to obtain a mixture of diacetates **5** and **6** (21 mg) that was separated by LC on Partisil (20% EtOAc/hexane) to obtain diacetate **5** (12 mg, 54% yield) and diacetate **6** (7.8 mg, 35% yield).

Diacetate 5: oil; IR ($CHCl_3$) 1800, 1765, 1750 cm^{-1}; UV (MeOH) 203 nm (ϵ 7570); ^1H NMR ($CDCl_3$) δ 0.70 (d, 3 H, J = 7 Hz), 1.60 (br s, 3 H), 1.67 (br s, 3 H), 2.13 (s, 3 H), 2.18 (s, 3 H), 4.63 (br s, 1 H), 4.68 (ddd, 1 H, J = 11.5, 3.8, 1.2 Hz), 4.82 (br s, 1 H), 5.05 (br t, 1 H, J = 6 Hz), 5.81 (br d, 1 H, J = 4.5 Hz), 6.21 (br s, 1 H), 6.33 (s, 1 H), 6.97 (s, 1 H); HRMS, m/z 440.2569, $C_{27}H_{36}O_5$ (M - AcOH) requires 440.2553.

Diacetate 6: oil; IR ($CHCl_3$) 1800, 1765, 1750 cm^{-1}; UV (MeOH) 203 nm (ϵ 7240); ^1H NMR ($CDCl_3$) δ 0.70 (d, 3 H, J = 7 Hz), 1.59 (br s, 3 H), 1.68 (br s, 3 H), 2.10 (s, 3 H), 2.15 (s, 3 H), 4.63 (br s, 1 H), 4.69 (br t, 1 H, J = 8 Hz), 4.83 (br s, 1 H), 5.04 (br t, 1 H, J = 6.5 Hz), 5.82 (br s, 1 H), 6.13 (s, 1 H), 6.26 (s, 1 H), 7.06 (s, 1 H); HRMS, m/z 440.2560, $C_{27}H_{36}O_5$ (M - AcOH) requires 440.2553.

Preparation of Keto Acetate 8. A stream of ozone was bubbled through a cooled solution of luffariellin A (**3**, 26.2 mg) in methanol (10 mL) at -78 °C until the solution attained a blue coloration. After the excess ozone was removed by bubbling dry nitrogen through the solution, silver oxide (20 mg) was added, and the mixture was stirred at -78 °C for 1 h then allowed to warm to 25 °C, and stirred for 16 h. The product was filtered through Celite, the solvent was evaporated, and the residual oil was partitioned between ether and water. The ether soluble material was purified by LC on Partisil (1:1 ether/hexane) to obtain a diketone **7** (5.4 mg, 44% yield): IR ($CHCl_3$) 1710, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (d, 3 H, J = 7 Hz), 2.11 (s, 3 H), 2.13 (s, 3 H).

Pyrrolidine (6 μL) and acetic acid (9 μL) were added to a solution of the diketone **7** (5.0 mg) in dry methanol (1 mL), and the mixture was allowed to stand overnight under an atmosphere of dry nitrogen. The solvents were evaporated, and the residue was purified by LC on Partisil (1:1 ether/hexane) to obtain the keto acetate **8** (3.6 mg, 58% yield): oil; IR ($CHCl_3$) 1710 (br) cm^{-1}; ^1H NMR (C_6D_6) δ 0.65 (d, 3 H, J = 7 Hz), 1.04 (s, 3 H), 1.13 (m, 1 H), 1.19 (m, 1 H), 1.46 (m, 2 H), 1.54 (qdd, 1 H, J = 7, 7, 3 Hz), 1.66 (ddd, 1 H, J = 14, 11, 5 Hz), 1.69 (s, 3 H), 1.79 (m, 1 H), 1.84 (ddd, 1 H, J = 14, 11, 5 Hz), 2.01 (d, 1 H, J = 5 Hz), 2.36 (ddd, 1 H, J = 18, 11, 5 Hz), 2.45 (d, 1 H, J = 5 Hz), 2.63 (ddd, 1 H, J = 18, 11, 5 Hz); NOEDS measurements [$\delta_{irr} \rightarrow \delta_{obsd}$ (% enhancement)] 0.65 → 1.54 (16), 0.65 → 2.45 (12), 1.04 → 1.84 (15), 1.04 → 2.01 (20).

Acknowledgment. We thank Toshiro Paulis for assistance in Palau and Mary Kay Harper and Joaquin Caso for technical assistance. The research was generously supported by Allergan Corporation and by a grant from the California Sea Grant College Program (NOAA, NA85AA-D-SG140, R/MP-30).

C-Glycosides from Palladium-Mediated Reactions of Pyranoid Glycals. Stereochemistry of Formation of Intermediate Organopalladium Adducts and Factors Affecting Their Stability and Decomposition

Jane Chi-Ya Cheng and G. Doyle Daves, Jr.*

Department of Chemistry, Lehigh University, Bethlehem, Pennsylvania 18015

Received February 13, 1987

Palladium-mediated reactions of eight 3-O-substituted pyranoid glycals with (1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)mercuric acetate occurred regio- and stereospecifically to form, in each case, a single organopalladium adduct by attack of the organopalladium reagent on the glycal double bond from the face of the glycal opposite the allylic 3-O-substituent. Yields of C-glycosides formed by adduct decomposition were higher for glycals with pseudoequatorial 3-O-substituents than for glycals with this substituent pseudoaxial. Intermediate adduct stability and decomposition modes were sensitive to reaction medium composition. The presence of chloride ions resulted in relatively stable organopalladium adducts for which subsequent medium changes influenced decomposition modes. Reaction mixtures containing only acetate anions did not lead to stabile adducts and C-glycoside products appeared early. Conformational constraints on glycals, achieved by incorporation of 4- and 6-oxygen atoms into a ring, resulted in highly selective adduct decomposition producing a single C-glycoside product; unfortunately, this constraint also lowered product yields.

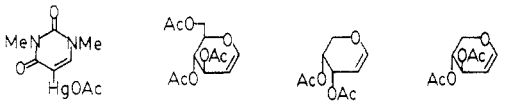
Palladium-mediated coupling reactions of pyranoid and furanoid glycals[1,2] are key to an efficient synthetic route to C-nucleosides (C-glycosides).[3] The coupling process leading to C-nucleosides involves four discrete organometallic reactions:[4] (1) formation of an organopalladium reagent from an aglycon precursor (aromatic or heterocyclic),[4] (2) complexation (usually stereospecific)[5] of the palladium center with the glycal (enol ether) double bond,[1,2,5,6] (3) collapse of the π-complex by regiospecific insertion of the enol ether double bond into the Pd–C bond of the aglycon reagent to form a C-glycoside σ-adduct,[1,2,5-8] and (4) adduct decomposition with elimination of palladium and a β-substituent (H,[1,3,5-8] OH,[6,9] OAc,[1,4,7] alkoxy[1,7]) and C-nucleoside product formation.

Efficient synthesis of C-glycosides using this palladium-mediated procedure depends on control of each step

(1) Arai, I.; Lee, T. D.; Hanna, R.; Daves, G. D., Jr. *Organometallics* **1982**, *1*, 742–747.
(2) Hacksell, U.; Daves, G. D., Jr. *J. Org. Chem.* **1983**, *48*, 2870–2876.
(3) (a) Hacksell, U.; Daves, G. D., Jr. *Prog. Med. Chem.* **1985**, *22*, 1–65. (b) Daves, G. D., Jr.; Cheng, C. C. *Prog. Med. Chem.* **1976**, *13*, 303–349. (c) Hanessian, S.; Pernet, A. G. *Adv. Carbohyrd. Chem. Biochem.* **1976**, *33*, 111–188. (d) Buchanan, J. G. *Prog. Chem. Org. Natl. Prod.* **1983**, *44*, 243–299.
(4) Kalinoski, H. T.; Hacksell, U.; Barofsky, D. F.; Barofsky, E.; Daves, G. D., Jr. *J. Am. Chem. Soc.* **1985**, *107*, 6476–6482.
(5) We have encountered only two examples in which products resulting from two stereoisomeric complexes were isolated (ref 6; Kwok, D. I.; Daves G. D., Jr., unpublished results).
(6) Cheng, J. C.-Y.; Hacksell, U.; Daves, G. D., Jr. *J. Org. Chem.* **1986**, *51*, 3093–3098.
(7) Arai, I.; Daves, G. D., Jr. *J. Am. Chem. Soc.* **1981**, *103*, 7683.
(8) Lee, T. D.; Daves, G. D., Jr. *J. Org. Chem.* **1983**, *48*, 399–402.
(9) Hacksell, U.; Daves, G. D., Jr. *Organometallics* **1983**, *2*, 772–775.

