d, 3H, CH_3C, J= 6.6Hz), 3.14 (ddd, 1H, CHC, J= 6.5Hz, 5.0Hz, 4.2Hz), 3.77 (s, 3H, CH_3O), 4.50 (abx, 1H, HC<u>H</u>, J= 11.6Hz, 5Hz), 4.62 (abx, 1H, HC<u>H</u>, J= 11.6Hz, 6.5Hz), 4.83 (dq, 1H, HCO, J= 4.2Hz, 6.6Hz).

Methyl (2<u>R</u>, 3<u>R</u>)-2-[(benzyloxy)methyl]-3-(<u>tert</u>-butyldimethylsiloxy)-butyrate. To a stirred solution of 24.9 g (97.7 mmol) of the alcohol **15** in 250 mL of N,N-dimethylformamide were added 19.8 g (131.4 mmol) of <u>tert</u>-butylchlorodimethylsilane and 18.0 g (264.4 mmol) of imidazole. After 3 h, the reaction mixture was

diluted with 750 mL of ether and 150 mL of 10% aqueous HCl. The phases were separated and the organic phase was extracted with two portions of 150 mL of water and one portion of 100 mL of saturated aqueous $NaHCO_3$. The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was flash chromatographed using 9:1 petroleum ether/ether to afford 29.6 g (85.9%) of the desired silyl ether as a colorless oil: R_f= 0.15 (95:5 petroleum ether/ether); evaporative distillation 100-105°C (0.04 mm Hg); $[\alpha]^{21}_D$= -8.95 (c 1.62, $CHCl_3$); IR ($CHCl_3$) 2950, 2930, 2850, 1730, 1455, 1440, 1380, 1365, 1255, 1100, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ0.0 (s, 6H, $(CH_3)_2Si$), 0.82 (s, 9H, $(CH_3)_3C$), 1.12 (d, 3H, CH_3, J= 6Hz), 2.7-2.8 (m, 1H, CHC), 3.6-3.7 (m, 2H, CH_2O), 3.74 (s, 3H, CH_3O), 4.03 (dq, 1H, CHOSi, J= 6Hz, 6Hz), 4.43 (s, 2H, CH_2Ph), 7.24 (s, 5H, PhH); Cap GC (DB1701, 120°C 2 min, 10°C/min to 200°C) major= 14.74; minor= 14.24; ratio= 9.8:1. Analysis calculated for $C_{19}H_{32}O_4Si$: C, 64.73; H, 9.15. Found: C, 64.80; H, 9.06.

(2R, 3R)-2-[(Benzyloxy)methyl]-3-(tert-butyldimethylsiloxy)-butyric acid (17). To a stirred solution of 3.0 g (8.51 mmol) of the above ester in 90 mL of methanol were added 30 mL of 1N aqueous lithium hydroxide. After 81 h, the methanol was removed under

reduced pressure and the reaction mixture was acidified to pH 2. The reaction mixture was extracted with four portions of 150 mL of ether,then the combined organic extracts were dried ($MgSO_4$) and the solvent was removed under reduced pressure. The residue was chromatographed on 250 g of silicar CC-4 special silica gel to afford 2.1 g (72.9%) of the acid **17** as a colorless oil: R_f= major 0.32, minor 0.22; IR ($CHCl_3$) 3530-2400 (br), 2950, 2930, 2850, 1750, 1710, 1450, 1380, 1360, 1255, 1100, 1025, 960, 840, 695 cm^{-1}; ^1H NMR ($CDCl_3$) δ0.03 (s, 6H, $(CH_3)_2Si$), 0.81 (s, 9H, $(CH_3)_3C$), 1.15 (d, 3H, CH_3C, J= 6Hz), 2.7-2.8 (m, 1H, CHC), 3.62 (d, 2H, CH_2O, J= 6.5Hz), 4.1-4.2 (m, 1H, HCO), 4.44 (s, 2H, CH_2Ph), 7.24 (s, 5H, PhH), 8.06 (br s, 1H, CO_2H) A small portion of the acid before chromatography was treated with excess ethereal diazomethane to afford a sample for Cap GC (DB1701, 120°C 2 min, 10°C/min to 200°C) major= 14.85; minor= 14.43; ratio= 3.36:1.

(3ξ)-(2R)-2-[(benzyloxy)methyl]-3-(tert-butyldimethylsiloxy)-5-(triphenylphosphoranylidene)-4-hexanone (18). To a stirred solution of 786.9 mg (2.32 mmol) of the acid **17** in 15 mL of benzene were added 5 drops of N,N-dimethylformamide then 0.22 mL (2.52 mmol) of oxalyl chloride. After 25 min, the solvent was removed under reduced pressure then the residue was

diluted with 10 mL of benzene and the solvent once again removed under reduced pressure. The dilution-solvent removal sequence was repeated then the residue diluted with 40 mL of ether and filtered through dry celite. The solvent was removed under reduced pressure and the residue was dissolved in 16 mL of benzene then warmed to 80°C. To a slurry of 1.89 g (5.09 mmol) of ethyltriphenylphosphonium bromide in 36 mL of benzene were added 2.10 mL of 2.02 M n-butyllithium in hexanes. After 30 min, the slurry was centrifuged. The supernatant red solution was transferred into the acid chloride solution via cannula over 6 min. After 30 min, the reaction was allowed to cool to room temperature then diluted with 400 mL of ether and 75 mL of 10% aqueous K_2CO_3. The phases were separated and the organic phase was dried ($MgSO_4$). The solvent was removed under reduced pressure to afford 1.4210 g (100%) of the α-ketophosphoranylidene **18** as a red oil: IR ($CHCl_3$) 3060, 2950, 2920, 2850, 1720, 1490, 1435, 1380, 1255, 1170, 1110, 1075, 1030, 1000, 840, 695 cm^{-1}; ^1H NMR ($CDCl_3$) δ0.02, 0.04 (2s, 6H, $(CH_3)_2Si$), 0.87 (s, 9H, $(CH_3)_3C$), 1.09 (d, 3H, CH_3C, J= 6Hz), 1.68 (d, 3H, $CH_3C=P$, J= 17Hz), 2.3-2.4 (m, 1H, CHC), 3.7-4.8 (m, 5H, HCO, H_2CO), 7.2-7.9 (m, 20H, PhH).

(9ξ)-Benzyl-(E)-9-[(benzyloxy)methyl]-10-O-(tert-

butyldimethylsilyl)-6,7,9,11-tetradeoxy-2,3-O-isopropylidene-7-C-methyl-D-glycero-α-D-lyxo-undec-6-enofuranosido-5,8-diulose (19). To a stirred solution of 53 μL (0.61 mmol) of oxalyl chloride in 3.0 mL of dichloromethane at -78°C were added 49 μL (0.69 mmol) of dimethylsulfoxide. After 15 min, a solution of 85.8 mg (0.28 mmol) of the diol **12** in 4.0 mL of dichloromethane was added to the reaction mixture over 2 min. After 27 min, 0.19 mL (1.36 mmol) of triethylamine were added over 0.5 min. After 20 min, a solution of 844.5 mg (1.38 mmol) of the α-ketophosphoranylidene **18** in 5.0 mL of dichloromethane was added to the reaction mixture over 5 min. After 5 min, the reaction mixture was allowed to warm to 0°C. After 1 h, the reaction mixture was diluted with 200 mL of ether and 20 mL of saturated aqueous NaCl. The organic phase was separated and dried ($MgSO_4$), then the solvent was removed under reduced pressure. The residue was chromatographed on 10 g of silica gel with 9:1 petroleum ether/ether to afford 65.4 mg (37%) of the enedione **19** as a colorless oil: R_f= 0.56 (1:1 petroleum ether/ether); IR ($CHCl_3$) 3020, 2960, 2930, 2850, 1710, 1680, 1610, 1380, 1365, 1260, 1100, 1085, 1035, 845 cm^{-1}; ^1H NMR ($CDCl_3$) δ0.02, 0.07 (2s, 6H, $(CH_3)_2Si$), 0.78, 0.82 (2s, 9H, $(CH_3)_3C$), 1.09 (d, 3H, CH_3COSi, J= 6Hz), 1.18, 1.30 (2s, 6H, $(CH_3)_2C$), 2.01, 2.15 (2s, 3H, $CH_3C=C$), 3.0-3.1 (m, 1H, CHC=O),

3.4-4.7 (m, 9H, OCH, H_2CO), 4.92 (2d, 1H, HCO, J= 5Hz), 5.16 (br s, 1H, CHOBn), 7.07 (s, 1H, CH=C), 7.25 (s, 10H, PhH). Analysis calculated for $C_{36}H_{50}O_8Si$: C, 67.68; H, 7.89. Found: C, 67.76; H, 7.80.

(7,9ξ)-Benzyl-7,10-anhydro-9-[(benzyloxy)methyl]-6,9,11-trideoxy-2,3-O-isopropylidene-7-C-methyl-D-glycero-α-D-lyxo-undecofuranosido-5,8-diulose (20). To a stirred solution of 13.3 mg (0.021 mmol) of the enedione **19** in 0.4 mL of 1:1 acetone/dichloromethane were added 22.0 mg (0.235 mmol) of lithium tetrafluoroborate and 0.8 mg (0.042 mmol) of p-toluenesulfonic acid. After 3 h, the reaction was diluted with 0.5 mL of carbon tetrachloride and directly chromatographed on 5 g of silica gel with 4:1 petroleum ether/ether to afford 9.1 mg (83.3%) of the furanone **20** as a colorless oil: R_f= 0.42 (1:1 petroleum ether/ether); evaporative distillation 220-225°C (0.03 mm Hg); IR ($CHCl_3$) 3040, 3000, 2970, 2930, 2860, 1755, 1720, 1455, 1390, 1380, 1365, 1230, 1165, 1090, 1030, 980, 870, 705 cm^{-1}; ^1H NMR ($CDCl_3$) 400MHz δ1.17, 1.23, 1.25, 1.29 (4s, 6H, $(CH_3)_2C$), 1.36, 1.38 (2s, 3H, CH_3), 1.41, 1.45 (2d, 3H, CH_3CH, J= 4.6Hz, J'= 6.1Hz), 2.56, 2.57 (2ddd, 1H, CHC=O, J= 9.5Hz, 7.8Hz, 3.9Hz, J'= 9.5Hz, 4.6Hz, 3.1Hz), 2.96 (ab, 0.5H, HCHC=O, J= 17.8Hz), 3.04 (ab, 0.5H, HCHC=O, J= 17.2Hz), 3.07 (ab, 0.5H, HCHC=O, J= 17.2Hz), 3.18 (ab, 0.5H, HCHC=O,

J= 17.8Hz), 3.61 (abx, 0.5H, HCHOBn, J= 9.7Hz, 3.1Hz), 3.81 (abx, 0.5H, HCHOBn, J= 9.7Hz, 4.6Hz), 3.92 (abx, 0.5H, HCHOBn, J= 18Hz, 7.8Hz), 3.98 (abx, 0.5H, HCHOBn, J= 18Hz, 3.9Hz), 4.32, 4.35 (2dq, 1H, $HCCH_3$, J= 9.5Hz, 4.6Hz, J'= 9.5Hz, 6.1Hz), 4.4-4.7 (m, 6H, CHOCOCH, CH_2Ph), 4.93, 5.03 (2dd, 1H, OCHC=O, J= 6.2Hz, 4.7Hz, J'= 6.2Hz, 5.0Hz), 5.20 (d, 1H, CHOBn, J= 3.4Hz), 7.2-7.4 (m, 10H, PhH). Analysis calculated for $C_{30}H_{36}O_8$: C, 68.69; H, 6.97. Found: C, 68.85; H, 7.00.

1-O-Benzyl-2,4-O-isopropylidene-3-deoxy-3-methyl-D-threitol. To a stirred solution of 3.1 g (14.8 mmol) of the diol **21** in 100 mL of acetone were added 1.82 mL (14.8 mmol) of dimethoxypropane and 0.2 g (1.05 mmol) of p-toluenesulfonic acid. After 14 h, the reaction mixture was diluted with 150 mL of ether and 25 mL of saturated aqueous $NaHCO_3$. The phases were separated and then the organic phase was extracted with 25 mL of saturated aqueous NaCl. The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography on silica gel with 9:1 petroleum ether/ether afforded 3.7 g (100%) of the desired acetonide as a colorless oil. Spectral properties were identical with those reported previously.[27]

2,4-O-Isopropylidene-3-deoxy-3-methyl-D-threitol (22).

To a stirred solution of 0.208 g (29.98 mmol) of lithium in 120 mL of anhydrous ammonia at -78°C was added a solution of 3.7 g (14.8 mmol) of the above benzyl ether in 15 mL of tetrahydrofuran over 5 min. After 15 additional min, dry NH_4Cl was added cautiously and the resulting colorless mixture was diluted with 100 mL of ether and the ammonia was allowed to evaporate. The slurry was diluted with 20 mL of water and the aqueous phase was extracted with four portions of 200 mL of ether. The combined organic phases were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed on silica gel with 1:1 petroleum ether/ether to afford 2.30 g (97.5%) of the alcohol **22** as a colorless oil: R_f= 0.25 (ether); evaporative distillation 110°C (35 mm Hg); $[\alpha]^{21}_D$= -4.32 (c 0.90, $CHCl_3$); IR ($CHCl_3$) 3580, 3450 (br), 2995, 1940, 2870, 1460, 1380, 1275, 1240, 1195, 1120, 1030, 1010, 935, 905, 835, 815 cm^{-1}; ^1H NMR ($CHCl_3$) 1.05 (d, 3H, CH_3C, J= 6Hz), 1.40, 1.46 (2s, 6H, $(CH_3)_2C$), 1.4-1.5 (m 1H, CH), 2.02 (br s, 1H, OH), 3.4-3.7 (m, 3H, HCO, CH_2O), 3.9-4.2 (m, 2H, CH_2OH). Analysis calculated for $C_8H_{16}O_3$: C, 59.98; H, 10.06. Found: C, 59.70; H, 10.05.

(2ξ)-1-O-Benzyl-3,5-O-isopropylidene-4-deoxy-4-methyl-D-threo-pentitol. To a stirred solution of 0.69 mL (7.97

mmol) of oxalyl chloride in 9.0 mL of tetrahydrofuran at -78°C was added a solution of 0.63 mL (8.88 mmol) of dimethylsulfoxide in 4.0 mL of tetrahydrofuran over 1.75 min. After 10 min, a solution of 1.0196 g (6.36 mmol) of the alcohol **22** in 8 mL of tetrahydrofuran was added to the reaction mixture over 3 min. After 15 min, 2.20 mL (15.78 mmol) of triethylamine were added over 30 seconds and the reaction mixture was allowed to warm to 0°C. After 15 min, the reaction mixture was cooled to -78°C and a solution of 10.6 mL (25.6 mmol) of benzyloxymethyl-tri-n-butyltin and 11.5 mL of 2.22 M n-butyllithium in hexanes in 55 mL of tetrahydrofuran, according to the procedure of Still[28], was added over 12 min. After 1 h, 50 mL of saturated aqueous NH_4Cl was added and the phases were separated. The aqueous phase was extracted with four portions of 100 mL of ether. The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography on silica gel with 3:1 petroleum ether/ ether afforded 917.2 mg (51.4%) of a mixture of the desired, diastereomeric benzyl ethers as a clear oil: R_f= major: 0.30, minor: 0.25 (1:1 petroleum ether/ether); evaporative distillation 130°C (0.20 mm Hg); IR ($CHCl_3$) major 3590, 2990, 2930, 2870, 1455, 1385, 1275, 1195, 1105, 1015, 855, 700 cm^{-1}; ^1H NMR ($CDCl_3$) major δ1.05 (d, 3H, CH_3C, J= 6Hz), 1.29 (s, 6H,

$(CH_3)_2C$), 1.6-1.7 (m, 1H, CH), 2.52 (d, 1H, OH, J= 4Hz), 3.3-4.2 (m 6H, OCH, OCH_2), 4.42 (s, 2H, CH_2Ph), 7.28 (s, 5H, PhH); Cap GC (DB1701, 130°) major: 11.78 min minor: 12.02 min, ratio= 9.4:1. Analysis calculated for $C_{16}H_{24}O_4$: C, 68.55; H, 8.63. Found: C, 68.58; H, 8.50.

(2ξ)-3,5-isopropylidene-4-deoxy-4-methyl-D-threo-pentitol (23). To a stirred solution of 32 mg (4.61 mmol) of lithium in 25 mL of anhydrous ammonia at -78°C was added a solution of 451.8 mg (1.61 mmol) of the above benzyl ethers in 5 mL of tetrahydrofuran. After 25 min, dry NH_4Cl was added cautiously and the resulting colorless mixture was diluted with 25 mL of ether and the ammonia was allowed to evaporate. The resulting slurry was diluted with 10 mL of half-saturated aqueous NaCl then the phases were separated. The aqueous phase was extracted with five portions of 40 mL of ether. The combined organics were dried ($MgSO_4$) then concentrated under reduced pressure. Chromatography on 10 g of silica gel with ether afforded 188.8 mg (61.6%) of the diols **23** as a colorless oil: R_f= 0.12 (ether); IR ($CHCl_3$) 3520 (br), 2990, 2930, 2880, 1455, 1385, 1235, 1195, 1140, 1085, 1010, 910, 850 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.10 (d, 3H, CH_3C, J= 6Hz), 1.38, 1.42 (2s, 6H, $(CH_3)_2C$), 1.7-1.8 (m, 1H, CH), 3.32 (br s, 2H, OH), 3.4-

4.3 (m, 6H, HCO, H_2CO). Analysis calculated for $C_9H_{18}O_4$: C, 56.82; H, 9.54; Found: C, 56.77; H, 9.45..

