Recent Improvements In The Palladium Assisted Synthesis Of C-glycosides Related To The Gilvocarcins.

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Recent improvements in the palladium assisted synthesis of *C*-glycosides related to the gilvocarcins

Farr, Roger N., Ph.D.

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RECENT IMPROVEMENTS IN THE PALLADIUM ASSISTED SYNTHESIS OF *C*-GLYCOSIDES RELATED TO THE GILVOCARCINS

by

ROGER N. FARR

A Dissertation

Presented to the Graduate Committee

of Lehigh University

in Candidacy for the Degree of

Doctor of Philosophy

in

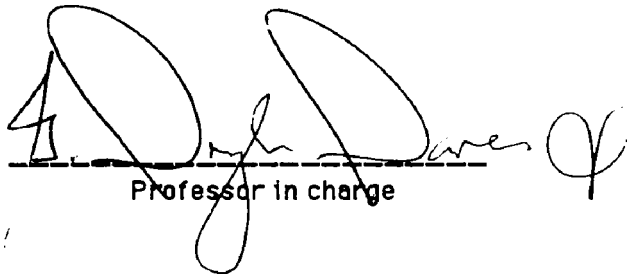
Department of Chemistry

Lehigh University

1991

Approved and recommended for acceptance as a dissertation in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

October 30, 1991
(date)



Professor in charge

Accepted October 30, 1991
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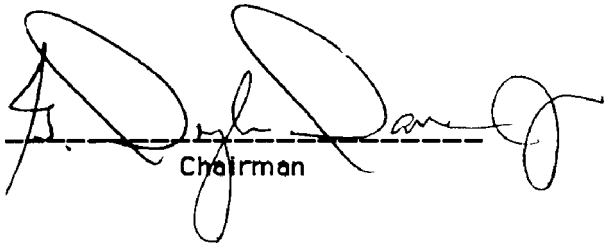

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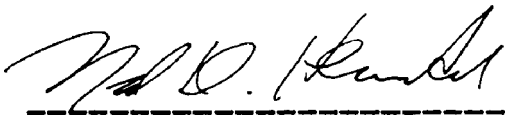

Dr. Ned Heindel

Dr. Natalie Foster

Dr. Richard Conley

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This dissertation is dedicated to Geri Ann Masessa whose constant encouragement and patience are greatly appreciated.

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ABSTRACT

A synthetic approach to the preparation of *C*-glycosides related to Gilvocarcin V has been developed and has resulted in the syntheses of 8-ethenyl-1-hydroxy-4-(2'-deoxy-β-D-ribofuranosyl)benzo[d]naphtho[1,2-b]pyran-6-one (**38**) and 8-ethyl-1-hydroxy-4-(2'-deoxy-β-D-ribofuranosyl)benzo[d]naphtho[1,2-b]pyran-6-one (**39**).

The development of a palladium-catalyzed coupling reaction between an aryl iodide and a glycal (1,2-unsaturated carbohydrate) has been accomplished[18,45] and is applicable to the synthesis of both *C*-glycopyranosides and *C*-glycofuranosides. Together with the synthesis of 1,4-anhydro-2-deoxy-3-*O*-(t-butyl-diphenylsilyl)-D-*erythro*-pent-1-enitol (**15**), a glycal specifically designed for efficient production of β-*C*-glycosides,[18,20] the palladium-mediated coupling reaction is an attractive convergent synthetic route to the gilvocarcin class of antibiotics.

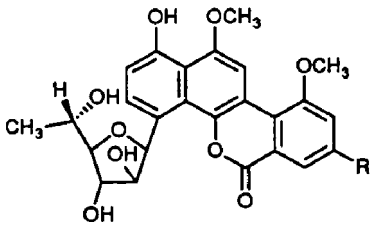
C-glycosyl product characterization was facilitated by a variety of one and two dimensional NMR experiments including the employment of NOE difference spectroscopy in order to assign the anomeric configuration of our compounds. In every case studied, the anomeric configuration of *C*-glycosides was assigned clearly based on the NOE results between the appropriate pairs of carbohydrate protons of both α- and β-*C*-glycosides respectively.

CHAPTER 1: INTRODUCTION

1. Background

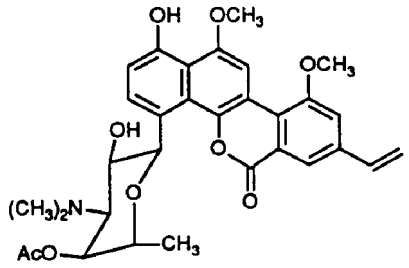
The C-glycosides are a class of compounds in which the sugar moiety and aglycon (non-sugar moiety) are attached by a carbon-carbon bond. Since the isolation of the first *C*-glycoside, pseudouridine in 1959,[1] a variety of other natural *C*-glycosides have been isolated which exhibit both antitumor and antibacterial activities.[2] Except for pseudouridine, all *C*-nucleosides and *C*-glycosides appear to be antibiotics; many of which also exhibit antiviral and anticancer activities.[2]

Currently, we are interested in a class of aromatic *C*-glycosides which include the gilvocarcins[3], ravidomycin[4], and the chrysomycins[5] which share the benzo[d]naphtho[1,2-b]pyran-6-one aglycone ring system. Several of these antibiotics possess the same aglycon, defucogilvocarcin V, which is itself a natural product.[6]

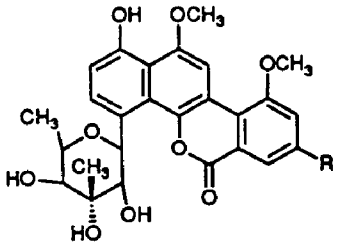


M : R = CH_3
V : R = $CH{=}CH_2$
E : R = CH_2CH_3

GILVOCARCINS

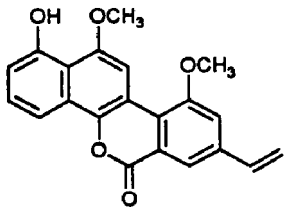


RAVIDOMYCIN



A : R = $CH{=}CH_2$
B : R = CH_3

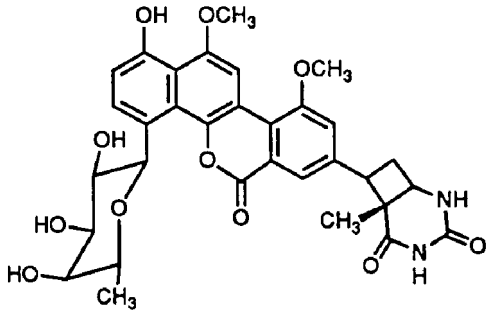
CHRYSOMYCIN



DEFUCOGILVOCARCIN V

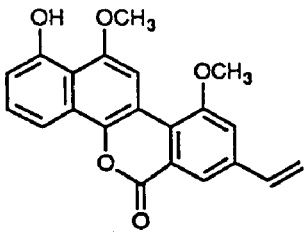
To date, eight syntheses of defucogilvocarcin V[7] as well as the synthesis of (-)-methyl ravidosaminide,[8] the carbohydrate portion of ravidomycin, have been reported. The synthesis of any naturally occurring *C*-glycoside related to this class of natural products has not been reported.

After evaluating the potency of the natural benzo[d]naphtho[1,2-b]pyran-6-one *C*-glycosides, it has been suggested that the nature of the sugar is relatively unimportant. The carbohydrate moiety of these antibiotic *C*-glycosides seems to function by aiding in cellular transport and may stabilize non-covalent binding of the *C*-glycoside to DNA[7c]. Quite recently, McGee and Misra[9] succeeded in isolating a photocycloadduct formed upon irradiation of a mixture of gilvocarcin V with double stranded DNA. It seems likely that the mode of action of these compounds is intercalation into DNA followed by light dependent single strand nicking by way of the photocycloadduct intermediate.

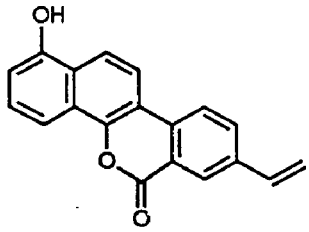


Scheme 1.1 Photocycloadduct Intermediate.

A synthetic analog of defucogilvocarcin V, lacking the C-10 and C-12 methoxy groups was essentially as effective as defucogilvocarcin V.[7c] This suggests that the minimum structural requirements neccessary for bioactivity are the vinyl group and the free phenol of the aglycon.



Defucogilvocarcin V



Scheme 1.2 Analog of Defucogilvocarcin

1.2. Specific Aims

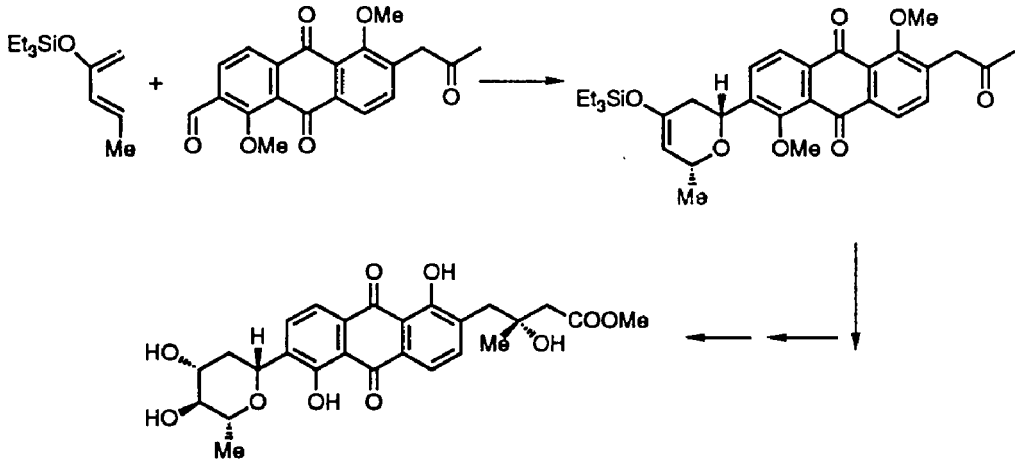
In the past several years, synthetic efforts towards the synthesis of complex *C*-glycosides has increased considerably. The development of methods to link preformed aglycon derivatives to carbohydrates would allow convergent synthetic sequences to be realized. In our laboratory, we have developed an aglycon-carbohydrate coupling reaction between glycals (1,2-unsaturated sugars) and the appropriate aglycon derivatives which forms the *C*-glycosyl bond both regio- and stereospecifically.

The specific aims of the present study were a) to make key improvements upon previous methodology to optimize the synthesis of β-*C*-glycosides and b) to apply the improved methodology to the synthesis of *C*-glycosides possessing the benzo[d]naphtho[1,2-b]pyran-6-one aglycone ring system for submission and biological evaluation.

CHAPTER 2: SYNTHETIC METHODOLOGY

2.1. Previous Synthetic Approaches

There are several available methods for formation of *C*-glycosyl linkages.[2] Among the available methods, the construction of the aglycon from a C-1 functionalized carbohydrate is a common strategy. This method was utilized in the synthesis[10] of the first *C*-nucleoside, pseudouridine.[1] An alternative linear synthetic method for synthesizing *C*-glycosides is the stepwise construction of the sugar moiety onto a preexisting aglycon. Danishefsky and co-workers have developed a method which utilizes a hetero Diels-Alder reaction to form the *C*-glycosyl bond. The synthesis of vineomycine B_2 demonstrated the utility of this process.[11]

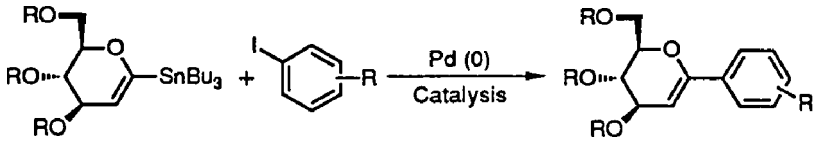


Vineomycine B_2 methyl ester

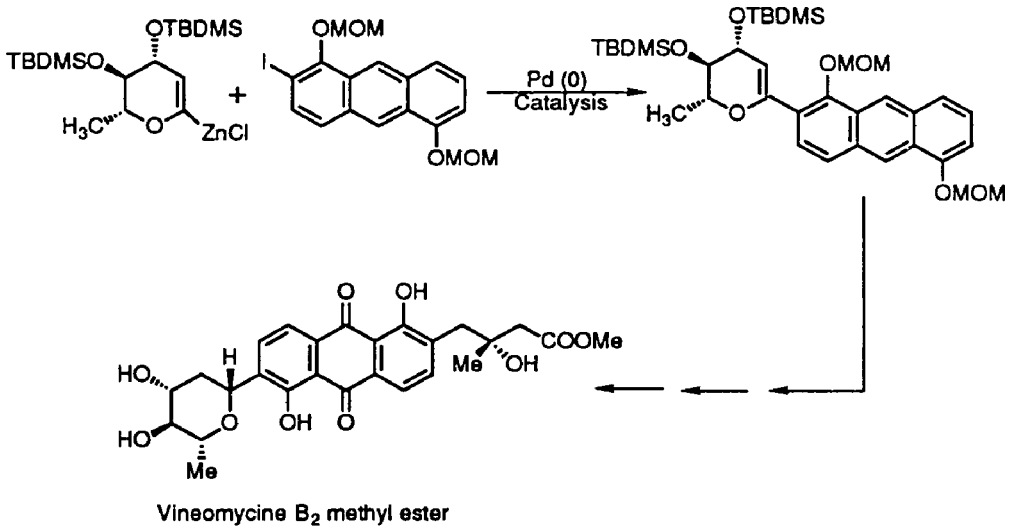
Scheme 2.1 Danishefsky Synthesis of Vineomycine B_2

Linkage of preformed carbohydrate and aglycon derivatives to form the desired *C*-glycosides has been achieved. The key bond has been formed by addition of organolithium derivatives to protected carbohydrate lactones [2,12] and also by Lewis acid-catalyzed condensation.[13] In both processes, however, the formation of the new carbon-carbon bond exhibited little or no stereoselectivity.

A recent convergent strategy for synthesizing *C*-glycosides has been reported[14] which utilizes various palladium-catalyzed cross coupling reactions to form the glycosidic bond. Tius and coworkers have recently reported[15] the synthesis of vineomycine B_2 involving as the key step a palladium-catalyzed cross coupling reaction to form the *C*-glycosidic bond.



Scheme 2.2 Example of Palladium-Catalyzed Cross Coupling Method



Scheme 2.3 Tius Synthesis of Vineomycine B_2

2.2. Palladium Chemistry

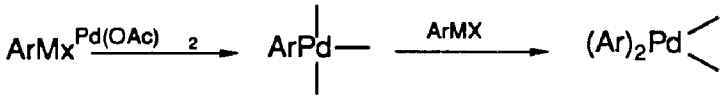
Over the past decade, we have developed a palladium-mediated coupling reaction which yields *C*-glycosides in both a regio- and stereospecific manner. The reaction proceeds in four discrete steps.

1) Formation of the Organopalladium Reagent

There are two distinct processes in which the organopalladium reagent may be formed.

Type 1. Transmetallation

The organopalladium reagent can be formed by transmetallation of either an arylstannane[16] or organomercury derivative[17] to give an unstable σ-bonded palladium intermediate.[18] The process requires stoichiometric quantities of a palladium (II) salt and may be complicated by diorganopalladium intermediate formation followed by reductive elimination to give dimeric or even trimeric products.[19]

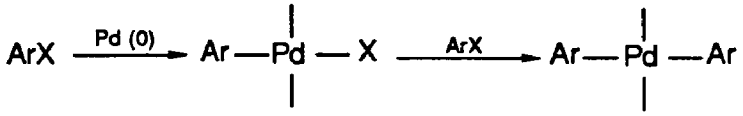


where Ar = aromatic, heteroaromatic, or vinyl
M = Sn or Hg
X = Ligand

Scheme 2.4 Formation of Organopalladium Reagent by Transmetallation

Type 2. Oxidative addition

A second way in which the organopalladium reagent is formed involves the oxidative addition of palladium to an organohalide. Unlike transmetallation which requires palladium (II) complexes, oxidative addition involves a Pd(0) species which can be either a soluble form such as $Pd(PPh_3)_4$ or may be generated in situ by reduction of Pd(II). As in the transmetallation reaction, dimerization may occur.

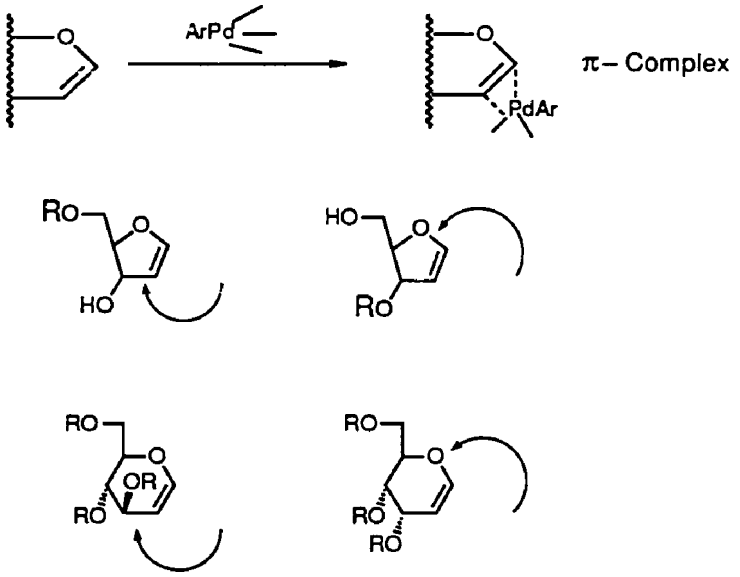


Ar = aryl, heteroaryl, or vinyl
X = I, Br

Scheme 2.5 Formation of Organopalladium Reagent by Oxidative Addition

2. π–Complex Formation

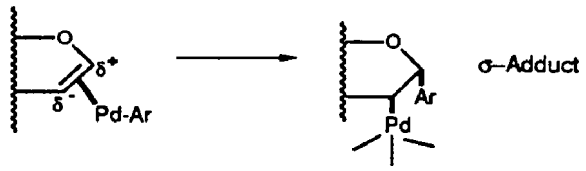
The organopalladium reagent, formed either by transmetallation or oxidative addition, forms a π-complex with the glycal double bond. Since the formation of the π-complex is sensitive to steric factors affecting access to the glycal double bond, the stereochemistry of the coupling reaction can be programmed by proper selection of glycal substituents.[18]



Scheme 2.6 π-Complex Formation

3. Formation of the σ–Palladium Adduct

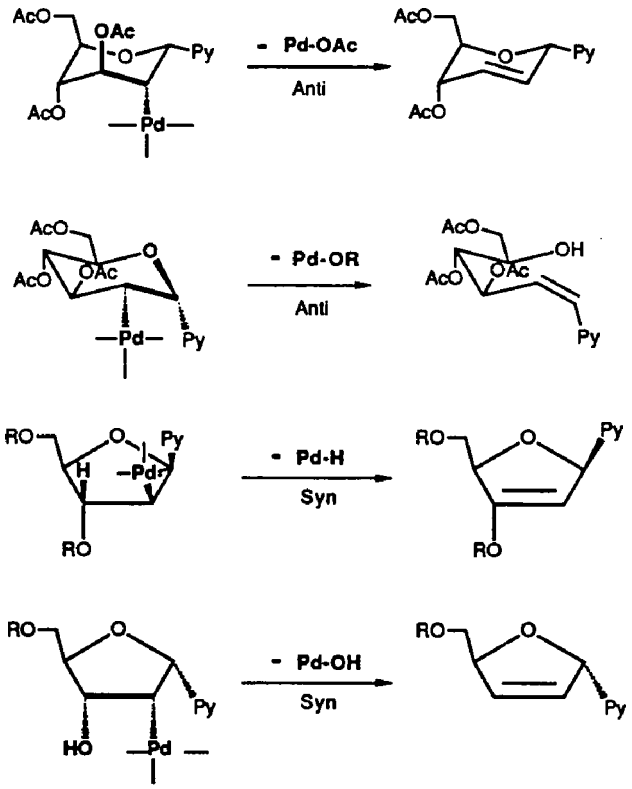
During this new carbon-carbon bond forming reaction, the π-complex collapses by insertion of the C-C double bond into the C-Pd bond which gives rise to an adduct with Pd(II) σ-bonded to carbon. Since the glycal double bond is in conjugation with the lone pair electrons of the ring oxygen, the new carbon-carbon bond is formed at the electron-deficient anomeric carbon.[18,21] The net result of π-complex formation and collapse is the syn addition of the organopalladium reagent to the glycal double bond in a regio- and stereospecific manner to form a σ-adduct. In some cases, stabilized σ-palladium adducts have been isolated in this laboratory.[22]



Scheme 2.7 Formation of the σ-Palladium Adduct

4) Decomposition of the Palladium Adduct

The decomposition of the σ-palladium adduct usually involves an elimination reaction in which palladium and a substituent on carbon β to palladium are lost. To date, four distinct modes of decomposition have been observed in this laboratory.[18] Both palladium acetate and palladium alkoxide eliminations (i.e. ring opening of the carbohydrate)[22a] require an anti-periplanar arrangement of palladium and oxygen substituent whereas palladium hydride[18,21,23a] and palladium oxide[25] eliminations require a syn periplanar arrangement of palladium and β-hydrogen or oxygen substituent respectively.