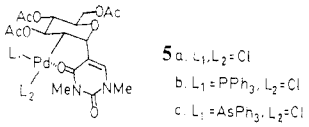
0022-3263/87/1952-3083$01.50/0

in the sequence. The present study was undertaken to (a) extend our investigation of stereocontrol of π-complex formation in pyranoid glycal coupling reactions and (b) elucidate decomposition modes of σ-adducts derived from pyranoid glycals. Previously, we have studied[1,10] palladium-mediated coupling reactions of (1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)mercuric acetate[11] (**1**) with three pyranoid glycals, 3,4,6-tri-*O*-acetal-D-glucal[12] (**2**), 3,4-di-*O*-acetyl-D-arabinal[13] (**3**), and 3,4-di-*O*-acetyl-D-xylal[14] (**4**). In each case, a mixture of C-nucleoside



1 PyHgOAc **2** **3** **4**

products was isolated and, in each case, the product mixture resulted from competing decomposition modes of a single σ-adduct (e.g., **5**), which was derived from attack of the pyrimidinyl–palladium reagent on the enol ether double bond from the face of the carbohydrate ring opposite the allylic acetate substituent.[15] These initial studies have now been extended by examination of the palladium-mediated coupling reactions of five additional pyranoid glycals.



5 a. L_1, L_2 = Cl
b. L_1 = PPh_3, L_2 = Cl
c. L_1 = $AsPh_3$, L_2 = Cl

Stereochemistry of Pyranoid Glycal–Organopalladium Complex Formation

In Table I are summarized available data for palladium-mediated reactions of pyranoid glycals with aryl or heterocyclic aglycons. Included are results from our earlier studies[1,4,7,10,16] and from studies of Czernecki and coworkers.[17,18] As noted in earlier studies[1,4,7,10,16] (Table I, entries 1a–d, 3, 5), coupling reactions involving stoichiometric portions of organomercurial **1** and pyranoid glycals **2–4** in the presence of palladium(II) salts in acetonitrile solution at room temperature led to products derived from a single organopalladium adduct, i.e., the reaction occurred stereo- and regiospecifically. Czernecki[17,18] who used elevated reaction temperatures (80–120 °C) and large excesses of aglycon precursors (benzene, anisole, resorcinol dimethyl ether) isolated product mixtures derived from stereoisomeric glycal–organopalladium adducts (e.g., Table I, entry 1f).[5] In the present study, coupling reactions of **2** and five additional pyranoid glycals, 3,4,6-tri-*O*-acetyl-D-galactal[20] (**6**), 3-*O*-acetyl-4,6-*O*-(phenylmethylene)-D-glucal[21] (**7**), 3,4,6-tri-*O*-acetyl-D-allal[22] (**8**), 3-*O*-acetyl-4,6-*O*-(phenylmethylene)-D-allal[23] (**9**), and 3-*O*-(triisopropylsilyl)-4,6-*O*-(phenylmethylene)-D-allal (**10**) were carried out under reaction conditions used in our earlier studies.[1,10] In each case, π-complex and σ-adduct formation resulted from attack of the organopalladium reagent derived from **1**[4] on the face of the glycal ring opposite the allylic (C-3) substituent.[24]

It is unclear why attack of the organopalladium reagent on the pyranoid glycal double bond for π-complex and σ-adduct formation should be stereospecific. In furanoid glycals, significant differences in the relative steric shielding of the two faces of the glycal ring by 3-O and 5-O substituents appear to account for the stereoselectivity of π-complex formation.[2,5] However, the half-chair conformation of pyranoid glycals in solution[25] is such that the double bond appears to be accessible to bulky reagents from either face. It is surprising that π-complex formation is so sensitive to the allylic oxy substituent (whether pseudoaxial or pseudoequatorial). It is likely that stereoelectronic effects[26] including the anomeric effect[27] and the more recently described vinylogous anomeric effect[28,29] control the stereochemistry of the palladium-mediated coupling of pyranoid glycals. It is pertinent that glycals in which the C-3 substituent is pseudoequatorial in the lowest energy conformation (**2**, **4**, **6**, **7**)[30] appear to undergo palladium-mediated coupling in higher yield (Table I) than the corresponding glycals in which the C-3 substituent is pseudoaxial (**3**, **8–10**).

Decomposition Modes of Pyranoid Glycal Organopalladium σ-Adducts

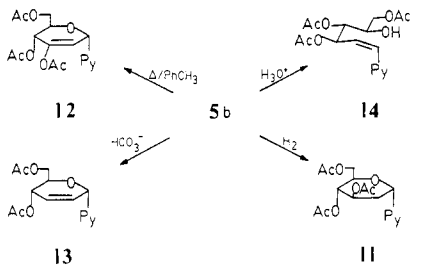
It was recognized earlier[1,10] that the anion content of reaction mixtures and conformational factors affecting the intermediate σ-organopalladium adduct are important in determining decomposition reactions. In the present work, the effects on decomposition modes of pyranoid glycal configuration, conformation, and 3-O substituent type were studied. The effect of added salts was also investigated.

Reaction Media Effects on Adduct Stability and Decomposition Modes. In coupling reactions of 3,4,6-tri-*O*-acetal-D-glucal[12] (**2**) with **1** the anion (ligand) content of the reaction mixture affects importantly the reaction

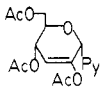
(10) Arai, I.; Daves, G. D., Jr. *J. Am. Chem. Soc.* **1978**, *100*, 287–288.
(11) Arai, I.; Daves, G. D., Jr. *J. Org. Chem.* **1978**, *43*, 4110–4112.
(12) Roth, W.; Pigman, W. *Methods in Carbohydrate Chemistry*; Academic Press: New York, 1963; Vol. II, pp 405–408.
(13) Humoller, F. L. *Methods in Carbohydrate Chemistry*; Academic Press: New York, 1962; Vol. I, pp 83–88.
(14) Weygand, F. *Methods in Carbohydrate Chemistry*; Academic Press: New York, 1962; Vol I, pp 182–185.
(15) Reversible attack of the organopalladium reagent on both faces of the ring to form a mixture of two isomeric π-complexes cannot be ruled out assuming that only one complex leads to products. In the one instance where a stable σ-adduct was isolated, the adduct was that from which products were derived; no evidence was found for the presence of the isomeric adduct (ref 7, 16).
(16) Hacksell, U.; Kalinoski, H. T.; Barofsky, D. F.; Daves, G. D., Jr. *Acta Chem. Scand. Ser. B* **1985**, *39*, 469–476.
(17) Czernecki, S.; Dechavanne, V. *Can. J. Chem.* **1983**, *61*, 533–540.
(18) Czernecki, S.; Gruy, F. *Tetrahedron Lett.* **1981**, *22*, 437–440.
(19) For a different approach to palladium-mediated coupling, see: Dunkerton, L. V.; Serino, A. J. *J. Org. Chem.* **1982**, *47*, 2812–2814.
(20) Rosenthal, A.; Read, D. *Methods Carbohydr. Chem.* **1963**, *2*, 457. For ^{1}H nuclear magnetic resonance spectrum, see: Chalmers, A. A.; Hall, R. H. *J. Chem. Soc., Perkin Trans. 2* **1974**, 728–732.
(21) Sharma, M.; Brown, R. K. *Can. J. Chem.* **1966**, *44*, 2825–3835.
(22) (a) Richtmyer, N. *Methods in Carbohydrate Chemistry*; Academic Press; New York, 1962; Vol. I, pp 107–113. (b) Lemieux, R. U.; Fraga, E.; Watanabe, K. A. *Can. J. Chem.* **1968**, *46*, 61–69. (c) Guthrie, R. D.; Irvine, R. W. *Carbohydr. Res.* **1979**, *72*, 285–288.
(23) Feast, A. A.; Overend, W. G.; Williams, N. R. *J. Chem. Soc.* **1965**, 7378–7388.
(24) In the coupling reaction of 3,4,6-tri-*O*-acetyl-D-allal (**8**) an anomolous result was obtained (Table I, entry 6). In addition to the expected product **22**, a significant amount of **15** was also formed. No mechanism to account for this product from either π-complex derived from **8** is evident; it seems likely that isomerization of **8** to **2** accounts for the formation of **15**.
(25) (a) Hall, L. D.; Johnson, L. F. *Tetrahedron* **1964**, *20*, 883–889. (b) Chalmers, A. A.; Hall, R. H. *J. Chem. Soc., Perkin Trans. 2* **1974**, 728–732. (c) Achmatowicz, O., Jr.; Gluzinski, P.; Szechner, B. *Bull. Acad. Pol. Sci. Ser. Sci. Chim.* **1975**, *23*, 911. (d) Rico, M.; Santoro, J. *Org. Magn. Reson.* **1976**, *8*, 49–55.
(26) (a) Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon Press: New York, 1983. (b) Houk, K. N.; Paddon-Row, M. N.; Rondan, N. G.; Wu, Y.-D.; Brown, F. K.; Spellmeyer, D. C.; Metz, J. T.; Li, Y.; Loncharich, R. J. *Science (Washington, D.C.)* **1986**, *231*, 1108–1117.
(27) Kirby, A. J. *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*; Springer-Verlag: New York, 1983.
(28) Curran, D. P.; Suh, Y.-G. *J. Am. Chem. Soc.* **1984**, *106*, 5002–5004.
(29) Denmark, S. E.; Dappen, M. S. *J. Org. Chem.* **1984**, *49*, 798–806.
(30) Coupling constants in ^{1}H nuclear magnetic resonance spectra suggests that the ring-flipped conformer with the C-3 substituent pseudoaxial coexists in solution; see ref 24d.