(9ξ)-(2R, 3S, 5E)-1,3-O-isopropylidene-9-(tert-butyldimethylsiloxy)-1,3-dihydroxy-2,6-dimethyl-5-decene-4,7-dione (24). To a stirred solution of 76 μL (0.87 mmol) of oxalyl chloride in 3.0 mL of dichloromethane at -78°C were added 70 μL of dimethylsulfoxide. After 10 min, a solution of 74.9 mg (0.39 mmol) of the diols **23** in 3.0 mL of dichloromethane was added to the reaction mixture over 4 min. After 20 min, 0.27 mL (1.94 mmol) of triethylamine were added and the reaction mixture was allowed to warm to -40°C, then a solution of 1.1789 g (2.33 mmol) of the α-ketophosphoranylidene **11** in 5.0 mL of dichloromethane was added over 6 min. After 30 min, the reaction mixture was diluted with 50 mL of ether and 10 mL of saturated aqueous NaCl. The phases were separated and the organic phase was dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was chromatographed on 10 g of silica gel with 9:1 petroleum ether/ether to afford 87.2 mg (56.1%) of the desired the enediones **24** as a mixture of diastereomers: R_f= 0.59 (1:1 petroleum ether/ether); evaporative distillation 140-145°C (0.06 mm Hg); IR ($CHCl_3$) 3020, 2960, 2930,

2860, 1685, 1610, 1460, 1385, 1260, 1140, 1110, 1010, 935, 840 cm^{-1}; ^1H NMR ($CDCl_3$) 400 MHz -0.03, -0.02, 0.03,. 0.04 (4s, 6H, $(CH_3)_2Si$), 0.80, 0.81 (2s, 9H, $(CH_3)_3C$), 0.99 (2d, 3H, CH_3, J= 6.8Hz), 1.18 (2d, 3H, CH_3COSi, J= 6.1Hz), 1.45, 1.49 (2s, 6H, $(CH_3)_2C$), 2.01-2.05 (m, 1H, $CHCH_3$), 2.16 (s, 3H, $CH_3C=C$), 2.62 (abx, 1H, $HCHC=O$, J= 15.4Hz, 5.1Hz), 2.96 (abx, 1H, $HCHC=O$, J= 15.4Hz, 7.3Hz), 3.61 (d, 1H, $HCH_{eq}O$, J= 11.5Hz), 4.16 (dd, 1H, $HCH_{ax}O$, J= 11.5Hz, 2.6Hz), 4.32-4.36 (m, 1H, CHOSi), 4.49, 4.50 (2d, 1H, CHC=O, J= 2.5Hz), 7.12, 7.15 (2s, 1H, HC=C). Analysis calculated for $C_{21}H_{38}O_5Si$: C, 63.28; H, 9.61. Found: C, 63.49; H, 9.42.

1-O-Benzyl-3-deoxy-3-methyl-D-threitol diethyl carbonate. To a mixture of 1.03 g (4.9 mmol) of the diol **21** and 1.76 g (14.9 mmol) of diethyl carbonate was added a sliver of sodium metal. After 18 h at 80°C, the reaction mixture was diluted with 100 mL of ether and 15 mL of 10% aqueous HCl. The organic phase was separated and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was flash chromatographed on 40 g of silica gel with 1:1 petroleum ether/ether to afford 0.63 g (36.3%) of the desired dicarbonate as a colorless oil: R_f= 0.63 (ether); evaporative distillation 155-165°C (0.04 mm Hg); $[\alpha]^{21}_D$= -10.26° (c 1.15, $CHCl_3$); IR ($CHCl_3$) 2995, 1740, 1470,

1460, 1375, 1260, 1100, 1010, 900 cm^{-1}; ^1H NMR ($CDCl_3$) δ0.96 (d, 3H, CH_3C, J= 6Hz), 1.20 (t, 6H, CH_3CH_2, J= 7Hz), 2.2-2.3 (m, 1H, CHC), 3.53 (d, 2H, CH_2OBn, J=5.5Hz), 3.7-4.3 (m, 6H, $CH_2OC=O$), 4.46 (s, 2H, CH_2Ph), 4.91 (q, 1H, CHOC=O, J= 5.5Hz), 7.25 (s, 5H, PhH). Analysis calculated for $C_{18}H_{26}O_7$: C, 61.00; H, 7.39. Found: C, 61.06; H, 7.40.

3-Deoxy-3-methyl-D-threitol 1,2-cyclic carbonate 4-ethyl carbonate (25). To a stirred solution of 0.53 g (1.50 mmol) of the above dicarbonate in 7 mL of absolute ethanol were added 0.30 g of 10% palladium on carbon. The reaction mixture was stirred under a hydrogen atmosphere for 4 h. The catalyst was removed by filtration and the solvent was removed under reduced pressure. The residue was chromatographed on 10 g of silica gel with 2:1 petroleum ether/ether to afford 107.9 mg (33%) of the cyclic carbonate **25** as a colorless oil: R_f= 0.49 (ether); evaporative distillation 130-140°C (1.0 mm Hg); $[\alpha]^{21}_D$= -44.68 (c 0.77, $CHCl_3$); IR ($CHCl_3$) 2995, 2930, 1810, 1740, 1470, 1385, 1265, 1175, 1080, 915 cm^{-1}; ^1H NMR δ1.03 (d, 3H, CH_3C, J= 6Hz), 1.22 (t, CH_3CH_2, J= 7Hz), 2.1-2.2 (m, 1H, CHC), 3.8-4.8 (m, 7H, H_2CO, HCO). Analysis calculated for $C_9H_{14}O_6$: C, 49.54; H, 6.47. Found: C, 49.53; H, 6.48.

1-O-Benzyl-3-deoxy-3-methyl-D-threitol cyclic carbonate. To a stirred solution of 201.6 mg (0.96 mmol) of the diol **21** in 4 mL of pyridine at 0°C were added 4 mL of a 1M solution of phosgene in benzene. After 0.5 h, the reaction mixture was allowed to warm to room temperature. After 4 h, the reaction mixture was diluted with 20 mL of 10% aqueous HCl and 100 mL of ether. The phases were separated and the aqueous phase was extracted with two portions of 50 mL of ether. The combined organics were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed on 10 g of silica gel with ether to afford 166.2 mg (73.4%) of the desired cyclic carbonate as a colorless oil: R_f= 0.26 (ether); evaporative distillation 182-185°C (1.0 mm Hg); $[\alpha]^{21}_D$= +10.3° (c 0.98, $CHCl_3$); IR ($CHCl_3$) 2970, 2930, 2860, 1745, 1450, 1405, 1225, 1130, 915 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.03 (d, 3H, CH_3, J= 6Hz), 2.3-2.4 (m, 1H, CHC), 3.62 (d, 2H, H_2CO, J= 5Hz), 4.28 (abx, 1H, HCHOC=O, J= 10Hz, 3Hz), 4.36 (abx, 1H, HCHOC=O, J= 10Hz, 2Hz), 4.54 (s, 2H, CH_2Ph), 4.6-4.7 (m, 1H, HCO), 7.25 (s,5H, PhH). Analysis calculated for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 66.18; H, 6.79.

3-Deoxy-3-methyl-D-threitol 1,2-cyclic carbonate (26). To a stirred solution of 150 mg (0.64 mmol) of the above

benzyl ether in 5 mL of absolute ethanol and 5 drops of glacial acetic acid were added 65 mg of 10% palladium on carbon. The reaction mixture was stirred under a hydrogen atmosphere for 16 h. The catalyst was removed by filtration and the solvent was removed under reduced pressure. The residue was chromatographed on 5 g of silica gel with ether to afford 73.7 mg (79.4%) of the five membered cyclic carbonate **26** as a colorless oil: R_f= 0.11 (ether); evaporative distillation 140°C (1.0 mm Hg); $[\alpha]^{21}_D$= -50.57 (c 1.34, $CHCl_3$); IR ($CHCl_3$) 3630, 3500 (br), 2970, 2920, 2880, 1780, 1575, 1395, 1370, 1170, 1070, 1050, 915 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.02 (d, 3H, CH_3, J= 6Hz), 2.0-2.1 (m, 2H, OH, CHC), 3.4-3.5 (m, 2H, CH_2OH), 4.2-5.0 (m, 3H, $HCOCOCH_2$), decoupling at 2.02 collapsed the doublet at 1.02 to a singlet, but did not affect the lower field multiplet at 4.2-5.0. Analysis calculated for $C_6H_{10}O_4$: C, 49.31; H, 6.90. Found: C, 49.16; H, 6.80.

1-O-Benzyl-3-deoxy-3-methyl-D-threitol dipivaloate. To a stirred solution of 657.0 mg (3.12 mmol) of the diol **21** in 6.0 mL of dichloromethane were added 1.55 mL (19.2 mmol) of pyridine, 1.15 mL (9.34 mmol) of pivaloyl chloride and 76.3 mg (0.62 mmol) of N',N'-dimethylaminopyridine. After 24 h, the reaction mixture was diluted with 100 mL of ether and extracted

successively with: two portions of 25 mL of 10% aqueous HCl, 25 mL of saturated aqueous $NaHCO_3$, and 25 mL of water. The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. Flash chromatography on silica gel with 9:1 petroleum ether/ether afforded 1.1503 g (97.3%) of the desired diester as a colorless oil: R_f= 0.38 (9:1 petroleum ether/ether); evaporative distillation 140°C (0.05 mm Hg); $[\alpha]^{21}_D$= -6.15 (c 1.74, $CHCl_3$); IR ($CHCl_3$) 2995, 2950, 1710, 1470, 1415, 1280, 1150, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.00 (d, 3H, CH_3, J= 6Hz), 1.15 (s, 18H, $(CH_3)_3C$), 2.2-2.3 (m, 1H, CHC), 3.51 (d, 2H, CH_2OBn, J= 5Hz), 3.90 (d, 2H, $CH_2OC{=}O$, J= 6Hz), 4.46 (s,2H, CH_2Ph), 5.09 (q, 1H, HCO, J= 5Hz), 7.24 (s, 5H, PhH). Analysis calculated for $C_{22}H_{34}O_5$: C, 69.81; H, 9.05. Found: C, 69.66; H, 8.92.

3-Deoxy-3-methyl-D-threitol 2,4-dipivaloate (27). To a stirred solution of 996.0 mg (2.63 mmol) of the above benzyl ether in 19.5 mL of absolute ethanol were added 850 mg of 10% palladium on carbon. The reaction mixture was agitated under 50 psi of hydrogen for 18 h. The catalyst was removed by filtration and the solvent was removed under reduced pressure. The residue was flash chromatographed with 2:1 petroleum ether/ether to afford 683.1 mg (90%) of the alcohol **27** as a colorless oil:

R_f= 0.28 (1:1 petroleum ether/ether); evaporative distillation 95-100°C (0.04 mm Hg); $[\alpha]^{21}_D$= -7.11° (c 1.435, $CHCl_3$); IR ($CHCl_3$) 3490 (br), 2970, 2890, 1710, 1475, 1455, 1395, 1365, 1280, 1155, 1035 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.01 (d, 3H, CH_3, J= 6Hz), 1.15 (s, 18H, $(CH_3)_3C$), 2.1-2.2 (m, 2H, CHC, OH), 3.72 (t, 2H, CH_2OH, J= 5Hz), 3.94 (d, 2H, $CH_2OC{=}O$, J= 6Hz), 4.90 (q, 1H, CHOC=O, J= 5Hz). Analysis calculated for $C_{15}H_{28}O_5$: C, 62.47; H, 9.79. Found: C, 62.30; H, 9.70.

3-Deoxy-3-methyl-D-threose dipivaloate. To a stirred solution of 0.18 mL (2.06 mmol) of oxalyl chloride in 10.0 mL of dichloromethane at -78°C were added 0.30 mL (4.23 mmol) of dimethylsulfoxide. After 15 min, a solution of 301.8 mg (1.05 mmol) of the alcohol **27** in 6.0 mL of dichloromethane was added to the reaction mixture over 2 min. After 26 min, 1.1 mL (7.89) of triethylamine were added and then the reaction mixture was allowed to warm to room temperature. The reaction mixture was diluted with 50 mL of ether and 20 mL of saturated aqueous $NaHCO_3$. The phases were separated and the aqueous phase was extracted with two portions of 50 mL of ether. The combined organics were dried ($MgSO_4$) and concentrated under reduced pressure to afford the desired crude aldehyde: R_f= 0.56 (1:1 petroleum ether/ether); ^1H NMR ($CDCl_3$) δ0.94 (d, 3H, CH_3, J=

6.5Hz), 1.12, 1.21 (2s, 18H, $(CH_3)_3C$), 2.4-2.5 (m, 1H, CHC), 3.95 (d, 2H, CH_2O, J= 6.5), 5.02 (d, 1H, HCO, J= 3.5 Hz), 9.53 (s, 1H, HC=O).

(2R, 3R)-1,3-Dihydroxy-2-methyl-4-pentene dipivaloate (28). To a stirred solution of 301 mg (1.21 mmol) of Tebbe's reagent in 2.5 mL of benzene at 5°C were added a solution of the above crude aldehyde (roughly 1 mmol) in 2.5 mL of benzene and also 0.10 mL (1.23 mmol) of pyridine. After 20 min, 0.35 mL of 15% aqueous NaOH were added to the reaction mixture. After 15 min, the reaction mixture was diluted with 50 mL of petroleum ether, dried (Na_2SO_4) and filtered through a pad of dry celite. The solvent was removed under reduced pressure and the residue diluted with 50 mL of petroleum ether and filtered through a pad of dry celite. After the solvent was removed, the residue was chromatographed on 50 g of florisil with 98:2 petroleum ether/ether to afford 142.1 mg (47.7% from alcohol **27**) of the olefin **28** as a colorless oil: R_f= 0.67 (1:1 petroleum ether/ether); evaporative distillation 70-72°C (0.06 mm Hg); $[\alpha]_D^{21}$= +11.89° (c 1.06, $CHCl_3$); IR ($CHCl_3$) 3010, 2970, 2930, 2895, 2870, 1710, 1480, 1460, 1400, 1370, 1285, 1160, 1035, 995, 945 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.00 (d, 3H, CH_3, J= 6Hz), 1.15 (s, 18H, $(CH_3)_3C$), 2.1-2.2 (m, 1H, CHC), 3.82 (abx, 1H, CHH, J= 12Hz, 2Hz), 4.04

(abx, 1H, CHH, J= 12Hz, 3Hz), 5.1-5.2 (m, 1H, HCO), 5.2-5.3 (m, 2H, H_2C=C), 5.7-5.8 (m, 1H, HC=C). Analysis calculated for $C_{16}H_{28}O_4$: C, 67.57; H, 9.92. Found: C, 67.48; H, 9.76.

(2ξ)-4-Deoxy-4-methyl-D-threo-pentitol 3,5-dipivaloate (29). To a stirred solution of 109.5 mg (0.38 mmol) the olefin **28** in 7.5 mL of acetone and 3.0 mL of water were added 69.9 mg (0.52 mmol) of N-methylmorpholine-N-oxide and 0.39 mL (0.038 mmol) of a 2.5% solution of OsO_4 in tert-butanol. After 10.5 h, the reaction mixture was diluted with 15 mL of water and 1 g of celite then 200 mg of sodium hydrosulfite were added. After 20 min, the reaction mixture was filtered through a wet celite pad and acidified to pH 1.5. The solution was extracted with three portions of 150 mL of ethyl acetate. The combined organic extracts were dried ($MgSO_4$) then concentrated under reduced pressure. The residue was chromatographed on 10 g of silica gel with ether to afford 110.9 mg (90.5%) if the diols **29** as a mixture of diastereomers: R_f= major 0.08, minor 0.06 (1:1 petroleum ether/ether); evaporative distillation 135-140°C (0.05 mm Hg); IR ($CHCl_3$) 3690, 3540 (br), 2970, 2930, 2870, 1715, 1480, 1460, 1400, 1290, 1160 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.00 (d, 3H, CH_3, J= 6.8Hz), 1.18, 1.19 (2s, 18H, $(CH_3)_3C$), 2.5-2.6 (m, 2H, CHC, OH), 2.7-2.8

(m, 1H, OH), 3.4-3.5 (m, 1H, C<u>H</u>OH), 3.5-3.6 (m, 2H, $C\underline{H}_2OH$), 3.85 (abx, 1H, HC<u>H</u>OC=O, J= 11Hz, 9Hz), 3.91 (abx, 1H, HC<u>H</u>OC=O, J= 11Hz, 6.6Hz), 4.87 (dd, 1H, HCOC=O, J= 9.2Hz, 2.4Hz). Analysis calculated for $C_{16}H_{30}O_6$: C, 60.35; H, 9.50. Found: C, 60.46; H, 9.46

(8ξ)-(2<u>R</u>, 3<u>S</u>, 5<u>E</u>, 9<u>R</u>)-8-[(benzyloxy)methyl]-9-(<u>tert</u>-butyldimethylsiloxy)-1,3-dihydroxy-2,6-dimethyl-5-decene-4,7-dione dipivaloate (30). To a stirred solution of 1.43 mL (16.39 mmol) of oxalyl chloride in 65 mL of dichloromethane at -78°C were added 1.34 mL (18.88 mmol) of dimethylsulfoxide. After 15 min, a solution of 2.38 g (7.47 mmol) of the diol **30** in 45 mL of dichloromethane was added to the reaction mixture over 3 min. The reaction mixture was allowed to warm slowly to -30°C and after 15 min at that temperature, 5.24 mL (37.60 mmol) of triethylamine were added. After 6.5 min, a solution of 6.8489 g (11.21 mmol) of the α-ketophosphoranylidene **18** in 50 mL of dichloromethane was added over 3.5 min. After 20 min, the reaction mixture was allowed to warm to 0°C. After 1 h, the reaction mixture was diluted with 1.5 L of ether and 400 mL of saturated aqueous NaCl. The organic phase was separated and dried ($MgSO_4$) then the solvent was removed under reduced pressure. The residue was flash chromatographed

on 250 g of silica gel with 9:1 petroleum ether/ether to afford 2.0099 g (41.6%) of the enedione **30** as a slightly yellow oil. A small portion was further chromatographed at medium pressure on a size A Lobar silica column with 9:1 petroleum ether/ether to afford analytically pure samples of both diastereomers: R_f= major: 0.51, minor: 0.49 (3:1 petroleum ether/ether); IR ($CHCl_3$) major: 3020, 2965, 2925, 2850, 1725, 1665, 1610, 1480, 1460, 1365, 1285, 1255, 1150, 1105, 1035, 1005, 915, 840 cm^{-1}; minor: 3020, 2965, 2925, 2850, 1725, 1665, 1610, 1480, 1460, 1370, 1285, 1150, 1115, 920, 845 cm^{-1}; ^1H NMR ($CDCl_3$) major: δ-0.01, 0.02 (2s, 6H, $Si(CH_3)_2$), 0.82 (s, 9H, $(CH_3)_3C$), 0.85 (d, 3H, CH_3C, J= 7.1Hz), 1.02 (d, 3H, CH_3COSi, J= 6.5Hz), 1.19, 1.24 (2s, 18H, $(CH_3)_3CO$), 2.20 (s, 3H, $CH_3C=C$), 2.2-2.3 (m, 1H, CHCCO), 2.3-2.4 (m, 1H, CHC=O), 3.5-3.9 (m, 4H, CH_2O), 3.97 (dq, 1H, HCOSi, J= 2Hz, 6.5Hz), 4.36 (ab, 1H, HCHPh, J= 13Hz), 4.40 (ab, 1H, HCHPh, J= 13Hz), 5.19 (d, 1H, CHOC=O, J= 4.0Hz), 6.83 (s, 1H, HC=C), 7.2-7.4 (m, 5H, PhH); minor: δ-0.07, -0.01 (2s, 6H, $(CH_3)_2$), 0.77 (s, 9H, $(CH_3)_3CSi$), 0.84 (d, 3H, CH_3C, J= 6.7Hz), 1.13 (d, 3H, CH_3CO, J= 6.3Hz), 1.19, 1.26 (2s, 18H, $(CH_3)_3C$), 2.0-2.1 (m, 1H, CHCO), 2.22 (s, 3H, $CH_3C=C$), 2.28 (ddd, 1H, CHC=O, J= 12.0 Hz, 6.5Hz, 2.5Hz), 3.4-3.6 (m, 2H, CH_2OBn), 3.94 (d, 2H, $CH_2OC=O$, J= 7Hz), 4.02 (dq, 1H, CHOSi, J= 6.3Hz, 12Hz), 4.40 (s, 2H, CH_2Ph), 5.22 (d, 1H, CHOC=O, J=

4.0Hz), 6.85 (s, 1H, HC=C), 7.2-7.4 (m, 5H, PhH). Analysis Calculated for $C_{36}H_{58}O_8Si$: $(M+H)^+$, 647.3979. Found: $(M+H)^+$, major - 647.3969, minor - 647.3949.