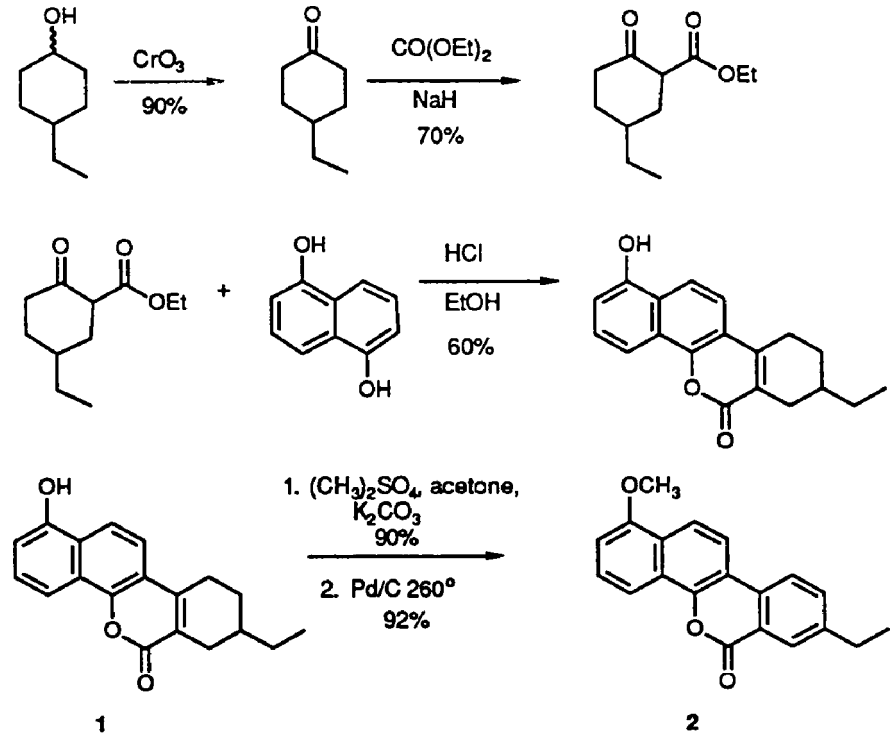


Scheme 2.8 Decomposition of the σ-Palladium Adducts

CHAPTER 3: PRELIMINARY STUDIES OF THE BENZO[d]-NAPHTHO-[1,2,-b]PYRAN-6-ONE SYSTEM

3.1. Aglycon Synthesis

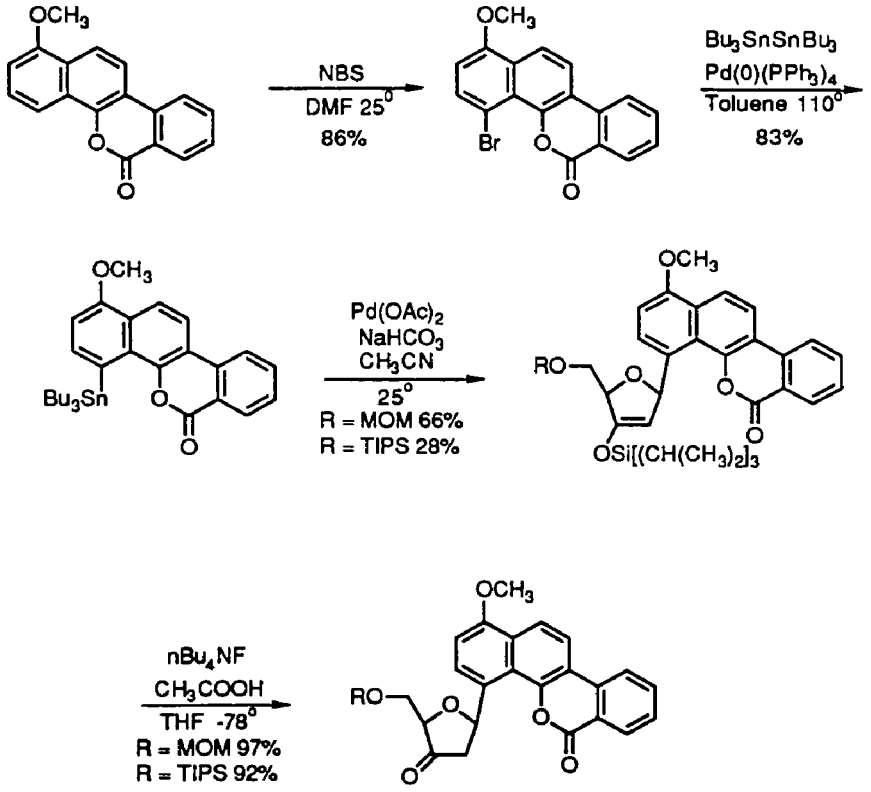
Previously in our laboratory, Outten reported the synthesis[16] of the first benzo[d]naphtho[1,2-b]pyran-6-one *C*-glycosides related to the gilvocarcins.[3] The aglycons were obtained by a sequence developed by Chebaane and coworkers.[25] In the following scheme, the aglycon was obtained[7c] starting from commercially available 4-ethyl cyclohexanol. Oxidation of the alcohol with Jones reagent gave 4-ethyl cyclohexanone which was then treated with sodium hydride and diethylcarbonate to give the corresponding β-keto ester in 70 % yield. Acid-catalyzed condensation of the β-keto ester with 1,5-dihydroxynaphthalene afforded the tetracyclic phenol (**1**),which contains the complete carbon framework of defucogilvocarcin V, in 60% yield. Phenolic methylation followed by dehydrogenation gave the fully aromatized aglycon (**2**) in 80% yield.



Scheme 3.1 Aglycon Synthesis

3.2. *C*-Glycoside Synthesis

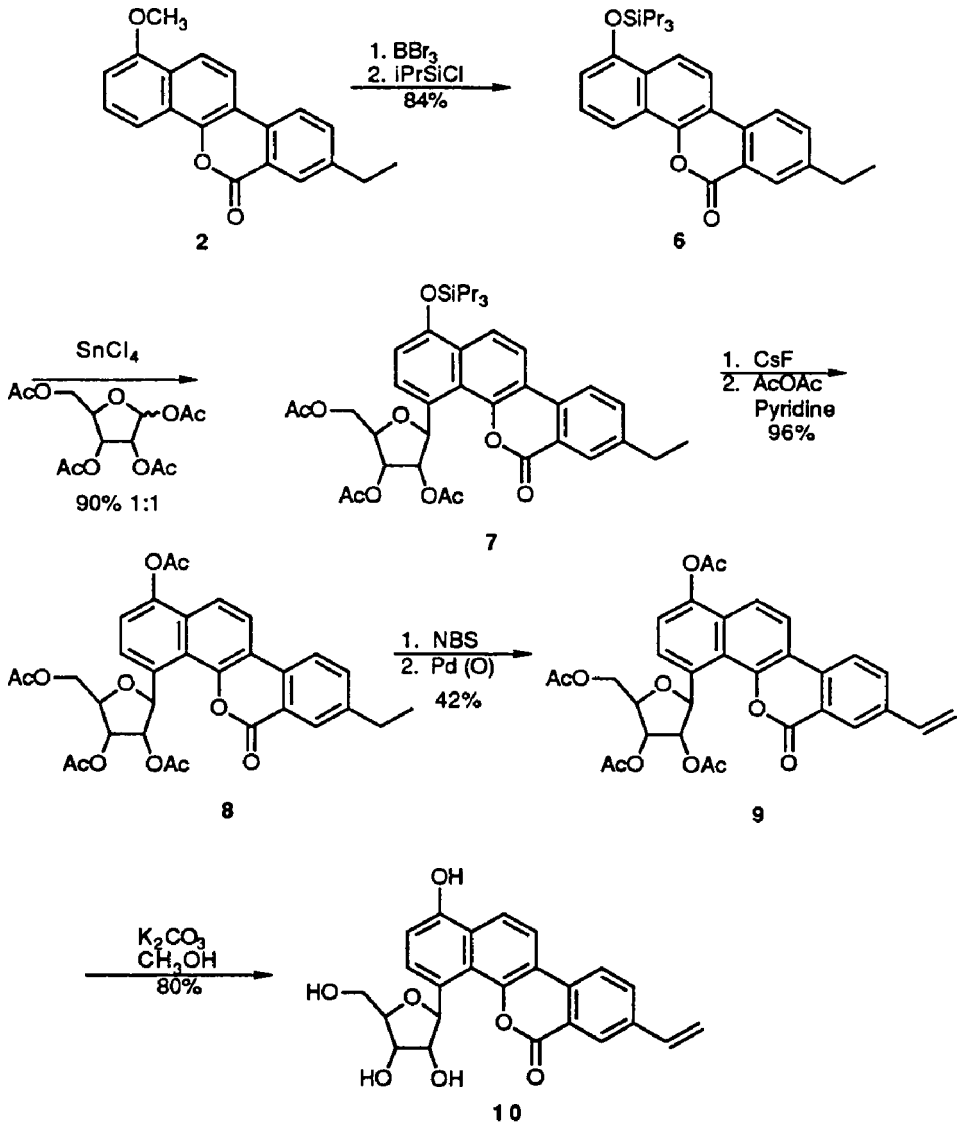
The readily available tetracyclic aglycon (**3**)[25,26] was brominated using N-bromosuccinimide in dimethylformamide and subsequently subjected to the palladium-mediated coupling reaction with ribofuranoid glycals. Unfortunately, no *C*-glycoside formation was observed. The bromo derivative (**4**) was then treated with hexabutyl ditin in the presence of a palladium(0) catalyst to give the arylstannane (**5**) in good yield. Upon treating the arylstannane with several different glycals, in the presence of stoichiometric amounts of palladium acetate, the desired *C*-glycosides were obtained.[16]



Scheme 3.2 *C*-Glycoside Synthesis

Quite recently, we reported the synthesis[27] of the first *C*-glycoside which has the minimum structural requirements thought necessary for bioactivity.[7c,9] The synthesis utilizes a Lewis acid catalyzed condensation reaction of the aglycon and peracetylated

ribofuranose to give the α– and β–*C*-glycosides in a 1:1 mixture. Desilylation, acetylation, and free radical bromination-dehydrobromination gave the peracetylated *C*-glycoside **9**. Upon treating **9** with potassium carbonate in methanol, the target compound (**10**) was obtained.[27]



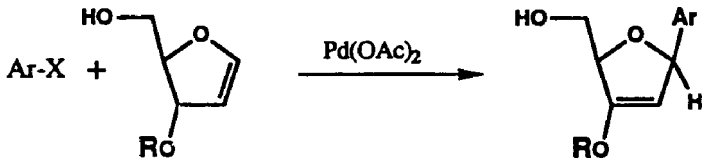
Scheme 3.3 Synthesis of Gilvocarcin V Analog

CHAPTER 4: KEY IMPROVEMENTS IN SYNTHETIC METHODOLOGY

The palladium-catalyzed coupling reaction between a glycal and the appropriate aglycon derivatives allows convergent synthetic routes to complex *C*-glycosides to be realized. The coupling reaction is both regio- and stereospecific and by proper selection of an appropriate glycal, the selective syntheses of α- and β-*C*-glycosides can be achieved. However, one of the specific aims of this study is to make key improvements upon previous methodology to optimize the synthesis of β-*C*-glycosides.

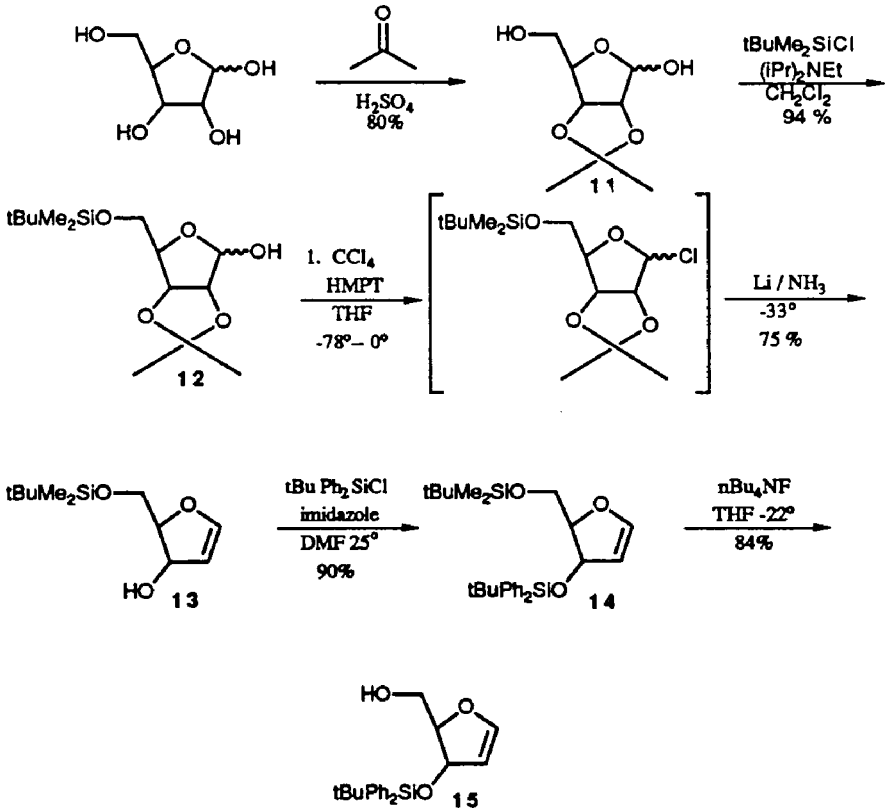
4.1. New Glycal for Synthesizing β-*C*-Glycosides

In palladium-mediated coupling reactions of furanoid glycals, the substituted hydroxyl groups direct the attack of the organopalladium reagent on the glycal double bond.[18,20] When only one of the hydroxyls of a ribofuranoid glycal is substituted (either the C-3 or C-5 hydroxyl),[28] palladium-mediated coupling occurs from the face of the glycal ring opposite the substituted (directing) hydroxyl to form a single *C*-glycosidic product.[18] Therefore, 5-hydroxy-3-*O* -substituted ribofuranoid glycals yield β-*C*-glycosides stereospecifically. However, all glycals designed to produce β-*C*-glycosides which were available[28] have had C-3-O-alkyl groups which could not be removed without epimerizing the anomeric center of the carbohydrate in the *C*-glycosidic product.[17c] To circumvent this problem, readily deprotected[17,29] 3,5-disilylated glycals,[28] which are known[18] to produce β-*C*-glycosides were utilized. Unfortunately, a bulky group on the face of the glycal experiencing organopalladium reagent attack leads to significantly depressed yields (25-50%) [17c,29]



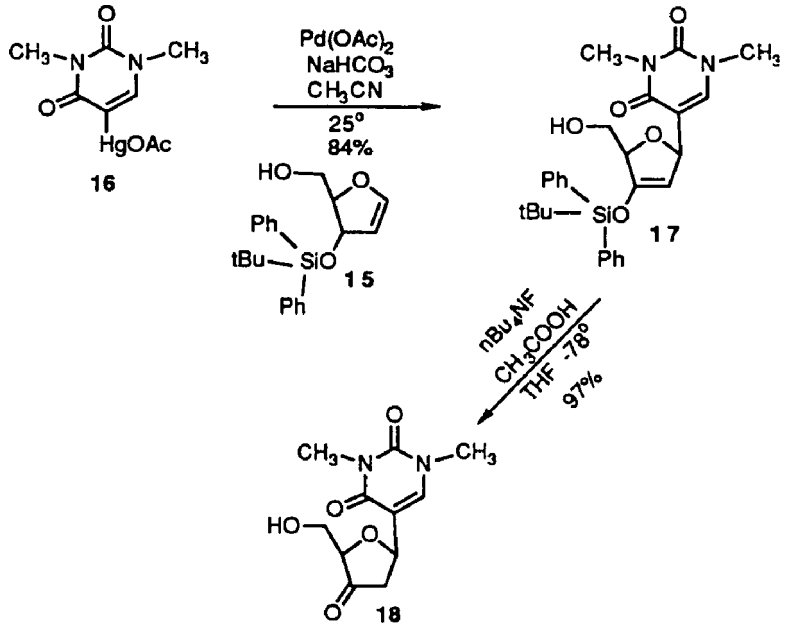
Scheme 4.1 Design of β-*C*-Glycoside Synthesis

In order to optimize the production of β-*C*-glycosides, we required a glycal that would direct the formation of β-*C*-glycosides in high yield and which could then be fully deprotected. A glycal of this description has now been synthesized[20]. 1,4-Anhydro-2-deoxy-3-*O*-(t-butyldiphenylsilyl)-D-*erythro*-pent-1-enitol (**15**) was synthesized via the method of Ireland[30] starting from the commercially available D-ribose. Following acetonation[31], the primary alcohol was selectively silylated[32] in 94% yield. Chlorination followed by a dissolving metal reduction gives the 5'*O*-tertbutyldimethylsilyl-glycal (**13**) in 75% yield. Protection of the allylic alcohol of **13** was accomplished using tertbutyldiphenylsilyl chloride in dimethylformamide to give the diprotected glycal **14** in 90% yield followed by selective unmasking of the primary hydroxyl using flouride ion at low temperature to give the desired glycal (**15**) in 84% yield.



Scheme 4.2 Synthesis of the Tailor-Made Glycal

Palladium-mediated coupling of **15** with(1,3-dimethyl-2,4-dioxo-1,3-dihydro-pyrimidin-5-yl)mercuric acetate (**16**)[21], in the presence of one equivalent of palladium acetate, resulted in an 84% yield of the corresponding β-furanosyl *C*-glycoside **17**. The silyl-stereodirecting group was then readily removed with flouride ion to give the 2'-deoxy-3'-keto-*C*-glycoside (**18**) in essentially quantitative yield.

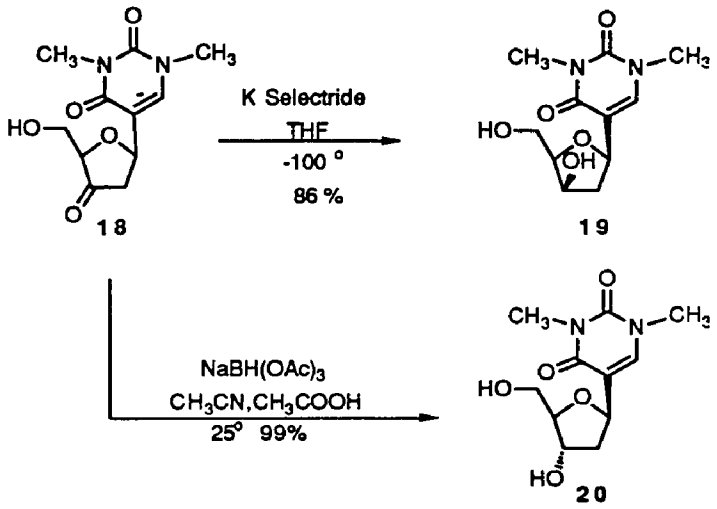


Scheme 4.3 Palladium Coupling With the Tailor-Made Glycal

4.2. Stereoselective Reduction of 3'-Keto-*C*-Glycosides

In earlier work[17c], reduction of the intermediate keto C-glycoside (**18**) employing sodium or lithium borohydride resulted in mixtures of **19** and **20**. Complementary methods for the stereoselective reduction of the carbohydrate carbonyl carbon of **18** has now been developed.[20] The stereoselective reduction of **18** from the least hindered face of the carbohydrate was accomplished using potassium tri-sec-butylborohydride (K-Selectride) at low temperature to give **19** as a sole product in 86% yield. Reduction of the ketone from the most hindered face of the carbohydrate was accomplished using sodium triacetoxyborohydride, a reagent that involves initial coordination to, and

activation by the proximal 5' OH,[33] to give **20** in essentially quantitative yield. A 500 MHz ^{1}H nmr spectrum of the reaction mixture showed no trace of isomer **19**.

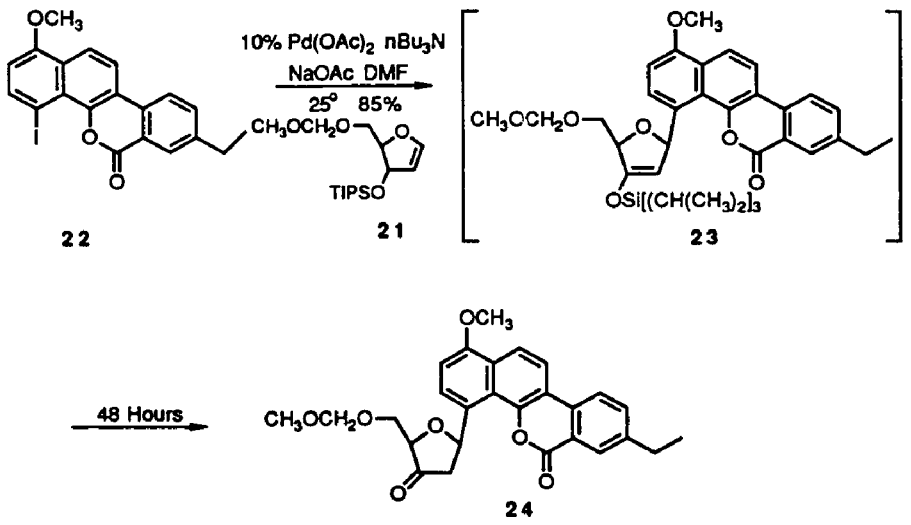


Scheme 4.4 Stereoselective Reductions

4.3 Catalytic Palladium-Mediated Coupling Reaction

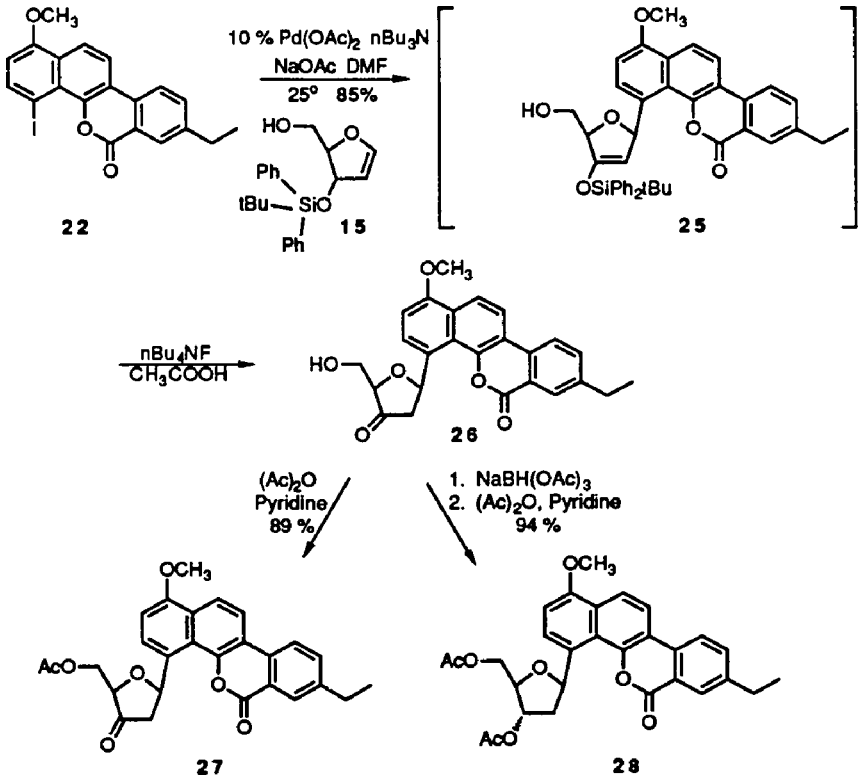
In previous reports, we[21,34] and others[35-41] have had little success in achieving catalytic versions of the palladium-mediated coupling reaction between enol ethers and aryl compounds. In each case, achievement of an acceptable yield of coupled product required elevated reaction temperatures and several equivalents of either the enol ether or aglycone precursor. Further understanding of the factors affecting the palladium-mediated coupling reaction between enol ethers and aryl compounds, roles of various ligands and salts, nature of the catalyst, as well as solvent effects on the coupling reaction,[18,42-44] has led to the development of an improved coupling procedure.[45] The new glycal-aglycon coupling reaction (a) is catalytic in palladium, (b) occurs rapidly at room temperature, (c) requires only stoichiometric portions of reactants, (d) and is as effective as the previously reported method for synthesizing *C*-glycosides[18] which requires stoichiometric quantities of palladium to affect glycosidic bond formation.

With the initial attempts to synthesize *C*-glycosides by the palladium catalyzed coupling of aryl bromides with functionalized glycals having been unsuccessful, we then began studying the coupling reactions between glycals and aryl iodides using catalytic portions of palladium. For these experiments, we prepared 8-ethyl-4-iodo-1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one (**22**)[45] from the corresponding aryl bromide by a halogen exchange reaction.[46,47] The reaction of **22** with furanoid glycal (**21**)[28] was carried out in a reaction medium containing 10 mol % palladium acetate, two equivalents of tributylamine per palladium and one equivalent of sodium acetate in dimethylformamide[42,43] at room temperature. Under these conditions, palladium-catalyzed coupling of equivalent portions of iodo derivative **22** with furanoid glycal **21**[28] occurred during 48 hours both regio- and stereospecifically to form a single *C*-glycoside product. Under these reaction conditions, desilylation (presumably by iodide ion) occurred to produce the corresponding 3'-keto-β-*C*-glycoside (**24**) as the only isolated product in 85% yield. A companion experiment, in which tributylamine was replaced by one equivalent of tetra-n-butylammonium chloride[44] and sodium bicarbonate was used as the base rather than sodium acetate, was equally successful.