course and outcome.[31] When this reaction is carried out[1,10] in a medium containing 2 or 3 equiv of chloride ion,[32] the resulting σ-adduct (**5a**) is relatively stable; after 3 days reaction time the adduct remains largely intact. In coupling reactions involving only acetate anions the resulting σ-adduct is much less stable and was not detected in the reaction mixture.

Attempts to isolate adduct **5a** were unsuccessful; however, when the adduct was further stabilized by addition of triphenylphosphine[7] (triphenylarsine[16]) to the reaction mixture (after 2 or 3 days reaction time), isolation and purification of **5b** or **5c** was accomplished.[7,16] The isolation[7] and characterization[16] of the σ-adduct (**5**) provided a firm basis for study of the various adduct decomposition modes and factors that influence their selection. Variation of reaction media and conditions for decomposition of isolated adduct **5b** permitted four separate C-nucleoside products to be obtained in selective decomposition reactions.[7] When a solution of **5b** in tetrahydrofuran was shaken under 2 atm of hydrogen, the 2′-deoxy C-nucleoside **11**[1] was formed. Heating **5b** in toluene resulted in syn β-hydride elimination with formation of **12**[1,10] as the sole product. In the presence of aqueous sodium bicarbonate, **5b** selectively underwent anti elimination of palladium and 3′-acetoxy to yield **13**.[1,10] Treatment of **5b** with aqueous hydrochloric acid caused a rupture of the pyranosyl ring with formation of the acyclic C-nucleoside **14**.[1,10]



In coupling reactions of **1** and **2** in which the intermediate σ-adduct (**5**) was not isolated, changing the composition and concentration of salts in the reaction mixture and changing conditions used to effect adduct decomposition caused significant differences in the nature and/or ratios of pyranosyl C-nucleoside decomposition products that were formed (Tables I and II). As noted (vida supra), inclusion of chloride ions in the reaction mixture served to stabilize the intermediate σ-adduct and relatively little adduct decomposition occurred until a change was made to facilitate decomposition. In early studies,[1,10] decomposition of the chloride-stabilized adduct was accomplished by passing hydrogen sulfide through the reaction mixture. When this was done, a black precipitate, presumably palladium sulfide, formed during several hours. Isolation and fractionation of the remaining palladium-free material from reaction of organomercurial **1** and glycal **2** yielded a mixture of C-nucleosides that consisted of the products (**12–14**) obtained in controlled decomposition reactions of adduct **5b** (Table I, entry 1a) plus an additional enol acetate product (**15**) resulting from a shift of acetate from glycal C-3 to C-2 (vida infra).[33]



15

When the coupling reaction was carried out with acetate as the only anion, the resulting product mixture contained **13** formed by anti elimination of palladium acetate and isomeric enol ethers **12** and **15**, resulting from hydridopalladium eliminations, in comparable amounts (Table I, entry 1b). In these reactions, no acyclic carbohydrate product was isolated. It is likely that in reactions in which ring opening occurred (Table I, entries 1a,d, 5), hydrochloric acid formation facilitated protonation of the pyranosyl ring oxygen of the undecomposed Pd adduct assisting ring opening with palladium elimination.[7] Indeed, when the concentration of chloride in the reaction mixture was higher and hydrogen sulfide was used to effect adduct decomposition (Table I, entry 1d) the acyclic C-nucleoside (**14**) was the sole product isolated. Use of sodium sulfide to effect adduct decomposition led to a mixture of cyclic C-nucleosides **12** and **13** (Table I, entry 1b). The data summarized in Table II reveal other effects of reaction media on adduct decomposition.

Conformational Effects on Adduct Decomposition. The steric requirements for elimination reactions, anti-periplanar for loss of palladium acetate (alkoxide)[1,6,34] and syn-periplanar for loss of palladium hydride[1,2,6,34] and palladium oxide[6,9] suggested that conformational constraints might favor a particular adduct decomposition mode.[34] To test this hypothesis, pyranoid glycal hydroxyls at C-4 and C-6 were incorporated into a six-membered ring (by reaction with benzaldehyde[22a]) to reduce conformational flexibility. When the phenylmethylene derivative of glucal[21] (**7**), organomercurial **1**,[11] and an equivalent of palladium(II) acetate in acetonitrile were allowed to react for 3 days, a single C-nucleoside product, **17**, was formed by syn elimination of palladium hydride (Table I, entry 4). Anti elimination of palladium acetate was suppressed, apparently because the intermediate σ-adduct **16** cannot achieve the conformation required for anti-periplanar arrangement of palladium and β-acetate.[34] Similarly, glycal **9**,[23] which is the C-3 epimer of **7**, undergoes coupling to yield only the C-nucleoside (**19**) formed by anti elimination of palladium acetate (Table I, entry 7). In this case the intermediate adduct (**18**) has palladium on the β face of the glycal and anti-periplanar to C′-3 acetoxy. These selective adduct decompositions that yield single C-nucleoside products (Table I, entries 4 and 7) stand in sharp contrast to those exhibited by adducts derived from the corresponding conformationally mobile tri-*O*-acetylglycals (**2**[12] and **8**[22]), which yield mixtures of C-nucleoside products (Table I, entries 1 and 6).