(6,8ξ)-6,9-Anhydro-8-[(benzyloxy)methyl]-2,5,8,10-tetradeoxy-2-methyl-6-C-methyl-D-glycero-D-threo-4,7-decodiulsoe dipivaloate (31). To a stirred solution of 1.0 g (1.70 mmol) of the enedione **30** in 46 mL of 1:1 acetone/dichloromethane were added 1.99 g (21.23 mmol) of lithium tetrafluoroborate and 0.67 g of p-toluenesulfonic acid. After 12 h, the reaction mixture was diluted with 300 mL of ether and 75 mL of saturated aqueous NaCl slightly acidified with 10% aqueous HCl. The phases were separated and the aqueous phase washed with 300 mL of ether. The combined organics were dried ($MgSO_4$) and the solvent removed under reduced pressure. The residue was chromatographed on 100 g of silica gel with 4:1 petroleum ether/ether to afford 588.2 mg (71.4%) of the furanone **31** as a colorless oil: R_f= 0.43 (1:1 petroleum ether/ether); IR ($CHCl_3$) 2970, 2925, 2865, 1755, 1725, 1480, 1455, 1370, 1285, 1150 cm^{-1}; ^1H NMR ($CDCl_3$) 400MHz δ0.84, 0.87 (2d, 3H, CH_3CCO, J= 7.1Hz, J'= 6.8Hz), 1.17, 1.21 (2s, 18H, $(CH_3)_3C$), 1.23, 1.25 (2s, 3H, CH_3), 1.34, 1.43 (2d, 3H, CH_3CO, J= 6.6Hz, J'= 6.1Hz), 2.4-2.6 (m, 2H, CHC), 2.78 (ab, 0.5H, HCHC=O, J= 17.6Hz), 2.90 (s, 1H, $CH_2C=O$), 2.94 (ab,

0.5H, HCHC=O, J= 17.6Hz), 3.68 (abx, 0.5H, HCHOBn, J= 9.7Hz, 3.3Hz), 3.73 (abx, 0.5H, HCHOBn, J= 9.7Hz, 6.6Hz), 3.88 (d, 2H, $CH_2OC=O$, J= 8.3Hz), 3.91 (abx, 0.5H, HCHOBn, J= 9.5Hz, 2.1Hz), 3.93 (abx, 0.5H, HCHOBn, J= 9.5Hz, 4.0Hz), 4.27 (dq, 0.5H, $OCHCH_3$, J= 9.4Hz, 6.1Hz), 4.46, 4.52 (2s, 2H, CH_2Ph), 4.60 (dq, 0.5H, $OCHCH_3$, J= 8.3Hz, 6.6Hz), 5.12 (d, 0.5H, HCOC=O, J= 2.9Hz), 5.16 (d, 0.5H, HCOC=O, J= 2.7Hz), 7.2-7.4 (m, 5H, PhH). Analysis calculated for $C_{30}H_{44}O_8$: $(M+H)^+$, 533.3114. Found: $(M+H)^+$, 533.3133.

(4,6ξ) 6,9-Anhydro-8-[(benzyloxy)methyl]-2,5,8,10-tetradeoxy-2-methyl-6-C-methyl-4,7-bis-O-(trimethylsilyl)-D-glycero-D-threo-decitol-4,7-diene dipivaloate. To a stirred solution of 50.4 mg (0.0946 mmol) of the furanone **31** in 0.95 mL of dichloromethane at 0°C were added 80 μL (0.5740 mmol) of triethylamine and 85 μL (0.4685 mmol) of trimethylsilyl triflate. After 9 h, the reaction mixture was diluted with 50 mL of 3:1 petroleum ether/ether and 5 mL of saturated aqueous $NaHCO_3$. The phases were separated and the organic layer dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue was chromatographed on 2.5 g of silica gel to afford 56.2 mg (87.7%) of the relatively unstable bis-silyl enol ether as a colorless oil: R_f= 0.63 (3:1 petroleum

ether/ether); IR ($CHCl_3$) 3000, 2960, 2900, 1750, 1650, 1495, 1475, 1410, 1385, 1300, 1265, 1170, 1100, 1040, 1020, 910, 860, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.02, 0.04 (2s, 18H, $(CH_3)_3Si$), 0.82 (d, 3H, CH_3CC, J= 7Hz), 1.18 (s, 21H, $(CH_3)_3C$, CH_3CO), 1.48 (s, 3H, CH_3), 2.1-2.2 (m, 1H, CHC), 3.35 (abx, 1H, HC<u>H</u>OC=O, J= 10Hz, 6Hz), 3.61 (abx, 1H, HC<u>H</u>OC=O, J= 10Hz, 5Hz), 4.3-4.5 (m, 4H, CH_2OCH_2Ph), 4.8-4.9 (m, 1H, CH=C), 5.3-5.5 (m, 2H, HCO), 7.26 (s, 5H, PhH).

(4,6ξ) 6,9-Anhydro-8-[(benzyloxy)methyl]-2,5,8,10-tetradeoxy-2-methyl-6-<u>C</u>-methyl-4,7-bis-<u>O</u>-(trimethylsilyl)-D-<u>glycero</u>-D-<u>threo</u>-decitol-4,7-diene (32). To a stirred solution of 5.8 mg (0.0086 mmol) of the above enol ether in 0.10 mL of THF at -78°C were added 5 μL of 1.6 M lithium tetrahydridoaluminate in THF. After 1 h the reaction mixture was allowed to warm to R.T. After 6 h, the reaction mixture was treated sequentially with 5 μL of water, 5 μL of 15% aqueous NaOH, and 15 μL of water. The solution was diluted with 10 mL of ether and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was chromatographed on 1 g of silica gel with ether to afford 2.8 mg (64.2%) of the diol **32** as a colorless oil: R_f= 0.46 (ether); IR ($CHCl_3$) 3470 (br), 3000, 2990, 2950, 2890, 1640, 1455, 1390, 1250, 1110, 1090, 1010,

910, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ0.03 (s, 18H, $(CH_3)_2Si$), 0.86 (d, 3H, CH_3CC, J= 7Hz), 1.15 (d, 3H, CH_3CO, J= 6Hz), 1.52 (s, 3H, CH_3), 1.8-2.2 (m, 3H, CHC, OH), 3.3-3.6 (m, CH_2O), 4.2-4.9 (m 6H, CHOH, HC=C, CH_2OCH_2Ph), 5.4-5.5 (m, 1H, HCOC), 7.28 (s, 5H, PhH).

(4,6,7,8ξ)-6,9-Anhydro-8-[(benzyloxy)methyl]-2,5,8,10-tetradeoxy-2-methyl-6-C-methyl-D-glycero-D-threo-decitol. To a stirred solution of 99.4 mg (0.1866 mmol) of the furanone **31** in 1.8 mL of THF at -78°C were added 0.36 mL of 1.6 M lithium tetrahydridoaluminate. After 1 h, the reaction mixture was allowed to warm to R.T. After 4 h total, the reaction mixture was treated sequentially with 18 μL of water, 18 μL of 15% aqueous NaOH and 54 μL of water. After 0.5 h, the resultant slurry was diluted with THF and filtered through a celite pad. The solvent was removed under reduced pressure to afford 75.8 mg (100+%) of the crude tetraol as a colorless oil which was not further purified: R_f= 0.14 (EtOAc); IR ($CHCl_3$) 3450 (br), 3005, 2990, 2940, 2880, 1455, 1380, 1245, 1075, 1040, 840 cm^{-1}. ^1H NMR ($CDCl_3$) δ0.90 (d, 3H, CH_3CC, J= 7Hz), 1.2-1.3 (m, 6H, CH_3), 1.7-1.9 (m, 2H, CCH_2C), 2.0-2.2 (m, 2H, CHC), 2.6-2.9 (m, 4H, OH), 3.4-4.1 (m, 8H, CH_2O, CHO), 4.52 (s, 2H, CH_2Ph), 7.28 (s, 5H, PhH).

(4,6,7,8ξ)-6,9-Anhydro-1,3-O-benzylidene-8-[(benzyloxy)methyl]-2,5,8,10-tetradeoxy-2-methyl-6-C-methyl-D-glycero-D-threo-decitol (33). To a stirred solution of 55.6 mg (0.15 mmol) of the above tetra-ol in 1mL of benzene were added 20 μL (0.20 mmol) of benzaldehyde and 2.0 mg (0.01 mmol) of p-toluenesulfonic acid. After 22 h, the reaction mixture was directly chromatographed on 10 g of silica gel with 3:2 ether/petroleum ether affording 38.7 mg (56.2%) of the mono-benzylidene acetal **33** as a colorless oil: R_f= 0.65 (ether); evaporative distillation 230°C (0.03 mm Hg); IR ($CHCl_3$) 3460 (br), 3010, 3000, 2960, 2890, 1475, 1260, 1120, 1055, 1040, 1015, 715 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.1-1.4 (m, 9H, CH_3), 1.5-2.4 (m, 6H, OH, CCH_2C, CHC), 3.5-4.2 (m, 8H, CH_2O, CHO), 4.45 (s, 2H, CH_2Ph), 5.42 (s, 1H, CHPh), 7.2-7.5 (m, 10H, PhH). Analysis calculated for $C_{27}H_{36}O_6$: C, 71.03; H, 7.95. Found: C, 71.03; H, 8.09.

(6,8ξ)-6,9-Anhydro-1,3-O-benzylidene-8-[(benzyloxy)methyl]-2,5,8,10-tetradeoxy-2-C-methyl-D-glycero-D-threo-4,7-decodiulose (34). To a stirred solution of 10 L (0.1146 mmol) of oxalyl chloride in 400 μL of dichloromethane at -78°C were added 10 μL (0.1409 mmol) of dimethylsulfoxide. After 10 min, a solution of 12.4 mg (0.0272 mmol) of the diol **33** in 400

μL of dichloromethane was added to the reaction mixture over 1.0 min. After 19 min, the reaction mixture was treated with 40 μL (0.2870 mmol) of triethylamine, allowed to warm to room temperature then diluted with 50 mL of ether and 2 mL of 1 N aqueous HCl. The phases were separated and the organic phase was extracted with 4 mL of saturated aqueous $NaHCO_3$. The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue on 1 g of silica gel with 1:1 petroleum ether/ether afforded 10.0 mg (81.3%) of the diketone **34** as a colorless oil: R_f= 0.31 (1:1 petroleum ether/ether); evaporative distillation 240-245°C (0.03 mm Hg); IR ($CHCl_3$) 3005, 2980, 2940, 2860, 1760, 1725, 1455, 1390, 1365, 1240, 1165, 1110, 1040, 1030, 1005, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.07, 1.16 (2d, 3H, CH_3CC, J=J'= 7.0Hz), 1.24 (s, 3H, CH_3), 1.38, 1.43 (2d, 3H, CH_3CO, J= 6.3Hz, J'= 5.6Hz), 2.0-2.1 (m, 1H, CHC), 2.6-2.7 (m, 1H, CHC=O), 2.92, 2.98 (2ab, 1H, HC<u>H</u>C=O, J= 18.4Hz, J'= 17.8Hz), 3.28, 3.32 (2ab, 1H, HC<u>H</u>C=O, J= 17.8Hz, J'= 18.4Hz), 3.6-4.4 (m, 6H, CH_2O, CHO), 4.54 (s, 2H, CH_2Ph), 5.47 (s, 1H, CHPh), 7.2-7.6 (m, 10H, PhH). Analysis calculated for $C_{27}H_{32}O_6$: C, 71.66; H, 7.13. Found: C, 71.55; H, 7.22.

(6,8ξ)-6,9-Anhydro-8-[(benzyloxy)methyl]-2,5,8,10-tetradeoxy-2-methyl-6-<u>C</u>-methyl-D-<u>glycero</u>-D-<u>threo</u>-4,7-

decodiulo-1,4-furano-3,7-pyranose (35). To a stirred solution of 6.9 mg (0.0153 mmol) of the diketone **34** in 0.15 mL of THF were added 0.05 mL of 10% aqueous HCl. After 5.5 h, the reaction mixture was diluted with 50 ml of ethyl acetate and solid K_2CO_3 was added to neutralize the acid. The solution was filtered and the solvent was removed under reduced pressure. The residue was chromatographed on 1 g of silica gel with 2:1 ether/petroleum ether to afford 4.0 mg (72.0%) of the bis-hemi-acetal **35** as a colorless oil: R_f= 0.26 (ether); evaporative distillation 160-165°C (0.02 mm Hg); IR ($CHCl_3$) 3540, 3005, 2970, 2940, 2880, 1450, 1380, 1135, 1105, 1060, 1005, 960, 905, 815, 690; ^1H NMR ($CDCl_3$) δ1.05, 1.13 (2d, 3H, CH_3CC, J=J'= 6.8Hz), 1.23, 1.28 (2s, 3H, CH_3), 1.33, 1.49 (2d, 3H, CH_3CO, J= 3.9Hz, J'= 6.1Hz), 2.0-2.4 (m, 6H, CHC, CH_2C, OH), 3.3-4.1 (m, 6H, CH_2O, CHO), 4.48, 4.50 (2ab, 1H, HC<u>H</u>Ph, J= 11.9Hz, J'= 12.4Hz), 4.57, 4.58 (2ab, 1H, HC<u>H</u>Ph, J= 12.4Hz, J'= 11.9Hz), 7.2-7.5 (m, 5H, PhH). Analysis calculated for $C_{20}H_{28}O_6$: C, 65.92; H, 7.74. Found: C, 66.15; H, 7.87.

(4,6,7,8ξ)-6,9-Anhydro-8-[(benzyloxy)methyl]-1-<u>O</u>-(<u>tert</u>-butyldiphenylsilyl)-2,5,8,10-tetradeoxy-2-methyl-6-<u>C</u>-methyl-D-<u>glycero</u>-D-<u>threo</u>-decitol. To a stirred solution of 39.2 mg (0.1064 mmol) of the crude tetra-ol in 1.0 mL

of dichloromethane were added 30.4 μL (0.1169 mmol) of tert-butylchlorodiphenylsilane and 26 mg (0.2128 mmol) of N',N'-dimethylaminopyridine. After 2.25 h, the reaction mixture was diluted with 50 mL of ether and 4 mL of 1 N HCl. The phases were separated and the organic phase was washed with 4 mL of saturated aqueous $NaHCO_3$. The organic phase was diluted with 50 mL of petroleum ether and dried ($NaSO_4$). The solvent was removed under reduced pressure to afford 60.9 mg (94.3%) of the desired crude silyl ether as a colorless oil: R_f= 0.32 (ether); IR ($CHCl_3$) 3865 (br), 3080, 3000, 2970, 2950, 2860, 1460, 1420, 1380, 1360, 1240, 1100, 1080, 900, 810, 790 cm^{-1}; ^1H NMR ($CDCl_3$) δ0.90 (s, 12H, $(CH_3)_3C$, CH_3CC), 1.1-1.2 (m, 6H, CH_3CO, CH_3), 1.5-2.1 (m, 4H, CCHC, CCH_2C), 2.8-3.1 (br s, 3H, OH), 3.3-4.0 (m, 8H, CH_2O, CHO), 4.52 (s, 2H, CH_2Ph), 7.2-7.7 (m, 15H, PhH). Analysis calculated for $C_{36}H_{50}O_6Si$: $(M+H)^+$, 607.3455. Found: $(M+H)^+$, 607.3471.