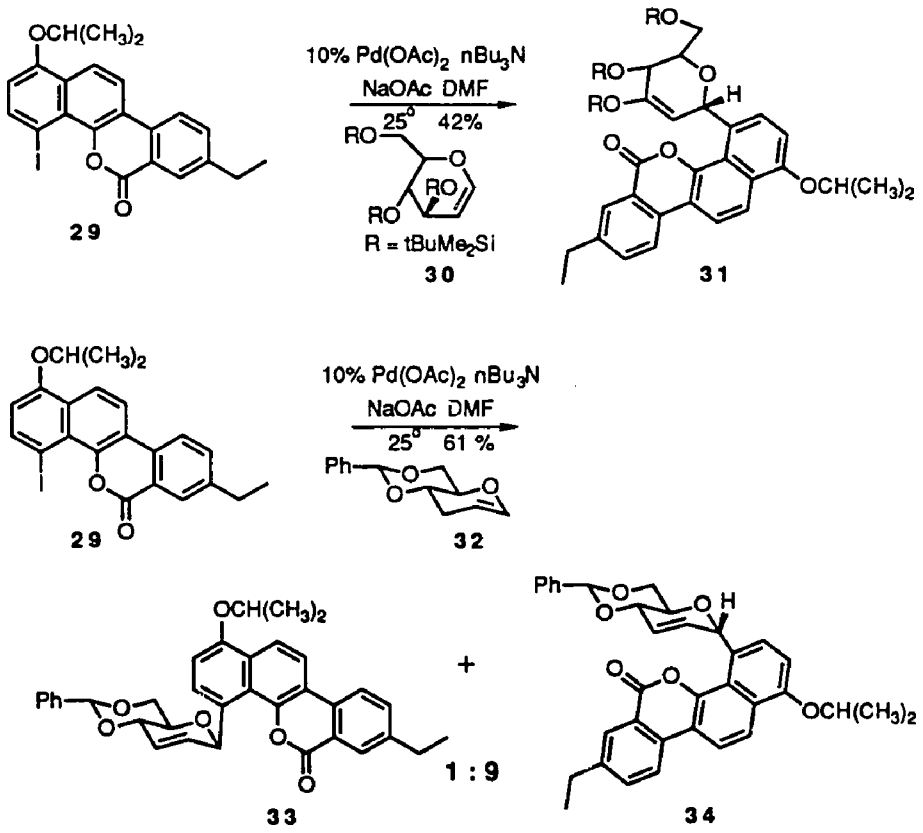
Scheme 4.5 Catalytic Palladium Coupling Reaction

The utility of the recent improvements in the syntheses of β-*C*-glycosides was demonstrated with the synthesis of compounds **27** and **28**. The desired *C*-glycoside was obtained by mixing **22**, in the presence of 10 mol % palladium acetate, with our tailor-made glycal **15**[20]. In this case, the reaction was complete after ten hours; tetrabutylammonium fluoride was then added to complete desilylation of the intermediate silyl enol ether (**25**) and the free 5'-hydroxyl of the resulting 5'-hydroxy-3'-keto *C*-glycoside (**26**) was acetylated *in situ* to facilitate product isolation. This one-pot three-step reaction sequence yielded *C*-glycoside **27** as the single isolated product in 89% yield. More dramatically, a one-pot four-step synthetic sequence, which includes the stereospecific reduction of the 3'-keto group with sodium triacetoxyborohydride[33], was accomplished to yield 4-[2'-deoxy-3',5'-diacetyl-β-D-ribo(=arabino)furanosyl]-8-ethyl-1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one (**28**) in an isolated yield of 94 %.



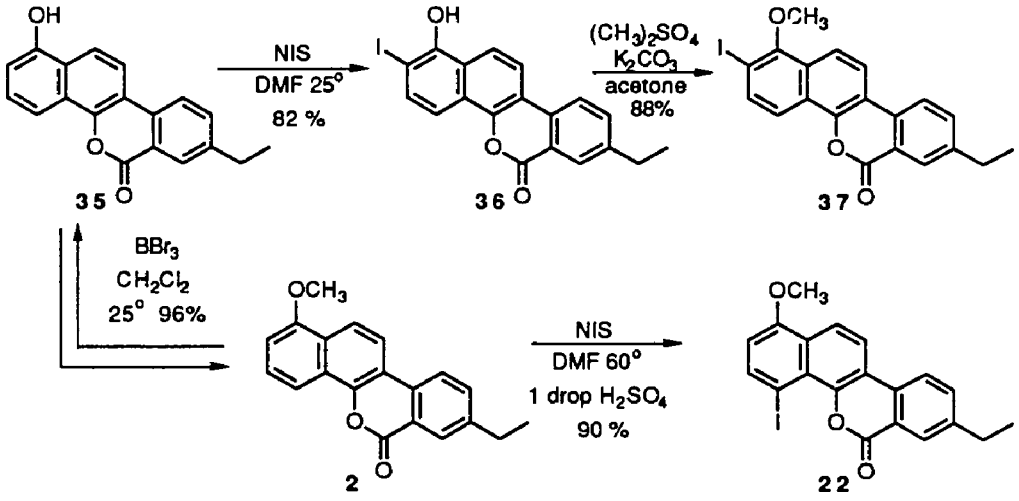
Scheme 4.6 One Pot-Multiple Step Synthesis

Further extension of the catalytic palladium-mediated coupling reaction was accomplished by treating aryl iodide **29** with pyranoid glycal **30**[14c,d] to give α-C-glycoside **31** in 42% yield. However, by mixing **29**[48] with glycal **32**[49], in which the allylic (C-3) carbon bears only hydrogen, an anomeric pair of anthracyclic C-glycosides (**33** and **34**) were produced in a ratio of 1:9 (61% combined yield).[48] In previous studies involving pyranoid glycals,[18] attack of the intermediate organopalladium reagent derived from the aglycon derivative has occurred invariably from the face of the glycal opposite the C-3 oxy substituent. In this example, stereochemical induction was affected by more remote (i.e. C-4 and C-5) sites of the glycal. This suggests that a stereo-directing group at C-3 of the glycal is not essential for synthetically efficient construction of a stereocontrolled C-glycosyl linkage.



Scheme 4.7 Catalytic Coupling with Pyranoid Glycals

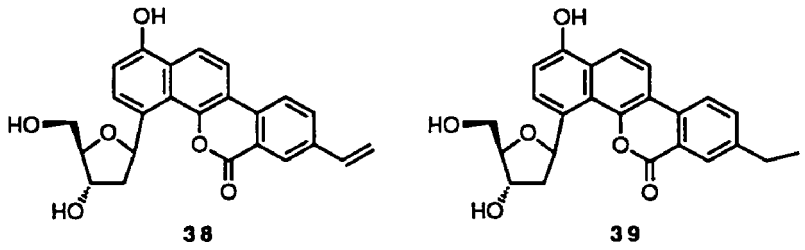
With the palladium-mediated coupling reaction between aryl iodides and both furanoid and pyranoid glycals having been accomplished,[45] a direct iodination method of the benzo[d]naphtho[1,2-b]pyran-6-one ring system was desired. Iodination conditions were developed to selectively synthesize ortho (C-2) and para (C-4) iodo derivatives.[48,50] By treating the free phenol **35**[27] with N-iodosuccinimide in dimethylformamide[46], the ortho iodinated product (**36**) was obtained in 82% yield. Methylation of **36** yielded **37**, whereas protection of the phenol prior to iodination produced the isomeric 4-iodo compound **22**.



Scheme 4.8 Direct Iodination of the Aglycon

CHAPTER 5: SYNTHESIS OF 8-ETHYL- AND 8-ETHENYL-1-HYDROXY-4-(2'-DEOXY-β-D-RIBOFURANOSYL)-BENZO[d]NAPHTHO[1,2-b]PYRAN-6-ONES

We have reported the synthesis of *C*-glycosides[16] structurally related to the benzo[d]naphtho[1,2-b]pyran-6-one antibiotics ravidomycin,[4] chrysomycin,[5] and the gilvocarcins.[3] Quite recently, we reported the synthesis[27] of the first *C*-glycoside which possesses the minimum structural requirements (1-hydroxy, 8-ethenyl) necessary for bioactivity.[7c,9] The present study has culminated with the syntheses of 8-ethenyl-1-hydroxy-4-(2'-deoxy-β-D-ribofuranosyl)benzo[d]naphtho[1,2-b]pyran-6-one (**38**) and 8-ethyl-1-hydroxy-4-(2'-deoxy-β-D-ribofuranosyl)benzo[d]naphtho[1,2-b]pyran-6-one (**39**).[50] The synthesis of these compounds was not straightforward as unexpected complications arose.



38 **39**

Scheme 5.1 Target *C*-Glycosides

5.1. Attempted Formation of the Aglycon Vinyl Group By Radical Bromination-Dehydrobromination

The ultimate utility of the recent improvements in the syntheses of β-C-glycosides has been demonstrated with the synthesis of 4-[2'-deoxy-3',5'-diacetyl-β–D-ribo (=arabino)furanosyl]-8-ethyl-1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one(**28**).[45] Compound **28** is a potential intermediate in the synthesis of the target compounds **38** and **39** provided hydrolysis of the methyl ether at C-1 of the aglycon and radical bromination-dehydrobromination of the ethyl sidechain can be accomplished.

Subsequently, all attempts to effect demethylation of 28 resulted in either no reaction or epimerization of the anomeric center of the sugar moiety.

Attempted radical bromination of the ethyl group of 28 was equally unsuccessful. When 28 was treated with N-bromosuccinimide in the presence of benzoyl peroxide, the desired brominated *C*-glycoside was not obtained. Instead, two highly unstable products were isolated from the reaction mixture which exhibited none of the ^{1}H NMR resonances characteristic of the ribofuranosyl moiety. (figure 5.1).

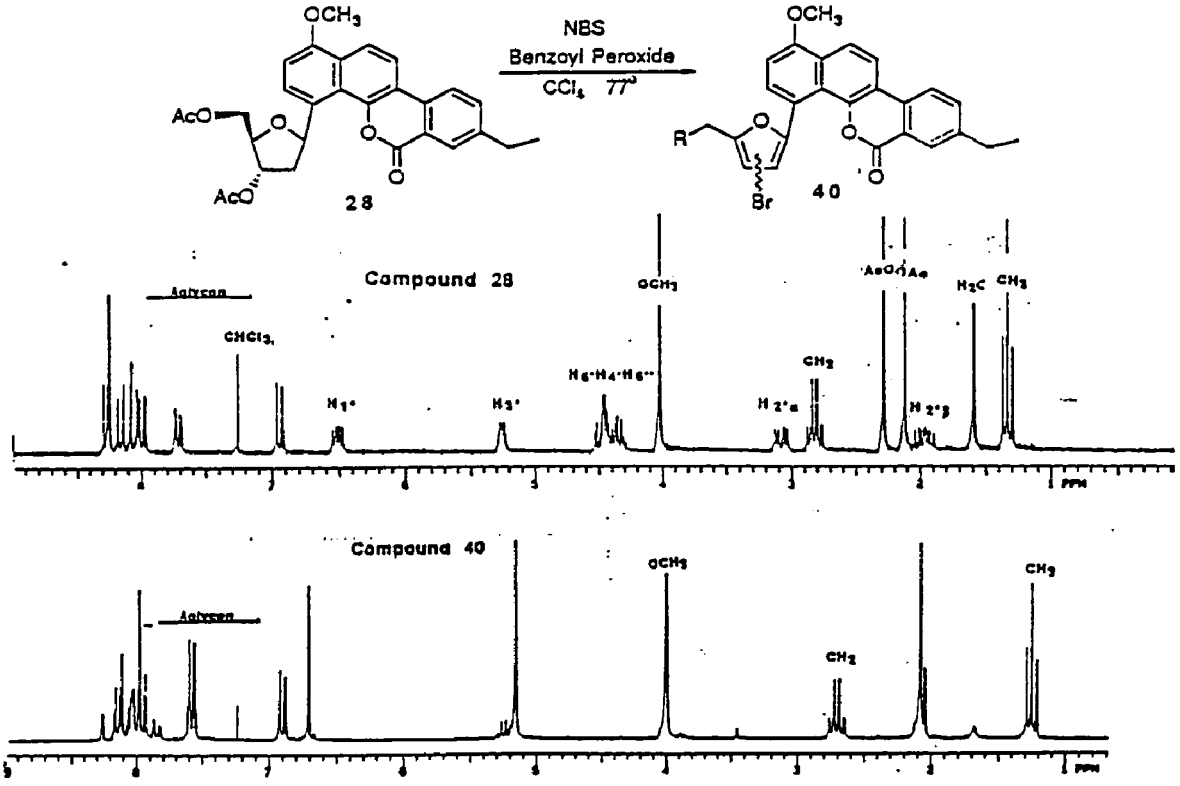
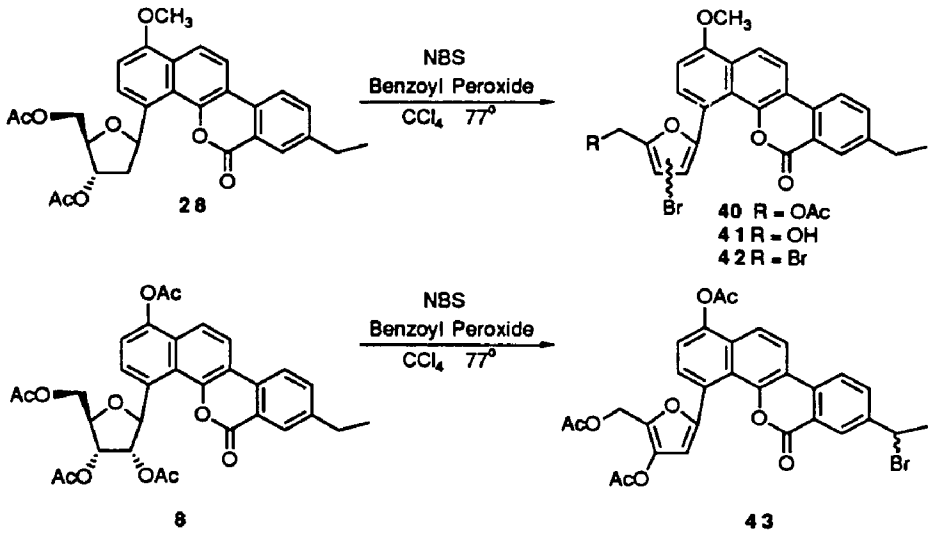


Figure 5.1 Results of Radical Bromination of 28

The presence of two new resonances (δ 5.17 and 6.70 ppm for 40, δ 4.61 and 6.70 ppm for 41), indicated that the sugar moiety had aromatized to the furan under the reaction conditions. These ^{1}H NMR resonances are consistent with disubstituted furfuryl alcohols.[51] Mass spectral data of compound 40 clearly established the

composition to be $C_{27}H_{21}O_6Br$, however, the regiochemistry (C-2' or C-3') of the furan bromo-substituent could not be established from the available data. In the ^1H NMR spectrum of compound **41**, no acetyl methyl resonances are present and the two hydrogen resonance has shifted from δ 5.17 (compound **40**) to 4.61 ppm. This can be explained by either hydrolysis of the ester to give **41** or by radical bromination of C-5' to give **42**. Unfortunately, mass spectral data were not obtained for this material due to the highly unstable nature of this compound. Based on the available spectral studies, the products were assigned structures **40** and **41**.



Scheme 5.2 Radical Bromination Results

Reinvestigation of the radical bromination of **8**[27] resulted in the isolation of a highly unstable product which was difficult to characterize. Based on mass and nuclear magnetic resonance spectra, the compound was assigned structure **43**.

These reactions illustrate that radical bromination occurs at both the aglycon ethyl sidechain and the anomeric carbon of the sugar moiety in a competitive manner. In the case of *C*-glycoside **8**, attack occurs preferentially at the more accessible ethyl group of the aglycon since the presence of the 2'-acetate undoubtedly limits the steric

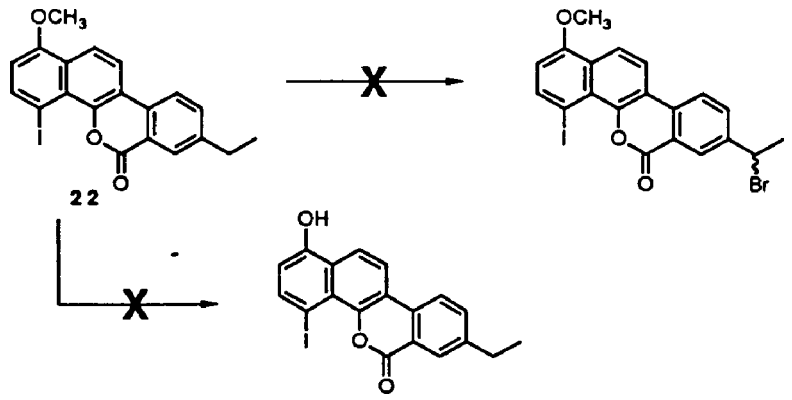
accessibility of C-1 of the carbohydrate. In the case of 2'-deoxy-*C*-glycoside **28**, which does not possess a neighboring C-2'-substituent, radical bromination occurs almost exclusively at the anomeric carbon of the ribofuranosyl moiety.

Two conclusions were made as a result of the unsuccessful demethylation of the C-1 ether of the aglycon and the failure to get the vinyl group by radical bromination-dehydrobromination to produce the desired *C*-glycosides **38** and **39**. A new protective group for the anthracyclic phenol must be chosen which is both compatible with subsequent reactions and readily removable without disrupting the stereochemical integrity of the anomeric center of the carbohydrate. Secondly, the vinyl substituent must be made prior to the aglycon-glycal coupling in order to circumvent the aromatization of the sugar moiety via radical bromination.

5.2. Aglycon Chemistry

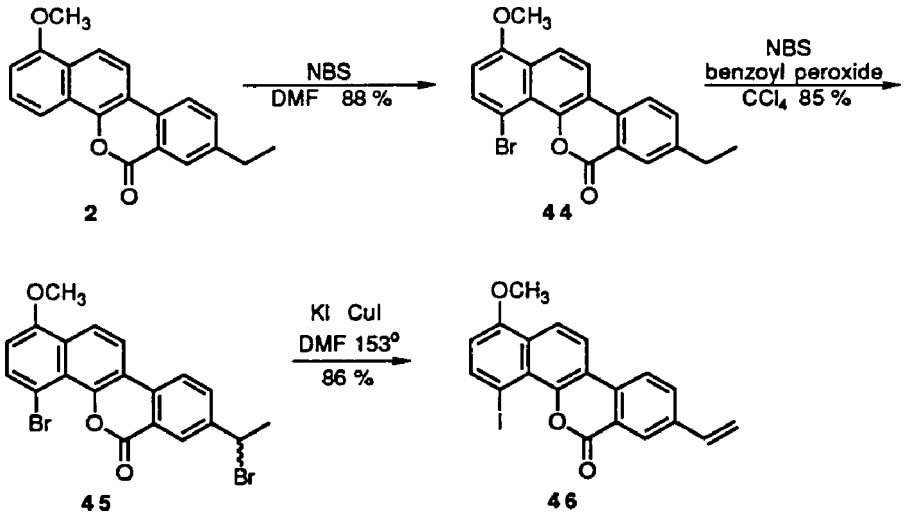
In order to synthesize an aglycon derivative having both the iodo and vinyl substituents intact prior to *C*-glycoside bond formation, a number of routes were explored. The first of the schemes tested involved the formation of the iodo substituent prior to conversion of the ethyl group to a vinyl substituent. When aryl iodide **22** was treated with N-bromosuccinimide in the presence of benzoyl peroxide, radical bromination in the ethyl group did not occur, but instead, rapid deiodination took place.

All attempts to remove the methyl group (boron and aluminum tri-halides or various nucleophiles including sodium thioethoxide, and potassium trimethylsilyloxide)[52] from the C-1 oxygen of **22** also resulted in either no reaction or rapid deiodination. It became apparent that iodination must therefore be delayed until after the vinyl substituent had been constructed.



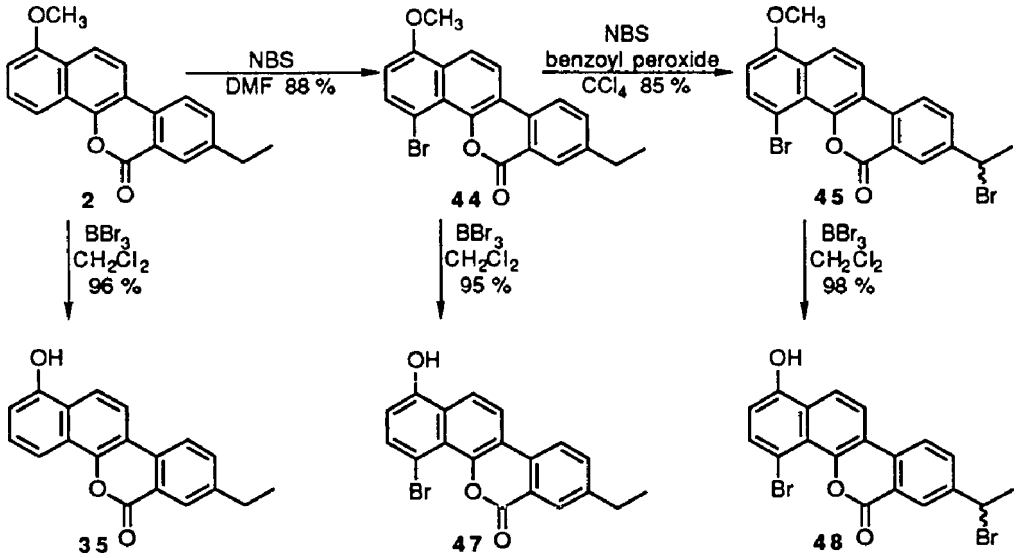
Scheme 5.3 Step Ordering

Compound **2**[7c,13a] was synthesized and brominated selectively at C-4 to give **44** (88%) followed by radical bromination of the benzylic carbon to give **45**. When **45** was subjected to the halogen exhange reaction conditions, iodination as well as dehydrobromination was effected to give **46** in 86% yield which contains the desired iodo and vinyl substituents.