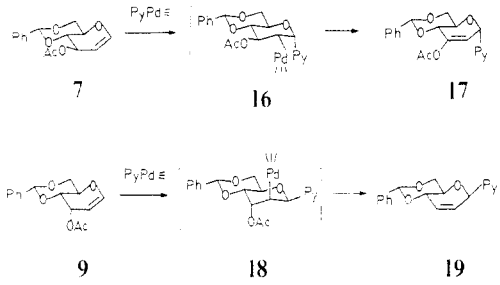
Effect of Glycal C-3-O-Substituent on Adduct Decomposition. The conformational constraints of a 4,6-phenylmethylene unit on decomposition of organopalladium adduct derived from pyranoid glycals permitted selective elimination of a C-3′-oxy substituent when the group anti-periplanar to palladium was acetoxy[34] (**18**). However, when a much poorer leaving group, (triisopropylsilyl)oxy was present (in the adduct derived from

(31) For other examples of palladium-mediated reactions affected by choice of anions, see: (a) Kende, A. S.; Roth, B.; Sanfilippo, P. J. *J. Am. Chem. Soc.* **1982**, *104*, 1784–1785. (b) Backvall, J. E.; Nordberg, R. E. *J. Am. Chem. Soc.* **1981**, *103*, 4959–4960. (c) Hosaka, S.; Tsuji, J. *Tetrahedron* **1971**, *27*, 3821–3829. (d) Tsuji, J.; Mori, Y.; Hara, M. *Tetrahedron* **1972**, *28*, 3721–3725. (e) Billups, W. E.; Walker, W. E.; Schield, T. C. *J. Chem. Soc., Chem. Commun.* **1971**, 1067–1068. (f) Trost, B. M.; Strange, P. E.; Weber, L.; Fullerton, T. J.; Dietsche, T. J. *J. Am. Chem. Soc.* **1978**, *100*, 3407–3415. (g) Trost, B. M.; Metzner, P. *J. Am. Chem. Soc.* **1980**, *102*, 3572–3577.

(32) If a large excess (5 equiv) of chloride ion is present the glycal coupling reaction does not occur[1] and pyrimidine dimerization takes place: Arai, I.; Hanna, R.; Daves, G. D., Jr. *J. Am. Chem. Soc.* **1981**, *103*, 7684–7685.

(33) In previous reports (ref 1 and 10), this product was assigned structure **12**. Compound **15** was not formed during the controlled decomposition of **5b** (ref 7).

(34) Cheng, J. C.-Y.; Daves, G. D., Jr. *Organometallics* **1986**, *5*, 1753–1755.



glycal **10**) anti elimination was completely suppressed and the adduct decomposed by syn palladium hydride elimination (to yield **20** and **21**, Table I, entry 8). Presumably, this decomposition required a change to a strained conformation in which the palladium and β-hydrogen are syn-periplanar.[34]

Structural Assignments

Assignments of structures to the C-nucleoside products were made on the basis of spectrometric and chemical data. ^1H and ^{13}C nuclear magnetic resonance (NMR) data for all the C-nucleosides prepared are summarized in Tables III and IV, respectively. In most instances, the assignments were straightforward; however, assignments of structures for the two enol acetate products resulting from the palladium-mediated reaction of 3,4,6-tri-*O*-acetyl-D-glucal (**2**)[12] with **1**[11] required more detailed study.

Isomeric Enol Acetates Derived from Adduct 5. Fractionation of the mixture of C-nucleoside products derived from coupling[1,10] of **1**[11] and **2**[12] (Table I, entry 1) was difficult and was accomplished only by using high performance liquid chromatography (HPLC). From this mixture two products were obtained that were characterized as enol acetate isomers by using mass spectrometry (Experimental Section) and NMR (Tables III and IV) and assigned structures[33] **12** and **15** on the basis of spectroscopic and chemical data.

Circular dichroism (CD) spectroscopy was used to assign the configurations of the anomeric carbons[35] of the two enol acetate isomers **12** and **15**. CD spectra for 2′,3′-unsaturated C-nucleosides **12**, **13**, **15**, **22**, and **23** are recorded in Figure 1. For the C-1′ anomeric pair **13** and **22**, the CD spectra are impressively different and serve to distinguish the stereochemical difference between the two.

The stereochemistry of chiral olefins has been correlated with CD spectra in the range 185–230 nm;[36] in this range di- (cis) and trisubstituted[37] chiral olefins exhibit two CD bands: λ_1, a very steep curve below about 195 nm, with a maximum at 185–190 nm and λ_2 with a maximum at 198–210 nm.[38] The CD spectra and stereochemical differences for **13** and **22** correlate well with reported chiral olefins.[36] Thus, in the CD spectrum of the α C-nucleoside **13** a negative Cotton effect is observed at λ_1 (i.e., the band is consignate, obeying the "right-hand" octant rule with respect to allylic substituents)[39] and a positive Cotton effect at λ_2 (the band is dissignate, obeying the "left-hand" octant rule).[39] The sign of λ_1 in the CD spectrum of the anomeric β C-nucleoside **22** is reversed (Figure 1). Since a small vinylic substituent (e.g., acetoxy on the C-2′–C-3′ carbohydrate double bond) has almost no effect on λ_1 and only a slight effect on λ_2,[36] the CD spectra of enol acetates **12**, **15**, and **23** are directly comparable to those of the disubstituted olefinic C-nucleosides. The CD spectra of **12** and **15** correlate with that of **13** and both isomers are assigned to the α C-nucleoside series.

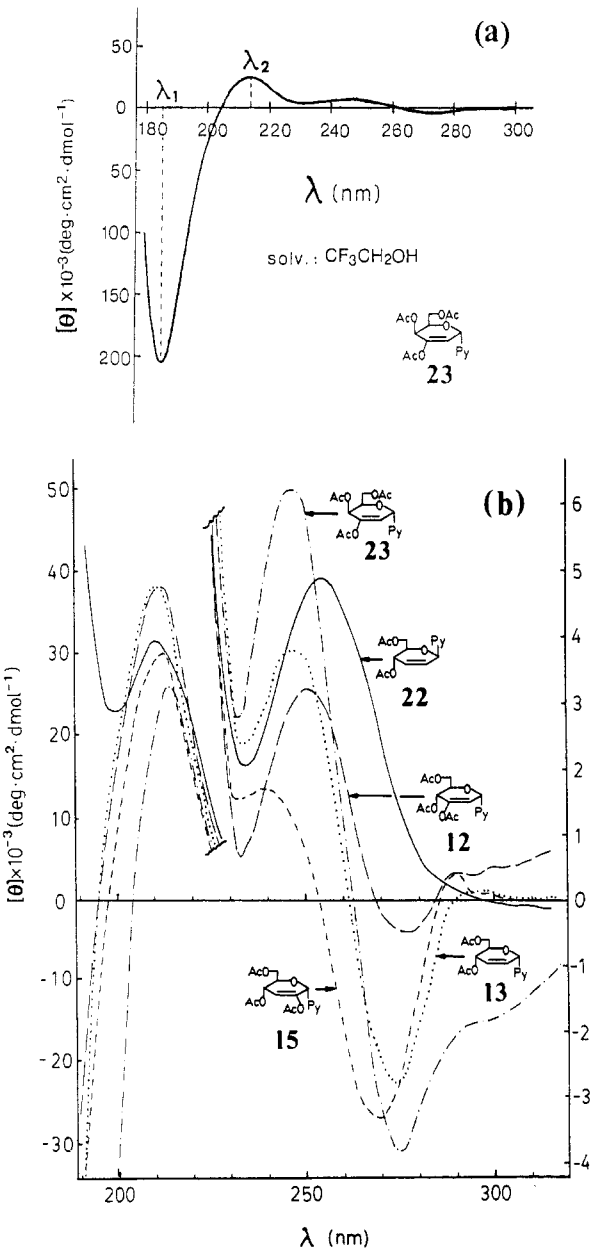


Figure 1. (a) Circular dichroism spectrum of C-nucleoside **23**. (b) Circular dichroism spectra of pyranoid C-nucleosides recorded in trifluoroethanol (190–230 nm) and methanol (225–320 nm).

Further information concerning the structures of enol acetate isomers **12** and **15** was obtained by comparison of products resulting from hydrolysis of the enol acetate functionality. ^1H NMR analysis of the product mixture obtained by treatment of **12** with methanolic potassium bicarbonate revealed the presence of an anomeric pair of 3′-keto-2′-deoxy C-nucleosides (**24**). Analysis of coupling constants ($J_{1',2\alpha'}$ = 3.6 Hz, $J_{1',2\beta'}$ = 7.2 Hz for the α-anomer, and $J_{1',2\alpha'}$ = 10.7 Hz, $J_{1',2\beta'}$ = 2.9 Hz for the β-anomer) indicated that the α-anomer of **24** was the major one. The β-anomer was presumably formed by abstraction of the C-1′ (anomeric) proton during the hydrolysis procedure.

