Enantio- and Diastereoisomers of 2,4-Dimethoxy-5-(2,3-dideoxy-5-*O*-tritylribofuranosyl)pyrimidine. 2′,3′-Dideoxy Pyrimidine C-Nucleosides by Palladium-Mediated Glycal–Aglycon Coupling

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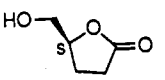
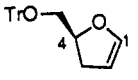
Newly available enantiomeric 2,3-dideoxy glycals, (5*S*)- and (5*R*)-4,5-dihydro-5-[(triphenylmethoxy)-methyl]furans and 2,4-dimethoxy-5-iodopyrimidine undergo palladium-mediated coupling by two different, complementary procedures to form enantiomeric pairs of (2′,3′-dideoxy-2′,3′-didehydrofuranosyl)- and (2′,3′-dideoxy-3′,4′-didehydrofuranosyl)pyrimidine C-nucleosides. Stereoselective reductions of the carbohydrate unsaturations produce all four enantio- and diastereoisomers of 2,4-dimethoxy-5-(2,3-dideoxy-5-*O*-tritylribofuranosyl)pyrimidine. The facile two-step syntheses of 2′,3′-deoxy C-nucleosides which involves preparation of a D-series C-nucleoside from an L-series glycal (and vice versa) represents a new strategy for C-nucleoside synthesis.

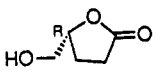
The (*S*)- and (*R*)-γ-(hydroxymethyl)-γ-butyrolactones (**1a** and **1b**), derived from L-and D-glutamic acids, respectively, in two steps,[1] have been used widely as chiral synthons[2] (chirons[3]). Chiral lactones **1a** and **1b** have been readily converted into the corresponding 2,3-dideoxyfuranoid glycal enantiomers **2a** and **2b**,[4] new chiral synthons of impressive synthetic utility. In the present report, we demonstrate the use of these glycal enantiomers for stereoselective preparation of 2′,3′-dideoxy C-nucleosides,[5] potential human immunodeficiency virus reverse transcriptase inhibitors.[6]



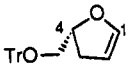
1a



2a, D

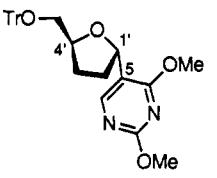


1b

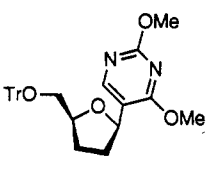


2b, L

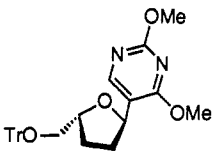
By an efficient two-step procedure involving transfer of chirality from the C-4 stereocenter[7] of glycal **2a** or **2b** to a newly formed C-glycosyl bond at C-1 each of the four enantio- and diastereoisomers, α-D (**3a**), β-D (**4a**), α-L (**3b**), and β-L (**4b**), of 2,4-dimethoxy-5-(2,3-dideoxy-5-*O*-tritylribofuranosyl)pyrimidine[7] was prepared. This new procedure, developed in connection with our interest in palladium-mediated glycal–aglycon coupling reactions[8] for C-glycosyl bond formation,[9] involves a synthetic strategy not previously used for C-glycoside synthesis.[10]



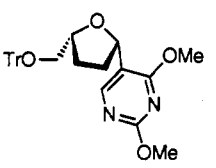
3a, α-D



4a, β-D



3b, α-L



4b, β-L

The strategy for synthesis of the four enantio- and diastereoisomers **3a**, **3b**, **4a**, and **4b** from 2,3-dideoxyfuranoid glycal enantiomers **2a** and **2b**[4] takes advantage of two key mechanistic features[8,9] of the palladium-mediated coupling reaction between a glycal (e.g., **2a** or **2b**) and an appropriate aglycon derivative (in the present case, iodopyrimidine **5**). First, in the palladium-mediated coupling reaction, the glycal stereocenter at C-4[7] directs aglycon–palladium reagent attack on the glycal double bond from the less hindered face of the glycal so that, in the intermediate σ-organopalladium adduct, the new C-glycosyl bond at C-1 forms stereospecifically trans to the C-4 substituent.[8,9] Second, depending on the reaction conditions selected for coupling, subsequent σ-organopalladium adduct decomposition and β-palladium hydride elimination occurs either with retention of the original

(1) Ravid, U.; Silverstein, R. M.; Smith, L. R. *Tetrahedron* **1978**, *34*, 1449–1452.

(2) Coppola, G. M.; Schuster, H. F. *Asymmetric Synthesis Construction of Chiral Molecules Using Amino Acids*; John Wiley & Sons: New York, 1987; pp 216–256.