Scheme 5.4 Halide Exchange Reaction

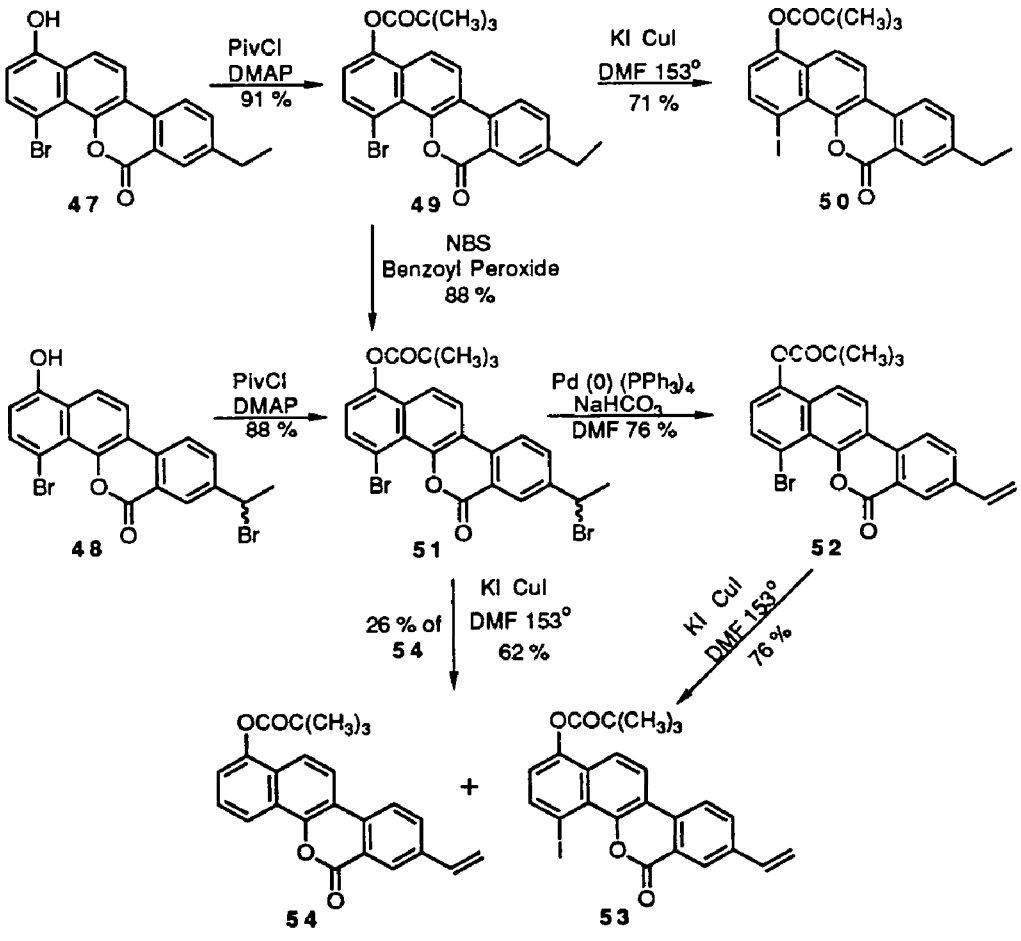
To incorporate this two-step process into a useful synthetic sequence, several phenolic derivatives were synthesized (**35**,[27]**47**,**48**) After attempted halogen exchange[47] of **47** and **48** resulted in the formation of intractable tars, a variety of derivatives was synthesized. The phenols were silylated, acetylated and also protected as the isopropyl ethers and subsequently subjected to the halide exchange reaction conditions. The silylated and acetylated derivatives were not compatible with the strong conditions required for halogen exchange[47] and resulted in rapid desilylation and deacetylation. The isopropyl ether derivatives survived the halogen exchange reactions but subsequent removal of the isopropyl protective group was not straightforward.



Scheme 5.5 Demethylation

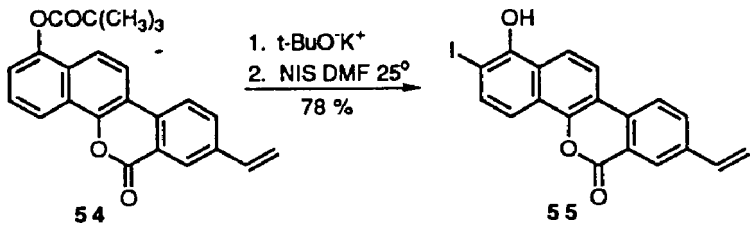
Since a more hindered ester should be stable under the halogen exchange reaction conditions, the phenols (**47**and **48**) were then esterified with pivaloyl chloride in the presence of 4-dimethylaminopyridine[7c] to give **49** and **51** in excellent yield. Treatment of **49** with cuprous and potassium iodides[47] resulted in halogen exchange to give aryl iodide **50**. The desired aglycon precursor containing both the 4-iodo and 8-

vinyl substituents, was synthesized from **51** in either of two ways. Dehydrobromination was effected using catalytic tetrakis(triphenylphosphine) palladium(0)[27] to form **52** which subsequently underwent halogen exchange in the presence of cuprous iodide and potassium iodide[47] to yield **53** in 76 % isolated yield. Compound **53** was also obtained directly from **51** under the halogen exchange conditions. From this reaction mixture, the desired aglycon precursor **53** was isolated in 62 % yield. During this reaction, complete dehalogenation also occurred to give **54**[7c] as a side product in 26 % yield.



Scheme 5.6 Synthesis of the Desired Aglycon

Side product **54** was deprotected[7c] and iodinated to give **55** (74%) which should prove to be a key intermediate in the synthesis of isomeric C-2 *C*-glycosides.

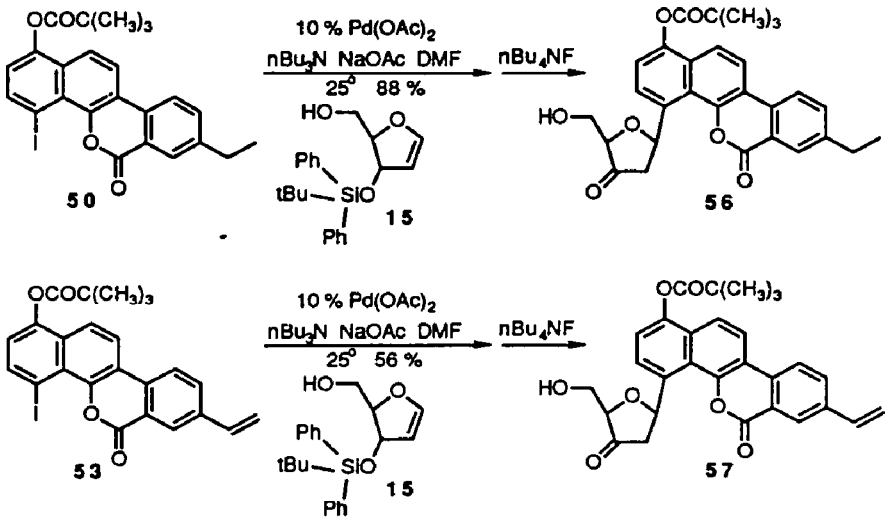


54 **55**

Scheme 5.7 Iodination of Byproduct

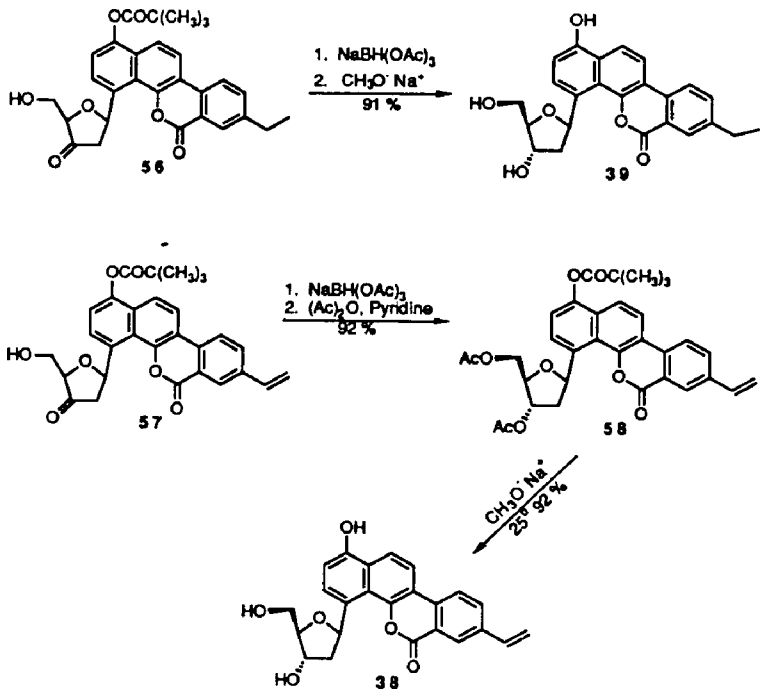
5.3. Synthesis of *C*-Glycosides

The full potential of a pivaloyl-protected aglycon derivative was realized by reaction of 8-ethyl-4-iodo-1-trimethylacetoxybenzo[d]naphtho[1,2-b]pyran-6-one (**50**) with furanoid glycal **15**,[20] a glycal specifically designed for synthesizing β-*C*-glycosides. In the presence of catalytic quantities of palladium acetate, *C*-glycosyl bond formation was effected in a stereo- and regiospecific manner to produce, following the *in situ* desilylation of the intermediate silyl enol ether, 8-ethyl-4-(β–D-glycero-pentofuran-3'-ulos-1'-yl)-1-trimethylacetoxybenzo[d]naphtho[1,2-b]pyran-6-one (**56**) in 88% isolated yield. Equally straightforward was the synthesis of 8-ethenyl-4-(β–D-glycero-pentofuran-3'-ulos-1'-yl)-1-trimethylacetoxybenzo[d]naphtho [1,2-b]pyran-6-one (**57**). Coupling of **53** with **15**[20], in the presence of catalytic quantities of palladium acetate afforded β-*C*-glycoside **57** which contains the aglycon vinyl substituent necessary for the photolytic nicking of DNA. [7c,9]



Scheme 5.8 *C*-Glycoside Formation

Reduction of the carbohydrate carbonyl carbon from the β-face was achieved using sodium triacetoxyborohydride.[33] Treatment of compound **56** with sodium triacetoxyborohydride at room temperature resulted in rapid stereospecific carbonyl reduction which followed by hydrolysis gave 4-[2'-deoxy-β-D-ribo-(=arabino)-furanosyl]-8-ethyl-1-hydroxybenzo[d]naphtho[1,2-b]pyran-6-one (**39**) in excellent yield (91%). Following the stereospecific reduction of compound **57**, in situ acetylation produced **58** in 92% isolated yield. Removal of the three ester protecting groups was effected by sodium methoxide to give the target compound (**38**) in high yield (92%).

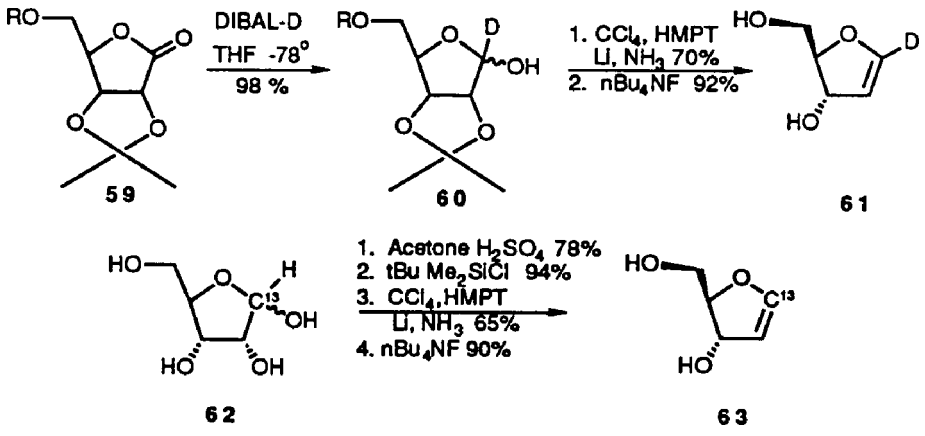


Scheme 5.9 Target Compounds

CHAPTER 6: SYNTHESIS OF ^{2}H AND ^{13}C-LABELLED GLYCALS

As an outgrowth of our work with ribofuranoid glycals, we became interested in the synthesis of labelled D-ribal. Quite recently, D-ribal (1,4-anhydro-2-deoxy-D-*erythro*-pent-1-enitol)[28] has been shown to be a key intermediate in the biosynthesis of 2'-deoxyribonucleotides.[53] In the absence of acceptors, nucleoside 2-deoxyribosyltransferase catalyzes the hydrolysis of 2'-deoxyribonucleosides. During this hydrolysis reaction, D-ribal is generated spontaneously. In the absence of nucleic acid bases, D-ribal is quickly hydrated to give 2'-deoxy-ribose, whereas the presence of nucleic acid bases resulted in the formation of 2'-deoxyribonucleotides.

In order to further study the mechanism of 2'-deoxyribonucleotide biosynthesis, compounds **61** and **63** were synthesized via the method of Ireland.[30] Compound **60** was obtained via reduction[54] of the protected ribonolactone (**59**)[28] using diisobutylaluminum deuteride (98% D).[55] Following reduction of the lactone (98 %), **61** was obtained directly from a two step procedure in 63 % overall yield. Compound **63** was synthesized in a straightforward manner[18,30] from the commercially available 1-^{13}C-D-ribose (99% ^{13}C).[56] Following a four step synthesis, **63** was obtained directly in 45 % overall yield.



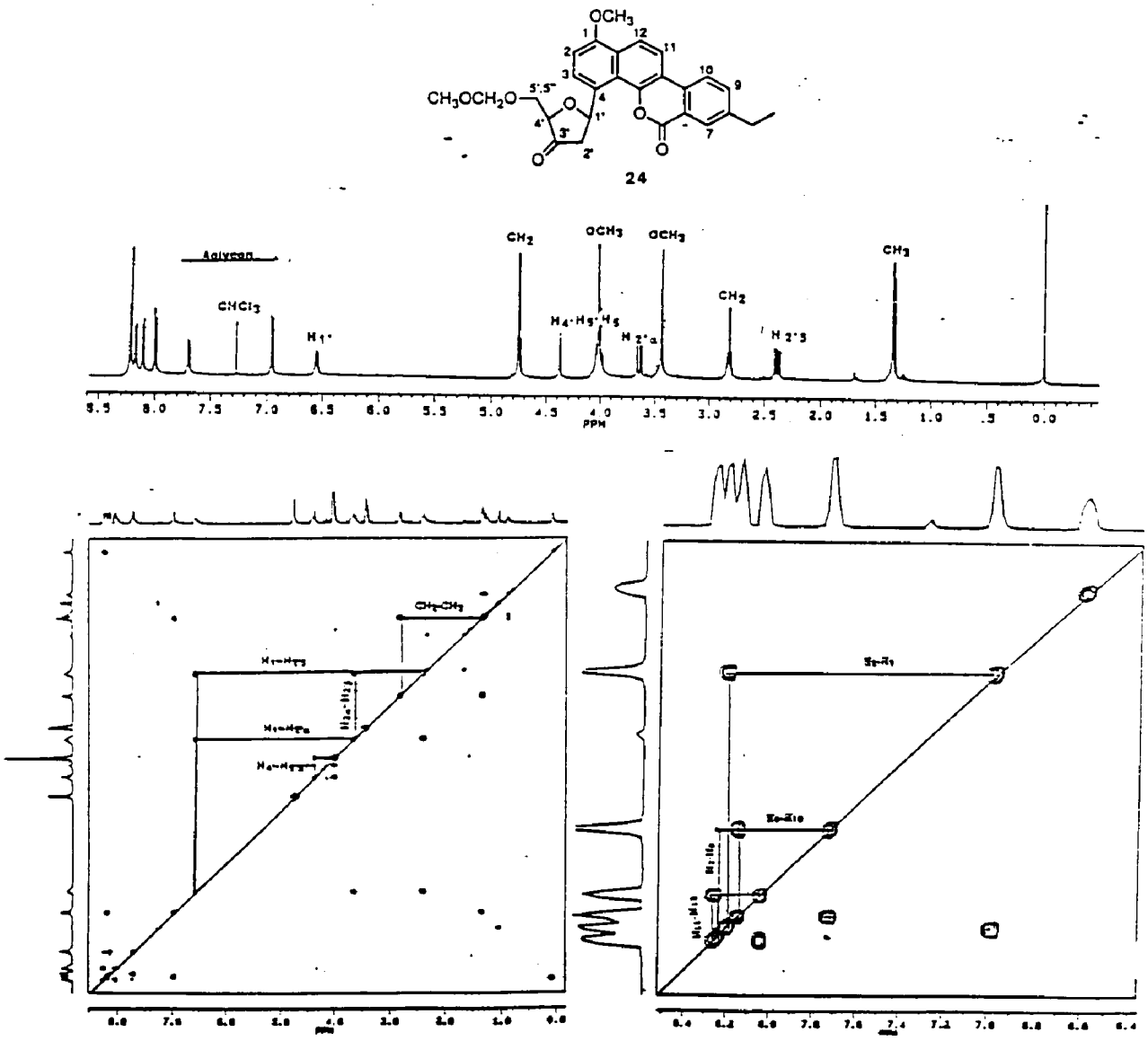
Scheme 6.1 Synthesis of Labelled Glycals

CHAPTER 7: STRUCTURAL ASSIGNMENT OF *C*-GLYCOSIDES

The *C*-glycosides that were synthesized in this study were characterized by mass spectroscopy, elemental analysis, and detailed nuclear magnetic resonance (nmr) spectroscopy. Due to the complexity of the resulting benzo[d]naphtho[1,2-b]pyran-6-one *C*-glycosides, the complete assignment of all resonances in both the ^{1}H nmr and ^{13}C nmr was difficult but full characterization of these materials was accomplished by utilization of several two-dimensional nmr experiments.

7.1 Assignment of ^{1}H NMR Spectrum

C-Glycosides of the benzo[d]naphtho[1,2-b]pyran-6-one family exhibit a complex ^{1}H nmr spectrum due to the nature of both the aglycon (seven aromatic protons) and sugar moiety. For this reason, we employed a two-dimensional homonuclear experiment (COSY[57]) to establish the relationship of the different resonances in question. (Figure 7.1) The COSY experiment was most useful in differentiating H_3 from H_{10} of the aglycon since ambiguity had arisen from identical coupling constants for H_2, H_3, and H_{10}, whereas in the case of 2,3-dideoxy-pyranosyl *C*-glycosides, the assignment of $H_{2'}$ and $H_{3'}$ was impossible based on the COSY experiment. The definitive assignment of $H_{2'}$ and $H_{3'}$ was accomplished through the use of n.O.e. experiments. (section 7.3)



24

Figure 7.1 ^{1}H Assignment of *C*-Glycosides Using COSY Experiment

7.2 Assignment of ^{13}C NMR Spectrum

In order to accomplish a more detailed assignment of the ^{13}C spectrum of our materials, the ^{13}C APT (attached proton test) and HETCOR (heteronuclear correlation test)[57] experiments were performed. Direct correlation between ^{1}H and ^{13}C signals

was established by utilizing the HETCOR experiment which made possible the detailed assignment of the ^{13}C nmr spectrum.(see for example Figure 7.2)

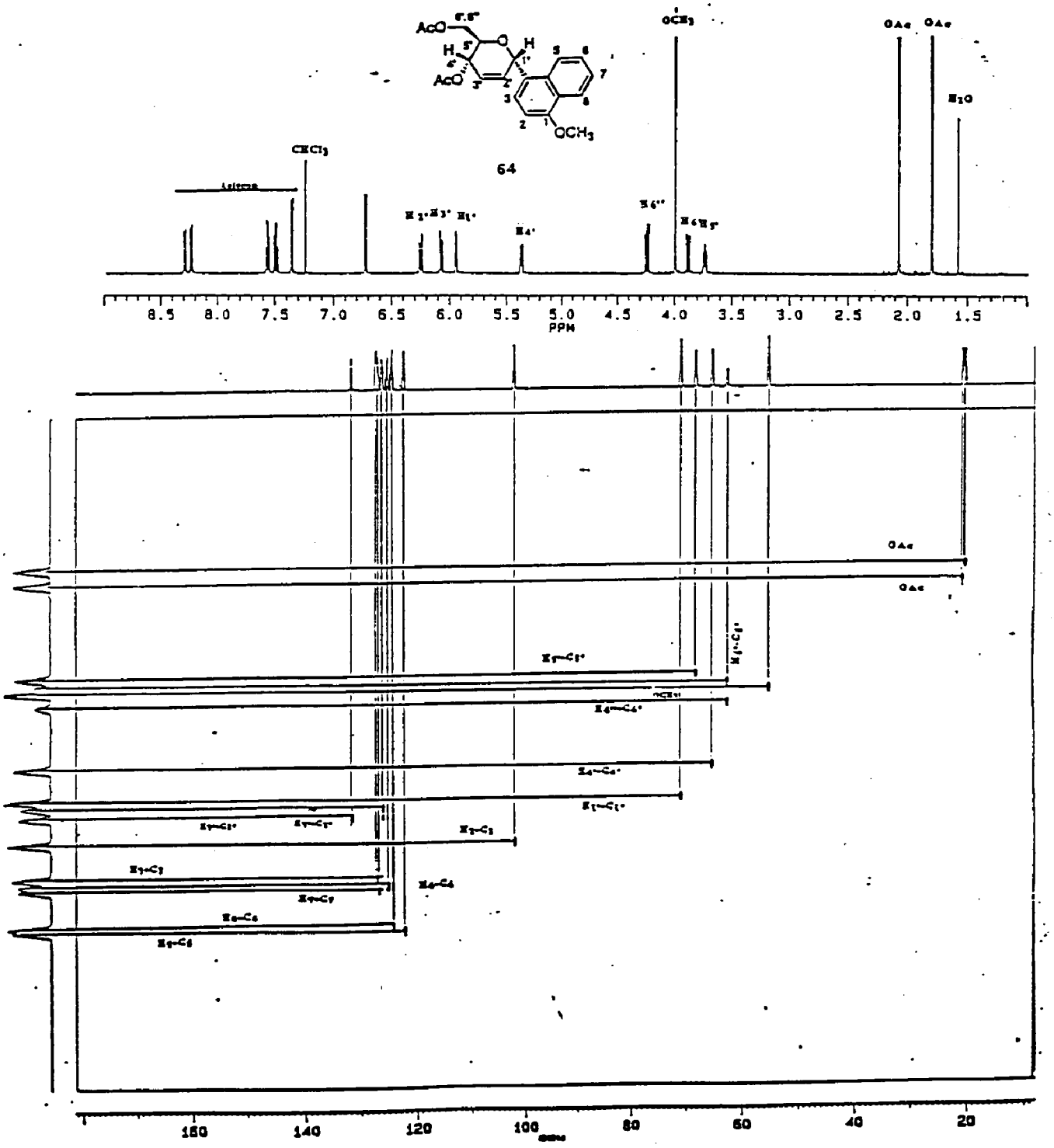


Figure 7.2 ^{13}C Assignment of *C*-Glycosides Using HETCOR Experiment

7.3 Assignment of the Anomeric Configuration of C-Glycosides

In syntheses of chiral molecules, a key analytical step is the determination of the configuration of the newly formed asymmetric center. The methods that are currently used to determine the anomeric configuration of C-glycosides include the comparison of chemical shifts or coupling constants of anomeric pairs[58,59] and more recently, the comparison of $^{1}J_{C1,H1}$ values[60] for anomeric pairs has been used to assign the stereochemistry at the C1 carbon. The available methods rely on close comparisons of spectral data for both members of an anomeric pair. Since the palladium-mediated coupling reaction is stereospecific,[18] we require an analytical procedure which confidently determines the anomeric configuration of a single *C*-glycoside in a quick and reliable fashion without the need for comparison with data for the complementary anomer.

An additional method that has been reported[61] for the unambiguous assignment of the anomeric configuration of *C*-glycosides utilizes homonuclear Overhauser enhancement (NOE) spectroscopy.[57] Since the magnitude of NOEs diminishes rapidly as the interproton distance is increased, one expects to observe a larger NOE from a proton with a syn relationship to the ring proton being irradiated than when the two protons are anti to one another. In the case of ribofuranosyl *C*-glycosides, strong NOEs between $H_{1'}$ and $H_{4'}$ protons are expected[61a,g,i] whereas α-*C*-glycosides exhibit a strong $H_{1'}$-$H_{3'}$ NOE due to thier relative proximity.[61g,i] *C*-Glycopyranosides have also been reported to exhibit similar behavior when studied by NOE difference spectroscopy.[61f] α-*C*-Glycopyranosides exhibit a strong NOE between the syn protons $H_{1'}$ and $H_{4'}$, whereas β-*C*-glycopyranosides exhibit a strong NOE between $H_{1'}$ and $H_{5'}$ protons which are within the effective distance[57] of the NOE experiment.