(4,6,7,8ξ)-6,9-Anhydro-8-[(benzyloxy)methyl]-1-O-(tert-butyldiphenylsilyl)-2,5,8,10-tetradeoxy-2-methyl-6-C-methyl-D-glycero-D-threo-decitol 3,4-cyclic carbonate (36). To a stirred solution of 60.9 mg (0.1003 mmol) of the above crude triol in 2.0 mL of pyridine were added 0.5 mL of a 1M solution of phosgene in benzene. After 30 min, the reaction mixture was diluted with 75 mL of

ether and 10 mL of 10% aqueous HCl. The phases were separated and the aqueous was washed with 40 mL of ether. The combined organics were diluted with 100 mL of petroleum ether and dried (Na_2SO_4). The solvents were removed under reduced pressure and the residue was chromatographed on 5 g of silica gel with 3:2 ether/petroleum ether to afford 32.1 mg (50.5%, 52.4% from furanone **31**, 80.6%/step) of the carbonate **36** as a colorless oil: R_f= 0.48, 0.43 (ether); IR ($CHCl_3$) 3600, 3010, 2990, 2950, 2870, 1810, 1460, 1430, 1380, 1190, 1010, 1000, 825, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ0.90 (d, 3H, CH_3CC, J= 7Hz), 1.01 (s, 9H, $(CH_3)_3C$), 1.1-1.3 (m, 6H, CH_3), 1.8-2.3 (m, 4H, CH_2C, CHC), 2.4-2.5 (m, 1H, OH), 3.4-4.3 (m, 6H, CHO, CH_2O), 4.50 (s, 2H, CH_2Ph), 4.9-5.1 (m, 2H, HCOC=OOCH), 7.2-7.7 (m, 15H, PhH). Analysis calculated for $C_{37}H_{48}O_7Si$: C, 70.22; H, 7.64. Found: C, 70.31; H, 7.62.

(4,6,8ξ)-6,9-Anhydro-8-[(benzyloxy)methyl]-1-O-(tert-butyldiphenylsilyl)-2,5,8,10-tetradeoxy-2-methyl-6-C-methyl-D-glycero-D-threo-deco-7-ulose 3,4-cyclic carbonate (37). To a stirred solution of 10 μL (0.1146 mmol) of oxalyl chloride in 0.40 mL of dichloromethane at -78°C were added 10 μL (0.1409 mmol) of dimethylsulfoxide. After 11 min, a solution of 9.7 mg (0.0153 mmol) of the alcohol **36** in 0.40 mL of

dichloromethane was added to the reaction mixture over 2 min. After 20 min, the reaction mixture was treated with 40 μL (0.2870 mmol) of triethylamine, allowed to warm to room temperature and then diluted with 30 mL of ether and 2 mL of 10% aqueous HCl. The phases were separated and the organic phase was extracted with 4 mL of saturated aqueous $NaHCO_3$. The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure to afford 9.0 mg (93.1%) of the ketone **37** as a colorless oil: R_f= 0.69 (ether); IR ($CHCl_3$) 3010, 2990, 2940, 2870, 1810, 1765, 1480, 1460, 1430, 1390, 1370, 1190, 1160, 1120, 915, 830, 810, 705, 620 cm^{-1}; ^1H NMR ($CDCl_3$) 0.91 (d, 3H, CH_3CC, J= 7Hz), 1.08 (s, 9H, $(CH_3)_3C$), δ1.2-1.7 (m, 8H, CH_3CO, CH_3, CCH_2C), 1.9-2.6 (m, 2H, CHC), 3.4-3.9 (m, 4H, CH_2O), 4.2-4.3 (m, 1H, CHO), 4.52 (s, 2H, CH_2Ph), 4.9-5.1 (m, 2H, CHOC=OOCH), 7.2-7.7 (m, 15H, PhH). Analysis calculated for $C_{37}H_{46}O_7Si$: C, 70.45; H, 7.35. Found: C, 70.41; H, 7.43.

(4,6,7,8ξ)-6,9-Anhydro-8-[(benzyloxy)methyl]-1-O-(tert-butyldiphenylsilyl)-2,5,8,10-tetradeoxy-3,4-O-isopropylidene-2-methyl-6-C-methyl-D-glycero-D-threo-decitol (38). To a stirred solution of 56.2 mg (0.0926 mmol) of the crude triol in 0.25 mL of acetone were added 45 μL of 0.1N p-toluenesulfonic acid in THF.

After 2.5 h, an additional 45 μL of acid solution were added. After 1 h, the reaction mixture was diluted with 40 mL of ether and 4 mL of saturated aqueous $NaHCO_3$. The phases were separated and the organic phase was diluted with 50 mL of petroleum ether and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue was chromatographed on 5 g of silica gel with 2:1 petroleum ether/ether to afford 29.4 mg (50%, 54% from furanone **31**) of the acetonide **38** as a colorless oil: R_f= 0.38 (1:1 petroleum ether/ether); IR ($CHCl_3$) 3480, 3010, 2980, 2940, 2870, 1460, 1430, 1390, 1380, 1260, 1120, 1030, 920, 880, 830, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ0.93 (d, 3H, CH_3CC, J= 7Hz), 1.10 (s, 9H, $(CH_3)_3C$), 1.1-1.3 (m, 6H, CH_3CO, CH_3), 1.40 (s, 6H, $(CH_3)_2C$), 1.5-2.2 (m, 4H, CCH_2C, CHC), 3.4-4.3 (m, 9H, CH_2O, CHO, OH), 4.53 (s, 2H, CH_2Ph), 7.2-7.7 (m, 15H, PhH). Analysis calculated for $C_{39}H_{54}O_6Si$: C, 72.41; H, 8.41. Found: C, 72.45; H, 8.37.

(4,6,8ξ)-6,9-Anhydro-8-[(benzyloxy)methyl]-1-O-(tert-butyldiphenylsilyl)-2,5,8,10-tetradeoxy-3,4-O-isopropylidene-2-methyl-6-C-methyl-D-glycero-D-threo-deco-7-ulose (39). To a stirred solution of 10 μL (0.1146 mmol) of oxalyl chloride in 0.4 mL of dichloromethane at -78°C were added 10 μL (0.1409 mmol) of dimethylsulfoxide. After 11 min, a solution of 16.6

mg (0.0257 mmol) of the alcohol **38** in 0.4 mL of dichloromethane was added to the reaction mixture over 1.5 min. After 23 min, the reaction mixture was treated with 40 μL (0.2870 mmol) of triethylamine, allowed to warm to room temperature and then diluted with 30 mL of ether and 2 mL of 10% aqueous HCl. The phases were separated and the organic phase was extracted with 6 mL of saturated aqueous $NaHCO_3$. The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue on 1 g of silica gel with 4:1 petroleum ether/ether afforded 13.7 mg (82.7%) of the ketone **39** as a colorless oil: R_f= 0.47 (1:1 petroleum ether/ether); IR ($CHCl_3$) 3010, 3000, 2980, 2940, 2870, 1760, 1460, 1430, 1390, 1380, 1230, 1180, 1115, 1030, 830, 705 cm^{-1}; ^1H NMR ($CDCl_3$) δ0.93 (d, 3H, CH_3CC, J= 7Hz), 1.04 (s, 9H, $(CH_3)_3C$), 1.1-1.3 (m, 6H, CH_3CO, CH_3), 1.31, 1.40 (2s, 6H, $(CH_3)_2C$), 1.45-1.7 (m, 3H, CCH_2C, CHC), 2.0-2.2 (m, 1H, CHC=O), 3.28 (d, 2H, CH_2OSi, J= 5Hz), 3.60 (t, 2H, CH_2OBn, J= 5Hz), 3.9-4.3 (m, 3H, CHO), 4.48 (s, 2H, CH_2Ph), 7.2-7.7 (m, 15H, PhH); irradiation at 2.1 collapsed the triplet at 3.60. Analysis calculated for $C_{39}H_{52}O_6Si$: C, 72.63; H, 8.13. Found: C, 72.47; H, 8.18.

(4,6,8ξ)-6,9-Anhydro-8-[(benzyloxy)methyl]-1-O-(tert-butyldiphenylsilyl)-2,5,8,10-tetradeoxy-2-methyl-6-C-

methyl-D-glycero-D-threo-deco-7-ulo-7,3-furanose (40). To a stirred solution of 8.2 mg (0.0127 mmol) of the ketone **39** in 0.4 mL of methanol were added 0.1 mL of 10% aqueous HCl. After 1.5 h, the reaction mixture was diluted with 25 mL of ethyl acetate and $NaHCO_3$ was added. After filtration, the solvent was removed under reduced pressure and the residue was chromatographed on 1 g of silica gel with 2:1 petroleum ether/ether to afford 7.4 mg (96.2%) of the hemi-ketal **40** as a colorless oil: R_f= 0.18 (1:1 petroleum ether/ether); IR ($CHCl_3$) 3560 (br), 3010, 2980, 2940, 2870, 1450, 1435, 1385, 1110, 1040, 820, 705 cm^{-1}; ^1H NMR ($CDCl_3$) 400 MHz δ0.93 (d, 3H, CH_3CC, J= 7.1Hz), 0.98 (s, 9H, $(CH_3)_3C$), 1.11 (d, 3H, CH_3CO, J= 6.1Hz), 1.26 (s, 3H, CH_3), 1.6-2.2 (m, 5H, CCH_2C, CHC, OH), 2.77 (bs, 1H, OH), 3.4-3.9 (m, 6H, CH_2O, CHO), 4.23 (q, 1H, CHO, J= 7.1Hz), 4.50 (ab, 1H, HCHPh, J= 11.6 Hz), 4.52 (ab, 1H, HCHPh, J= 11.6Hz), 7.2-7.7 (m, 15H, PhH). Analysis calculated for $C_{36}H_{48}O_6Si$: $(M+H)^+$, 605.3300. Found: $(M+H)^+$, 605.3298.

(4,6,8ξ)-6,9-Anhydro-8-[(benzyloxy)methyl]-1-O-(tert-butyldiphenylsilyl)-2,5,8,10-tetradeoxy-2-methyl-6-C-methyl-D-glycero-L-glycero-3,7-decodiulo-7,3-furanose. To a stirred solution of 10 μL (0.1146 mmol) of oxalyl chloride in 0.40 mL of dichloromethane at -78°C were

added 10 μL (0.1409 mmol) of dimethylsulfoxide. After 10 min, a solution of 2.1 mg (0.0035 mmol) of the hemiketal **40** in 0.40 mL of dichloromethane was added to the reaction mixture over 1 min. After 21 min, the reaction mixture was treated with 40 μL (0.2870 mmol) of triethylamine, allowed to warm to room temperature and then diluted with 30 mL of ether and 3 mL of 10% aqueous HCl. The phases were separated and the organic phase was extracted with 6 mL of saturated aqueous $NaHCO_3$. The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue on 1 g of silica gel with 4:1 petroleum ether/ether afforded 1.6 mg (76.2%) of the acyclic ketone as a colorless oil: R_f= 0.61 (1:1 petroleum ether/ether); IR ($CHCl_3$) 2980, 2950, 2870, 1730, 1460, 1430, 1390, 1260, 1110, 1010, 820, 710 cm^{-1}; ^1H NMR ($CDCl_3$) 400 MHz δ0.8-1.0 (m, 3H, CH_3CC), 1.01 (s, 9H, $(CH_3)_3C$), 1.1-1.5 (m, 6H, CH_3CO, CH_3), 1.9-2.0 (m, 1H, CHC), 2.32 (d, 2H, CCH_2C, J= 8.2Hz), 2.4-2.5 (m, 1H, OH), 3.0-3.2 (m, 1H, CHC=O), 3.51 (dd, 1H, J= 9.9Hz, 5.5Hz), 3.70 (dd, 1H, J= 9.3Hz, 8.6Hz), 3.81 (t, 1H, J= 9.1Hz), 3.92 (dd, 1H, J= 9.6Hz, 5.9Hz), 4.05 (dd, 1H, J= 9.6Hz, 4.4Hz), 4.52 (ab, 1H, HC<u>H</u>Ph, J= 12.6Hz), 4.56 (ab, 1H, HC<u>H</u>Ph, J= 12.6Hz), 4.72 (t, 1H, CHC=O, J= 8.2Hz), 7.2-7.7 (m, 15H, PhH). Analysis calculated for $C_{36}H_{46}O_6Si$: $(M-OH)^+$, 585.3036. Found: $(M-OH)^+$, 585.3037.

(4,6,7,8ξ)-6,9-Anhydro-7-O-benzyl-1,3-O-benzylidene-8-[(benzyloxy)methyl]-2,5,8,10-tetradeoxy-2-methyl-8-C-methyl-D-glycero-D-threo-decitol. To a stirred solution of 11.2 mg (0.0245 mmol) of the diol **33** in 0.10 mL of N,N-dimethylformamide were added 9.5 mg (0.0620 mmol) of barium oxide, 2.5 mg (0.0146 mmol) of barium hydroxide and 3.6 μL (0.0303 mmol) of benzyl bromide. After 0.5 h at room temperature, the reaction mixture was warmed to 40°C. After 22 h, to the reaction mixture were added 7.2 μL (0.0606 mmol) of benzyl bromide, 9.5 mg (0.0620 mmol) of barium oxide and 2.5 mg (0.0146 mmol) of barium hydroxide. After 12 h more, the reaction mixture was diluted with 50 mL of dichloromethane and 5 mL of saturated aqueous $NaHCO_3$. The phases were separated and the aqueous phase was extracted with 40 mL of ether. The combined organics were dried (Na_2SO_4) and concentrated under reduced pressure. The residue was chromatographed on 1 g of silica gel with 4:1 petroleum ether/ether then 1:1 petroleum ether/ether to afford 9.9 mg (73.8%) of mono-benzylated product. Further elution afforded 2.6 mg of starting material (96.1% based on unrecovered starting material). The product was a colorless oil: R_f= 0.27 (1:1 ether/petroleum ether); evaporative distillation 240-245°C (0.02 mm Hg); IR ($CHCl_3$) 3460, 3005, 2970, 2930, 2860, 1450, 1385, 1360,

1240, 1110, 1030, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ0.8-1.0 (m, 3H, CH_3CC), 1.15 (s, 3H, CH_3), 1.19 (d, 3H, CH_3CO, J= 7Hz), 1.4-2.2 (m, 5H, CCH_2C, CCHC, OH), 3.4-4.1 (m, 8H, CH_2O, CHO), 4.33 (ab, 1H, HCHPh, J= 12Hz), 4.36 (ab, 1H, HCHPh, J= 6Hz), 4.49 (ab, 1H, HCHPh, J= 6Hz), 4.54 (ab, 1H, HCHPh, J= 12Hz), 5.47 (s, 1H, CHPh), 7.2-7.5 (m, 15H, PhH). Analysis calculated for $C_{34}H_{42}O_6$: C, 74.70; H, 7.74. Found: C, 74.87; H, 7.80.

(6,7,8ξ)-6,9-Anhydro-7-O-benzyl-1,3-O-benzylidene-8-[(benzyloxy)methyl]-2,5,8,10-tetradeoxy-2-methyl-8-C-methyl-D-glycero-D-threo-deco-4-ulose. To a stirred solution of 10 μL (0.1146 mmol) of oxalyl chloride in 0.40 mL of dichloromethane at -78°C were added 10 μL (0.1409 mmol) of dimethylsulfoxide. After 15 min, a solution of 3.5 mg (0.0064 mmol) of the above alcohol in 0.40 mL of dichloromethane was added to the reaction mixture over 1 min. After 22 min, the reaction mixture was treated with 40 μL (0.2870 mmol) of triethylamine, allowed to warm to room temperature and then diluted with 50 mL of ether and 6 mL of 10% aqueous HCl. The phases were separated and the organic phase was extracted with 10 mL of saturated aqueous $NaHCO_3$. The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue on 1 g of silica gel with 4:1 petroleum ether/ether afforded

2.6 mg (74.6%) of the acyclic ketone as a colorless oil: R_f= 0.36 (1:1 ether/petroleum ether); IR ($CHCl_3$) 3005, 2965,. 2860, 1720, 1455, 1390, 1360, 1115, 1040, 1030, 1010, 700 cm^{-1}; ^1H NMR ($CDCl_3$) 400MHz δ0.97, 1.08 (2d, 3H, CH_3CC, J=J'= 7.0Hz), 1.23 (s, 3H, CH_3), 1.24, 1.29 (2d, 3H, CH_3CO, J=J'= 6.2Hz), 1.9-2.2 (m, 2H, CHC), 2.66 (ab, 1H, HC<u>H</u>C=O, J= 17.0Hz), 2.99 (ab, 1H, HC<u>H</u>C=O, J= 17.0Hz), 3.39 (abx, 1H, HC<u>H</u>OCO, J= 9.8Hz, 5.4Hz), 3.44 (abx, 1H, HC<u>H</u>OCO, J= 9.8Hz, 4.3Hz), 3.82, 3.85 (2d, 1H, CHOBn, J= 6.2Hz, J'= 6.0Hz), 3.99 (abx, 0.66H, HC<u>H</u>OBn, J= 12.5Hz, 1.4Hz), 4.00 (d, 0.66H, CH_2OBn, J= 6.7Hz), 4.04 (abx, 0.66H, HC<u>H</u>OBn, J= 12.5Hz, 2.5Hz), 4.20 (d, 1H, CHC=O, J= 2.7Hz), 4.2-4.3 (m, 1H, CHOC), 4.33 (ab, 1H, HC<u>H</u>Ph, J= 11.9Hz), 4.38 (ab, 1H, HC<u>H</u>Ph, J= 11.9Hz), 4.52 (ab, 1H, HC<u>H</u>Ph, J= 12.1Hz), 4.63 (ab, 1H, HC<u>H</u>Ph, J= 12.1Hz), 7.2-7.6 (m, 15H, PhH). Analysis calculated for $C_{34}H_{40}O_6$: $(M+H)^+$, 545.2905. Found: $(M+H)^+$, 545.2880.