(35) Assignment of configuration at the anomeric center of furanosyl C-nucleosides can be accomplished on the basis of the magnitude of $^4J_{1',4'}$ as measured in the ^1H NMR spectrum (ref 2 and 6); unfortunately, this method is not available for pyranosyl C-nucleosides.

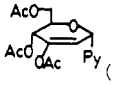
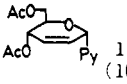
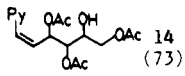
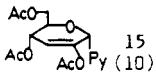
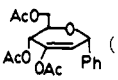
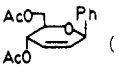
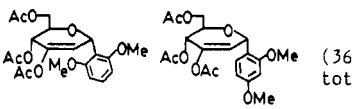
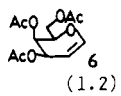
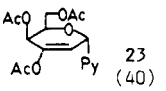
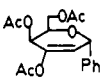
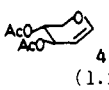
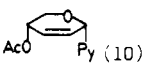
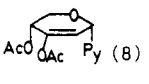
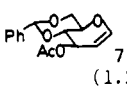
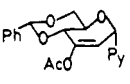
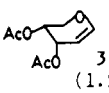
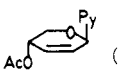
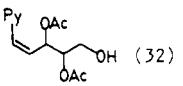
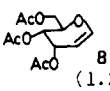
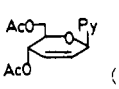
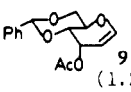
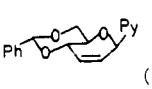
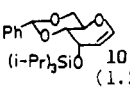
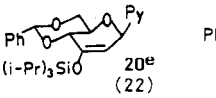
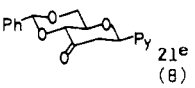
(36) Hudec, J.; Kirk, D. N. *Tetrahedron* **1976**, *32*, 2475–2506, and references cited therein.

(37) Trisubstituted olefins usually exhibit a third CD band (190–195 nm); in some cases it appears to be missing and may be obscured by more intense λ_1 and λ_2 bands.

(38) The pyrimidinyl aglycon may give rise to CD absorption in this region (its UV spectrum exhibits two absorption bands: λ_{max} (CF_3CH_2OH), 200–210 nm, log ε 3.93; λ_{max} (CH_3OH), 265–270 nm, log ε 3.91).

(39) Klyne, W.; Kirk, D. N. *Tetrahedron Lett.* **1973**, *1483*–1486, and refernces cited therein.

Table I. Pyranoid C-Nucleoside Synthesis[a]

entry	glycal (equiv)	aglycon (equiv)	PdX_2 (equiv)	added salt (equiv)	time[f] (days or h)	workup	product(s) (yield, %)[b]	ref
1a	 2(1.5)	PyHgOAc (1.0)	X=OAc (1.0)	LiCl (2.0)	2 d	H_2S	 12 (?)  13 (10)  14 (73)  15 (10)	Arai[c], this work
1b	2 (1.5)	PyHgOAc (1.0)	X=OAc (1.0)	LiCl (2.0)	2 d	Na_2S	12(5) 13(26) 15(54)	this work
1c	2 (1.5)	PyHgOAc (1.0)	X=OAc (1.0)	LiOAc (2.0)	2 d	H_2S	13(40) 15(40)	Arai[c]
1d	2 (1.5)	PyHgCl (1.0)	X=Cl (1.0)	LiOAc (2.0)	2 d	H_2S	14(40)	Arai[c]
1e	2 (1.5)	PyHgOAc (1.0)	X=OAc (1.0)	-	3 d	-	12(15) 13(31) 15(31)	this work
1f	2 (1.0)	benzene (166)	X=OAc (1.0)	-	2-8 h	-	 (54)  (10)	Czernecki[d]
1g	2 (1.0)	3-dimethoxy-benzene (166)	X=OAc (0.2)	$Cu(OAc)_2$ (1.6)	1.5 h	-	 (36) total	Czernecki[d]
2a	 6 (1.2)	PyHgOAc (1.0)	X=OAc (1.0)	$NaHCO_3$ (4.0)	1.5 d	-	 23 (40)	this work
2b	6 (1.0)	benzene (166)	X=OAc (1.0)	-	2-8 h	-	 (51)	Czernecki[d]
2c	6 (1.0)	benzene (166)	X=OAc (0.3)	$Cu(OAc)_2$ (1.6)	13 h	-	" (30)	Czernecki[d]
3	 4 (1.5)	PyHgOAc (1.0)	X=OAc (1.0)	LiCl (2.0)	2 d	H_2S	 (10)  (8)	Arai[c]
4	 7 (1.2)	PyHgOAc (1.0)	X=OAc (1.0)	$NaHCO_3$ (4.0)	3 d	-	 17 (25)	this work
5	 3 (1.5)	PyHgOAc (1.0)	X=OAc (1.0)	LiCl (2.0)	1 d	H_2S	 (20)  (32)	Arai[c]
6	 8 (1.2)	PyHgOAc (1.0)	X=OAc (1.0)	-	3 d	-	 22 (22) 15 (10)	this work
7	 9 (1.2)	PyHgOAc (1.0)	X=OAc (1.0)	$NaHCO_3$ (4.0)	3 d	-	 19 (20)	this work
8	 10 (1.2)	PyHgOAc (1.0)	X=OAc (1.0)	$NaHCO_3$ (4.0)	3 d	60°C 2 h	 20[e] (22)  21[e] (8)	this work

[a] All the reactions were run in acetonitrile at room temperature except Czernecki's reactions (see entries 1f, 1g, 2b, and 2c, ref 17) which were run at 80–120 °C in excess of aglycon (e.g., benzene, anisole, etc.) in the presence of acetic acid. [b] Isolated yields. [c] See ref 1. [d] See ref 17. [e] Resulted from partial cleavage of the silyl group. [f] d = days.

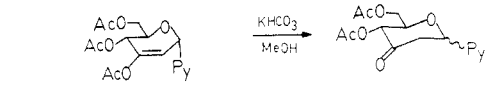
Similar hydrolysis of **15** yielded a single product (**25**), which, based on mass spectrometric and NMR analysis, possesses (a) only one acetoxy group, (b) an α,β-unsaturated carbonyl in the carbohydrate moiety, and (c) a one-hydrogen singlet at δ 5.18 in the ^1H NMR spectrum assignable to a (noncoupled) anomeric hydrogen. On the

Table II. Effect of Salts on the Distribution of C-Nucleoside Products from Coupling of 3,4,6-Tri-*O*-acetyl-D-glycal (2) with (1,3-Dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)-mercuric Acetate in the Presence of Equimolar Palladium(II) Acetate

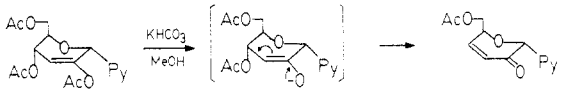
salt added	% total yield[a]	C-nucleoside products ratio[b] 12:13:15
no[c]	77	1:2:2
LiCl (2.0)		1:6:2
Na_2CO_3 (10.0)		5:1:1
$NaHCO_3$ (10.0)		5:1:1
NaOAc (10.0)	62	9:1:3

[a] Isolated yield. [b] Determined by high performance liquid chromatography; see Experimental Section. [c] Entry 1e in Table I.

basis of these results, the position of the carbonyl of **25** is assigned as C-2′ and leads to assignment of structures **15** and **25**.



12 **24**



15 **25**

The origin of **15** is not clear. A plausible mechanism would involve rearrangement of σ-adduct **5** by migration of acetate (C-3′ → C-2′) with concomitant movement of palladium from C-2′ to C-3′.[40]

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 × 20 cm^2, 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. A Varian 5000 liquid chromatograph equipped with an IBM LC/9522 UV detector (254 nm) was used for high pressure liquid chromatographic (HPLC) analyses (Whatman Partisil PXS 5/25 ODS column) and separations (Whatman Partisil M9 10/50 ODS-3 column). Nuclear magnetic resonance spectra were obtained on a JEOL FX 90Q spectrometer and are referenced to tetramethylsilane. High-field (400 MHz) spectra were recorded by Dr. G. A. Gray, Varian Associates, Palo Alto, CA. Mass spectra (EI) were obtained with a Finnegan 4023 GC/MS/DS system operating at 70 eV using a direct insertion probe. High resolution mass spectra were performed by Dr. I. Wachs, Department of Chemistry, Cornell University. Melting points were measured with a Thomas-Hoover capillary apparatus and are uncorrected. Circular dichroism spectra were recorded on a JASCO J500-C spectropolarimeter by Dr. Michael J. Behe. Elemental analyses were carried out by Dr. G. Robinson, Florham Park, NJ.