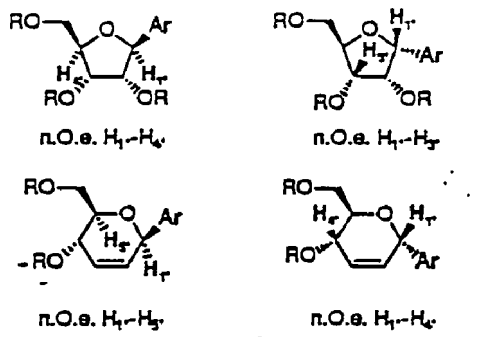


Figure 7.3.1 Observed N.O.E.s of *C*-Glycosides

N.O.e. difference spectroscopy was used in the characterization of each of the *C*-glycosides that were synthesized in this study. In every case studied, the anomeric configuration was assigned clearly based on the n.O.e. results between the appropriate protons of both α- and β-*C*-glycosides respectively. Previous assignments of the stereochemistry of the anomeric center which were based on either the homoallylic coupling constant $J_{1',4'}$[23b](*C*-glycofuranosides) or comparison of the available literature, were further corroborated by n.O.e. difference spectroscopy. To illustrate the effectiveness of n.O.e. difference spectroscopy, spectral data for compounds 28, 33 and 34 are presented (Figures 7.3.2, 7.3.3).

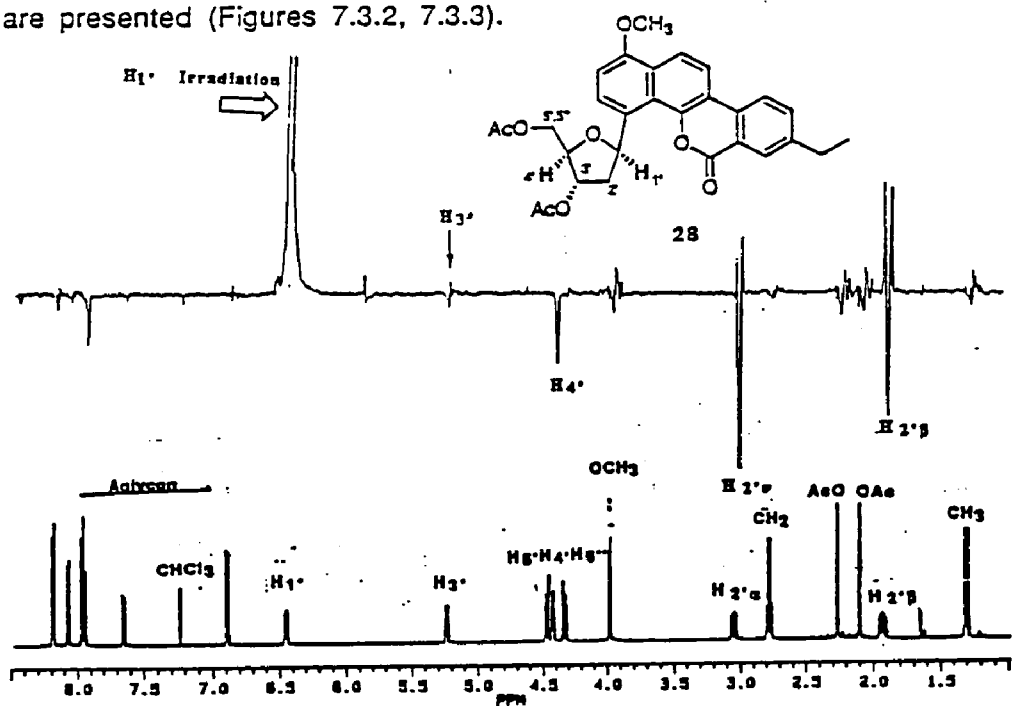


Figure 7.3.2 Assignment of the Anomeric Configuration of *C*-Ribofuranoside 28 by Irradiation of $H_{1'}$

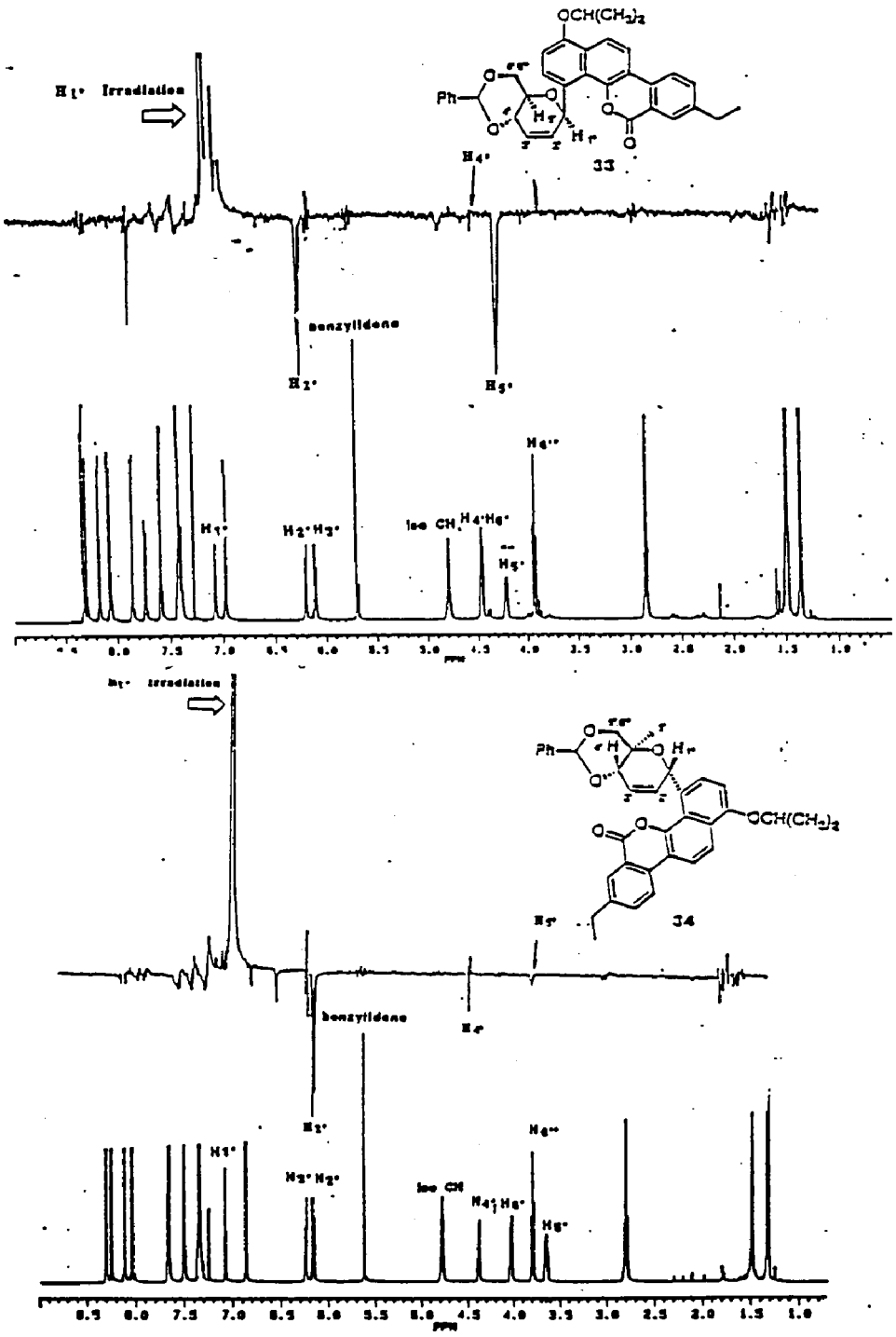
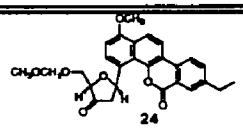
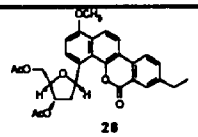
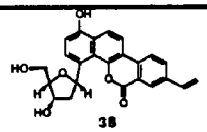
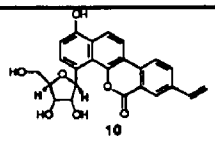
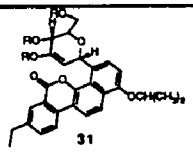
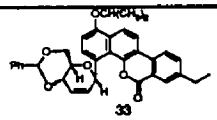
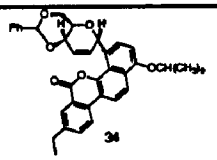
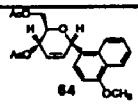
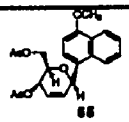


Figure 7.3.3 Assignment of the Anomeric Configuration of *C*-Glycopyranosides 33 and 34 by Irradiation of $H_{1'}$

C-Glycoside 28 (Figure 7.3.2) exhibits the expected n.O.e.[61agi] for β-*C*-ribofuranosides ($H_{1'}$-$H_{4'}$), whereas 33 and 34 clearly exhibit the characteristic $H_{1'}$-$H_{4'}$ or

$H_{1'}$-$H_{5'}$ n.O.e.s expected[61f] for α- and β-*C*-glycopyranosides respectively. The results of the n.O.e. experiments are summarized in Table 7.1.

Table 7.1 N.O.E. Data of *C*-Glycosides

COMPOUND	n.O.e. $H_{1'}$-$H_{4'}$	n.O.e. $H_{1'}$-$H_{5'}$
 24	YES	- - -
 28	YES	- - -
 38	YES	- - -
 10	YES	- - -
 31	YES	- - -
 33	- - -	YES
 34	YES	- - -
 64	YES	- - -
 65	- - -	YES

CHAPTER 8: CONCLUSIONS

This study has resulted in the synthesis of 8-ethenyl-1-hydroxy-4-(2'-deoxy-β-D-ribofuranosyl)benzo[d]naphtho[1,2-b]pyran-6-one (**38**) and 8-ethyl-1-hydroxy-4-(2'-deoxy-β-D-ribofuranosyl)benzo[d]naphtho[1,2-b]pyran-6-one (**39**)[50] which are structurally related to the Gilvocarcin family of antibiotics. The palladium-catalyzed coupling reaction between an aryl iodide and a glycal (1,2-unsaturated carbohydrate) has been developed[18,45] and is applicable to the synthesis of both *C*-glycopyranosides and *C*-glycofuranosides.

1,4-Anhydro-2-deoxy-3-*O*-(t-butyldiphenylsilyl)-D-*erythro*-pent-1-enitol (**15**), a glycal specifically designed for efficient production of β-*C*-glycosides, has been synthesized[20]. This glycal has been employed in the synthesis of β-*C*-ribofuranosides in both stoichiometric[20] and catalytic[45,50] palladium-mediated coupling reactions.

The synthesis of ribofuranoid glycals **61** and **63** in which the C-1 carbon is labelled (^{2}H or ^{13}C), has been accomplished. This methodology may be employed in the study of the biosynthesis of 2'-deoxyribonucleotides[53] or in the synthesis of C-1'-labelled (anomeric center of the sugar moiety) *C*-glycosides.

The catalytic palladium-mediated coupling reaction, which was developed during the course of this study,[45] may be applied to the synthesis of the naturally occurring Gilvocarcin V.[3] Together with the furanoid glycal **15** and 3-deoxy pyranoid glycal **32**,[49] the palladium-mediated coupling reaction is an attractive route to the gilvocarcins[3] as well as ravidomycin.[4] Following *C*-glycoside formation via the palladium-mediated coupling reaction, various subsequent modifications of the carbohydrate moieties will give rise to a variety of synthetic analogs as well as the corresponding natural products.

Experimental Section

General Comments. Thin-layer chromatography (TLC) was carried out on prescored silica gel GF plates (Analtech). Preparative TLC was carried out on 1 mm thick, 20 x 20 cm, silica gel GF plates (Analtech). For flash chromatography, silica gel 60 (230-400 mesh ASTM, E. Merck) was used. Columns were eluted with a positive nitrogen pressure. Nuclear magnetic resonance (nmr) spectra were obtained on either a JEOL FX-90Q, a Varian Associates XL-200 or a Bruker AM 500 spectrometer and are referenced to tetramethylsilane. Melting points were measured with a Thomas-Hoover capillary apparatus and are uncorrected. Elemental analyses were carried out by Quantitative Technologies, Bound Brook, NJ.

1,4-Anhydro-2-deoxy-5-*O*-[(1,1-dimethylethyl)dimethylsilyl]-3-*O*-[(1,1-dimethylethyl)diphenylsilyl]-D-*erythro*-pent-1-enitol (14). A mixture of **13**[28] (5.80 g, 25.2 mmol), imidazole (4.29 g, 63.0 mmol), and *t*-butyldiphenylsilyl chloride (7.60 g, 27.7 mmol) in 20 mL of dimethylformamide was stirred at room temperature for 18 hours. The reaction mixture was then poured into 300 mL of diethyl ether and the organic layer was separated and washed with brine and distilled water and then dried over sodium sulfate. After evaporation of the volatiles in vacuo, purification was accomplished by flash chromatography (ether/hexane 1:5) on silica gel to afford 11.33 g (96%) of **14** as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 0.13 (6H, s, Si-CH_3), 0.89 (9H, s, t-butyl), 1.10 (9H, s, t-butyl), 3.38 (2H, ddd, $J_{4,5}$ = 5.0 Hz, $J_{4,5'}$ = 6.2 Hz, $J_{5,5'}$ = 10.9 Hz, H-5,5'), 4.49 (1H, m, H-4), 4.87 (2H, m, H-2,3), 6.46 (1H, dd, $J_{1,2}$ = 2.2 Hz, $J_{1,3}$ = 0.7 Hz, H-1), 7,46, 7.74 (10H, phenyl). ^{13}C NMR ($CDCl_3$) δ 5.44, 18.28, 19.05, 25.83, 26.88, 62.97 (C-5), 76.81 (C-3), 89.20 (C-4), 103.30 (C-2), 127.55, 127.68, 129.60, 129.69, 133.93, 134.19, 135.78, 149.08 (C-1).

Anal. Calcd. for $C_{27}H_{40}O_3Si_2$: C, 69.2; H, 8.60. Found: C, 69.5; H, 8.77.

1,4-Anhydro-2-deoxy-3-*O*-[(1,1-dimethylethyl)diphenylsilyl]-D-*erythro*-pent-1-enitol (15). To a stirred solution of **14** (5.60 g, 12.0 mmol) in 25 mL of tetrahydrofuran at -22 °C, was added a 1M solution of tetra-n-butylammonium fluoride in tetrahydrofuran (14.4 mL, 14.4 mmol). The resulting mixture was then stirred for 2 hours during which time the reaction was completed based on TLC. 1,2-Dichloroethane (100 mL) was then added to the reaction mixture and the volatiles were removed in vacuo. The crude product was then purified by flash chromatography (ether/hexane, 1:3) to give 3.56 g (84%) of **15** as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 1.10 (9H, s, t-butyl), 3.25 (2H, ddd, $J_{4,5}$ = 3.4 Hz, $J_{4,5'}$ = 7.2 Hz, $J_{5,5'}$ = 11.8 Hz, H-5,5'), 4.47 (1H, m, $J_{3,4}$ = 3.4 Hz, H-4), 4.77 (1H, dd, $J_{2,3}$ =2.8 Hz, $J_{3,4}$ = 3.4 Hz, H-3), 4.97 (1H, dd, $J_{1,2}$ = 2.6 Hz, H-2), 6.47 (1H, m, H-1), 7,45, 7.72 (10H, phenyl). ^{13}C NMR ($CDCl_3$) δ 18.93, 26.79, 62.69 (C-5), 76.39 (C-3), 89.23 (C-4), 103.92 (C-2), 127.60, 127.62, 127.75, 129.73, 129.85, 133.68, 133.69, 135.68, 135.69, 148.67 (C-1).

Anal. Calcd. for $C_{21}H_{26}O_3Si$: C, 71.1; H, 7.39. Found: C, 70.8; H, 7.57.

1,3-Dimethyl-5-(β-D-*glycero*-pentofuran-3'-ulos-1'-yl)-2,4(*1H, 3H*)-pyrimidinedione (18). To a stirred solution of **16**[21] (460 mg, 11.56 mmol) in acetonitrile (25 mL) was added palladium acetate (260 mg, 11.56 mmol). The mixture was stirred for five minutes, and then a solution of **15** (491 mg, 13.87 mmol) in acetonitrile (5 mL) was added. After two hours, sodium bicarbonate (243 mg, 28.9 mmol) was added and the resulting mixture was stirred for an additional 18 hours. The mixture was then filtered through Celite, and volatiles were removed in vacuo. Column chromatography (ethyl acetate) of the residue yielded 478 mg (84%) of **17** as a colorless oil.

To a solution of **17** (200 mg, 0.41 mmol) and acetic acid (48.8 mg, .82 mmol) in tetrahydrofuran (25 mL) at -78 °C was added a 1M solution of tetra-n-butylammonium fluoride (0.82 mL, .82 mmol) in tetrahydrofuran. The reaction was complete in 15

minutes based on tlc. Volatiles were removed in vacuo and the resulting residue was purified by column chromatography to yield 100 mg (97%) of **18** as a colorless oil. Compound **18** exhibited spectrometric properties indistinguishable from those previously reported.[17c]

5-[2'-Deoxy-β-D-*ribo(=lyxo)*furanosyl]-1,3-dimethyl-2,4-(*1H,3H*)-pyrimidinedione[17c] (19). To a solution of **18** (120 mg, 0.47 mmol) in tetrahydrofuran (25 mL) at -78 °C was added a 1M solution of potassium selectride in tetrahydrofuran (0.95 mL, 0.95 mmol). After the reaction mixture was stirred for two hours, the reaction was complete based on tlc. Several drops of acetic acid were then added and cooling was discontinued. Ater removing the volatiles in vacuo, a 500 MHz NMR spectrum of the residue showed that **19** was the sole product. The residue was purified by column chromatography (ethyl acetate) to give 104 mg (86%) of **19** as a white solid which exhibited spectrometric properties indistinguishable from those previously reported.[17c]

5-[2'-Deoxy-β-D-*ribo(=arabino)*furanosyl]-1,3-dimethyl-2,4-(*1H,3H*)-pyrimidinedione[17c] (20). To a solution of **18** (80 mg, 0.31 mmol) in acetic acid (10 mL) and acetonitrile (10 mL) at room temperature was added sodium triacetoxyborohydride (168 mg, 0.79 mmol). The reaction was complete in 10 minutes based on tlc. Volatiles were then removed in vacuo. A 500 MHz NMR spectrum of the residue showed no trace of isomer **19**. The residue was purified by column chromatography (ethyl acetate) to give 80 mg (99%) of **20** as a white solid which exhibited spectrometric properties indistinguishable from those previously reported.[17c]

8-Ethyl-4-Iodo-1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one (22). To a mixture of 4-bromo-8-ethyl-1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one[45] (1.05 g, 2.7 mmol) and potassium iodide (9.1 g, 54.8 mmol) in 25 mL of dimethylformamide was added cuprous iodide (2.6 g, 13.7 mmol). The mixture was

heated under reflux for two hours at which time tlc indicated that reaction was complete. After cooling the reaction mixture to room temperature, the solvent was removed *in vacuo*. Chloroform (100 mL) was added and the suspension was filtered through a small amount of silca gel. The filtrate was washed with a saturated solution of sodium thiosulfate, distilled water, and then dried over sodium sulfate. The solvent was removed and the residue was recrystallized from chloroform : ethanol to give 1.06 g (90%) of 8-ethyl-4-iodo-1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one (**22**) as white crystals, mp 205°. ^{1}H nmr ($CDCl_3$): δ 1.30 (3 H, t, CH_3), 2.75 (2 H, q, benzylic), 3.91 (3 H, s, OCH_3), 6.44 (1 H, d, $J_{2,3}$ = 8.4 Hz, H-2), 7.60 (1 H, dd, $J_{7,9}$ = 1.9 Hz, $J_{9,10}$ = 8.1 Hz, H-9), 7.87 (1 H, d, $J_{11,12}$ = 9.0 Hz), 8.01 (1H, d, $J_{9,10}$ = 8.1 Hz, H-10), 8.05 (1 H, d, J $_{11,12}$ = 9.0 Hz) 8.10 (1 H, d, $J_{2,3}$ = 8.4 Hz, H-3), 8.13 (1 H, d, $J_{7,9}$ =1.9 Hz, H-7);^{13}C nmr ($CDCl_3$): δ 15.19, 28.58, 55.75, 73.80, 107.05, 114.69, 118.67, 118.94, 120.88, 122.35, 123.62, 127.53, 128.70, 132.55, 134.93, 142.29, 144.91, 145.51, 155.42, 160.04.

Anal. Calcd. for $C_{20}H_{15}IO_3$: C, 55.8; H, 3.51. Found: C, 55.8; H, 3.41.

4-[2'-Deoxy-5'-[(methoxy)methyl]-β-D-*glycero*-pentofuran-3'-ulos-1'yl]-8-ethyl-1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one (24). To a mixture of 8-ethyl-4-iodo-1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one (**22**) (50 mg, 0.12 mmol), sodium acetate (10 mg, 0.12 mmol), and tributylamine (6 µl, .024 mmol), in 5 mL of dry dimethylformamide was added 1,4-anhydro-2-deoxy-5-*O*-(methoxymethyl)-3-*O*-[tris(1-methylethyl)silyl]-D-*erythro*-pent-1-enitol (**21**)[28](44 mg, 0.14 mmol), and palladium acetate (3 mg, 0.012 mmol). After stirring at room temperature for 48 hours, the volatiles were removed *in vacuo*. The residue was dissolved in chloroform and purified by column chromatography (methylene chloride/ether, 10:1) to give 46 mg (85%) of **24** as white crystals, mp 194°. ^{1}H nmr ($CDCl_3$): δ 1.34 (3 H, t, CH_3), 2.39 (1 H, dd, $J_{1',2'a}$= 10.0 Hz, $J_{2'a2'b}$ = 18.5 Hz, H-2'a), 2.83 (2 H, q, benzylic), 3.43 (3 H, s, OCH_3),

3.65 (1 H, dd, $J_{1',2'b}$ =6.1 Hz, H-1'), 4.00 (2 H, ddd, $J_{4',5'}$ = 2.6 Hz, $J_{4',5''}$ = 4.4 Hz, $J_{5',5''}$ = 11.1 Hz, H-5',5''), 4.04 (3 H, s, $ArOCH_3$), 4.38 (1 H, dd, H-4), 4.75 (2 H, dd, J = 11.1 Hz, OCH_2O), 6.58 (1 H, dd, H-1'), 6.97 (1 H, d, $J_{2,3}$ = 8.4 Hz, H-2), 7.71 (1 H, dd, $J_{7,9}$ = 1.8 Hz, $J_{9,10}$ = 8.4 Hz, H-9), 8.02 (1 H, d, $J_{11,12}$ = 9.0 Hz), 8.13 (1 H, d, H-3), 8.18 (1 H, d, H-10), 8.23 (1 H, d, H-7), 8.25 (1 H, d, $J_{11,12}$ = 9.0 Hz). ^{13}C nmr ($CDCl_3$) δ 15.22, 28.58, 46.37, 55.31, 55.68, 66.39, 75.87, 81.15, 96.61, 105.51, 114.79, 118.40, 119.19, 120.30, 121.93, 122.43, 125.01, 126.76, 128.69, 129.60, 132.94, 135.19, 145.51, 147.05, 154.49, 160.62, 213.96.

Anal. Calcd. for $C_{27}H_{26}O_7$: C, 70.1; H, 5.67. Found: C,70.0; H, 5.68.