(4,6,7,8ξ)-6,9-Anhydro-7-<u>O</u>-benzyl-1,3-<u>O</u>-benzylidene-8-[(benzyloxy)methyl]-2,5,8,10-tetradeoxy-2-methyl-6-<u>C</u>-methyl-D-<u>glycero</u>-D-<u>threo</u>-decitol pivaloate (41). To a stirred solution of 19.1 mg (0.0349 mmol) of the above alcohol in 0.20 mL of dichloromethane were added 8.6 μL (0.0713 mmol) of pivaloyl chloride and 12.8 mg (0.1048 mmol) of N',N'-dimethylaminopyridine. After 20 h, a further 4.3 μL (0.356 mmol) of pivaloyl chloride and 6.4

mg (0.0524 mmol) of N',N'-dimethylaminopyridine were added. After 8 h, the reaction mixture was diluted with 120 mL of ether and 5 mL of 10% aqueous HCl. The phases were separated and the organic was extracted with 10 mL of saturated aqueous $NaHCO_3$. The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography on 5 g of silica gel with 2:1 petroleum ether/ether afforded 16.4 mg (74.5%) of the desired ester **41** as a colorless oil: R_f= 0.54 (1:1 petroleum ether/ether); IR ($CHCl_3$) 2980, 2940, 2870, 1730, 1460, 1380, 1295, 1175, 1120, 770, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.1-1.3 (m, 18H, CH_3), 1.6-2.2 (m, 4H, CCHC, CCH_2C), 3.4-4.1 (m, 7H, CH_2O, CHO), 4.40 (ab, 1H, HC<u>H</u>Ph, J= 12Hz), 4.44 (s, 2H, CH_2Ph), 4.50 (ab, 1H, HC<u>H</u>Ph, J= 12Hz), 5.26 (dt, 1H, HCOC=O, J= 1.5Hz, 8Hz), 5.49 (s, 1H, HCPh), 7.2-7.5 (m, 15H, PhH). Analysis calculated for $C_{39}H_{50}O_7$: C, 74.26; H, 7.99. Found: C, 74.34; H, 7.99.

(4,6,7,8ξ)-6,9-Anhydro-7-<u>O</u>-benzyl-8-[(benzyloxy)methyl]-2,5,8,10-tetradeoxy-2-methyl-6-<u>C</u>-methyl-D-<u>glycero</u>-D-<u>threo</u>-decitol pivaloate. To a stirred solution of 54.2 mg (0.0859 mmol) of the ester **41** in 0.75 ml of THF at 50°C were added 0.25 ml of 10% aqueous HCl. After 26 h, the reaction was diluted with 100 mL of ether and 10 mL of 2% aqueous HCl. The phases were separated and the

aqueous phase was extracted with 100 mL of ether. The combined organics were diluted with 150 mL of petroleum ether and dried (Na_2SO_4). The solvent was removed under reduced pressure to afford the crude diol which was not purified, but used directly in the next reaction: R_f= 0.07 (1:1 petroleum ether/ether); IR ($CHCl_3$) 3400 (br), 3005, 2985, 2950, 2880, 1725, 1480, 1455, 1400, 1375, 1280, 1160, 1105, 1030, 970, 700 cm^{-1}; ^1H NMR ($CDCl_3$) 200MHz δ0.85, 0.91 (2d, 3H, CH_3CC, J=J'= 7.1Hz), 1.15 (s, 9H, $(CH_3)_3C$), 1.1-1.3 (m, 6H, CH_3C), 1.6-2.1 (m, 4H, CCH_2C, CCHC), 2.6-3.1 (br s, 2H, OH), 3.3-4.1 (m, 7H, CH_2O, CHO), 4.2-4.4 (m, 4H, CH_2Ph), 4.8-5.0 (m, 1H, HCOC=O), 7.2-7.4 (m, 10H, PhH).

(4,6,7,8ξ)-6,9-Anhydro-7-O-benzyl-8-[(benzyloxy)methyl]-2,5,8,10-tetradeoxy-1,3-O-isopropylidene-2-methyl-6-C-methyl-D-glycero-D-threo-decitol pivaloate. To a stirred solution of the above crude diol in 0.80 mL of acetone were added 0.10 mL (0.813 mmol) of dimethoxypropane and 0.10 mL of a 0.1 M solution of p-toluenesulfonic acid in THF. After 6 h, the reaction mixture was diluted with 100 mL of ether and 5 mL of saturated aqueous $NaHCO_3$. The phases were separated and the organic phase was dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was chromatographed on 5 g of silica gel with 4:1 petroleum

ether/ether to afford 31.8 mg (70%) of the desired acetonide as a colorless oil: R_f= 0.59 (1:1 ether/petroleum ether); IR ($CHCl_3$) 3010, 2990, 2950, 2880, 1730, 1490, 1450, 1385, 1360, 1280, 1240, 1150, 1110, 1040, 1020, 940, 840, 700 cm^{-1}; ^1H NMR ($CDCl_3$) 200MHz δ1.09 (d, 3H, CH_3CC, J=7.2Hz), 1.15 (s, 9H, $(CH_3)_3C$), 1.1-1.4 (m, 12H, CH_3), 1.6-2.1 (m, 4H, CCH_2C, CCHC), 3.2-4.1 (m, 7H, CH_2O, CHO), 4.4-4.6 (m, 4H, CH_2Ph), 5.09 (dt, 1H, CHOC=O, J= 1.5Hz, 8.0Hz), 7.2-7.4 (m, 10H, PhH). Analysis calculated for $C_{35}H_{50}O_7$: C, 72.13; H, 8.65. Found: C, 72.19; H, 8.71.

(4,6,7,8ξ)-6,9-Anhydro-2,5,8,10-tetradeoxy-8-hydroxymethyl-1,3-O-isopropylidene-2-methyl-6-C-methyl-D-glycero-D-threo-decitol 4-pivaloate (42). To a stirred solution of 28.7 mg (0.0492 mmol) of the above ester in 2.0 mL of ethyl acetate were added 10 μL of acetic acid and 20 mg of 10% palladium on carbon. The reaction mixture was stirred vigorously under a hydrogen atmosphere for 7 h. The catalyst was removed by filtration and the solvent was removed under reduced pressure. The residue was chromatographed on 1 g of silica gel with ether to afford 17.9 mg (90.4%) of the diol **42** as a colorless oil: R_f= 0.14 (ether); evaporative distillation 170°C (0.03 torr); IR ($CHCl_3$) 3500 (br), 2980, 2940, 2880, 1730, 1480, 1460, 1385,

1280, 1165, 1080, 1035, 1010 cm^{-1}; ^1H NMR ($CDCl_3$) 200MHz δ0.84 (d, 3H, CH_3CC, J= 7.0Hz), 1.02 (d, 3H, CH_3CO, J= 6.4Hz), 1.2-1.6 (m, 18H, CH_3), 1.9-2.4 (m, 6H, CCH_2C, CCHC, OH), 3.3-4.4 (m, 7H, CH_2O, CHO), 5.10 (apparent t, 1H, CHOC=O, J=8Hz). Analysis calculated for $C_{21}H_{38}O_7$: C, 62.66; H, 9.52. Found: C, 62.56; H, 9.55.

(4,6,7,8ξ)-6,9-Anhydro-8-[(tert-butyldiphenylsilyloxy)methyl]-2,5,8,10-tetradeoxy-1,3-O-isopropylidene-2-methyl-6-C-methyl-D-glycero-D-threo-decitol 4-pivaloate. To a stirred solution of 13.6 mg (0.0338 mmol) of **42** in 0.50 mL of dichloromethane were added 17.6 μL (0.0676 mmol) of tert-butylchlorodiphenylsilane and 14.5 mg (0.1183 mmol) of N',N'-dimethylaminopyridine. After 2.25 h, the reaction mixture was diluted with 100 mL of ether and 4 mL of 10% aqueous HCl. The phases were separated and the organic phase was extracted with 8 mL of saturated aqueous $NaHCO_3$ then dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was chromatographed on 1 g of silica gel with 4:1 petroleum ether/ether to afford 19.8 mg (91.4%) of the desired silyl ether as a colorless oil: R_f= 0.40 (1:1 petroleum ether/ether); IR ($CHCl_3$) 3500, 3000, 2980, 2940, 2870, 1730, 1460, 1430, 1380, 1280, 1160, 1110,

1000, 820, 700 cm^{-1}; ^1H NMR ($CDCl_3$) 200MHz δ0.73 (d, 3H, CCH_3C, J=7.0Hz), 0.9-1.5 (m, 30H, CH_3), 1.7-2.1 (m, 4H, CCH_2C, CCHC), 1.80 (br s, 1H, OH), 3.3-4.4 (m, 7H, CH_2O, CHO), 4.96 (apparent t, 1H, CHOC=O, J= 8Hz), 7.3-7.7 (m, 10H, PhH). Analysis calculated for $C_{37}H_{56}O_7Si$: C, 69.34; H, 8.81. Found: C, 69.27; H, 8.97.

(4,6,8ξ)-6,9-Anhydro-8-[(tert-butyldiphenylsilyloxy)methyl]-2,5,8,10-tetradeoxy-1,3-O-isopropylidene-2-methyl-6-C-methyl-D-glycero-D-threo-7-decoulose pivaloate (43). To a stirred solution of 10 μL (0.1146 mmol) of oxalyl chloride in 0.40 mL of dichloromethane at -78° were added 10 μL (0.1409 mmol) of dimethylsulfoxide. After 10 min, a solution of 13.8 mg (0.0215 mmol) of the above alcohol in 0.40 mL of dichloromethane was added to the reaction mixture over 1.5 min. After 20 min, the reaction mixture was treated with 40 μL (0.2870 mmol) of triethylamine, allowed to warm to room temperature and then diluted with 100 mL of ether and 4 mL of 10% aqueous HCl. The phases were separated and the organic phase was extracted with 8 mL of saturated aqueous $NaHCO_3$. The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue on 1 g of silica gel with 9:1 petroleum ether/ether afforded 13.3 mg (96.7%) of the ketone **43** as a colorless oil: R_f= 0.55 (1:1

petroleum ether/ether); IR ($CHCl_3$) 3000, 2980, 2940, 2870, 1760, 1730, 1480, 1460, 1425, 1380, 1280, 1160, 1110, 1005, 830, 700 cm^{-1}; ^1H NMR ($CDCl_3$) 200MHz δ0.71, 0.83 (2d, 3H, CH_3CC, J=J'= 6.5Hz), 1.00 (s, 9H, $(CH_3)_3CSi$), 1.09 (d, 3H, CH_3CO, J= 6.1Hz), 1.16 (s, 9H, $(CH_3)_3CC=O$), 1.22, 1.30 (2s, 6H, $(CH_3)_2C$), 1.37, 1.40 (2s, 3H, CH_3), 1.9-2.4 (m, 4H, CCH_2C, CCHC), 3.2-4.4 (m, 6H, CH_2O, CHO), 5.08 (m, 1H, CHOC=O), 7.3-7.7 (m, 10H, PhH). Analysis calculated for $C_{37}H_{54}O_7Si$: $(M+H)^+$, 639.3717. Found: $(M+H)^+$, 639.3705.

1,7:6,9-Dianhydro-8-[(tert-butyldiphenylsiloxy)methyl]-2,5,8,10-tetradeoxy-2-methyl-6-C-methyl-α-D-threo-D-ido-7-decoulo-7,3-pranose pivaloate (44). To a stirred solution of 10.1 mg of the ketone **43** in 0.5 mL THF were added 0.17 mL of 10% aqueous HCl. After 1 h, the reaction mixture was diluted with 50 mL of ether and 6 mL of 3% aqueous HCl. The phases were separated and the aqueous phase was extracted with 50 mL of ether. The combined organics were diluted with 75 mL of petroleum ether and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue was chromatographed on 1 g of silca gel with a solvent gradient starting with 3:1 petroleum ether/ether and ending with ether to afford 3.3 mg (35.9%) of the ketal **44** as a colorless oil: R_f= 0.24 (1:1 petroleum ether/ether); IR ($CHCl_3$)

3000, 2980, 2870, 1730, 1460, 1380, 1280, 1140, 1110, 1080, 1050, 1030, 700 cm^{-1}; ^1H NMR ($CDCl_3$) 400 MHz δ0.89 (d, 3H, CH_3CC, J= 7.1Hz), 1.02 (d, 3H, CH_3CO, J= 6.1Hz), 1.05 (s, 9H, $(CH_3)_3CSi$), 1.15 (s, 9H, $(CH_3)_3CC=O$), 1.22 (s, 3H, CH_3), 1.89 (dddq, 1H, $CH_3C\underline{H}C$, J= 1.8Hz, 4.9Hz, 6.6Hz, 7.1Hz), 2.22 (dd, 1H, $HC\underline{H}CO$. J= 13.4Hz, 4.6Hz), 2.31 (dd, 1H, $HC\underline{H}CO$, J= 13.4Hz, 10.3Hz), 2.32 (dt, 1H, J= 10.0Hz, 6.4Hz), 3.56 (dq, 1H, CHO, J= 10.0Hz, 6.1Hz), 3.60 (dd, 1H, $HC\underline{H}O$, J= 9.8Hz, 4.9Hz), 3.66 (d, 2H, CH_2OSi, J= 6.4Hz), 4.03 (dd, 1H, $OC\underline{H}CHCH_3$, J= 10.3Hz, 1.8Hz), 4.09 (dd, 1H, $HC\underline{H}O$, J= 9.8Hz, 6.6Hz), 4.89 (dt, 1H, CHOC=O, J=4.6Hz, 10.3Hz), 7.4-7.5 (m, 6H, p-, m-PhH), 7.6-7.7 (m, 4H, o-PhH); irradiation at 0.89 collapses 1.89 to a ddd; irradiation at 1.02 collapses 3.56 to a d; irradiation at 4.89 collapses 2.22 to a d, 2.31 to a d and 4.09 to a d; NOE difference with irradiation at 1.22 enhances d at 0.89, dd at 2.22 and dt at 2.32; NOE difference with irradiation at 0.89 enhances s at 1.22. Analysis calculated for $C_{34}H_{48}O_6Si$: $(M+H)^+$, 581.3298. Found: $(M+H)^+$, 581.3294.

Further elution afforded 2.3 mg (24.3%) of a hemi-ketal: R_f= 0.17 (1:1 petroleum ether/ether); IR ($CHCl_3$) 3350, 2970, 2940, 2890, 2830, 1725, 1460, 1430, 1390, 1360, 1260, 1170, 1110, 1080, 1050, 700 cm^{-1}; ^1H NMR ($CDCl_3$) 400MHz δ0.88 (d, 3H, CH_3CC, J= 6.8Hz), 1.04 (s, 9H,

$(CH_3)_3CSi$), 1.05 (d, 3H, CH_3CO, J= 6.0Hz), 1.19 (s, 9H, $(CH_3)_3C$), 1.34 (s, 3H, CH_3), 1.88 (dd, 1H, HCHC, J= 13.4Hz, 6.8Hz), 2.13 (dd, 1H, HCHC, J= 13.4Hz, 7.3Hz), 2.16 (ddd, 1H, CHCO, J= 11.0Hz, 10.5Hz, 5.0Hz), 2.2-2.3 (m, 1H, $CHCH_3$), 3.0-3.1 (m, 3H, CH_2OH), 3.54 (dq, 1H, CHO, J= 10.5Hz, 6.0Hz), 3.61 (dd, 1H, HCHOSi, J= 11.0Hz, 9.5Hz), 4.03 (dd, 1H, HCHOSi, J= 9.5Hz, 5.0Hz), 4.23 (s, 1H, OCOH), 4.44 (ddd, 1H, CHOC=O, J= 8.5Hz, 7.3Hz, 6.8Hz), 5.03 (dd, 1H, CHO, J= 8.5Hz, 2.2Hz), 7.3-7.7 (m, 10H, PhH); irradiation at 1.05 collapses 3.54 to a d; irradiation at 4.03 collapses 3.61 to a d and 2.16 to a dd; irradiation at 4.44 collapses 1.88 to a d, 2.13 to a d and 5.03 to a d; irradiation at 5.03 collapses 4.44 to a d and 2.2-2.3 m; NOE difference with irradiation at 1.34 gave no definite enhancements. Analysis calculated for $C_{34}H_{50}O_7Si$: $(M-OH)^+$, 581.3298. Found: $(M-OH)^+$, 581.3311.

Further elution afforded 2.9 mg (30.6%) of a mixture of two additional compounds that were converted to a single compound by treatment with 0.1 N p-toluenesulfonic acid in $CHCl_3$. This material was again chromatographed on 0.5 g of silica gel with 2:1 petroleum ether/ether to afford 2.7 mg of a colorless oil: R_f= 0.16 (1:1 petroleum ether/ether); IR ($CHCl_3$) 3500, 2970, 2940, 2860, 1725, 1470, 1430, 1400, 1290, 1170, 1120, 1030,

700 cm^{-1}; ^1H NMR ($CDCl_3$) 400MHz δ1.02 (d, 3H, CH_3CC, J= 7.1Hz), 1.04 (s, 9H, $(CH_3)_3CSi$), 1.09 (d, 3H, CH_3CO, J= 5.9Hz), 1.19 (s, 9H, $(CH_3)_3CCO$), 1.30 (s, 3H, CH_3), 2.01 (abx, 1H, HCHCO, J= 13.2Hz, 8.4Hz), 2.10 (abx, 1H, HCHCO, J= 13.2Hz, 6.7Hz), 2.1-2.2 (m, 1H, $CHCH_2OSi$), 2.2-2.3 (m, 1H, $CHCH_3$), 2.94 (br s, 1H, OH), 3.62 (abx, 1H, HCH, J= 10.7Hz, 4.9Hz), 3.72 (dq, 1H, $OCHCH_3$, J= 5.0Hz, 5.9Hz) 3.75 (dd, 1H, CHO, J= 3.2Hz, 6.5Hz), 3.78 (abx, 1H, HCH, J= 10.7Hz, 10.0Hz), 3.87 (abx, 1H, HCH, J= 11.1Hz, 5.8Hz), 4.06 (abx, 1H, HCH, J= 11.1Hz, 6.5Hz), 4.36 (ddd, 1H, CHOC=O, J= 8.4Hz, 6.7Hz, 3.2Hz), 5.43 (s, 1H, COH), 7.3-7.8 (m, 10H, PhH); irradiation at 1.09 collapses 3.72 to a d; irradiation at 4.36 collapses 3.75 to a d and 2.2-2.3 m; NOE difference with irradiation at 1.30 gave no definite enhancements. Analysis calculated for $C_{34}H_{50}O_7Si$: $(M-OH)^+$, 581.3298. Found: $(M-OH)^+$, 581.3289.

To stirred solutions of each of these three products in acetone was added excess Jones reagent. The ketal **44** was not affected whereas the two hemi-ketals were both rapidly consumed.