(3) Hanessian, S. *Total Synthesis of Natural Products: The "Chiron" Approach*; Pergamon Press: New York, 1983.

(4) The 5-*O*-*tert*-butyldimethylsilyl analog of L-glycal enantiomer **2b** has been reported. Takle, A.; Kocienski, P. *Tetrahedron* **1990**, *46*, 4503–4516.

(5) (a) Zhang, H.-C.; Daves, G. D., Jr. *J. Org. Chem.* **1992**, *57*, 4690–4696. (b) Chu, C. K.; Schinazi, R. F.; Ahn, M. K.; Ullas, G. V.; Gu, Z. P. *J. Med. Chem.* **1989**, *32*, 612–617. (c) Sochacka, E.; Nawrot, B.; Pankiewicz, K. W.; Watanabe, K. A. *J. Med. Chem.* **1990**, *33*, 1995–1999. (d) Doboszewski, B.; Chu, C. K.; Van Halbeek, H. *J. Org. Chem.* **1988**, *53*, 2777–2782. (e) Chu, C. K.; Schinazi, R. F.; Arnold, B. H.; Cannon, D. L.; Doboszewski, B.; Bhadti, V. B.; Gu, Z. *Biochem. Pharmacol.* **1988**, *37*, 3543–3548. (f) Serafinowski, P. *Synthesis* **1990**, 411–415.

(6) Mitsuya, H.; Yarchoan, R.; Broder, S. *Science* **1990**, *249*, 1533–1543.

(7) In the Discussion, we use carbohydrate notation for convenience; Chemical Abstracts names are used in the Experimental Section.

(8) Daves, G. D., Jr. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press: Greenwich, CT, 1991; Vol. 2, pp 59–99. Daves, G. D., Jr.; Hallberg, A. *Chem. Rev.* **1989**, *89*, 1433–1445.

(9) Daves, G. D., Jr. *Acc. Chem. Res.* **1990**, *23*, 201–206. Daves, G. D., Jr. In *Carbohydrates–Synthetic Methods and Applications in Medicinal Chemistry*; Suami, T., Hasegawa, A., Ogura, H., Eds.; Kodansha Ltd.: Tokyo, 1992; pp 52–68.

(10) Reviews: Hacksell, U.; Daves, G. D., Jr. *Prog. Med. Chem.* **1985**, *22*, 1–65. Buchanan, J. G. *Prog. Chem. Org. Nat. Prod.* **1983**, *44*, 243–299.

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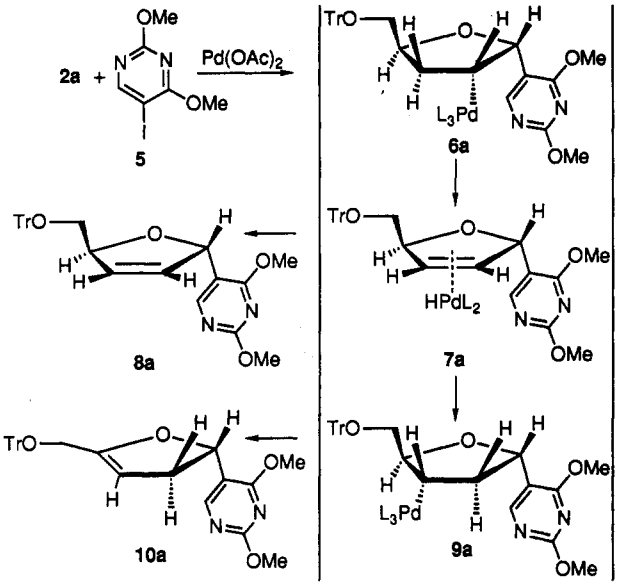
Scheme I. Palladium-Mediated Coupling of Glycal 2a with 2,4-Dimethoxy-5-iodopyrimidine (5)

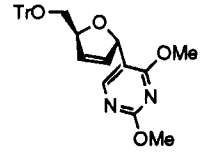
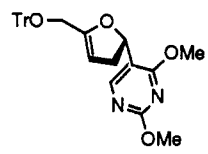
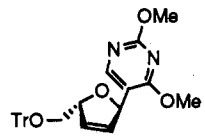
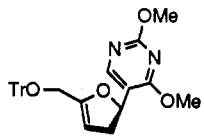


asymmetric center at C-4 forming a 2′,3′-unsaturated C-glycoside or, by palladium migration,[11] with loss of chirality at C-4 by formation of a 3′,4′-unsaturation. The option to direct the mode of σ-organopalladium adduct decomposition by permitting or suppressing palladium migration,[11d,12] not available with glycals possessing an oxygen substituent at C-3,[8,9] permits the original configuration at C-4 to be either retained or inverted after its use to set the stereochemistry of the C-glycosyl bond formation at C-1. In instances where the C-4 stereocenter is inverted, a D-series C-glycoside is prepared from an L-series glycal and vice versa.