4-[5'-Acetyl-2'-deoxy-β-D-*glycero*-pentofuran-3'-ulos-1'yl]-8-ethyl-1-methoxybenzo[d]naptho[1,2-b]pyran-6-one. (27). To a mixture of 8-ethyl-4-iodo-1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one (**22**) (700 mg, 1.63 mmol), sodium acetate (133 mg, 1.63 mmol), and tributylamine (77 μL, 0.33 mmol), in 25 mL of dry dimethylformamide was added 1,4-anhydro-2-deoxy-3-*O*-[(1,1-dimethylethyl)diphenylsilyl]-D-*erythro*-pent-1-enitol[20] (**15**) (692 mg, 1.95 mmol) and palladium acetate (37 mg, 0.17 mmol). After stirring for 6 hours at room temperature, acetic acid (195 mg, 3.26 mmol) and a 1 M solution of tetrabutylammonium flouride in tetrahydrofuran (2.0 mL, 2.0 mmol) were added. After stirring for an additional 10 minutes, pyridine (10 mL), and acetic anhydride (1 mL) were added. The reaction was then stirred for an additional 8 hours at which time tlc indicated the reaction was complete. The volatiles were removed *in vacuo* and the residue was purified by column chromatography (methylene chloride/ether, 10:1) to give 666 mg (89%) of **27** as off-white crystals, mp 190°. ^1H nmr ($CDCl_3$): δ 1.34 (3 H, t, CH_3), 2.12 (3 H, s, $COCH_3$), 2.35 (1 H, dd, $J_{1',2'\beta}$ = 9.9 Hz, $J_{2'\alpha,2'\beta}$ =18.7 Hz, H-2'β), 2.81 (2 H, q, benzylic), 3.67 (1 H, dd, $J_{1',2'\alpha}$ =6.2 Hz, H-2α), 4.02 (3 H, s, $ArOCH_3$), 4.42 (2 H, dd, $J_{4',5'}$ = 4.6 Hz, $J_{5',5''}$ = 15.1 Hz, H-5',5''), 4.69 (1

H, dd, $J_{4',5''}$ = 5.5 Hz, H-4'), 6.52 (1 H, dd, H-1'), 6.94 (1 H, d, $J_{2,3}$ = 8.4 Hz, H-2), 7.69 (1 H, dd, $J_{7,9}$ =1.8 Hz, $J_{9,10}$ = 8.2 Hz, H-9), 7.98 (1 H, d, $J_{11,12}$ = 9.0 Hz), 8.04 (1 H, dd, $J_{1',3}$ =.8 Hz, H-3), 8.08 (1 H, d, H-10), 8.19 (1 H, d, $J_{11,12}$ = 9.0 Hz), 8.20 (1 H, d, H-7). ^{13}C nmr ($CDCl_3$) δ 15.19, 20.86, 28.56, 46.11, 55.67, 62.92, 75.98, 79.56, 105.40, 114.78, 118.44, 119.17, 120.22, 121.79, 122.41, 124.57, 126.76, 128.64, 129.23, 132.85, 135.19, 145.54, 146.90, 154.53, 160.55, 170.68, 212.95.

Anal. Calcd. for $C_{27}H_{24}O_7$: C, 70.4; H, 5.17. Found: C, 70.0; H, 5.19.

4-[2'-Deoxy-3',5'-diacetyl-β-D-*ribo(=arabino)*furanosyl]-8-ethyl-1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one (28). To a solution of 8-ethyl-4-iodo-1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one (**22**) (1.80 g, 4.19 mmol), sodium acetate (0.34 g, 4.19 mmol), and tributylamine (200 μL, 0.84 mmol) in 50 mL of dry dimethylformamide was added 1,4-anhydro-2-deoxy-3-*O*-[(1,1-dimethylethyl)diphenylsilyl]-D-*erythro*-pent-1-enitol[20] (**15**) (1.78 g, 5.02 mmol) and palladium acetate (94 mg, 0.42 mmol). The reaction mixture was stirred at room temperature for 10 hours at which time acetic acid (0.50 g, 8.37 mmol) and a 1 M solution of tetrabutylammonium flouride in tetrahydrofuran (6.28 mL) were added. After 10 minutes, the volatiles were removed *in vacuo* and the residue was dried under high vacuum for 2 hours. Dimethylformamide (100 mL) and acetic acid (100 mL) were then added. Sodium triacetoxyborohydride (2.65 g, 12.56 mmol) was added and the reaction was complete in 10 minutes based on TLC. Volatiles were removed *in vacuo* and pyridine (40 mL) and acetic anhydride (2 mL) were added. The reaction mixture was then stirred for an additional 10 hours. Volatiles were removed and the residue was dissolved in chloroform. Purification was accomplished by column chromatography (methylene chloride/ether, 10:1) to give 1.98 g (94%) of **28** as an off white solid. The product was then recrystallized from chloroform : ethanol, mp 169° C. ^1H nmr ($CDCl_3$): d 1.30 (3 H, t, CH_3), 1.94 (1 H, ddd, $J_{1',2'\beta}$ = 9.7 Hz, $J_{2'\alpha,2'\beta}$

= 13.7 Hz, $J_{2'\beta,3'}$ = 6.0 Hz, H-2'β), 2.10, 2.27 (6 H, 2 s, $COCH_3$), 2.78 (2 H, q, benzylic), 3.05 (1 H, ddd, $J_{1',2'\alpha}$ = 5.2 Hz, $J_{2'\alpha,3'}$ = 5.3 Hz, H-2'α), 3.98 (3 H, s, $ArOCH_3$), 4.32 (1 H, dd, $J_{4',5'}$ = 4.6 Hz, $J_{5',5''}$ =11.3 Hz, H-5'), 4.42 (1 H, m, H-4), 4.48 (1 H, dd, $J_{4',5''}$ = 4.2 Hz, H-5"), 5.23 (1 H, m, H-3'), 6.45 (1 H, dd, H-1'), 6.90 (1 H, d, $J_{2,3}$ = 8.4 Hz, H-2), 7.66 (1 H, dd, $J_{7,9}$ =1.7 Hz, $J_{9,10}$ =8.4 Hz, H-9), 7.96 (1 H, d, H-3), 7.97 (1 H, d, $J_{11,12}$ = 9.0 Hz), 8.08 (1 H, d, H-10), 8.18 (1 H, d, $J_{11,12}$ = 9.0 Hz), 8.19 (1 H, d, H-7). ^{13}C nmr ($CDCl_3$) d 15.24, 20.95, 21.27, 28.58, 41.89, 55.66, 64.48, 76.54, 79.16, 81.01, 105.47, 114.68, 118.33, 119.09, 120.39, 121.92, 122.40, 124.26, 126.84, 128.63, 129.97, 132.99, 135.05, 145.34, 147.29, 154.26, 160.49, 170.88, 171.25.

Anal. Calcd. for $C_{29}H_{28}O_8$: C, 69.0; H, 5.59 Hz. Found: C,69.2; H, 5.46.

8-Ethyl-4-iodo-1-(1-methylethyl)oxybenzo[d]naphtho[1,2-b]pyran-6-one (29). To a mixture of 8-ethyl-1-(1-methylethyl) oxybenzo[d]naphtho[1,2-b]pyran-6-one [48] (150 mg, 0.464 mmol) and N-iodosuccinimide (132 mg, 0.586 mmol) in 10 mL of dry dimethylformamide was added 1 drop of concentrated sulfuric acid. The reaction mixture was then stirred at 60° for 2 hours at which time tlc indicated that reaction was complete. The residue was dissolved in chloroform and washed with a saturated solution of sodium thiosulfate and then with distilled water. The organic layer was dried over sodium sulfate and the solvent was then removed. The residue was recrystallized from chloroform : ethanol to give 191 mg (92%) of 8-ethyl-4-iodo-1-(1-methylethyl)oxybenzo[d]naphtho[1,2-b]pyran-6-one (29) as off-white crystals, mp 215°. ^1H nmr ($CDCl_3$): δ 1.30 (3 H, t, CH_3), 1.44 (6 H, d, isopropyl), 2.76 (2 H, q, benzylic), 4.69 (1 H, m, isopropyl), 6.54 (1 H, d, $J_{2,3}$ =8.3 Hz, H-2), 7.64 (1 H, dd, $J_{7,9}$ =1.8 Hz, $J_{9,10}$ = 8.3 Hz, H-9), 7.99 (1 H, d, $J_{11,12}$ =9.0 Hz), 8.05 (1 H, d, H-10), 8.16 (1 H, d, H-3), 8.20 (1 H, d, $J_{11,12}$ = 9.0 Hz), 8.21 (1 H, d, H-7). ^{13}C nmr ($CDCl_3$): d 15.21, 21.94, 28.59,

70.90, 73.28, 109.32, 114.67, 118.74, 119.15, 120.94, 122.34, 124.08, 128.60, 128.76, 132.66, 134.98, 142.38, 145.02, 145.50, 153.78, 160.13.

Anal. Calcd. for $C_{22}H_{19}IO_3$: C, 57.7; H, 4.18. Found: C, 57.8; H,4.01.

4-(2'-Deoxy-3',4',6'-tri-*O*-[(1,1-dimethylethyl)dimethylsilyl]-α-D-*erythro*-hex-2-enopyranosyl)-8-ethyl-1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one (31). To a solution of 8-ethyl-4-iodo-1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one (**22**) (200 mg, 0.47 mmol), sodium acetate (38 mg, 0.47 mmol), and tributylamine (22 μL, 0.09 mmol) in 10 mL of dry dimethylformamide was added 3,4,6-tri-*O*-[(1,1-dimethylethyl)dimethylsilyl]-D-glucal[14c,d] (**30**) (340 mg, 7.00 mmol) and palladium acetate (21 mg, 0.09 mmol). The reaction mixture was stirred for 4 days at room temperature and the volatiles were removed *in vacuo*. The residue was purified by column chromatography (ether/hexane, 5:1) to give 154 mg (42%) of **31** as a pale yellow solid which was then recrystallized from chloroform : ethanol to yield crystals, mp 172°. ^{1}H nmr ($CDCl_3$): δ 0.05-0.21 (18 H, br, Si-CH_3), 0.85-0.97 (27 H, br, *t*-butyl), 1.33 (3 H, t, CH_3), 2.80 (2 H, q, benzylic), 3.84 (1 H, d, $J_{5',6'}$ = 4.6 Hz, H-6'), 4.00 (1 H, d, $J_{5',6''}$ =4.7 Hz, H-6''), 4.01 (3 H, s, ArOCH_3), 4.12 (1 H, dd, $J_{4',5'}$ = 6.3 Hz, H-5'), 4.70 (1 H, d, H-4), 5.29 (1 H, d, $J_{1',2'}$ =2.3 Hz), 6.77 (1 H, s, H-1'), 6.93 (1 H, d, $J_{2,3}$ = 8.4 Hz, H-2), 7.68 (1 H, dd, $J_{7,9}$ = 1.9 Hz, $J_{9,10}$ = 8.3 Hz, H-9), 8.01 (1 H, d, $J_{11,12}$ = 9.1 Hz), 8.08 (1 H, d, H-3), 8.13 (1 H, d, H-10), 8.23 (1 H, d, $J_{11,12}$ = 9.1 Hz), 8.25 (1 H, d, H-7). ^{13}C nmr ($CDCl_3$): δ -5.23, -5.17, -4.52, -4.21, -2.76,15.27, 18.17, 18.22, 25.79, 25.87, 25.93, 25.98, 28.62, 55.73, 62.18, 67.28, 70.07, 80.16, 105.88, 108.37, 114.69, 118.04, 119.13, 120.62, 122.46, 126.86, 128.50, 128.69, 130.61, 133.22, 134.97, 145.21, 147.32, 154.40, 160.51.

Anal. Calcd. for $C_{44}H_{66}O_7Si_3$: C, 66.8; H,8.41. Found: C, 66.7; H, 8.31.

Coupling of 1,5-anhydro-2,3-dideoxy-4,6-O-phenylmethylene-

D-*erythro*-hex-1-enitol[49] (32) with 8-ethyl-4-iodo-1-(1-methyl ethyl)oxybenzo[d]naphtho[1,2-b]pyran-6-one (29). To a stirred solution of **29** (317 mg, 0.69 mmol), **32** (300 mg, 1.38 mmol), sodium acetate (57 mg, 0.69 mmol), and tri-n-butyl amine (33 μL, 0.14 mmol) in 25 mL of dry dimethylformamide was added palladium acetate (16 mg, 0.069 mmol). The solution was stirred at room temperature for six days and the volatiles were then removed *in vacuo*. The resulting residue was dissolved in chloroform and passed through a short column of silica gel. An NMR spectrum of the crude reaction mixture indicated a 1:9 ratio of anomeric C-glycosides **33** and **34** respectively. Purification was accomplished using preparatory tlc (methylene chloride/ether, 50:1) to give 30 mg (8%) of 4-(2',3'-dideoxy-4',6'-O-phenylmethylene-β-*erythro*-hex-2-enopyranosyl)-8-ethyl-1-(1-methylethyl)oxybenzo[d]naphtho[1,2-b] pyran-6-one (**33**), mp 218 °C and 201 mg (53%) of 4-(2',3'-dideoxy-4',6'-O-phenylmethylene-α-D-*erythro*-hex-2-enopyranosyl)-8-ethyl-1-(1-methylethyl)oxybenzo[d]naphtho[1,2-b]pyran-6-one (**34**), mp 238 °C as white solids. For **33**, ^{1}H NMR ($CDCl_3$): δ 1.34 (t, 3H, J = 6.6 Hz, CH_3), 1.47 (dd, 6H, isopropyl), 2.83 (q, 2H, benzylic), 3.92 (dd, 1H, $J_{5',6'}$ = 10.2 Hz, $J_{6',6''}$ = 10.3 Hz, H-6'), 4.21 (ddd, 1H, $J_{4,'5'}$ = 4.7 Hz, $J_{5',6''}$ = 4.7 Hz, H-5'), 4.47 (m, 2H, H-4', H-6''), 4.79 (m, 1H, isopropyl), 5.70 (s, 1H, benzylidene), 6.09 (d, 1H, $J_{2',3'}$ = 10.3 Hz, H-2'), 6.20 (ddd, 1H, $J_{1',3'}$ = 2.1 Hz, $J_{3',4'}$ = 4.1 Hz, H-3'), 6.96 (d, 1H, $J_{2,3}$ = 8.4 Hz, H-2), 7.07 (br, 1H, H-1'), 7.40, 7.58 (m, 5H, Ph), 7.72 (dd, 1H, $J_{7,9}$ = 1.8 Hz, $J_{9,10}$ = 8.2 Hz, H-9), 7.84 (d, 1H, H-10), 8.07 (d, 1H, $J_{11,12}$ = 9.1 Hz, H-11), 8.17 (d, 1H, H-3), 8.28 (d, 1H, H-7), 8.32 (d, 1H, H-12). ^{13}C NMR ($CDCl_3$): δ 15.28, 21.96, 22.09, 28.63, 69.73, 70.70, 71.71, 75.54, 76.32, 102.16, 107.72, 115.02, 118.33, 119.60, 120.62, 122.46, 122.76, 125.73, 126.34, 126.38, 127.85, 128.07,128.32, 128.36, 128.80, 129.04, 129.12, 132.24, 133.08, 135.09, 137.73, 145.41, 147.56, 153.29, 160.56.

Anal. Calcd. for $C_{35}H_{32}O_6$: C, 76.6; H, 5.88. Found: C, 76.4; H, 5.67.

For **34**: ^{1}H NMR ($CDCl_3$): δ 1.32 (t, 3H, J = 7.6 Hz, CH_3), 1.48 (d, 6H, J = 6.0 Hz, isopropyl), 2.80 (q, 2H, benzylic), 3.63 (ddd, 1H, $J_{4',5'}$ = 8.6 Hz, $J_{5',6'}$ = 4.6 Hz, $J_{5',6''}$ = 10.1 Hz, H-5'), 3.80 (dd, 1H, $J_{6',6''}$ =10.3 Hz, H-6''), 4.02 (dd, 1H, H-6'), 4.38 (m, 1H, H-4), 4.76 (m, 1H, isopropyl), 5.62 (s, 1H, benzylidene), 6.15 (ddd, 1H, $J_{1',2'}$ = 5.1 Hz, $J_{2',3'}$ = 10.3 Hz, $J_{2',4'}$ = 2.5 Hz, H-2), 6.24 (d, 1H, H-3), 6.86 (d, 1H, $J_{2,3}$ = 8.3 Hz, H-2), 7.08 (dd, 1H, H-1'), 7.34, 7.50 (m, 5H, Ph), 7.66 (d, 1H, $J_{9,10}$ = 8.2 Hz, H-10), 7.67 (dd, 1H, $J_{7,9}$ =1.8 Hz, H-9), 8.02 (d, 1H, $J_{11,12}$ = 9.1 Hz, H-11), 8.12 (d, 1H, H-3), 8.24 (d, 1H, H-7), 8.30 (d, 1H, H-12). ^{13}C NMR ($CDCl_3$): δ 15.29, 22.02, 28.59, 64.14, 69.87, 70.59, 73.09, 75.69, 101.75, 106.35, 115.06, 118.43, 119.48, 120.73, 122,40, 123.11, 126.17, 126.31, 127.20, 128.23, 128.54, 128.71, 128.89, 129.36, 131.10, 133.07, 134.98, 137.67,145.32, 153.45,160.83.

Anal. Calcd. for $C_{35}H_{32}O_6$: C, 76.6; H, 5.88. Found: C, 76.2; H, 5.76.

8-Ethyl-1-hydroxy-2-iodobenzo[d]naphtho[1,2-b]pyran-6-one (36). To a solution of 8-ethyl-1-hydroxybenzo[d]naphtho[1,2-b]pyran-6-one[27] (**35**) (400 mg, 1.38 mmol) in 10 mL of dimethylformamide was added N-iodosuccinimide (434 mg, 1.93 mmol). Volatiles were removed in vacuo and the residue was dissolved in chloroform and separated by column chromatography followed by recrystallization from chloroform-ethanol to give 471 mg (82%) of **36** as off-white crystals, mp 208-209 °C. ^{1}H NMR ($CDCl_3$) δ 1.32 (3H, t, J = 7.6 Hz, CH_3), 2.81 (2H, q, benzylic), 7.68 (1H, dd, $J_{7,9}$ =2.0 Hz, $J_{9,10}$ =8.3 Hz, H-9), 7.73 (1H, d, $J_{11,12}$ = 9.0 Hz), 7.88 (1H, dd, $J_{3,4}$ =8.9 Hz, H-3), 8.00 (1H, d, H-11,12), 8.08 (1H, d, H-10), 8.11 (1H, dd, H-4), 8.26 (1H, d, H-7). ^{13} C NMR ($CDCl_3$) δ 15.41, 28.62, 89.64, 113.65, 118.74, 119.76, 120.52, 121.09, 122.31, 125.17, 128.69, 129.24, 132.42, 135.23, 136.79, 145.87, 146.90, 156.31, 161.06.

Anal. Calcd. for $C_{19}H_{13}O_3I$: C, 54.8; H, 3.15. Found: C, 54.4; H, 3.34.

8-Ethyl-2-iodo-1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one (37). To a stirred solution of 8-ethyl-2-iodo-1-hydroxybenzo[d]naphtho[1,2-b]pyran-6-one (**36**) (340 mg, 0.82 mmol) and potassium carbonate (902 mg, 6.54 mmol) in 100 mL of acetone was added dimethyl sulfate (0.45 mL, 3.27 mmol). The mixture was heated to reflux for three hours at which time the reaction was complete based on tlc. The volatiles were removed in vacuo and 100 mL of chloroform added. The mixture was filtered and the filtrate was washed three times with distilled water. The organics were dried over anhydrous sodium sulfate and volatiles were removed in vacuo. The residue was purified by column chromatography (methylene chloride) followed by recrystallization from chloroform-ethanol to give 310 mg (88 %) of **37** as white crytals, mp 213-214 °C. ^{1}H NMR ($CDCl_3$): δ 1.33 (3H, t, J = 7.6 Hz, CH_3), 2.81 (2H, q, benzylic), 3.99 (3H, s, OCH_3), 7.68 (1H, dd, $J_{7,9}$ =1.9 Hz, $J_{9,10}$ =8.2 Hz, H-9), 7.88 (1H, $J_{11,12}$ = 8.9 Hz), 7.98 (1H, d, $J_{3,4}$ =9.1 Hz, H-3), 8.04 (2H, br. d, H-4, H-11,12), 8.06 (1H, d, H-10),8.24 (1H, d, H-7). ^{13} C NMR ($CDCl_3$): δ 15.17, 28.65, 61.83, 89.72, 113.85, 118.68, 119.92, 120.14, 121.12, 122.17, 125.17, 128.73, 129.29, 132.54, 135.26, 136.55, 145.67, 146.92, 156.27, 161.06.

Anal. Calcd. for $C_{20}H_{15}IO_3$: C, 55.8; H, 3.51. Found: C, 55.8; H, 3.34.

Radical bromination of 4-[2'-Deoxy-3',5'-di-O-acetyl-β-D-ribo-(= arabino)-furanosyl]-8-ethyl-1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one[45] (28). A solution of **15** (225 mg, 0.45 mmol), N-bromosuccinimide (103 mg, 0.58 mmol), and benzoyl peroxide (20 mg) in 30 mL of carbon tetrachloride was heated under reflux for 16 hours. The solution was then evaporated to almost dryness and separated by preparative TLC (chloroform:ethyl acetate, 40:1) to afford 122 mg (60%) of **40** as a light yellow solid and 26 mg (14%) of **41** as a light yellow solid. For **40**: ^{1}H nmr ($CDCl_3$) δ 1.23 (t, 3H, CH_3), 2.10 (s, 3H, acetyl), 2.81 (2d, 2H, benzylic), 4.03 (s, 3H, OCH_3), 5.15 (s, 2H, H-5',5"), 6.70 (s, 1H, H-2'), 6.93 (m,

1H, H-2), 7.55-8.28 (complex, 6H, H-3,7,9,10,11,12). MS (FAB, matrix: m-nitrobenzyl alcohol), m/z 521 ($M^{+\cdot}$), 462 (M -OAc, base peak), 382 (M-OAc,-Br). For **41**: ^{1}H nmr ($CDCl_3$) δ 1.30 (t, 3H, CH_3), 2.85 (2d, 2H, benzylic), 4.10 (s, 3H, OCH_3), 4.62 (s, 2H, H-5'5"), 6.60 (s, 1H, H-2'), 7.00-8.35 (complex , 7H, aromatic).