References and Notes

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42. This acetonide was completely hydrolyzed in 1 h while the corresponding benzylidene acetal required

about 24 h at 50°C using the same mixture of 1:3 10% aqueous HCl/THF.

43. Two of the hemi-ketals could be converted under acid catalysis to a single compound (see experimental) which was also a hemi-ketal. Nuclear Overhauser effect experiments failed to provide information about the stereochemistry of this compound or the other hemi-ketal formed during the hydrolysis.

44. More complete verification would require that all possible stereoisomers at the centers in question be submitted to these reaction conditions. Since we were submitting a mixture of only 3 compounds (determined by the number of products), and could state the stereochemistry of only one of them (the ketal) with certainty, our result shows only that the desired configuration is relatively favorable.

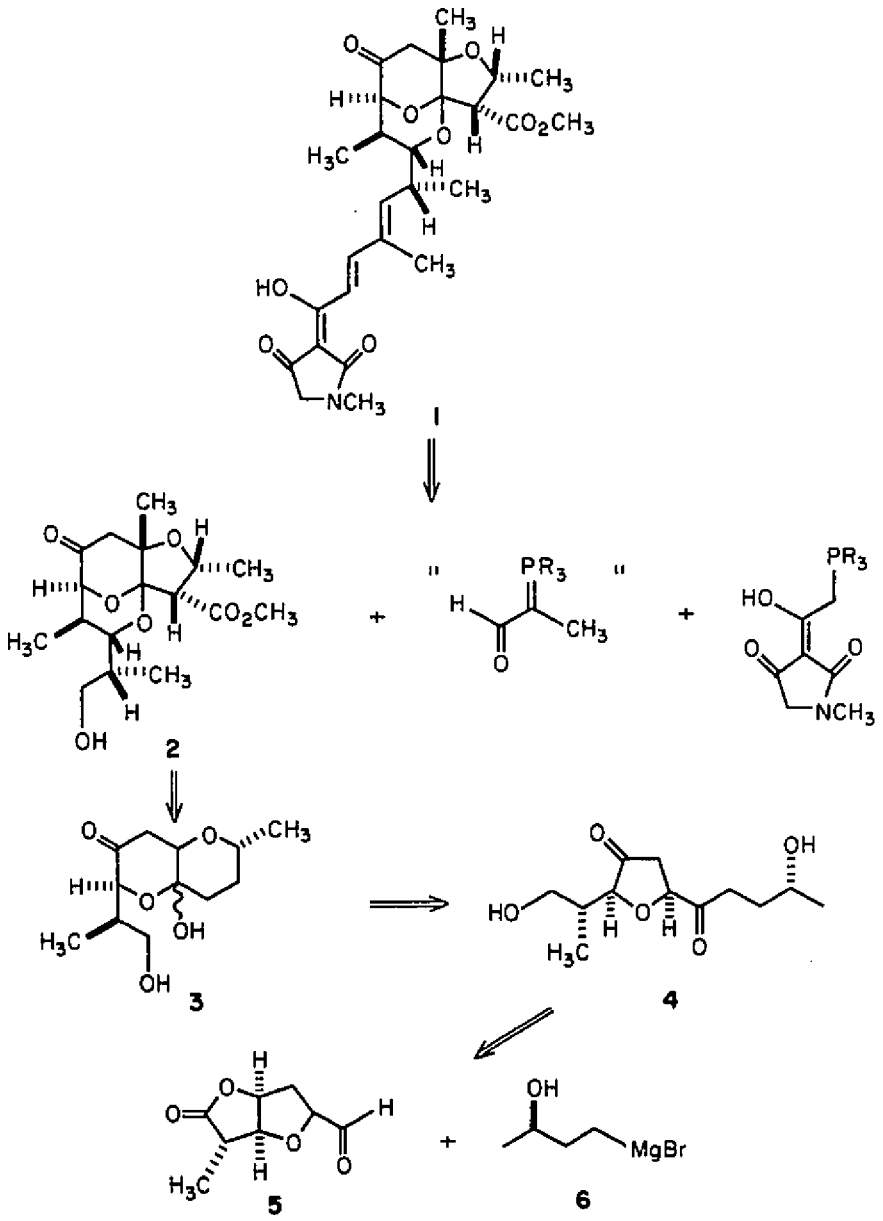
Appendix

The furan cleavage route to Bu-2313 (1).

Prior to the synthetic effort reported in the preceding section, an alternate, but conceptually similar approach was investigated. The key antithetic step is the conversion of **3** to **4** (Scheme I). This step is analogous to the closure of the enedione to the tetrahydrofuran in the preceding section and indeed was proposed to proceed through an intermediate enedione. The aim of the work reported here was to determine whether the linchpin reaction could be executed successfully.

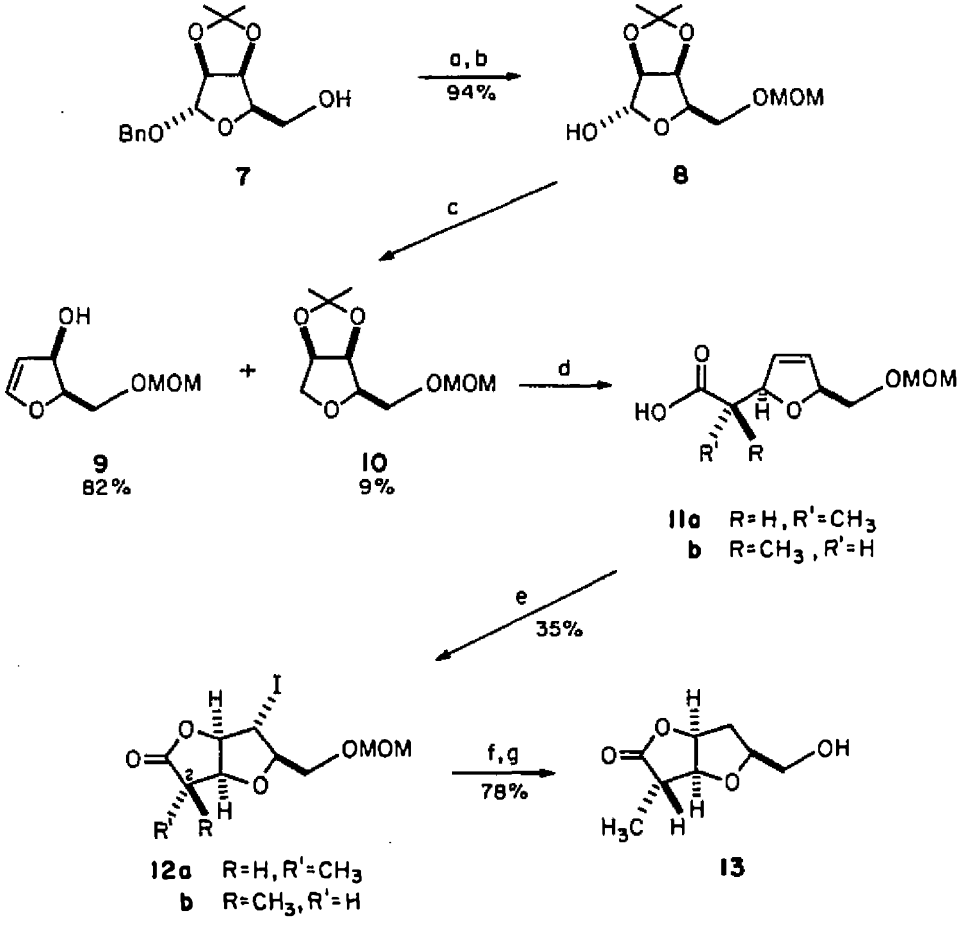
Protection of the known[1] alcohol **7** (Scheme II), prepared in 56% yield from D-mannose, as the methoxymethyl (MOM) ether proceeded only sluggishly using dimethoxymethane and P_2O_5, but went smoothly using chloromethylmethyl ether. Removal of the benzyl protecting group with lithium in ammonia afforded the desired hemi-acetal **8**. Formation of the glycal **9** proceeded according to literature precedent[2] through the intermediate furanosyl chloride. The glycal was esterified with propionyl chloride and n-butyllithium at low temperature then enolized in situ under conditions (LDA with 20% v/v HMPA) that favor formation of the E-enolate which was trapped as the Z-silyl ketene acetal

Scheme I Retrosynthetic Analysis for Bu-2313



with TMSCl. Warming to room temperature allowed the acetal to undergo a [3,3] sigmatropic rearrangement through a boat-like transition state[3] to afford, after aqueous workup, a 4:1 mixture (^{1}H NMR) of diastereomeric

Scheme II Synthesis of the Alcohol Precursor to 5[a]



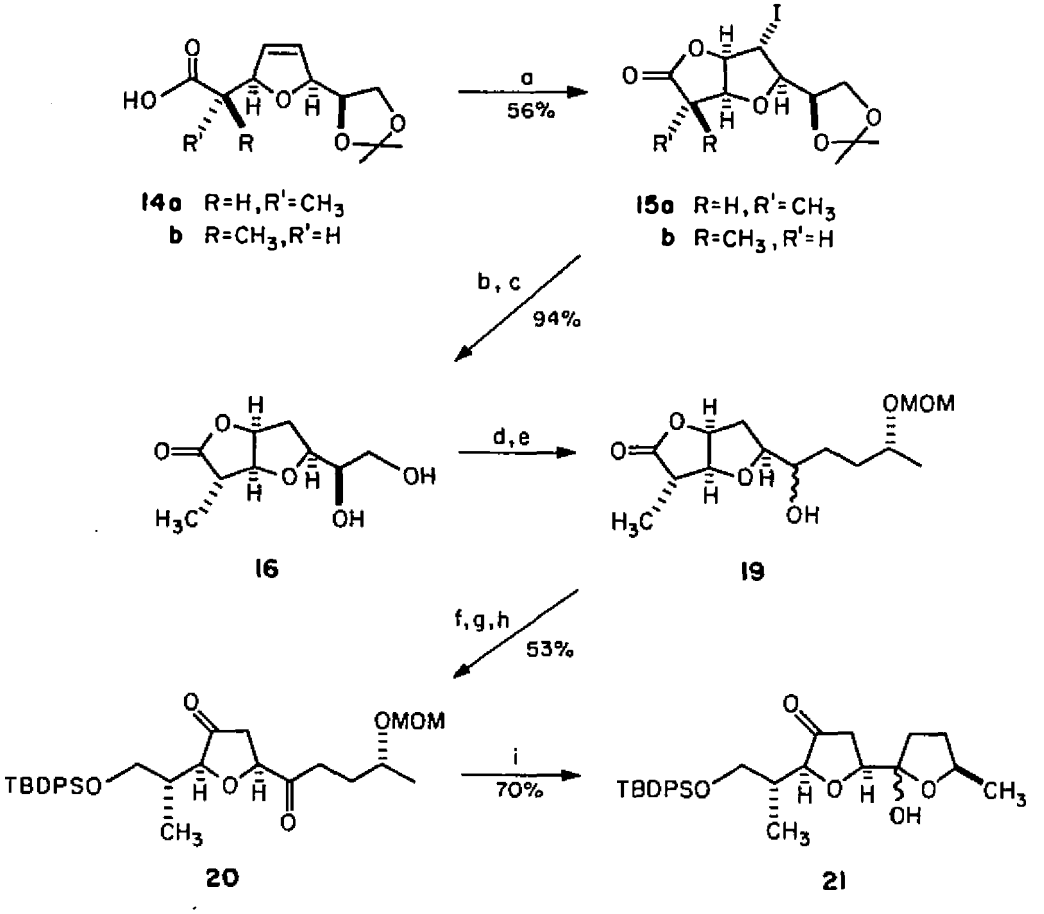
[a](a) MOMCl, $(i\text{-Pr})_2EtN$, CH_2Cl_2; (b) Li, NH_3, THF; (c) CCl_4, TDAP, THF; Li, NH_3; (d) n-BuLi, THF; propionyl chloride; LDA, HMPA, THF; TMSCl, Et_3N; 5% HCl; (e) Na_2CO_3, I_2, acetonitrile; (f) $(nBu)_3SnH$, MeOH; (g) 10% HCl, acetonitrile.

acids **11a,b** which normally were not separated from residual HMPA. Treatment of the crude mixture of acids and residual HMPA with I_2 and Na_2CO_3 in acetonitrile[4] afforded the iodolactones **12a,b.** These correspond to the mixture of acids, but in ratios that varied from 8:1 (**12a:12b**) up to exclusively **12a.** This enhancement of the diastereomeric ratio is most probably the result of a simple kinetic resolution. In **12b,** the C2 methyl group is on the endo face of the bicyclic structure and would appear to cause unfavorable steric interactions which would not exist in **12a** in which the C2 methyl group is on the exo face. This interaction would begin to be significant in the transition state and effects the relative transition state energies, causing **12a** to be formed more rapidly than **12b.** The variations in the ratio observed were due to differences in reaction length and concentration and generally followed the expected trend of lower ratio (**12a:12b**) with more advanced reaction. De-iodination with tri-n-butyltin hydride under conditions of rigorous oxygen exclusion followed by acidic cleavage of the MOM ether afforded the alcohol **13.** Unfortunately, no method of oxidation was found that provided aldehyde **5** in usable purity. Among those oxidations attempted were: Swern in various solvents,[5] buffered PCC,[6] SO_3:Pyr in DMSO,[7] and Collins.[8]

A solution to this problem was suggested by the manner in which mannose was converted to the alcohol **7**. The last transformation on the path to **7** is a periodate cleavage of a vicinal diol to an aldehyde then $NaBH_4$ reduction of this carbonyl to the alcohol. Since these reactions proceeded in high yield we proposed to unmask the aldehyde from a diol after the Claisen rearrangement and lactone formation.

The acids **14a,b** (Scheme III) were obtained as a 3:2 mixture according to literature procedure.[9] This ratio was obtained using either LDA in THF/HMPA or LiHMDSA in THF as the enolizing agent. Submission of this crude mixture with HMPA present to iodolactonization[4] afforded the crystalline iodolactone **15a** as the sole product in 56% yield (^1H, ^{13}C NMR). Conversely, the crude acids without HMPA placed under identical reaction conditions afforded a 3:2 mixture of iodolactones **15a,b** in 95% yield. These results suggest that the reaction rate is lowered by HMPA in the reaction mixture. The HMPA may serve to stabilize ionic intermediates so that the lactonization is not as rapid a process and only the exo methyl group iodolactone forms to any noticeable degree after one hour. Without the stabilizing effect of HMPA, the reaction is much faster and both iodolactones form under the reaction conditions. Two experiments could be done to verify this hypothesis.

Scheme III Synthesis of a Protected 4



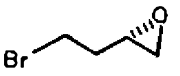
[a](a) Na_2CO_3, I_2, acetonitrile; (b) $(nBu)_3SnH$, MeOH; (c) 10% HCl, THF; (d) $NaIO_4$, H_2O, THF; (e) 18, THF; (f) LAH, ether; (g) TBDPSCl, DMAP, CH_2Cl_2; (h) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2; (i) TMSCl, $(Et)_4NBr$, CH_2Cl_2.

First, with HMPA present, the reaction could be allowed to proceed for an extended period of time. If the less favored iodolactone forms, then the hypothesis would be supported. Second, the iodolactonization in the absence of HMPA could be followed over much shorter intervals to

determine whether the kinetic differentiation also occurs under these conditions.

The iodolactone **15a**, obtained either as an exclusive product or by chromatographic separation from **15b**, was treated with tri-n-butyltin hydride to affect de-iodination, then with aqueous acid to cleave the acetonide. Treatment of the diol **16** with $NaIO_4$ in water/methanol afforded predominantly the methyl acetal of the desired aldehyde. Substitution of THF for methanol avoided this complication and provided the desired aldehyde in very good yield and purity, although it proved to be unstable to chromatography or storage for more than a few hours.

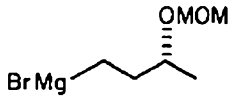
At this point, a chiral four carbon equivalent to **6** (Scheme I) was needed. The most obvious starting material for this purpose would be the biopolymer poly-(R)-3-hydroxybutyrate (PHB)[10] used in the previous section, but at the time of this work it was not commercially available and a more circuitous route was neccesary to obtain material with a high enantiomeric excess. The known epoxide **17**[11] is obtainable in about



17

50% yield over six steps from S-(-)-malic acid and contains the neccesary chirality and fuctionality. Careful reduction of **17** with lithium tetrahydridoaluminate (LAH) at low temperature followed by MOM ether formation afforded the desired Grignard precursor.

Attempted formation of the Grignard reagent **18** under standard conditions and trapping with an electrophile failed to provide any sign of the desired product. Presumably, the Grignard reagent is formed



18

which then cyclizes to the cyclopropane. This reaction of 3-halo ethers such as the substrate employed here is actually a general route to substituted cyclopropanes.[12] This undesired reaction was surpressed by forming the Grignard reagent through addition of the bromide to Rieke magnesium[13] at 0°C. Addition of the crude aldehyde described previously to this solution still at 0°C afforded the desired Grignard adduct **19** as a 1:1 mixture of diasteomers in 83% yield from the diol **16.** Shortly after this work was done, Rieke and coworkers[14] published a remarkably similar procedure to form similar

Grignard reagents.

The two diastereomers of **19** were separately reduced with LAH and the primary alchol then was protected selectively as the tert-butyldiphenylsilyl ether. The two diastereomeric diols were oxidized individually to afford a single diketone **20** proving that the diastereomers observed in **16** were epimeric at the secondary alcohol center formed in the Grignard reaction. The MOM ether was cleaved using trimethylsilyl bromide generated in situ according to the procedure of Woodward and coworkers[15] thereby affording the key retrosynthetic target **21** (a protected version of **4**).

Analysis of the desired ring opening shows it to be a retro-5-endo-trigonal reaction according to the Baldwin notation.[16] These are generally disfavored processes. However, it was hoped that if the desired reaction would not proceed under basic conditions, it would under protic or Lewis acid catalysis. Attempted equilibration of **21** to a protected version of **3** failed under all of these conditions, apparently because the tetrahydrofuran ring would not open. Bases provided only returned starting material although generation of enolates was verified by deuterium incorporation upon D_2O quenching. Attempted protic or Lewis acid catalyzed equilibration also provided only

returned starting material or, under forcing conditions, complete decomposition. Failure of this reaction prompted an abandonment of this route.