1,5-Anhydro-2-deoxy-4,6-*O*-(phenylmethylene)-3-*O*-[tris-(1-methylethyl)silyl]-D-*ribo*-hex-1-enitol (10). To a stirred solution of 4,6-*O*-(phenylmethylene)-D-allal[23] (2.6 g, 11.1 mmol) in 3.5 mL of dimethylformamide under nitrogen was added imidazole (1.89 g, 27.8 mmol) in one portion and then triisopropylsilyl chloride (2.93 mL, 97%, 13.3 mmol) dropwise. The resulting solution was stirred at room temperature for 19 h; the oily mixture was then extracted with ether. The precipitate was filtered and

(40) For a recent example of acetoxy migration to Pd-bearing carbon, see: Backvall, J. E.; Heumann, A. *J. Am. Chem. Soc.* **1986**, *108*, 7107–7108.

Table III. ^{1}H Nuclear Magnetic Resonance Spectral Data of Pyranoid C-Nucleosides[a]

	^{1}H NMR chemical shifts (δ)										proton–proton coupling constants, J (Hz)											
cmpd	H_6	$H_{1'}$	$H_{2'}$	$H_{3'}$	$H_{4'}$	$H_{5'}$	$H_{6'}$	$H_{6''}$	NMe	OAc	1′,6	1′,2′	1′,3′	1′,4′	2′,3′	2′,4′	3′,4′	4′,5′	5′,6′	5′,6″	6′,6″
12[b]	7.48	5.52	5.82		5.36	4.15	4.36	4.19	3.35,	2.08, 2.09,	0.8	2.8		1.7		0.5		4.3	6.6	4.4	11.5
	d	m	d		m	ddd	dd	dd	3.44	2.13											
13[b,c]	7.26	5.33	6.09	5.93	5.15	3.95	4.26	4.14	3.34,	2.06, 2.08	0.6	1.3	2.2		10.4	2.6	3.2	6.5	6.7	3.9	11.9
	d	m	ddd	ddd	ddd	ddd	dd	dd	3.41												
15[b,c]	7.35	5.37		5.75	5.33	3.93	4.28	4.15	3.33,	2.03, 2.06,	0.0		1.2	1.7			3.9	5.9	6.4	3.7	12.2
	s	m		ddd	ddd	ddd	dd	dd	3.40	2.07											
17[d]	7.44	5.63	5.43		4.48	3.78	4.25	3.85	3.38,	2.20	0.5	3.2		2.2		2.1		8.8	10.0	4.5	10.0
	d	m	dd		ddd	ddd	dd	dd	3.43												
19[d]	7.24	5.41	6.06	5.88	4.40	3.80	4.40	3.83	3.42,		0.9	0.0	1.4	0.0	10.3	1.0	3.0	*e*	*e*	*e*	*e*
	d	d	ddd	ddd	m	m	m	m	3.36												
20[d]	7.24	5.49	4.95		4.21	3.82	4.34	3.82	3.36,		0.7	2.0		3.4		2.0		6.5?	*e*	*e*	*e*
	d	m	dd		m	m	m	m	3.40												
22[b]	7.21	5.28–	5.99	5.76	5.28–	3.88	5.41–5.43		3.33,	2.08, 2.08	0.7	0.0	0.0		10.4	0.0	0.0	9.1	4.3	4.3	*e*
	d	5.30 (m)	d	d	5.30 (m)	ddd	m		3.40												
23	7.39	5.66	5.82		5.37		4.09–4.25		3.37,	2.02, 2.14,	0.5	3.9		0.0		0.0		2.0	*e*	*e*	*e*
	d	d	d		d		m		3.45	2.18											
25[f]	7.26	5.18		6.35	7.01	4.74	4.59	4.15	3.33,	2.10	0.0						10.6	2.9	6.6	3.2	11.5
	s	s		dd	dd	m	dd	dd	3.41												

[a] Chemical shifts in ppm, spectra were recorded in $CDCl_3$. Resonances for which no multiplicities are indicated are singlets; where multiplicities are noted the notation reflects the apparent multiplicities. d, doublet; dd, doublet of doublets; ddd, doublet of doublets of doublets; m, multiplet. [b] Spectra were recorded with a 400-MHz NMR spectrometer. [c] See also ref 1, in which compound **15** was originally assigned as **12**. [d] Chemical shifts for phenylmethylene. **17**: δ 7.27–7.58 (C_6H_5, m), 5.58 (PhCH, s). **19**: δ 7.28–7.54 (C_6H_5, m), 5.63 (PhCH, s). **20**: δ 7.25–7.55 (C_6H_5, m), 5.59 (PhCH, s). [e] Coupling constants were unresolved. [f] $J_{3',5'}$ = 1.7 Hz.

Table IV. ^{13}C NMR Chemical Shifts δ (ppm) of Pyranoid C-Nucleosides[a]

cmpd	N_1CH_3	C_2	N_3CH_3	C_4	C_5	C_6	$C_{2'}$	$C_{3'}$	$C_{6'}$	C_1,C_4,C_5[b]			other
12	37.34	151.47	27.93	162.09	110.47	142.00	119.03	142.46	61.83	72.36	66.17	64.80	OAc, 170.59, 170.14, 168.89, 20.71, 20.64
13	37.25	151.53	27.99	162.28	110.84	140.97	130.59	124.71	62.68	70.35	68.99	65.01	OAc, 170.71, 170.26, 21.07, 20.80
15	37.29	151.40	28.05	162.45	108.37	142.79	113.59	148.48	62.13	69.76	66.63	65.71	OAc, 170.65, 170.08, 168.20, 20.99, 20.84, 20.69
17	37.37	151.49	28.05	162.51	113.51	142.66	110.29	146.10	69.14	73.53	67.76	65.00	C_6H_5, 137.02, 128.98, 128.25, 125.95; PhCH, 101.60; OAc, 168.55, 20.47
19	73.13	151.44	27.89	162.05	112.08	140.52	129.01	126.98	69.25	74.94	71.53	71.53	C_6H_5, 137.30, 129.12, 128.28, 126.16; PhCH, 102.03
20	37.02	151.44	27.86	162.05	113.25	140.76	104.74	148.40	68.98	75.54	71.58	70.28	C_6H_5, 137.30, 128.79, 127.92, 126.14; PhCH, 101.92; $SiCH(CH_3)_2$, 17.79, 12.43
22	37.06	151.29	27.72	161.91	111.90	140.55	130.90	124.89	63.34	74.88	70.14	64.92	OAc, 170.59, 170.11, 20.80, 20.68
23	37.40	151.41	27.93	162.16	108.53	142.40	119.00	144.34	61.58	68.17	67.65	63.59	OAc, 170.35, 170.23, 169.78, 20.58
25	37.13	151.37	27.94	162.21	109.94	143.83	192.72	128.23	62.87	145.91[c]	74.49	71.11	OAc, 170.61, 20.83

[a] Spectra were recorded in $CDCl_3$. [b] Peaks were not assigned unless otherwise noted. [c] C_4.

the filtrate was concentrated in vacuo to give an oil. Two sequential flash chromatographic separations of this oil first with 1:9 ether–petroleum ether and then with hexanes for elution yielded 4.07 g (94%) of **10** as a colorless oil: ^1H NMR ($CDCl_3$) δ 7.55–7.27 (m, C_6H_5), 6.32 (d, H_1), 5.57 (s, PhCH), 4.93 (dd, H_2), 4.44 (dd, H_{6e}), 4.37 (dd, H_3), 4.31 (ddd, H_5), 3.77 (dd, H_{6a}; dd, H_4), 1.05 (s, $SiCH(CH_3)_2$), $J_{1,2}$ = 5.9 Hz, $J_{2,3}$ = 5.9 Hz, $J_{3,4}$ = 3.4 Hz, $J_{4,5}$ = 9.9 Hz, $J_{5,6e}$ = 5.0 Hz, $J_{5,6a}$ = 8.9 Hz, $J_{6e,6a}$ = 8.9 Hz; mass spectrum, m/z (relative intensity) 389 (0.9, M – H^+), 247 (11, M – $CH(CH_3)_2$). Anal. Calcd for $C_{22}H_{34}O_4Si$: C, 67.7; H, 8.8. Found: C, 67.5; H, 8.8.