Radical bromination of 1-acetoxy-8-ethyl-4-(2',3',5'-tri-O-acetyl-β-D-ribofuranosyl) benzo[d]naphtho[1,2-b]pyran-6-one (**8**). A solution of **8** (162 mg, 0.27 mmol), N-bromosuccinimide (63.5 mg, 0.36 mmol) and benzoyl peroxide (2 mg, 0.008 mmol) in 25 mL of carbon tetrachloride was heated under reflux for 18 hr. The solution was then evaporated to almost dryness and separated by preparative TLC (methylene chloride:ethyl acetate, 10:1) to afford 118 mg (65%) of 1-acetoxy-8-(1-bromoethyl)-4-(2',3',5'-tri-O-acetyl-β-D-ribofuranosyl)benzo[d]naphtho[1,2-b]pyran-6-one R_f= .42 as a light yellow solid: mp 194-196 °C (decomp.); and 52 mg (24 %) of **43** as a light brown solid. For **8**: MS, m/z 607 $(M\text{-}HOAc)^+$, 588 $(M\text{-}HBr)^+$; ^{1}H nmr ($CDCl_3$) δ 2.12, 2.13 (each d, 3H, J=6.8 Hz, CH_3), 2.00, 2.21, 2.32, 2.49 (4s, 12H, acetyl), 4.47 (dd, 1H, H-5'), 4.57 (dd, 1H, $J_{5',5'}$ = 7.9 Hz, H-5'), 4.60 (ddd, 1H, $J_{4',5'}$ = 2.4 , 4.1 Hz, H-4'), 5.19, 5.20 (each dd, 1H, $J_{3',4'}$ = 9.3 Hz, H-3'), 5.31 (2d, 1H, benzylic), 5.65 (d, 1H, $J_{2',3'}$ = 4.4 Hz, H-2'), 6.56 (s, 1H, H-1'), 7.32 (d, 1H, H-2), 7.82, 7.82 (each d, 1 H, $J_{11,12}$ = 9.0 Hz), 7.94 (apparent dt, 1H, J = 3.3, 9.1 Hz), 8.03, 8.04 (each d, 1H, $J_{11,12}$ = 9.0 Hz), 8.12 (d, 1H, $J_{9,10}$ = 8.2 Hz, H-10), 8.21 (d, 1H, $J_{2,3}$ = 8.2 Hz, H-3), 8.33, 8.36 (each d, 1H, $J_{7,9}$ = 2.0 Hz, H-7); ^{13}C nmr ($CDCl_3$) δ 20.47, 20.93, 21.03, 21.19, 26.30, 26.36, 47.30, 62.66, 69.23, 76.15, 76.59, 82.36, 114.62, 118.69, 119.37, 120.14, 120.30, 120.37, 122.12, 123.06, 123.11, 125.48, 127.77, 127.91, 128.79, 133.39, 133.96, 134.14, 134.53, 144.34, 144.37, 146.27, 147.95, 159.38, 169.65, 170.41, 170.58.

For **43** : ^1H nmr ($CDCl_3$) δ 2.06, 2.15, 2.50, (each s, 3H each, acetyls), 2.09 (d,3H, J = 6.9 Hz, CH_3), 5.12 (s, 2H, furan), 5.25 (m, 1H, benzylic), 6.74 (s, 1H, furan), 7.38-8.32 (complex, 7H, aglycon).

4-Bromo-8-ethyl-1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one (44). To a suspension of 8-ethyl-1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one[7c,13a] (**2**) (2.0 g, 6.6 mmol) in 50 mL of dry dimethylformamide was added N-bromosuccinimide (1.29 g, 7.2 mmol). After the solution became clear, an off-white precipitate formed. The reaction was complete in 2 hours based on tlc. The resulting mixture was poured into 500 mL of ice water and the precipitate which formed was collected and recrystallized from chloroform/ethanol to give 2.21 g (88%) of 4-bromo-8-ethyl-1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one (**44**) as off white crystals, mp 185°. ^1H nmr ($CDCl_3$): δ 1.32 (3 H, t, CH_3), 2.79 (2H, q, benzylic), 3.92 (s,3 H, OCH_3), 6.60 (1 H, d, $J_{2,3}$ = 8.3 Hz, H-2), 7.61 (1 H, q, $J_{7,9}$ = 1.7 Hz, $J_{9,10}$ = 8.2 Hz, H-9), 7.68 (1 H, d, $J_{2,3}$ = 8.3 Hz, H-3), 7.88 (1H, d, $J_{11,12}$ = 9.1 Hz), 7.98 (1 H, d, $J_{9,10}$ = 8.3 Hz, H-10), 8.04 (1 H, d, $J_{11,12}$ = 9.1 Hz), 8.15 (1 H, d, $J_{7,9}$ = 1.6 Hz, H-7); ^{13}C nmr ($CDCl_3$): δ 15.15, 28.56, 55.77, 106.13, 106.82, 115.02, 118.70, 119.13, 120.74, 122.13, 122.30, 127.77, 128.64, 132.47, 134.18, 134.89, 145.50, 145.85, 154.43, 160.23.

Anal. Calcd for $C_{20}H_{15}BrO_3$: C, 62.7; H, 3.95. Found: C, 62.5; H, 3.92.

4-Bromo-8-(1-bromo-ethyl)-1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one (45). A solution of 4-bromo-8-ethyl-1-methoxybenzo[d]naphtho [1,2-b]pyran-6-one[45] (**44**) (2.25 g, 5.88 mmol), N-bromosuccinimide (1.07 g, 5.99 mmol) and benzoyl peroxide (300 mg) in 200 mL of carbon tetrachloride was heated under reflux for 2 hours. Volatiles were removed in vacuo and the residue was dissolved in chloroform and separated by column chromatography (methylene chloride) followed by recrystallization from chloroform-ethanol to give 2.31 g (85%) of **45** as off-white crystals, mp 212-214° C. ^1H NMR ($CDCl_3$) δ 2.14 (3H, d, J = 7.0 Hz,

CH_3), 4.01 (3H, s , $ArOCH_3$), 5.34 (1H, q, benzylic), 6.76 (1H, d, $J_{2,3}$ = 8.4 Hz, H-2), 7.82 (1H, d, 1H, H-3), 7.98 (1H, dd, $J_{7,9}$ = 2.1 Hz, $J_{9,10}$ = 8.5 Hz, H-9), 8.07 (1H, d, $J_{11,12}$ = 9.1 Hz), 8.22 (1H, d, H-10), 8.26 (1H, d, H-11,12), 8.47 (1H, d, H-7). ^{13}C NMR ($CDCl_3$) δ 26.40, 47.44, 55.94, 106.74, 107.05, 114.69, 119.15, 119.24, 121.07, 122.37, 123.14, 124.96, 127.85, 128.37, 133.88, 134.60, 134.88, 144.32, 154.60, 159.80.

Anal. Calcd. for $C_{20}H_{14}O_3Br_2$: C, 52.0; H, 3.05. Found: C, 52.2,; H, 2.81.

8-Ethenyl-4-iodo-1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one (46). A solution of 4-bromo-8-(1-bromo-ethyl)-methoxybenzo[d]naphtho[1,2-b]pyran-6-one (**45**) (280 mg, 0.61 mmol), copper (I) iodide (806 mg, 4.24 mmol), and potassium iodide (2.01 g, 12.12 mmol) in 20 mL of dimethylformamide was heated under reflux for 6 hours. Volatiles were removed in vacuo and chloroform (100 mL) was then added. The reaction mixture was then filtered and the filtrate was washed with a saturated solution of sodium thiosulfate. The organics were dried over sodium sulfate and volatiles were removed in vacuo and the residue was dissolved in chloroform and purified by column chromatography followed by recrystallization from chloroform-ethanol to give 223 mg (86%) of **46**. ^1H NMR ($CDCl_3$) δ 4.02 (3H, s, OCH_3), 5.46 (1H, d, J_{cis} = 10.9 Hz), 5.98 (1H, d, J_{trans} = 17.6 Hz), 6.61 (1H, d, $J_{2,3}$ =8.3 Hz, H-2), 6.86 (1H,dd, vinyl), 7.92 (1H, dd, $J_{7,9}$ =1.7 Hz, $J_{9,10}$ =8.5 Hz, H-9), 8.10 (1H, d, $J_{11,12}$ =9.1 Hz), 8.18 (1H, d, H-10), 8.25 (1H, d, H-11,12), 8.26 (1H, d, H-3), 8.45 (1H, d, H-7).

4-Bromo-8-ethyl-1-hydroxybenzo[d]naphtho[1,2-b]pyran-6-one (47). To a stirred solution of 4-bromo-ethyl-1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one[45] (2.62 g, 6.84 mmol) in 100 mL of methylene chloride was added boron tribromide (20.5 mL of a 1M solution in methylene chloride). A bright yellow precipitate appeared instantly. After two hours the reaction mixture was a clear brown solution. The reaction mixture was then added dropwise to a solution of methanol and

water. The precipitate was collected by filtration to yield 2.40 g (95%) of **47** as an off white powder. ^{1}H NMR (DMSO) δ 1.24 (3H, t, J = 7.5 Hz, CH_3), 2.75 (2H, q, benzylic), 6.87 (1H, d, $J_{2,3}$ = 8.3 Hz, H-2), 7.73 (1H, d, H-3), 7.78 (1H, dd, $J_{7,9}$ =1.7 Hz, $J_{9,10}$ = 8.2 Hz, H-9), 8.06 (1H, d, H-7), 8.13 (1H, d, $J_{11,12}$ = 9.0 Hz), 8.29 (1H,d, H-11,12), 8.35 (1H,d, H-10), 10.74 (1H, s, PhOH).

4-Bromo-8-(1-bromo-ethyl)-1-hydroxybenzo[d]naphtho[1,2-b]pyran-6-one (48). To a stirred solution of 4-bromo-8-(1-bromo-ethyl)-1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one (**45**) (1.50 g, 3.25 mmol) in 200 ml of methylene chloride was added boron tribromide (9.7 mL of a 1M solution in methylene chloride). A bright yellow precipitate appeared instantly. After four hours the reaction mixture was a clear brown solution. The reaction mixture was then added dropwise to a solution of methanol and water. The precipitate was collected by filtration to give 1.43 g (98%) of **48** as a beige solid, mp 228-231 °C dec. ^{1}H NMR (DMSO) δ 2.07 (3H, d, J = 6.9 Hz, CH_3), 5.74 (1H, q, benzylic), 6.90 (1H, d, $J_{2,3}$ = 8.3 Hz, H-2), 7.75 (1H, d, H-3), 8.13 (1H, dd, $J_{7,9}$ =1.9 Hz, $J_{9,10}$ = 8.5 Hz, H-9), 8.16 (1H, d, $J_{11,12}$ = 9.0 Hz), 8.36 (1H, d, H-7), 8.37 (1H, d, H-11,12), 8.53 (1H, d, H-10). ^{13}C NMR (DMSO) δ 26.01, 49.06, 103.58, 111.21, 114.54, 119.22, 119.69, 120.36, 121.60, 124.08, 127.23, 127.33, 134.10, 134.48, 135.03, 144.41, 145.92, 153.09, 159.13.

Anal. Calcd. for $C_{19}H_{12}O_3Br_2$: C, 50.9; H, 2.70. Found: C, 51.2; H, 2.44.

4-Bromo-8-ethyl-1-trimethylacetoxybenzo[d]naphtho[1,2-b]pyran-6-one (22). To a stirred solution of 4-bromo-8-ethyl-1-methoxybenzo-[d]naphtho[1,2-b]pyran-6-one[45] (2.62 g, 6.84 mmol) in 100 mL of methylene chloride was added boron tribromide (20.5 mL of a 1M solution in methylene chloride). A bright yellow precipitate appeared instantly. After two hours the reaction mixture was a clear brown solution. The reaction mixture was then added dropwise to a solution of methanol and water. The precipitate was collected by filtration and was sufficiently

pure to be used in the following step. To an ice cooled mixture of the precipitate in 150 mL of toluene was added trimethylacetyl chloride (1.23 g, 10.26 mmol). 4-Dimethylaminopyridine (1.67 g, 13.68 mmol) was then added and the reaction mixture was brought to room temperature and stirred for six hours. Volatiles were removed in vacuo and the residue was dissolved in chloroform and separated by column chromatography (methylene chloride) followed by recrystallization from chloroform-ethanol to give 2.63 g (85%) of **49** as off-white crystals, mp 195-197 °C. ^{1}H NMR ($CDCl_3$) δ 1.31 (3H, t, CH_3), 1.48 (9H, s, t-butyl), 2.79 (2H, q, benzylic), 7.06 (1H, d, $J_{2,3}$ = 8.3 Hz, H-2), 7.67 (1H, dd, $J_{7,9}$ =1.8 Hz, $J_{9,10}$ = 8.3 Hz, H-9), 7.76 (1H, d, $J_{11,12}$ = 9.1 Hz), 7.88 (1H, d, H-3), 8.05 (1H, d, H-11,12), 8.22 (1H, d, H-7). ^{13}C NMR ($CDCl_3$) δ 15.16, 27.28, 28.62, 39.51, 113.65, 115.06, 117.85, 119.98, 120.76, 120.86, 122.28, 122.83, 128.92, 129.57, 132.28, 134.08, 135.15, 145.95, 146.14, 146.29, 160.03, 177.14.

Anal. Calcd. for $C_{24}H_{21}O_4Br$: C, 63.6; H, 4.67. Found: C, 63.2,; H, 4.55.

8-Ethyl-4-iodo-1-trimethylacetoxybenzo[d]naphtho[1,2-b]pyran-6-one (50). A solution of 4-bromo-8-ethyl-1-trimethylacetoxybenzo[d]naphtho-[1,2-b]pyran-6-one (**49**) (2.41 g, 5.32 mmol), copper(1) iodide (5.05 g, 26.60 mmol), and potassium iodide (17.66 g, 106.40 mmol) in 150 mL of dimethylformamide was heated under reflux for one hour. Volatiles were removed in vacuo and chloroform (200 mL) was then added. The reaction mixture was then filtered and the filtrate was washed with a saturated solution of sodium thiosulfate. The organics were dried over sodium sulfate, volatiles were removed in vacuo, and the residue was dissolved in chloroform and separated by column chromatography followed by recrystallization from chloroform-ethanol to give 1.89 g (71%) of **50** as off-white crystals, mp 208-209 °C. ^{1}H NMR ($CDCl_3$) δ 1.31 (3H, t, J = 7.5 Hz, CH_3), 2.78 (2H, q, benzylic), 6.95 (1H, d, $J_{2,3}$ = 8.1 Hz, H-2), 7.63 (1H, dd, $J_{7,9}$ =1.9 Hz, $J_{9,10}$ = 8.3 Hz, H-9), 7.72 (1H, d, $J_{11,12}$ = 9.1 Hz), 7.98 (1H, d, H-10), 8.03 (1H,

d, H-11,12), 8.17 (1H, d, H-7), 8.27(1H, d, H-3). ^{13}C NMR ($CDCl_3$) δ 15.12, 27.27, 28.57, 39.52, 81.63, 114.55, 117.76, 120.44, 120.84, 122.24, 124.21, 128.79, 129.02, 132.19, 135.09, 142.09, 145.13, 145.80, 147.16, 159.69, 176.41.

Anal. Calcd. for $C_{24}H_{21}O_4I$: C, 57.6; H, 4.23. Found: C, 57.6; H, 4.10.

4-Bromo-8-(1-bromo-ethyl)-1-trimethylacetoxybenzo[d]naphtho [1,2-b]pyran-6-one (51). From 48. To an ice cooled mixture of 4-bromo-8-(1-bromo-ethyl)-1-hydroxybenzo[d]naphtho[1,2-b]pyran-6-one (**48**) in 150 mL of toluene was added trimethylacetyl chloride (1.47 g, 12.22 mmol). 4-Dimethyl-aminopyridine (1.99 g, 16.30 mmol) was added and the reaction mixture was then brought to room temperature and stirred for ten hours. Volatiles were removed in vacuo and the residue was dissolved in chloroform and separated by column chromatography (methylene chloride) followed by recrystallization from chloroform-ethanol to give 3.81 g (88%) of **51** as off-white crystals, mp 187-189 °C.

From 49: A solution of 4-bromo-8-ethyl-1-trimethylacetoxybenzo[d]naphtho [1,2-b]pyran-6-one (**49**) (1.20 g, 2.65 mmol), N-bromosuccinimide (481 mg, 2.70 mmol) and benzoyl peroxide (150 mg) in 100 mL of carbon tetrachloride was heated under reflux for 30 minutes. Volatiles were removed in vacuo and the residue was dissolved in chloroform and purified by column chromatography (methylene chloride) followed by recrystallization from chloroform-ethanol to give 1.24 g (88%) of **51.** ^{1}H NMR ($CDCl_3$) δ 2.13 (3H, d, J = 7.0 Hz, CH_3), 5.31 (1H, q, benzylic), 7.10 (1H, d, $J_{2,3}$ = 8.2 Hz, H-2), 7.80 (1H, d, $J_{11,12}$ = 9.1 Hz), 7.89 (1H, d, H-3), 7.96 (1H, dd, $J_{7,9}$ =2.1 Hz, $J_{9,10}$ =8.4 Hz, H-9), 8.10 (1H, d, H-11,12), 8.15 (1H, d, H-10), 8.45 (1H, d, H-7). ^{13}C NMR ($CDCl_3$) δ 26.38, 27.29, 40.60, 47.30, 113.82, 114.54, 118.18, 120.45, 120.73, 121.04, 122.83, 123.04, 127.95, 129.99, 134.05, 134.36, 134.52, 144.60, 146.19, 146.96, 158.48, 176.49.

Anal. Calcd. for $C_{24}H_{20}O_4Br_2$: C, 54.2; H, 3.79. Found: C, 54.6; H, 3.70.

4-Bromo-8-ethenyl-1-trimethylacetoxybenzo[d]naphtho[1,2-b]pyran-6-one (52). A solution of 4-bromo-8-(1-bromo-ethyl)-1-trimethylacetoxybenzo[d]naphtho[1,2-b]pyran-6-one (**51**) (600 mg, 1.13 mmol), tetrakis-(triphenylphosphine)palladium (0) (119 mg, 0.11 mmol), and sodium bicarbonate (189 mg, 2.26 mmol) in 20 mL of dimethylformamide was stirred at room temperature for 24 hours. Volatiles were removed in vacuo and the residue was dissolved in chloroform and separated by column chromatography (methylene chloride) followed by recrystallization from chloroform-ethanol to give 387 mg (76%) of **52** as off-white crystals, mp 203-205 °C. ^{1}H NMR ($CDCl_3$) δ 1.50 (9H, s, t-butyl), 5.42 (1H, d, J_{cis} = 11.0 Hz), 5.91 (1H, d, J_{trans} = 17.6 Hz), 6.78 (1H, dd, vinyl), 7.06 (1H, d, $J_{2,3}$ = 8.3 Hz, H-2), 7.77 (1H, d, $J_{11,12}$ =9.0 Hz), 7.83 (1H, dd, $J_{7,9}$ =1.9 Hz, $J_{9,10}$ = 8.4 Hz, H-9), 7.85 (1H, d, H-3), 8.06 (2H, d, H-10, H-11,12), 8.32 (1H, d, H-7). ^{13}C NMR ($CDCl_3$) δ 27.14, 39.81, 113.92, 114.64, 116.82, 117.88, 120.41, 120.80, 121.21, 122.78,. 124.44, 127.64, 129.21, 132.32, 133.54, 135.00, 138.55, 142.25, 145.36, 147.24, 159.61, 176.41.

Anal. Calcd. for $C_{24}H_{19}O_4Br$: C, 63.9; H,4.24. Found: C, 63.9; H, 4.31.

8-Ethenyl-4-Iodo-1-trimethylacetoxybenzo[d]naphtho[1,2-b]pyran-6-one (53). A solution of 4-bromo-8-(1-bromo-ethyl)-1-trimethylacetoxybenzo[d]naphtho[1,2-b]pyran-6-one (**51**) (3.14 g, 5.90 mmol), copper(1) iodide (8.06 g, 41.32 mmol), and potassium iodide (29.39 g, 177.07 mmol) in 300 mL of dimethylformamide was heated under reflux for four hours. Volatiles were removed in vacuo and chloroform (500 mL) was then added. The reaction mixture was then filtered and the filtrate was washed with a saturated solution of sodium thiosulfate. The organics were dried over sodium sulfate and volatiles were removed in vacuo and the residue was dissolved in chloroform and purified by column chromatography (methylene chloride) followed by recrystallization from chloroform-

ethanol to give 1.82 g (62%) of **53** as off-white crystals, mp 228-230 °C, and 573 mg (26%) of **54** as a white crystal.[7c]

From 52: A solution of 4-bromo-8-ethenyl-1-trimethylacetoxybenzo[d]naphtho [1,2-b]pyran-6-one (**52**) (304 mg, 0.67 mmol), copper(I) iodide (512 mg, 2.70 mmol), and potassium iodide (1.19 g, 6.74 mmol) in 30 mL of dimethylformamide was heated under reflux for 1.5 hours. Volatiles were removed in vacuo and chloroform (100 mL) was then added. The reaction mixture was then filtered and the filtrate was washed with a saturated solution of sodium thiosulfate. The organics were dried over sodium sulfate and volatiles were removed in vacuo and the residue was dissolved in chloroform and purified by column chromatography (methylene chloride) followed by recrystallization from chloroform-ethanol to give 255 mg (76%) of **53** as off-white crystals, mp 228-230 °C. ^{1}H NMR ($CDCl_3$) δ 1.52 (9H, s, t-butyl), 5.41 (1H, d, J_{cis} = 10.7 Hz), 5.92 (1H, d, J_{trans} = 17.5 Hz), 6.77 (1H,dd, vinyl), 6.89 (1H, d, $J_{2,3}$ =7.9 Hz, H-2), 7.74 (1H, d, $J_{11,12}$ =9.0 Hz), 7.83 (1H, dd, $J_{7,9}$ = 1.4 Hz, $J_{9,10}$ = 8.3 Hz, H-9), 8.04 (1H, d, H-10), 8.05 (1H, d, H-11,12), 8.28 (1H, d, H-3), 8.30 (1H, d, H-7). ^{13}C NMR ($CDCl_3$) δ 27.29, 39.56, 81.72, 114.34, 116.64, 117.98, 120.42, 120.69, 121.13, 122.51, 124.24, 127.73, 129.27, 132.32, 133.66, 135.00, 138.59, 142.27, 145.48, 147.20, 159.52, 176.41.

Anal. Calcd. for $C_{24}H_{19}O_4I$: C, 57.8; H, 3.84. Found: C, 58.0; H, 3.73.

8-Ethenyl-1-hydroxy-2-iodobenzo[d]naphtho[1,2-*b*]pyran-6-one (55). To a solution of 8-ethenyl-1-hydroxybenzo[d]naphtho[1,2-b]pyran-6-one[7c] (400 mg, 0.50 mmol) in 10 mL of dimethylformamide was added N-iodosuccinimide (147 mg, 0.65 mmol). After stirring the reaction mixture for 6 hours at room temperature, the volatiles were removed in vacuo and the residue was dissolved in chloroform and purified by column chromatography (methylene chloride) followed by recrystallization from chloroform-ethanol to give 163 mg (78%) of **55** as off-white crystals, mp 202-204 °C dec. ^{1}H NMR ($CDCl_3$): δ 5.43 (1H, d, J_{cis} = 10.9 Hz),

5.96 (1H, d, J_{trans} = 17.6 Hz), 6.84 (1H, dd, vinyl), 7.78 (1H, d, $J_{11,12}$ =9.0 Hz), 7.90 (2H, m, H-3, H-9), 8.03 (1H, d, H-11,12), 8.12 (1H, d, $J_{9,10}$ = 8.4 Hz, H-10), 8.13 (1H, d, $J_{3,4}$ = 9.0 Hz, H-4), 8.43 (1H, d, $J_{7,9}$ = 1.6 Hz, H-7).

Anal. Calcd. for $C_{19}H_{11}O_3I$: C, 55.1; H, 2.68. Found: C, 55.0; H, 2.51.