Experimental Section

Melting points were measured in a Hoover melting point apparatus and are uncorrected. Proton nuclear magnetic resonance spectra were recorded with a Varian EM-390 spectrometer at 90 MHz unless otherwise specified. 500 MHz refers to a spectrum recorded with a Bruker WM-500. Data are reported as follows: chemical shift in parts per million downfield from tetramethylsilane (multiplicity, integrated relative intensity, assignment, coupling constants). Carbon-13 nuclear magnetic resonance spectra were recorded with a Jeol FX-90Q. Optical rotations were measured with a Jasco DIP-181 polarimeter in a 1 dm cell of 1 mL capacity; chloroform for these measurements was filtered through activity III alumina immediately prior to use. Infrared spectra were recorded with a Perkin-Elmer 1310 spectrometer.

Reaction solvents and liquid reagents were purified by distillation or dried over appropriate agents prior to use. Reactions were run under an atmosphere of argon which had been dried by passage through a drying tower filled with anhydrous $CaSO_4$. Reaction flasks were flame dried when possible and always purged with argon and evacuated under high vacuum several times using a

manifold system. Syringes and reaction flasks were dried at least 12 h in an oven (120-140°C) and cooled in a desiccator over anhydrous $CaSO_4$ prior to use. Elemental analyses were performed by Spang Microanalytical Laboratory, Star Route 1, Box 142, Eagle Harbor, MI 49951.

Benzyl 2,3-O-isopropylidene-5-O-(methoxymethyl)-D-lyxo-furanoside. To a stirred solution of 83.3 g (0.297 mol) of the alcohol **7** in 800 mL of dichloromethane were added 51.7 mL (0.297 mol) of di-iso-propylethylamine and 22.6 mL (0.297 mol) of chloromethylmethyl ether. After 2.5 h, a further 25.9 mL (0.149 mol) of di-iso-propylethylamine and 11.3 mL (0.149 mol) of chloromethylmethyl ether were added. After 6.5 h, 70 mL of saturated aqueous $NaHCO_3$ were added. After 0.5 h, the mixture was diluted with 100 mL more of saturated aqueous $NaHCO_3$ and the organic phase was separated. The aqueous phase was extracted with two portions of 600 mL of ether. The combined organic extracts were dried ($MgSO_4$) and then concentrated under reduced pressure. Flash chromatography of the residue on 1 kg of silica gel with 8:2 petroleum ether/ether afforded 90.9 g (94%) of the desired ether as a colorless oil: R_f= 0.48 (1:1 petroleum ether/ether); $[\alpha]^{21}_D$= +65.4 (c 1.18, $CHCl_3$); IR ($CHCl_3$) 3000, 2940, 2890, 1455, 1385, 1375, 1210, 1110,

1085, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.30, 1.45 (2s, 6H, $(CH_3)_2C$), 3.37 (s, 3H, OCH_3), 3.92 (m, 2H, $C-CH_2-O$), 4.23-4.84 (m, 7H, CHO, $PhCH_2$, OCH_2O), 5.10 (s, 1H, OCHO), 7.28 (s, 5H, PhH). Analysis calculated for $C_{17}H_{24}O_6$: C, 62.95; H, 7.46. Found: C, 63.10; H, 7.52.

2,3-O-isopropylidene-5-O-(methoxymethyl)-D-lyxo-furanoside (8). To a stirred solution of 428 mg (61.6 mmol) of lithium in 110 mL of anhydrous ammonia at -78°C was added a solution of 10.0 g (30.8 mmol) of the above ether in 20 mL of tetrahydrofuran over 15 min. After an additional 15 min, dry NH_4Cl was added cautiously and the resulting colorless mixture was diluted with 100 mL of ether and the ammonia was allowed to evaporate. The slurry was filtered, then the solids were dissolved in minimal water. The aqueous phase was extracted with four portions of 150 mL of ether and the combined organic extracts dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue placed under high vacuum for 8 h, yielding 7.2 g (100%) of the crude lactol **8**. A portion of this alcohol was chromatographed on silica gel with 2:1 ether/petroleum ether to afford an analytically pure sample: R_f= 0.44 (ether); $[\alpha]_D^{21}$= +4.35 (c 0.46, $CHCl_3$); IR ($CHCl_3$) 3620, 3000, 2980, 2895, 1385, 1220, 1105, 1040, 865, 710 cm^{-1}; ^1H NMR ($CDCl_3$) 1.30, 1.45 (2s, 6H, $(CH_3)_2C$), 3.37 (s, 3H, OCH_3), 3.52

(br s, 1H, OH), 3.65-3.98 (m, 2H, CH_2), 4.26-4.85 (m, 5H, CHO, OCH_2O), 5.40 (s, 1H, OCHO). Analysis calculated for $C_{10}H_{18}O_6$: C, 51.27; H, 7.75. Found: C, 51.03; H, 7.73.

1,4-Anhydro-2-deoxy-5-O-(methoxymethyl)-D-threo-pent-1-enitol (9). To a stirred solution of 7.2 g (30.7 mmol) of the lactol **8** and 3.6 mL (37.3 mmol) of carbon tetrachloride in 100 mL of tetrahydrofuran at -78°C were added 5.9 mL (32.5 mmol) of tris(dimethylamino)phosphine. After 30 min, the reaction mixture was allowed to warm to room temperature. After 1 h, the reaction mixture was added to a stirred solution of 2.56 g (369 mmol) of lithium in 150 mL of anhydrous ammonia at -78°C over 10 min. After 20 min, dry NH_4Cl was added cautiously to the reaction mixture. The resulting colorless mixture was diluted with 200 mL of ether and the ammonia was allowed to evaporate. The resulting ethereal solution was filtered, then concentrated under reduced pressure. Flash chromatography on 140 g of silica gel with ether afforded 4.0 g (82%) of the glycal **9** as a colorless oil: R_f= 0.38 (ether); evaporative distillation 70°C (0.001 mm Hg); $[\alpha]_D^{21}$= -73.6 (c 0.52, $CHCl_3$); IR ($CHCl_3$) 3580, 3480, 3005, 2940, 2890, 2820, 1608, 1450, 1390, 1210, 1143, 1107, 1030, 927, 870, 740, 665 cm^{-1}; ^1H NMR

($CDCl_3$) δ1.95 (d, 1H, OH, J= 8Hz), 3.41 (s, 3H, OCH_3), 4.00, 4.02 (2d, 2H, CH_2O, J= 5Hz J'= 6Hz), 4.43 (ddd, 1H, CHO, J= 6Hz, 5.5Hz, 5Hz), 4.73 (s, 2H, OCH_2O), 4.92 (m, 1H, C=C-CHO), 5.28 (t, 1H, CH=C, J= 3Hz), 6.66 (d, 1H, CH=C, J= 3Hz). Analysis calculated for $C_7H_{12}O_4$: C, 52.49; H, 7.55. Found: C, 52.56; H, 7.63.

Methyl 2(R) and 2(S)-[2,5-dihydro-5(S)-(methoxymethyleneoxymethyl)-2(S)-furyl]-propanoate (11a,b). To a stirred solution of 1.52 g (9.5 mmol) of the glycal **9** in 32 mL of tetrahydrofuran at -78°C were added 3.61 mL (9.5 mmol) of a 2.63 M solution of n-butyllithium in hexanes and then, after 5 min, 0.87 mL (10.0 mmol) of propionyl chloride were added. After 15 min at 0°C, the solution was recooled to -78°C and 6.4 mL of hexamethylphosphorustriamide were added. The solution was added via cannula to a stirred solution of 11.4 mmol of lithium di-iso-propylamide in 35 mL of tetrahydrofuran and 7.0 mL of hexamethylphosphorustriamide at -78°C. After 5 min, the reaction mixture was treated with 3.82 mL (26.6 mmol of chlorotrimethylsilane) of the supernatant centrifugate from a mixture of chlorotrimethylsilane and triethylamine. After 3.5 h at room temperature, the reaction mixture was diluted with 5 mL of 5% aqueous HCl and stirred for 20 min then 30 mL of 10% aqueous NaOH

were added. The phases were separated and the organic phase was extracted with 3 portions of 100 mL of 1N aqueous NaOH, and then the combined aqueous phases were extracted with 100 mL of ether, acidified to pH 2 with concentrated aqueous HCl and extracted with 3 portions of 150 mL of ether. The combined organics were dried ($MgSO_4$) and the solvent was removed under reduced pressure to yield a mixture of product and hexamethylphosphoroustriamide which was used in the next reaction without further purification. A small portion was placed under high vacuum for 24 h to remove volatiles, affording a crude orange oil: R_f= 0.26 (ethyl acetate); IR ($CHCl_3$) 3430 (br), 3000, 2940, 2880, 1715, 1455, 1380, 1210, 1148, 1107, 1030, 920 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.18,1.20 (2d, 3H, CH_3, J= 7Hz), 2.38, 2.61 (2dq, 1H, $CHCH_3$, J= 6Hz, 7Hz), 3.32 (s, 3H, OCH_3), 3.56 (d, 2H, CH_2O, J= 5Hz), 4.62 (s, 2H, OCH_2), 4.65 (m,2H, CHO), 4.98 (m, 2H, CH=CH).

3,6-Anhydro-2,5-dideoxy-7-O-(methoxymethyl)-2-methyl-5-iodo-D-erythro-L-arabino-heptoaldonic acid, γ-lactone (12a,b). To a stirred solution of an estimated 1.13 g (5.2 mmol) of the crude acids **11a,b** and 2.1 mL of hexamethylphosphorustriamide in 35 mL of acetonitrile were added 5.53 g (52.2 mmol) of anhydrous sodium carbonate and 6.63 g (26.1 mmol) of iodine. The mixture

was stirred in the dark for 1 h, diluted with 200 mL of ether and 100 mL of 10% aqueous Na_2SO_3. The organic layer was separated, extracted with 40 mL of saturated aqueous NaCl, and dried ($MgSO_4$). Removal of the solvent under reduced pressure and chromatography of the residue on 50 g of silica gel with 2:1 ether/petroleum ether afforded 1.0214 g (35% from glycal **9**) of the major diastereomeric iodolactone **12a** as a colorless oil that was not stable to heat or light: R_f= 0.24 (1:1 ether/petroleum ether); $[\alpha]^{21}_D$= -55.2 (c 0.55, $CHCl_3$); IR ($CHCl_3$) 2980, 1790, 1455, 1382, 1345, 1232, 1190, 1160, 1125, 1092, 1050, 955, 930, 770 cm^{-1}; ^1H NMR ($CDCl_3$) 500 MHz δ1.30 (d, 3H, CH_3, J= 8Hz), 2.84 (q, 1H, CHC=O, J= 8Hz), 3.34 (s, 3H, OCH_3), 3.64 (d, 1H, HCHO, J= 5Hz), 3.66 (d, 1H, HCHO, J= 6Hz), 4.18 (dd, 1H, CHI, J= 7Hz, 3Hz), 4.36 (ddd, 1H, CHOC, J= 7Hz, 6Hz, 5Hz), 4.52 (d, 1H, OCHCC=O, J= 5Hz), 4.63 (s, 2H, OCH_2O), 5.20 (dd, 1H, CHOC=O, J= 5Hz, 3Hz).

Also obtained were 127.6 mg of the minor isomeric iodolactone **12b**: **3,6-Anhydro-2,5-dideoxy-7-O-(methoxymethyl)-2-methyl-5-iodo-D-erythro-L-ribo-heptoaldonic acid, γ-lactone.** R_f= 0.21 (1:1 ether/petroleum ether); $[\alpha]^{21}_D$= -41.2 (c 0.26, $CHCl_3$); IR ($CHCl_3$) 2980, 1790, 1465, 1395, 1355, 1220, 1185, 1140, 1120, 1090, 1000, 940 cm^{-1}; ^1H NMR ($CDCl_3$) 500

MHz δ1.30 (d, 3H, CH_3C, J= 8Hz), 2.80 (dq, 1H, CHC=O, J= 0.5Hz, 8Hz), 3.33 (s, 3H, OCH_3), 3.63 (d, 1H, CHCHO, J= 6Hz), 3.65 (d, 1H, CHCHO, J= 5 Hz), 4.14 (dd, 1H, CHI, J= 7Hz, 2Hz), 4.31 (ddd, 1H, CHOC, J= 7Hz, 6Hz, 5Hz), 4.50 (dd, 1H, OCHCC=O, J= 5 Hz, 0.5 Hz), 4.65 (s, 2H, OCH_2O), 5.18 (dd, 1H, CHOC=O, J= 5Hz, 2Hz).

3,6-Anhydro-2,5-dideoxy-7-O-(methoxymethyl)-2-methyl-D-ido-heptoaldonic acid, γ-lactone. To a stirred solution of 951.5 mg (2.78 mmol) of the iodolactone **12a** in 45 mL of methanol were added 1.47 mL (5.57 mmol) of freshly prepared tri-n-butyltin hydride. After 20 min, the reaction mixture was diluted with 50 mL of ether and 25 mL of 10% aqueous KF, then stirred vigorously for 15 min. After filtration, the phases were separated and the aqueous phase extracted with three portions of 75 mL of ether. The combined organics were dried ($MgSO_4$) and the solvent removed under reduced pressure. The residue was chromatographed on 30 g of silica gel with ether affording 573.4 mg (95.4%) of the desired lactone: R_f= 0.20 (ether); evaporative distillation 105°C (0.005 mm Hg), $[\alpha]_D^{21}$= -65.3 (c 0.40, $CHCl_3$), IR ($CHCl_3$) 2950, 2890, 1780, 1515, 1360, 1190, 1160, 1120, 1095, 1050, 955, 925 cm^{-1}; ^1H NMR ($CHCl_3$) δ1.30 (d, 3H, CH_3C, J= 8Hz), 2.05 (abxy, 1H, HCHCOC=O, J= 14Hz, 7Hz, 2Hz), 2.37 (abxy, HCHCOC=O, J= 14Hz, 7Hz, 6.5Hz), 2.79 (q, 1H, CHC,

J= 8Hz), 3.32 (s, 3H, OCH_3), 3.57 (d, 1H, HC<u>H</u>O, J= 6Hz), 3.59 (d, 1H, HC<u>H</u>O, J= 5Hz), 4.20 (m, 1H, CHO), 4.25 (d, 1H, OCHCC=O, J= 5Hz), 4.60 (s, 2H, OCH_2O), 5.05 (ddd, 1H, CHOC=O, J= 6.5Hz, 5Hz, 2Hz). Analysis calculated for $C_{10}H_{16}O_5$: C, 55.55; H, 7.46. Found: C, 55.47; H, 7.46.

3,6-Anhydro-2,5-dideoxy-2-methyl-D-<u>ido</u>-heptoaldonic acid, γ-lactone (13). To a stirred solution of 573.4 mg (2.65 mmol) of the above ether in 18 mL of acetonitrile were added 4.5 mL of 10% aqueous HCl. The solution was heated to 45°C. After 10 h, the reaction mixture was cooled to room temperature and diluted with 50 mL of ethyl acetate and 20 mL of saturated aqueous NaCl. The phases were separated and the aqueous phase extracted with two portions of 50 mL of ethyl acetate. The combined organics were dried ($MgSO_4$) and the solvent removed under reduced pressure. The residue was chromatographed on 20 g of silica gel to afford 375.0 mg (82%) of the desired alcohol **13** as a colorless oil: R_f= 0.28 (ethyl acetate); $[\alpha]^{21}_D$= -55.5° (c 0.47, $CHCl_3$); IR ($CHCl_3$) 3600, 3500 (br), 2980, 2930, 2880, 1775, 1455, 1385, 1345, 1320, 1180, 1085, 1045, 1020, 990, 890, 850 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.30 (d, 3H, CH_3C, J= 8Hz), 1.90 (br s, 1H, OH), 2.07 (abxy, 1H, HC<u>H</u>COC=O, J= 15Hz, 7Hz, 2Hz), 2.27 (abxy, 1H, HC<u>H</u>COC=O, J= 15Hz,

6.5Hz, 6Hz), 2.79 (q, 1H, CHC, J= 8Hz), 3.52 (abx, 1H, HCHO, J= 12Hz, 6.5Hz), 3.70 (abx, 1H, HCHO, J= 12Hz, 3Hz), 4.10 (m, 1H, CHO), 4.26 (d, 1H, CHCC=O, J= 7Hz), 5.0 (m, 1H, CHOC=O). Analysis calculated for $C_8H_{12}O_4$: C, 55.81; H, 7.02. Found: C, 55.90; H, 7.04.

3,6-Anhydro-2,5-dideoxy-7,8-O-isopropylidene-2-methyl-5-iodo-D-ribo-L-arabino-octoaldonic acid, γ- lactone (15a). To a stirred solution of 3.84 g (15.1 mmol) of iodine and 3.2 g (30.2 mmol) of sodium carbonate in 25 mL of acetonitrile was added a solution of 730 mg (3.0 mmol) of the crude acids **14a,b** and 3.2 g of hexamethylphosphorustriamide in 10 mL of acetonitrile. After 1 h under exclusion of light, the reaction mixture was diluted with 150 mL of ether and 100 mL of 10% aqueous Na_2SO_3. The phases were separated and the organic phase extracted with 30 mL of saturated aqueous NaCl. The combined aqueous extracts were washed with two portions of 100 mL of ether. The combined organics were dried ($MgSO_4$) and the solvent removed under reduced pressure. Chromatography of the residue on 40 g of silica gel with 2:1 petroleum ether/ether afforded 624.3 mg (56%) of the white, crystalline iodolactone **15a** as a single diastereomer: R_f= 0.30 (1:1 petroleum ether/ether); melting point 121-122.5 °C (recrystallized from di-iso-propyl ether/petroleum

ether); IR ($CHCl_3$) 2990, 2978, 2960, 2870, 2850, 1780, 1450, 1380, 1370, 1170, 1065, 1000, 960, 880, 840 cm^{-1}; ^1H NMR ($CDCl_3$) 500 MHz δ1.28 (d, 3H, CH_3, J= 8Hz), 1.31, 1.45 (2s, 6H, $(CH_3)_2C$), 2.80 (q, 1H, CHC=O, J= 8Hz), 3.8-4.1 (m, 3H, $OCHCH_2O$), 4.41 (dd, 1H, OCHCI, J= 7Hz, 4Hz), 4.53 (d, 1H, OCHCC=O, J= 3Hz), 4.67 (d, 1H, CHI, J= 4Hz), 5.20 (d, 1H, CHOC=O, J= 3Hz); ^{13}C NMR ($CDCl_3$) partial δ 13.5 (CH_3), 21.2 ($\underline{C}CH_3$), 25.0, 26.8 ($\underline{C}H_3C\underline{C}H_3$), 43.0 (CI), 109.9 (OCO), 177.6 (C=O). Analysis calculated for $C_{12}H_{17}O_5I$: C, 39.15; H, 4.65. Found: C, 39.10; H, 4.62.