1,3-Dimethyl-5-(3,4,6-tri-*O*-acetyl-2-deoxy-α-D-*erythro*-hex-2-enopyranosyl)-2,4(1*H*,3*H*)-pyrimidinedione (12), 5-(4,6-Di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl)-1,3-dimethyl-2,4(1*H*,3*H*)-pyrimidinedione (13), and 1,3-Dimethyl-5-(2,4,6-tri-*O*-acetyl-3-deoxy-α-D-*erythro*-hex-2-enopyranosyl)-2,4(1*H*,3*H*)-pyrimidinedione (15). A solution of palladium acetate (824 mg, 3.66 mmol) in 120 mL of acetonitrile was stirred at room temperature for 23 h. To this orange solution was added (1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)mercuric acetate[11] (**1**) (1.46 g, 3.66 mmol), and the mixture was stirred for 5 min before the addition of 3,4,6-tri-*O*-acetyl-D-glucal[12] (**2**) (2.00 g, 7.32 mmol). The slowly darkening solution was then stirred for 3 days at room temperature. The black mixture was filtered through Celite and the filtrate was concentrated in vacuo. The resulting residue was then partitioned between dichloromethane and water. The aqueous layer was extracted twice with dichloromethane and the combined organic extract was dried over magnesium sulfate and 4 g of silica gel. The drying agents were removed, the solvent was evaporated, and the residue was separated by flash chromatography using chloroform and acetonitrile (4:1) as eluant to give 969 mg of a mixture of **12**, **13**, and **15** and 377 mg of an oil that was less pure. The latter oil was rechromatographed (same eluant) to give 107 mg of mixed **12**, **13**, and **15**. HPLC analysis of the combined product (1.08 g) exhibited the product ratio **12**:**13**:**15** = 1:2:2. The yields were then calculated: **13**, 393 mg, 31%; **15**, 458 mg, 31%; and **12**, 228 mg, 15%. A small sample of **15** was isolated from the above mixture by using preparative TLC: two bands were barely separated after the plate was developed six times with ether. Elution of the top band gave pure **15**[1,33] as an oil; the lower band contained **12**, **13**, and a trace of **15**. Pure **12**[1,7,33] and **13**[1,7] were obtained by HPLC separation with either the analytical column (3:2 water–methanol, flow rate 0.8 mL/min, t_R (min): **13**[1] 10.9, **15**[1,33] 13.2, **12** 13.8) or the semipreparative column (3:2, water–methanol, flow rate 2 mL/min). For **12**:[1,7,33] mass spectrum, m/z (relative intensity) 411 (0.03, M + H^+), 368 (0.04, $M^{\bullet+}$ – ketene), 350 (0.13, $M^{\bullet+}$ – AcOH).

Formation of 12, 13, and 15 in the Presence of Sodium Acetate, Sodium Carbonate, or Sodium Bicarbonate. A procedure similar to the one described above was used: to a solution of palladium acetate (412 mg, 1.83 mmol) and **1**[11] (730 mg, 1.83 mmol) in 60 mL of acetonitrile was added **2**[12] (1.00 g, 3.66 mmol) and sodium acetate (1.5 g, 18.3 mmol). The mixture was then stirred for 3 days at room temperature. The crude product was isolated as described and chromatographed over silica gel eluted with 4:1 chloroform–acetonitrile to afford 459 mg of oil; HPLC analysis (1:3 methanol–water, flow rate 1 mL/min): **13**:**15**:**12** = 1:3:9 (**13**, 31 mg, 5%; **15**, 107 mg, 14%; **12**, 321 mg, 43%).

When sodium carbonate (10 equiv) or sodium bicarbonate (10 equiv) was used instead of sodium acetate, the ratio of **13**:**15**:**12** was 1:1:5 (Table II).

Effect of Sodium Acetate-d_3 on the Formation of 12. When sodium acetate-d_3 (1.5 g, 17.6 mmol) was used, 311 mg of oil containing **13**, **15**, and **12** (1:3:9) was obtained by flash chromatography. HPLC separation using the semipreparative column (2:3 methanol–water) gave 100 mg of **12**.[1,7,33] ^1H NMR analysis showed no acetate-d_3 incorporation, i.e., three singlet acetyl peaks were observed with no decrease of the intensity on any of these peaks.

1,3-Dimethyl-5-(3,4,6-tri-*O*-acetyl-2-deoxy-α-D-*threo*-hex-2-enopyranosyl)-2,4(1*H*,3*H*)-pyrimidinedione (23). A mixture of 3,4,6-tri-*O*-acetyl-D-galactal[20] (**6**) (150 mg, 0.55 mmol), **1**[11] (183 mg, 0.46 mmol), and palladium acetate (103 mg, 0.46 mmol) in 15 mL of acetonitrile was stirred for 20 min; then sodium bi-

carbonate (154 mg, 1.84 mmol) was added and stirring was continued for 39 h. The mixture was then filtered through Celite and the filtrate was concentrated in vacuo. The oily residue was purified by preparative TLC (4:1 chloroform–acetonitrile) to afford 76 mg of pure **23** (40%) as an oil: mass spectrum, m/z (relative intensity) 411 (15, M + H^+), 368 (19, $M^{\bullet+}$ – ketene), 248 (21, $M^{\bullet+}$ – 2AcOH – ketene).

1,3-Dimethyl-5-[3-*O*-acetyl-2-deoxy-4,6-*O*-(phenylmethylene)-α-D-*erythro*-hex-2-enopyranosyl]-2,4(1*H*,3*H*)-pyrimidinedione (17). To a stirred solution of palladium acetate (44 mg, 0.20 mmol) and **1**[11] (78 mg, 0.20 mmol) in 7 mL of acetonitrile was added 3-*O*-acetyl-4,6-*O*-(phenylmethylene)-D-glucal[21] (**7**) (65 mg, 0.24 mmol). After 20 min, the slowly darkening solution was treated with sodium bicarbonate (66 mg, 0.78 mmol), and the mixture was stirred for 3 days at room temperature. The reaction mixture was filtered through Celite and the solvent was evaporated to give a crude oil, which was purified by preparative TLC using four developments with 20:1 chloroform–acetonitrile to yield 20 mg (25%) of **17** (R_f 0.16) as an oil: mass spectrum, m/z (relative intensity) 415 (12, M + H^+), 372 (5, $M^{\bullet+}$ – ketene); ^1H and ^{13}C NMR data are in Tables III and IV, respectively.

5-(4,6-Di-*O*-acetyl-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranosyl)-1,3-dimethyl-2,4(1*H*,3*H*)-pyrimidinedione (22) and 1,3-Dimethyl-5-(2,4,6-tri-*O*-acetyl-3-deoxy-α-D-*erythro*-hex-2-enopyranosyl)-2,4(1*H*,3*H*)-pyrimidinedione (15). To a stirred solution of palladium acetate (344 mg, 1.52 mmol) and **1**[11] (608 mg, 1.52 mmol) in 40 mL of acetonitrile at room temperature was added 3,4,6-tri-*O*-acetyl-D-allal[22] (**8**) (500 mg, 1.83 mmol) and the resulting mixture was stirred for 3 days. The reaction mixture was filtered through Celite and the solvent was removed to give a crude oil, which was purified by preparative TLC using 4:1 chloroform–acetonitrile for elution to afford 121 mg (22%) of **22** (Rf 0.57) and 65 mg (10%) of **15**[1,7,33] (R_f 0.47) as oil. Analytical samples were prepared by HPLC (analytical column), yielding 61 mg of **22** (t_R 18.5 min) as a solid and 22 mg of **15**[1,7,33] (t_R 13.3 min) as an oil. For **22**: mass spectrum, m/z (relative intensity) 353 (5, M + H^+), 292 (7, $M^{\bullet+}$ – AcOH), 232 (16, $M^{\bullet+}$ – 2AcOH). Anal. Calcd for $C_{16}H_{20}O_7N_2$: C, 54.5; H, 5.72; N, 7.95. Found: C, 54.2; H, 5.42; N, 7.96.