8-Ethyl-4-(β-D-*glycero*-pentofuran-3'-ulos-1'-yl)-1-trimethylacetoxybenzo[d]naphtho[1,2-b]pyran-6-one (56). To a stirred solution of 8-ethyl-4-iodo-1-trimethylacetoxybenzo[d]naphtho[1,2-b]pyran-6-one (**50**) (750 mg, 1.50 mmol), 1,4-anhydro-2-deoxy-3-O-[(1,1,dimethylethyl)-diphenylsilyl]-D-*erythro*-pent-1-enitol[20] (**15**) (637 mg, 1.80 mmol), sodium acetate (123 mg, 1.50 mmol), and tributylamine (71 μL, 0.30 mmol) in 25 mL of dimethylformamide was added palladium acetate (34 mg, 0.15 mmol). The reaction mixture was stirred for six hours at which time acetic acid (2 mL) and a 1M solution of tetrabutylammonium fluoride in tetrahydrofuran (1 mL) were then added. The volatiles were removed in vacuo and the residue was dissolved in chloroform, filtered through celite, and purified by column chromatography (methylene chloride/ethyl acetate, 5:1) followed by recrystallization from chloroform-ethanol to give 644 mg (88%) of **56** as white needles, mp 208-210 °C. ^1H NMR ($CDCl_3$) δ 1.31 (3H, t, J = 7.6 Hz, CH_3), 2.27 (1H, dd, OH), 2.37 (1H, dd, $J_{1',2'\alpha}$ =10.0 Hz, $J_{2'\alpha,2'\beta}$ = 18.6 Hz, H-2'α), 2.80 (2H, q, benzylic), 3.63 (1H, dd, $J_{1',2'\beta}$ = 6.2 Hz, H-2'β), 4.06 (2H, m, H-5',5''), 4.28 (1H, dd, $J_{4',5'}$ =3.8 Hz, $J_{4',5''}$ = 3.9 Hz, H-4'), 6.57 (1H, dd, H-1'), 7.29 (1H, d, $J_{2,3}$ = 8.2 Hz, H-2), 7.68 (1H, dd, $J_{7,9}$ =1.7 Hz , $J_{9,10}$ = 8.3 Hz, H-9), 7.78 (1H, d, $J_{11,12}$ = 9.0 Hz), 8.04 (1H, d, H-3), 8.17 (1H, d, H-10), 8.19 (1H, d, H-7). ^{13}C NMR ($CDCl_3$) δ 15.13, 27.29, 28.59, 39.49, 46.20, 61.74, 75.90, 82.00, 114.78, 118.25, 119.57, 119.97, 120.22, 122.13, 122.37, 124.30, 128.49, 128.82, 132.59, 135.38, 135.40, 145.89, 146.32, 147.17, 160.33, 176.74, 214.31.

Anal. Calcd. for $C_{29}H_{28}O_7$; C, 71.3; H, 5.78. Found: C, 71.1; H, 5.68.

8-Ethenyl-4-(β-D-*glycero*-pentofuran-3'-ulos-1'-yl)-1-trimethylacetoxybenzo[d]naphtho[1,2-b]pyran-6-one (57). To a stirred solution of 8-ethenyl-4-iodo-1-trimethylacetoxybenzo[d]naphtho[1,2-b]pyran-6-one (**53**) (350 mg, 0.70 mmol), 1,4-anhydro-2-deoxy-3-O-[(1,1,dimethylethyl)diphenylsilyl]-D-*erythro*-pent-1-enitol[20] (**15**) (299 mg, 0.84 mmol), sodium acetate (58 mg, 0.70 mmol), and tributylamine (33 μL, 0.14 mmol) in 8 mL of dimethylformamide was added palladium acetate (16 mg, 0.07 mmol). The reaction mixture was stirred for ten hours at which time acetic acid (1 mL) and a 1M solution of tetrabutylammonium fluoride in tetrahydrofuran (0.5 mL) were then added. Volatiles were removed in vacuo and the residue was dissolved in chloroform, filtered through Celite, and purified by column chromatography (methylene chloride/ethyl acetate, 5:1) followed by recrystallization from chloroform-ethanol to give 191 mg (56%) of **57** as yellow needles, mp 232-234 °C. ^{1}H NMR ($CDCl_3$) δ 1.50 (9H, s, t-butyl), 2.40 (1H, dd, $J_{1',2'\alpha}$ =10.0 Hz, $J_{2'\alpha,2'\beta}$ = 18.6 Hz, H-2'α), 3.65 (1H, dd, $J_{1',2'\beta}$ = 6.2 Hz, H-2'β), 4.08 (2H, br, H-5'5''), 4.29 (1H, dd, $J_{4',5'}$ =3.8 Hz, $J_{4',5''}$ = 3.9 Hz, H-4'), 5.43 (1H, d, J_{cis} = 10.9 Hz), 5.94 (1H, d, J_{trans} = 17.6 Hz), 6.60 (1H, dd, H-1'), 6.82 (1H, dd, vinyl), 7.33 (1H, d, $J_{2,3}$ = 8.2 Hz, H-2), 7.82 (1H, d, $J_{11,12}$ = 9.0 Hz), 7.91 (1H, dd, $J_{7,9}$ = 1.9 Hz, $J_{9,10}$ = 8.4 Hz, H-9), 8.08 (1H, d, H-11,12), 8.12 (1H, d, H-10), 8.20 (1H, d, H-3), 8.37 (1H, d, H-7). ^{13}C NMR ($CDCl_3$) δ 27.32, 39.61, 46.23, 61.78, 75.94, 81.97, 114.63, 116.78, 118.49, 119.86, 120.02, 120.54, 122.19, 122.68, 124.48, 127.76, 128.76, 132.63, 134.06, 134.96, 135.51, 138.68, 146.40, 147.53, 160.16, 176.75, 214.25.

Anal. Calcd. for $C_{29}H_{26}O_7 \cdot 0.5\ H_2O$: C, 70.3; H, 5.49. Found: C, 70.2; H, 5.14.

4-[2'-Deoxy-β-D-*ribo*-(=*arabino*)-furanosyl]-8-ethyl-1-hydroxy-benzo[d]naphtho[1,2-b]pyran-6-one (39). To a solution of 8-ethyl-4-(β-D-glycero-pentofuran-3'-ulos-1'-yl)-1-

trimethylacetoxybenzo[d]naphtho[1,2-b]pyran-6-one (78 mg, 0.16 mmol) (**56**) in 5 mL of dimethylformamide and 2 mL of acetic acid was added sodium triacetoxyborohydride (47 mg, 0.22 mmol). After 10 minutes, volatiles were removed in vacuo and the residue was dissolved in 5 mL of chloroform. The solution was then passed through a short column of silica gel and the fractions collected. Volatiles were removed in vacuo and methanol (20 mL) was added. A small piece of metallic sodium (approx. 1 mg) was added to the white suspension. The reaction mixture was a clear yellow solution after 15 minutes at which time the reaction was complete based on tlc. Acetic acid (1mL) and water (15 mL) were added and the resulting precipitate was collected to afford 59 mg (91 %) of **39** as an off white powder, mp 216-218°C dec. ^{1}H NMR (DMSO-d6) δ 1.25 (3H, t, J = 7.6 Hz, CH_3), 1.90 (1H, ddd, $J_{1',2'\beta}$ = 6.9 Hz, $J_{2'\alpha,2'\beta}$ = 13.0 Hz, H-2'β), 2.72 (1H, ddd, $J_{1',2'\alpha}$ = 7.0 Hz, H-2'α), 2.79 (2H, q, benzylic), 3.64 (1H, dd, $J_{4',5'}$ = 5.4 Hz, $J_{5',5''}$ =11.5 Hz, H-5'), 3.69 (1H, dd, $J_{4',5''}$ = 3.7 Hz, H-5''), 3.80 (1H, m, H-4'), 4.03 (1H,m, H-3'), 6.28 (1H, dd, H-1'), 6.97 (1H, d, $J_{2,3}$ = 8.2 Hz, H-2), 7.85 (1H, dd, $J_{7,9}$ = 1.3 Hz, $J_{9,10}$ = 8.3 Hz, H-9), 7.94 (1H,d, H-3), 8.12 (1H, br s, H-7), 8.16 (1H, d, $J_{11,12}$ = 9.0 Hz), 8.29 (1H, d, H-11,12), 8.44 (1H, d, H-10). ^{13}C NMR (DMSO-d6) δ 16.00, 28.50, 44.50, 62.49, 71.09, 77.75, 86.80, 110.27, 114.84, 119.10, 119.92, 120.51, 122.14, 124.03, 125.83, 126.51, 128.44, 131.59, 133.56, 136.22, 145.95, 147.86, 152.64, 160.65.

Anal. Calcd. for $C_{24}H_{22}O_6$: C, 70.9; H, 5.46. Found: C, 70.5; H, 5.36.

4-[2'-Deoxy-3',5'-diacetyl-β-D-*ribo*-(=*arabino*)-furanosyl]-8-ethenyl-1-trimethylacetoxybenzo[d]naphtho[1,2-b]pyran-6-one (58). To a solution of 8-ethenyl-4-(β-D-glycero-pentofuran-3'-ulos-1'-yl)-1-trimethylacetoxybenzo[d]naphtho[1,2-b]pyran-6-one (**57**) in 5 mL of dimethylformamide and 2 mL of acetic acid was added sodium triacetoxyborohydride (122 mg, 0.58 mmol). After ten minutes, acetaldehyde (1 mL) was added and the

reaction mixture was stirred for an additional five minutes. Volatiles were removed in vacuo and the residue was dissolved in pyridine (50 mL). Acetic anhydride (4 mL) was added and the reaction mixture was stirred overnight. Volatiles were removed in vacuo and the residue was dissolved in chloroform and purified by column chromatography followed by recrystallization from chloroform-ethanol to give 152 mg (92%) of **58** as white crystals, mp 162-163 °C. ^{1}H NMR ($CDCl_3$) δ 1.52 (9H, s, t-butyl), 2.01(1H, ddd, $J_{1',2'\alpha}$ = 9.8 Hz, $J_{2'\alpha,2'\beta}$ = 13.7 Hz, $J_{2'\alpha,3'}$ = 5.9 Hz, H-2'α), 2.12 (3H, s, OAc), 2.30 (3H, s, OAc), 3.11 (1H, ddd, $J_{1',2'\beta}$ = 5.3 Hz, $J_{2'\beta,3'}$ = 1.9 Hz, H-2'β), 4.36 (1H, dd, $J_{4',5'}$ = 4.1 Hz, $J_{5',5''}$ =11.1 Hz, H-5'), 4.47 (1H, m, H-4'), 4.50 (1H, dd, $J_{4',5''}$ = 4.1 Hz, H-5"), 5.28 (1H, m, H-3'), 5.46 (1H, d, J_{cis} = 11.0 Hz), 5.97 (1H, d, J_{trans} = 17.6 Hz), 6.54 (1H, dd, H-1'), 6.85 (1H, dd, vinyl), 7.32 (1H, d, $J_{2,3}$ = 8.2 Hz, H-2), 7.82 (1H, d, $J_{11,12}$ = 9.0 Hz), 7.91 (1H, dd, $J_{7,9}$ = 1.9 Hz, $J_{9,10}$ = 8.4 Hz, H-9), 8.09 (1H, d, H-11,12), 8.11 (1H, d, H-3), 8.16 (1H, d, H-10), 8.40 (1H, d, H-7). ^{13}C NMR ($CDCl_3$) δ 20.94, 21.26, 27.32, 39.51, 41.80, 64.35, 76.47, 79.14, 81.27, 114.44, 116.58, 118.38, 119.83, 119.84, 120.66, 122.19, 122.64, 124.15, 127.71, 128.73, 132.49, 134.21, 135.06, 136.42, 138.50, 146.05, 147.86, 160.06, 170.86, 171.23, 176.82.

Anal. Calcd. for $C_{33}H_{32}O_9$: C, 69.2; H, 5.63. Found: C, 69.3; H, 5.59.

4-[2'-Deoxy-β-D-*ribo*-(=*arabino*)-furanosyl]-8-ethenyl-1-trimethylacetoxybenzo[d]naphtho[1,2-b]pyran-6-one (38). To a solution of 4-[2'-deoxy-3',5'-diacetyl-β-D-ribo-(=arabino)-furanosyl]-8-ethenyl-trimethylacetoxybenzo[d]naphtho[1,2-b]pyran-6-one (**58**) (80 mg, .14 mmol) in 10 mL of methanol was added metallic sodium (3 mg). The suspension was then stirred for three hours at which time the reaction mixture was a clear yellow solution. Acetic acid (1 mL) and water (15 mL) was then added and the resulting precipitate was collected to afford 52 mg (92 %) of **38** as a light yellow powder, mp 258-260 °C dec. ^{1}H NMR (DMSO-d6) δ 1.91 (1H, ddd, $J_{1',2'\beta}$= 7.0 Hz, $J_{2'\alpha,2'\beta}$ = 12.9 Hz, $J_{2'\beta,3'}$ = 5.8 Hz,

H-2'β), 2.70 (1H, ddd, J $_{1',2'\alpha}$ = 7.0 Hz, H-2'α), 3.60 (1H, dd, J $_{4',5'}$ = 5.3 Hz, J $_{5',5''}$ =11.6 Hz, H-5'), 3.66 (1H, dd, J $_{4',5''}$ = 3.8 Hz, H-5''), 3.80 (1H, m, H-4'), 4.03 (1H,m, H-3'), 5.46 (1H, d, J $_{cis}$ = 11.0 Hz), 6.08 (1H, d, J $_{trans}$ = 17.6 Hz), 6.27 (1H, dd, H-1'), 6.90 (1H, dd, vinyl), 6.97 (1H, d, J $_{2,3}$ = 8.2 Hz, H-2), 7.91 (1H,d, H-3), 8.06 (1H, br d, J $_{9,10}$ =8.3 Hz, H-9), 8.12 (1H, d, J $_{11,\ 12}$ =9.0 Hz), 8.22 (2H, br, H-7, H-11,12), 8.40 (1H, d, H-10). ^{13}C NMR (DMSO-d6) δ 44.15, 62.21, 71.05, 77.73, 86.39, 110.27, 114.53, 117.45, 118.94, 119.97, 120.47, 121.84, 124.08, 125.72, 126.40, 127.27, 131.27, 133.05, 134.73, 135.51, 138.47, 147.81, 152.27, 160.61.

Anal. Calcd. for $C_{24}H_{20}O_6 \cdot 0.5\ H_2O$: C, 69.7; H, 5.12. Found: C, 69.8; H, 5.09.

1,4-Anhydro-2-deoxy-1-^{2}H-D-*erythro*-pent-1-enitol (61). A 1M solution of diisobutylaluminum deuteride[55] in ether (3.31 mL, 3.31 mmol) was added dropwise over 15 minutes to a stirred solution of **59**[28] (1.00 g, 3.31 mmol) in 40 mL of ether at -78 °C under nitrogen. After two hours, the reaction mixture was quenched by addition of 2 mL of methanol. The reaction mixture was then diluted with 100 mL of ether and washed with disodium tartrate solution (0.5 M aqueous) and the resulting ether extract was dried over magnesium sulfate. Volatiles were removed in vacuo to give 990 mg (98%) of **60** as a colorless oil which was used in the next step without further purification.

To a solution of the above oil (990 mg, 3.25 mmol) and carbon tetrachloride (0.376 mL, 3.90 mmol) in 25 mL of dry tetrahydrofuran at -78 °C, was added hexamethyl-phosphorous triamide (0.728 mL, 3.41 mmol). After 30 minutes, the reaction mixture was allowed to rise in temperature to 0 °C; the reaction mixture was then carefully added to a preprepared solution of lithium (275 mg, 38.95 mmol) in 100 mL of ammonia kept at -78 °C. After ammonia refluxing (dry ice condenser) for 2 hours, ammonium chloride (2.06 g, 38.95 mmol) was added. Ether (100 mL) was then added with 2 grams of magnesium sulfate. Ammonia was allowed to evaporate followed by

filtration and evaporation of volatiles in vacuo. Purification was accomplished by column chromatography to give 530 mg (71%).

To an ice-cooled solution of the above oil (530 mg, 2.31 mmol) in 15 mL of tetrahydrofuran was added a 1M solution of tetrabutylammonium fluoride in tetrahydrofuran (2.76 mL, 2.76 mmol). The reaction was complete in 5 minutes based on TLC. Evaporation of volatiles followed by flash chromatography of the residue yielded 248 mg (92%) of **61** as a colorless oil. ^{1}H NMR (DMSO-d6) δ 3.32 (2H,m, H-5,5'), 4.08 (1H, ddd, $J_{3,4}$ = 3.3 Hz, $J_{4,5}$ = 6.0 Hz, $J_{4,5'}$ = 9.4 Hz, H-4), 4.52 (1H, dd, H-3), 4.98 (1H, d, $J_{2,3}$ = 2.5 Hz, H-2). ^{13}C NMR (DMSO-d^6) δ 61.85, 74.20, 89.36, 104.05, 148.90 (t).

1,4-Anhydro-2-deoxy-1-^{13}C-D-*erythro*-pent-1-enitol (63).

To a mixture of 1-^{13}C-D-ribose (99% ^{13}C)[56] (480 mg, 3.18 mmol), and anhydrous copper (II) sulfate (500 mg) in 30 mL of dry acetone was added .060 mL of concentrated sulfuric acid. The mixture was stirred at room temperature for 10 hours and subsequently neutrallized with ammonia gas. Filtration followed by removal of volatiles in vacuo gave an oil which was purified by column chromatography to give 474 mg (78%) of 2,3-*O*-(1-methylethylidene)-1-^{13}C-D-ribose.

To a ice-cooled stirred solution of the above oil (474 mg, 2.48 mmol) and diisopropylethylamine (0.56 mL, 3.22 mmol) in 30 mL of dichloromethane was added tert-butyldimethylsilyl chloride (412 mg, 2.73 mmol). After 10 minutes, the reaction mixture was allowed to warm to room temperature and was stirred for an additional 6 hours. Ether (150 mL) was then added and the solution was then washed with a saturated solution of aqueous sodium bicarbonate. The organic layer was dried over sodium sulfate and volatiles were subsequently removed in vacuo. Column chromatography of the residue gave 706 mg (94%) of 5-O-[(1,1-dimethylethyl)dimethylsilyl]-2,3-*O*-(1-methylethylidene)-1-^{13}C-D-ribose.

To a solution of the above oil (706 mg, 2.33 mmol) and carbon tetrachloride (.267 mL, 2.80 mmol) in 25 mL of dry tetrahydrofuran at -78 °C, was added hexamethylphosphorous triamide (0.522 mL, 2.44 mmol). After 30 minutes, the reaction mixture was allowed to rise in temperature to 0 °C. The reaction mixture was then carefully added to a preprepared solution of lithium (196 mg, 27.96 mmol) in 100 mL of ammonia kept at -78 °C. After ammonia refluxing (dry ice condenser) for 2 hours, ammonium chloride (1.50 g, 27.96 mmol) was added. Ether (100 mL) was then added with 2 grams of magnesium sulfate. Ammonia was allowed to evaporate followed by filtration and evaporation of volatiles in vacuo. Purification was accomplished by column chromatography to give 371 mg (69%) of 1,4-anhydro-2-deoxy-5-O-[(1,1-dimethylethyl)dimethylsilyl]-1-^{13}C-D-erythro-pent-1-enitol as a colorless oil.

To an ice-cooled solution of the above oil (371 mg, 1.61 mmol) in 15 mL of tetrahydrofuran was added a 1M solution of tetrabutylammonium fluoride in tetrahydrofuran (1.80 mL, 1.80 mmol). The reaction was complete in 5 minutes based on tlc. Evaporation of volatiles followed by flash chromatography of the residue yielded 168 mg (90%) of **63** as a colorless oil.

4-(4',6'-Di-O-acetyl-2',3'-dideoxy-α-D-erythro-hex-2-enopyran-osyl)-1-methoxynaphthalene (64) and 4-(4',6'-di-O-acetyl-2',3'-dideoxy-β-D-erythro-hex-2-enopyranosyl)-1-methoxynaphthalene (65). To a stirred solution of 1-methoxynaphthalene (.50 g, 3.16 mmol) and 3,4,6-tri-O-acetyl-D-glucal (1.29 g, 4.74 mmol) in 50 mL of dry dichloroethane was added stannic chloride (0.32 mL of a 1M solution in dichloroethane, 0.32 mmol). The reaction mixture was then stirred for 1 hour at room temperature at which time 10 mL of tetrahydrofuran was added. The reaction mixture was then partitioned between dichloromethane and water. The organic phase was washed several times with water and then dried over sodium sulfate. The pink solution was then evaporated and the residue purified by column chromatography (methylene

chloride/ethyl acetate, 50:1) to give 1.10 g (94%) of a 1:1 mixture of **64** and **65**. The isomers were then further purified by preparative TLC (methylene chloride/ethyl acetate, 100:1) and recrystallized from chloroform: ethanol to give **64** as colorless crystals mp 133°, and **65** as colorless crystals mp 125°. For **64**: ^{1}H NMR ($CDCl_3$): δ 1.80 (3H, s, 4'-OAc), 2.07 (3H, s, 6'-OAc), 3.73 (1H, ddd, $J_{4',5'}$ = 8.6 Hz, $J_{5',6'}$ = 2.9 Hz, $J_{5',6''}$ = 6.1 Hz, H-5'), 3.88 (1H, dd, $J_{6',6''}$ =12.0 Hz, H-6'), 4.00 (3H, s, Ph-OCH_3), 4.24 (1H, dd, H-6''), 5.37 (m, 1H, H-4'), 5.94 (1H, m, H-1'), 6.08 (1H, m, $J_{2',3'}$ =10.3 Hz, H-2'), 6.26 (1H, m, H-3'), 6.73 (1H,d, $J_{2,3}$ = 7.9 Hz, H-2), 7.36 (1H,d, H-3), 7.48 (1H,m, $J_{7,8}$ = 8.5 Hz, H-7), 7.57 (1H, m, $J_{5,6}$ = 8.5 Hz, H-6), 8.24 (1H, d, H-5), 8.38 (1H, d, H-8). ^{13}C NMR ($CDCl_3$): δ 20.60 (OAc), 21.08 (OAc), 55.49 (OCH_3), 62.86 (C-6'), 65.57 (C-4'), 68.52 (C-5'), 71.15 (C-1'), 102.05 (C-2), 122.31 (C-8), 124.39 (C-5), 125.24 (C-7), 125.60, 126.16 (C-2'), 126.18, 126.91 (C-6), 127.31 (C-3), 131.86 (C-3'), 133.00, 156.13, 170.48, 170.76.

Anal. Calcd. for $C_{21}H_{22}O_6$: C, 68.1; H, 5.99. Found: C, 68.1; H, 6.01..

For **65**: ^{1}H NMR ($CDCl_3$): δ 2.05 (3H, s, OAc), 2.12 (3H, s, OAc), 3.98 (3H, s, Ph-OCH_3),4.12 (1H, ddd, $J_{4',5'}$ = 8.8 Hz, $J_{5',6'}$ = 2.5 Hz, $J_{5',6''}$ = 6.1 Hz, H-5'), 4.25 (1H, dd, $J_{6',6''}$ =12.0 Hz, H-6''), 4.30 (1H, dd, H-6'), 5.53 (m, 1H, H-4'), 5.82 (1H, m, H-1'), 5.92 (1H, m, $J_{2',3'}$ =10.3 Hz, H-2'), 6.12 (1H, m, H-3'), 6.76 (1H,d, $J_{2,3}$ = 8.0 Hz, H-2), 7.43 (1H, d, H-3), 7.46 (1H,m, $J_{7,8}$ = 8.1 Hz, H-7), 7.52 (1H, m, $J_{5,6}$ = 8.3 Hz, H-6), 8.08 (1H, d, H-5), 8.29 (1H, d, H-8). ^{13}C NMR ($CDCl_3$): δ 20.85 (OAc), 21.10 (OAc), 55.54 (OCH_3), 63.83 (C-6'), 65.72 (C-4'), 75.21 (C-5'), 75.25 (C-1'), 103.05 (C-2), 122.66 (C-8), 123.40 (C-5), 125.08 (C-7), 125.08 (C-2'), 125.87 (C-3), 126.06, 126.71 (C-6), 127.11, 131.91, 133.02 (C-3'), 155.89, 170.45, 170.95.

Anal. Calcd. for $C_{21}H_{22}O_6$: C, 68.1; H, 5.99. Found: C, 68.1; H, 5.86.

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