3,6-Anhydro-2,5-dideoxy-7,8-O-isopropylidene-2-methyl-D-erythro-L-arabino-octaldonic acid, γ-lactone. To a stirred solution of 613.2 mg (1.67 mmol) of the iodolactone **15a** in 20 mL of methanol were added 0.88 mL (3.34 mmol) of freshly prepared tri-n-butyltin hydride. After 3.5 h, the reaction mixture was diluted with 50 mL of ether and 15 mL of 10% aqueous KF then stirred vigorously for 15 min. After filtration, the phases were separated and the aqueous phase extracted with two portions of 50 mL of ether. The combined organic extracts were dried ($MgSO_4$) and the solvent was removed under reduced pressure. The residue was chromatographed on 60 g of silica gel with 1:1 petroleum ether/ether to afford 396.6 (98%) of the desired lactone as white

crystals: R_f= 0.16 (1:1 petroleum ether/ether); melting point 70-71°C (recrystalized from di-iso-propyl ether/petroleum ether); $[\alpha]^{21}_D$= -64.25° (c 1.035, $CHCl_3$); IR ($CHCl_3$) 3000, 2960, 1780, 1390, 1380, 1210, 1070, 935, 760, 670 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.30 (d, 3H, CH_3C, J= 8Hz), 1.35, 1.49 (2s, 6H, $(CH_3)_2C$), 2.3-2.5 (m, 2H, CCH_2C), 2.78 (q, 1H, CHC=O, J= 8Hz), 3.8-4.1 (m, 4H, $OCHCH(O)CH_2O$), 4.23 (d, 1H, OCHCC=O, J= 5Hz), 5.0-5.2 (m, 1H, CHOC=O). Analysis calculated for $C_{12}H_{18}O_5$: C, 59.49; H, 7.49. Found: C, 59.34; H, 7.48.

3,6-Anhydro-2,5-dideoxy-2-methyl-D-erythro-L-arabino-octaldonic acid, γ-lactone (16). To a stirred solution of 481.2 mg (1.98 mmol) of the above acetonide in 20 mL of tetrahydrofuran were added 5 mL of 10% aqueous HCl. After 3 h, the reaction was neutralized with 3.3 g of anhydrous sodium carbonate, then diluted with 100 mL of a 1:1 mixture of ether and dichloromethane. The solution was dried ($MgSO_4$) and the solvents were removed under reduced pressure. The residue was chromatographed on 20 g of silica gel with 95:5 chloroform/methanol to afford 385.0 mg (96%) of the desired diol **16** as a colorless oil: R_f= 0.12 (ethyl acetate); evaporative distillation 190-200°C (0.05 mm Hg); IR ($CHCl_3$) 3480 (br), 2995, 2930, 1780, 1460, 1385, 1355, 1230, 1170, 1060, 1020, 895 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.30 (d, 3H,

CH_3C, J= 8Hz), 2.3-2.4 (m, 2H, CCH_2C), 2.78 (q, 1H, CHC=O, J= 8Hz), 3.25 (br s, 2H, OH), 3.6-3.7 (m, 3H, $OCHCH_2O$), 3.9-4.0 (m, 1H, OCHCO), 4.22 (d, 1H, OCHCC=O, J= 4Hz), 5.02 (q, 1H, CHOC=O, J= 4Hz). Analysis calculated for $C_9H_{14}O_5$: C, 53.46; H, 6.98. Found: C, 53.60; H, 6.98.

2,5-Anhydro-3,6-dideoxy-6-methyl-D-ido-octauronic acid γ-lactone. To a stirred solution of 307.2 mg (1.52 mmol) of the diol **16** in 22 mL of tetrahydrofuran was added a solution of 357.4 mg (1.67 mmol) of sodium meta-periodate in 5 mL of water. After 20 min, the reaction mixture was diluted with 100 mL of dichloromethane and 20 mL of water. The phases were separated and the aqueous phase was extracted with two portions of 50 mL of dichloromethane and three portions of 50 mL of ethyl acetate. The combined organic extracts were dried ($MgSO_4$) and the solvent was removed under reduced pressure to afford 242.1 mg (93.6%) of the desired crude, unstable aldehyde which was used directly in the Grignard reaction: R_f= 0.25 (95:5 chloroform/methanol); IR ($CHCl_3$) 2970, 1780, 1740, 1450, 1380, 1350, 1180, 1085, 1015, 990 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.30 (d, 3H, CH_3, J= 8Hz), 2.48 (m, 2H, CH_2), 2.94 (q, 1H, CHC=O, J= 8Hz), 4.43 (m, 2H, HCO), 5.04 (m, 1H, CHOC=O), 9.58 (d, 1H, HC=O, J= 2Hz).

3(R)-3-Hydroxy-1-bromobutane. A stirred solution of 1.2 g (7.95 mmol) of the epoxide **17** in 6 mL of ether was added to a slurry of 0.36 g (15.90 mmol) of lithium tetrahydridoaluminate in 20 mL of ether at -78°C, then the reaction mixture was allowed to warm to -30°C. After 0.5 h, the reaction mixture was treated sequentially with 0.36 mL of water, 0.36 mL of 15% aqueous NaOH, and 1.1 mL of water. The solution was dried ($MgSO_4$) then the solvent was removed under reduced pressure to afford 1.2 g of the desired crude alcohol: R_f= 0.24 (1:1 ether/petroleum ether); ^1H NMR ($CDCl_3$) δ1.23 (d, 3H, CH_3, J= 6Hz), 1.9-2.0 (m, 3H, CCH_2C, OH), 3.50 (t, 2H, CH_2Br, J= 7Hz), 4.0-4.1 (m, 1H, HCO).

3(R)-3-(methoxymethyleneoxy)-1-bromobutane. To a stirred solution of 1.2 g (7.84 mmol) of the above alcohol in 20 mL of dichloromethane were added 1.4 mL (8.1 mmol) of di-iso-propylethylamine and 0.6 mL (7.9 mmol) of chloromethylmethyl ether. After 7 h, a further 1.4 mL (8.1 mmol) of di-iso-propylethylamine and 0.6 mL (7.9 mmol) of chloromethylmethyl ether were added. After 10 h, the reaction mixture was treated with 7 mL of saturated aqueous $NaHCO_3$ and stirred vigorously for 0.5 h. The reaction mixture was diluted with 50 mL of ether and 10 mL of saturated aqueous $NaHCO_3$ and the

organic phase was separated. The aqueous phase was extracted with two portions of 50 mL of ether. The combined organic extracts were dried ($MgSO_4$) and then concentrated under reduced pressure. The residue was chromatographed on 20 g of silica gel with 4:1 petroleum ether/ether to afford 1.1 g of the desired ether(70% from the epoxide **17**) as a colorless oil: R_f= 0.48 (1:1 petroleum ether/ether); evaporative distillation 75-80°C (30 mm Hg); $[\alpha]^{21}_D$= -65.4° (c 1.09, $CHCl_3$); IR ($CHCl_3$) 2970, 2930, 2890, 1440, 1375, 1140, 1100, 1030, 915 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.20 (d, 3H, CH_3, J= 6Hz), 1.9-2.0 (m, 2H, CCH_2C), 3.32 (s, 3H, CH_3O), 3.4-3.5 (m, 2H, CH_2Br), 3.80-3.9 (m, 1H, HCO), 4.66 (ab, 1H, OHCHO, J= 8Hz), 4.78 (ab, 1H, OHCHO, J= 8Hz).

(7ξ)-3,6-Anhydro-2,5,8,9,11-pentadeoxy-10-O-(methoxymethyl)-2-methyl-D-glycero-D-ido-undecoaldonic acid, γ-lactone (19). To 0.2102 g (5.37 mmol) of freshly cut potassium under 9 mL of tetrahydrofuran were added 0.29 g (3.05 mmol) of dry magnesium chloride and 0.49 g (2.95 mmol) of dry potassium iodide and the resulting slurry was heated to reflux for 2 h then cooled to 0°C. To the black suspension was added a solution of 266.5 mg (1.35 mmol) of the above bromide in 4.5 mL of tetrahydrofuran over 25 min. After 3 h at 0°C, to the crude Grignard reagent (**18**) solution was

added a solution of 70.7 mg (0.4155 mmol) of the crude aldehyde in 4.5 mL of tetrahydrofuran over 3 min. After 30 min at 0°C, the reaction mixture was treated with 15 mL of saturated aqueous NH_4Cl, then diluted with 100 mL of dichloromethane. The phases were separated and the aqueous phase was extracted with two portions of 100 mL of dichloromethane and then with 100 mL of ether. The combined organics were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed on 10 g of silica gel with 48:48:2 petroleum ether/ethyl acetate/pyridine to afford 99.8 mg (83%) of the Grignard adduct **19** as a colorless oil: R_f: 0.37 (95:5 chloroform/methanol); IR ($CHCl_3$) 3690, 3480, 2980, 2940, 2880, 1780, 1450, 1390, 1360, 1190, 1115, 1090, 1030, 915 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.18 (d, 3H, CH_3CO, J= 6Hz), 1.30 (d, 3H, CH_3C, J= 8Hz), 1.5-1.7 (m, 4H, CH_2CH_2), 2.2-2.3 (m, 3H, CH_2, OH), 2.82 (dq, 1H, CHC=O, J= 1.5Hz, 8Hz), 3.33 (s, 3H, CH_3O), 3.6-3.7 (m, 3H, HCO), 4.20 (dd, 1H, OCHCC=O, J= 4Hz, 1.5Hz), 4.56 (ab, 1H, OHC<u>H</u>O, J= 8Hz), 4.68 (ab, 1H, OHC<u>H</u>O, J= 8Hz), 5.0-5.1 (m, 1H, CHOC=O). Analysis calculated for $C_{14}H_{24}O_6$: C, 58.32; H, 8.39. Found: C, 58.28; H, 8.29.

(7ξ)-3,6-Anhydro-2,5,8,9,11-pentadeoxy-10-<u>O</u>-(methoxymethyl)-2-methyl-D-<u>glycero</u>-D-<u>ido</u>-undecitol. A solution of 342.6 mg (1.19 mmol) of the lactone **19** in 20

mL of ether was added to a slurry of 45.0 mg (1.19 mmol) of lithium tetrahydridoaluminate in 30 mL of ether at 0°C. After 20 min, the reation mixture was treated sequentially with 45 μL of water, 45 μL of 15% aqueous NaOH, and 135 μL of water. The solution was dried ($MgSO_4$) then the solvent was removed under reduced pressure to afford 256.6 mg (73.9%) of the desired crude triol. This material was used directly in the next reaction: R_f= 0.10 (95:5 chloroform/methanol); IR ($CHCl_3$) 3370 (br), 2940, 2890, 1500, 1380, 1210, 1140, 1100, 1030, 920 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.03 (d, 3H, CH_3C, J= 8Hz), 1.18 (d, 3H, CH_3CO, J= 6Hz), 1.4-2.4 (m, 7H), 3.35 (s, 3H, CH_3O), 3.4-4.4 (m, 10H), 4.56 (ab, 1H, OCH<u>H</u>O, J= 8Hz), 4.68 (ab, 1H, OCH<u>H</u>O, J= 8Hz).

(7ξ)-3,6-Anhydro-2,5,8,9,11-pentadeoxy-1-O-(<u>tert</u>-butyldiphenylsilyl)-10-O-(methoxymethyl)-2-methyl-D-<u>glycero</u>-D-<u>ido</u>-undecitol. To a stirred solution of 176.0 mg (0.60 mmol) of the above crude triol in 0.65 mL of dichloromethane were added 200 μL (0.77 mmol) of <u>tert</u>-butylchlorodiphenylsilane and 160 mg (1.30 mmol) of N',N'-dimethylaminopyridine. After 2 h, the reaction mixture was diluted with 20 mL of dichloromethane and 5 mL of 1% aqueous HCl. The phases were separated and the organic phase extracted with 5 mL of saturated aqueous $NaHCO_3$. The organic phase was dried ($MgSO_4$) and the

solvent removed under reduced pressure to yield 253.7 mg (79.4%) of the silyl ether as a mixture of diastereomers that were not further purified: R_f: 0.053, 0.080 (1:1 petroleum ether/ether); IR ($CHCl_3$) 3400 (br), 2995, 2960, 1930, 1850, 1460, 1430, 1370, 1120, 1040, 830, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.03 (d, 3H, CH_3C, J= 8Hz), 1.11 (s, 9H, $(CH_3)_3C$), 1.20 (d, 3H, CH_3CO, J= 6Hz), 1.4-1.8 (m, 6H, CH_2), 2.1-2.6 (m, 3H, CHC, OH), 3.35 (s, 3H, CH_3O), 3.4-4.3 (m, 7H, CH_2O, HCO), 4.54 (ab, 1H, OCHHO, J= 8Hz), 4.68 (ab, 1H, OCHHO, J= 8Hz), 7.3-7.4 (m, 6H, m-, p-PhH), 7.5-7.6 (m, 4H, o-PhH).

3,6-Anhydro-2,5,8,9,11-pentadeoxy-1-O-(tert-butyldiphenylsilyl)-10-O-(methoxymethyl)-2-methyl-D-glycero-D-arabino-4,7-undecadiulose (20). To a stirred solution of 150 μL (1.72 mmol) of oxalyl chloride in 2.5 mL of dichloromethane at -78°C were added 270 μL (3.8 mmol) of dimethylsulfoxide. After 15 min, a solution of 207.1 mg (0.39 mmol) of the above diol in 2.5 mL of dichloromethane was added to the reaction mixture. After 25 min, the reaction mixture was treated with 1.10 mL (7.9 mmol) of triethylamine, allowed to warm to room temperature and then diluted with 75 mL of dichloromethane and 25 mL of 1% aqueous HCl. The phases were separated and the organic phase was extracted with 10 mL of saturated aqueous $NaHCO_3$. The organic phase

was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue on 20 g of silica gel with 2:1 petroleum ether/ether afforded 185.9 mg (90.5 %) of the diketone **20** as a colorless oil: R_f= 0.33 (1:1 petroleum ether/ether); evaporative distillation 230°C (0.03 mm Hg); $[\alpha]^{21}_D$= -26.95° (c= 0.59, $CHCl_3$); IR ($CHCl_3$) 2940, 2860, 1760, 1720, 1460, 1430, 1380, 1260, 1110, 1103, 1030, 910, 825, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ0.94 (d, 3H, CH_3C, J= 8Hz), 1.10 (s, 9H, $(CH_3)_3C$), 1.20 (d, 3H, CH_3CO, J= 6Hz), 1.6-1.9 (m, 3H, CHC, CH_2C), 2.4-2.8 (m, 4H, $CH_2C=O$), 3.35 (s, 3H, CH_3O), 3.4-3.6 (m, 3H, HCO, H_2CO), 4.24 (d, 1H, O=CCHOCC, J= 3Hz), 4.5-4.6 (m, 3H, OCH_2O, O=CHCO), 7.3-7.4 (m, 6H, m-, p-PhH), 7.5-7.6 (m, 4H, o-PhH). Analysis calculated for $C_{30}H_{42}O_6Si$: C, 68.41; H, 8.04. Found: C, 68.23; H, 7.94.

3,6-Anhydro-2,5,8,9,11-pentadeoxy-1-O-(tert-butyldiphenylsilyl)-2-methyl-D-glycero-D-arabino-4,7-undecadiulo-7,10-furanose (21). To a stirred solution of 16.5 mg (0.0785 mmol) of tetraethylammonium bromide in 0.40 mL of dichloromethane was added a solution of 6.1 mg (0.0166 mmol) of the diketone **20** in 0.60 mL of dichloromethane. The resulting solution was treated with 10 μL (0.0788 mmol) of chlorotrimethylsilane. After 2.5 h, the reaction mixture was diluted with 30 mL

of dichloromethane and 5 mL of 1% aqueous HCl. The phases were separated and the organic phase was extracted with 5 mL of saturated aqueous $NaHCO_3$ then 5 mL of saturated aqueous NaCl. The organics were dried ($MgSO_4$) and the solvent was removed under reduced pressure. Chromatography on 1 g of silica gel with 2:1 petroleum ether/ether afforded 13.9 mg (70%) of the hemi-acetal **21**: R_f= 0.14 (1:1 petroleum ether/ether); evaporative distillation 200°C (0.05 mm Hg); IR ($CHCl_3$) 3560, 2990, 2940, 2870, 1760, 1610, 1470, 1435, 1400, 1120, 1010, 950, 920, 830, 710, 620 cm^{-1}; ^1H NMR ($CDCl_3$) δ0.80, 0.81 (2d, 3H, CH_3C, J= 8Hz), 1.02 (s, 9H, $(CH_3)_3C$), 1.16, 1.34 (2d, 3H, CH_3CO, J= 6Hz), 1.8-2.5 (m, 7H, CCHC, CCH_2C), 3.5-3.7 (m, 3H, CH_2O, OH), 4.0-4.2 (m, 3H, HCO), 7.3-7.4 (m, 6H, m-, p-PhH), 7.5-7.6 (m, 4H, o-PhH). Analysis calculated for $C_{28}H_{38}O_5Si$: C, 69.67; H, 7.94. Found: C, 69.75; H, 7.82.

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