Formation of 15 and 22 in the Presence of Sodium Acetate or Sodium Carbonate. A similar procedure to that described above was followed except that sodium acetate (10 equiv) or sodium carbonate (10 equiv) was used instead of sodium bicarbonate. The product ratio was 1:4 (**15**:**22**) in each reaction based on HPLC analysis.

22 from Hydrogenation of 13. A mixture of **13** and **12** (4:1, 274 mg) and 10% palladium on carbon (75 mg) in 100 mL of ethyl acetate was shaken under 2 atm of hydrogen for 2 days. The catalyst was removed and the filtrate was concentrated in vacuo. The resulting oily residue was separated by preparative TLC using 4:1 chloroform–acetonitrile for development to give three bands: top band, **22** (45 mg, 22%); middle band, unreacted **13** (20 mg, 10%); and lower band, a mixture of uncharacterized products. No **12** was recovered from the reaction mixture. The TLC, HPLC, and ^1H NMR properties of **22** obtained from this reaction were identical with those of **22** produced in the coupling reaction of 3,4,6-tri-*O*-acetyl-D-allal[22] (**8**) with **1**.[11]

5-[2,3-Dideoxy-4,6-*O*-(phenylmethylene)-β-D-*erythro*-hex-2-enopyranosyl]-1,3-dimethyl-2,4(1*H*,3*H*)-pyrimidinedione (19). To a stirred solution of palladium acetate (225 mg, 1.00 mmol) and **1**[11] (399 mg, 1.00 mmol) in 15 mL of acetonitrile was added 3-*O*-acetyl-4,6-*O*-(phenylmethylene)-D-allal[23] (**9**) (331 mg, 1.20 mmol). After 10 min, sodium bicarbonate (336 mg, 4.00 mmol) was added to the slowly darkening solution and stirring was continued for 3 days at room temperature. The reaction mixture was filtered through Celite and the solvent was evaporated to give a crude oil, which was purified by two consecutive preparative TLC steps using chloroform–acetonitrile (4:1) for development of the first plate and chloroform–acetonitrile (9:1) for the second plate (developed twice) to afford 70 mg (20%) of **19** as an oil. An analytical sample was obtained by crystallization of this oil with chloroform–petroleum ether, yielding 25 mg of fine needles: mp 190 °C dec; mass spectrum, m/z (relative intensity) 356 (1.3, $M^{\bullet+}$); HRMS, calcd for $C_{19}H_{20}N_2O_5$ 356.1352, found 356.1372.

1,3-Dimethyl-5-[2-deoxy-4,6-*O*-(phenylmethylene)-3-*O*-[tris(1-methylethyl)silyl]-β-D-*erythro*-hex-2-enopyranosyl]-2,4(1*H*,3*H*)-pyriminedione (20) and 1,3-Dimethyl-5-[2-deoxy-4,6-*O*-(phenylmethylene)-β-D-*erythro*-hexopyranos-3′-ulos-1′-yl]-2,4(1*H*,3*H*)-pyrimidinedione (21). A mixture of **10** (469 mg, 1.20 mmol), palladium acetate (225 mg, 1.00 mmol), **1**[11] (399 mg, 1.00 mmol), and sodium bicarbonate (336 mg, 4.0 mmol) in 15 mL of acetonitrile was stirred at room temperature for 3 days. The reaction mixture was then heated for 2 h at 60 °C and after cooling was filtered through Celite. The filtrate was concentrated in vacuo and the oily residue was separated by flash chromatography using 9:1 dichloromethane–ethyl acetate for elution to yield two products: 173 mg (33%) of **20** and 29 mg (8%) of **21** as oils. For **20**: mass spectrum, m/z (relative intensity) 528 (0.03, $M^{\bullet+}$), 485 (0.03, M – $CHMe_2$), 389 (0.03, M – pyrimidine), 379 (0.17, M – CH(Ph)OCH_2C=O).

5-(4,6-Di-*O*-acetyl-2-deoxy-α-D-*erythro*-hexopyranos-3-ulos-1-yl)-1,3-dimethyl-2,4(1*H*,3*H*)-pyrimidinedione (24a) and 5-(4,6-Di-*O*-acetyl-2-deoxy-β-D-*erythro*-hexopyranos-3-ulos-1-yl)-1,3-dimethyl-2,4(1*H*,3*H*)-pyrimidinedione (24b). A mixture of **12**[1,7,33] (34 mg, 0.08 mmol) and potassium bicarbonate (8 mg, 0.08 mmol) in 3.5 mL of methanol was stirred for 5.5 h at room temperature. TLC (4:1 chloroform–acetonitrile) indicated that no starting material (**12**) (R_f 0.49) remained and that three new materials were formed (R_f 0.33, 0.24, 0.02). The mixture was partitioned between dichloromethane and water, the aqueous layer was washed twice with dichloromethane, and the combined organic portion was dried (magnesium sulfate). After filtration and concentration, the oily residue was separated by preparative TLC (the plate was developed four times with 4:1 chloroform–acetonitrile) to give three bands. The top band yielded a mixture of unstable products that decomposed upon storage. The middle band gave 5 mg (17%) of **24** as an anomeric mixture (2:1, α:β) on the basis of ^1H NMR analysis. The lower band gave a mixture of overdeprotected products. No further attempt was made to separate the anomers of **24**. ^1H NMR ($CDCl_3$) of the middle band: **24α** δ 7.22 (d, H_6), 5.37 (ddd, $H_{1'}$) ($J_{1',6}$ = 0.7 Hz, $J_{1',2'}$ = 3.6 Hz, $J_{1',2'}$ = 7.2 Hz), **24β** δ 7.41 (d, H_6), 5.16 (ddd, $H_{1'}$) ($J_{1',6}$ = 0.7, $J_{1',2'}$ = 2.9 Hz, $J_{1',2'}$ = 10.7 Hz), 3.45, 3.43, 3.35, 3.34 (4s, NMes), 2.11, 2.08, 2.03, 2.02 (4s, AcO's). The remaining peaks were unresolved. Mass spectrum (mixture of α and β): m/z (relative intensity) 368 (0.3, $M^{\bullet+}$), 308 (1.8, $M^{\bullet+}$ – AcOH).

5-(6-*O*-Acetyl-3,4-dideoxy-α-D-hex-3-enopyranos-2-ulos-1-yl)-1,3-dimethyl-2,4(1*H*,3*H*)-pyrimidinedione (25). A mixture of **15**[1,7,33] (50 mg, 0.12 mmol) and potassium bicarbonate (12 mg, 0.12 mmol) in 5 mL of methanol was stirred for 3 h at 0 °C and then for 5.5 h at room temperature. TLC (4:1 chloroform–acetonitrile) indicated that further deprotection had begun to occur while the conversion from **15** (R_f 0.45) to **25** (R_f 0.38) was still incomplete. The mixture was concentrated immediately in vacuo and the oily residue was partitioned between dichloromethane and water. The aqueous layer was washed twice with dichloromethane and the combined organic portion was dried over magnesium sulfate. After filtration and concentration, the oil was separated by preparative TLC using 4:1 chloroform–acetonitrile for development (twice) to give three separated bands: top band, 12 mg (24%) of unreacted **15**, middle band, 15 mg (40%) of **25**. A mixture of several byproducts was obtained from the lower band. For **25**: mass spectrum, m/z (relative intensity) 308 (0.2, $M^{\bullet+}$), 248 (1.6, $M^{\bullet+}$ – AcOH), 235 (3.3, $M^{\bullet+}$ – $AcOCH_2$).

Acknowledgment. Support for this study from the American Cancer Society is greatly appreciated.