Stereospecific C-Glycosyl Bond Formation. 2,3-Dideoxyfuranoid glycal enantiomers **2a** and **2b** were prepared from the corresponding lactones[13] in 60% isolated yields by a procedure described previously[4] and coupled with 2,4-dimethoxy-5-iodopyrimidine[14] (**5**) in the presence of catalytic palladium acetate to form mixtures of carbohydrate-unsaturated C-glycosides (**2a** → **8a** and **10a**, Scheme I). The overall reaction process involves formation of an organopalladium reagent by oxidative addition of palladium(0) into the carbon–iodo bond of aglycon derivative **5** and π-complex formation by interaction of this reagent with the glycal double bond followed by π-complex collapse to σ-adduct **6a**.[8,9,15] σ-Adduct formation is stereospecific with the new carbon–carbon bond trans to the glycal ring substituent at C-4 as expected based on prior studies[8,9,15] and shown by the presence of a single 2′,3′-unsaturated C-glycoside (**8a**) in the reaction mixture.

Selectivity of Organopalladium Adduct Decomposition. The palladium-mediated coupling reaction

Table I. Palladium-Mediated Coupling Reactions of 2,4-Dimethoxy-5-iodopyrimidine (5) with Glycal Enantiomers 2a and 2b

glycal	procedure[a]	products (% yield)	
2a	A	 **8a** (53)	 **10a** (30)
2a	B	**8a** (20)	**10a** (58)
2a	C	**8a** (40)	**10a** (0)
2b	A	 **8b** (56)	 **10b** (31)
2b	B	**8b** (18)	**10b** (59)

[a] Procedure A: $Pd(OAc)_2$ (0.1 equiv), NaOAc (1.0 equiv), n-Bu_4NCl (0.5 equiv), Et_3N (2.0 equiv), dimethylformamide, rt, 20 h. Procedure B: $Pd(OAc)_2$ (0.1 equiv), $AsPh_3$ (0.2 equiv), Et_3N (2.0 equiv), CH_3CN, 75 °C, 10 h. Procedure C: $Pd(OAc)_2$ (0.1 equiv), PPh_3 (0.2 equiv), Et_3N (2.0 equiv), Ag_2CO_3 (2.0 equiv), CH_3CN, 75 °C, 10 h.

Table II. Hydrogenation of Carbohydrate-Unsaturated C-Nucleosides with Palladium and Ammonium Formate in Ethanol

unsaturated C-nucleoside	products (% yield)	
8a	**3a** (94)	
10a	**3a** (8)	**4b** (87)
8b	**3b** (90)	
10b	**3b** (7)	**4a** (85)

yields two products because intermediate π-complex **7a** formed by syn β-hydridopalladium elimination from σ-organopalladium adduct **6a** proceeds in two ways. Not only can **7a** dissociate to 2′,3′-unsaturated C-glycoside **8a** but also PdH can readd to the double bond to form a new σ-adduct **9a** and thereby effect double-bond migration[11] to form the thermodynamically more stable 3′,4′-unsaturated C-glycoside **10a** which possesses a newly formed asymmetric center at C-1′ but has lost the original asymmetric center at C-4′.

Table I summarizes the results of coupling reactions of enantiomeric glycals **2a** and **2b** with iodopyrimidine **5** carried out under different conditions. Modest selectivity for formation of either a 2′,3′-unsaturated C-glycoside (**8a** or **8b**) or a 3′,4′-unsaturated C-glycoside (**10a** or **10b**) was achieved. As expected,[11c] carrying out the palladium-mediated coupling reaction in the presence of tetra-*n*-butylammonium chloride and the absence of triphenylphosphine[16] (procedure A, Table I) facilitates dissociation of π-complex **7a** and favors formation of 2′,3′-unsaturated C-nucleoside **8a**, albeit only modestly. When tetra-*n*-butylammonium chloride was omitted from the reaction mixture and supporting triphenylarsine[5a,17] (or triphenylphosphine, data not shown) ligands for palladium were provided (procedure B), π-complexation was stabilized, and carbohydrate double-bond migration was fa-

(11) (a) Heck, R. F. *J. Am. Chem. Soc.* **1971**, *93*, 6896–6901. (b) Arai, I.; Daves, G. D., Jr. *J. Org. Chem.* **1978**, *43*, 4110–4112. (c) Lee, T. D.; Daves, G. D., Jr. *J. Org. Chem.* **1983**, *48*, 399–402. (d) Larock, R. C.; Gong, W. H.; Baker, B. E. *Tetrahedron Lett.* **1989**, *30*, 2603–2606. (e) Abelman, M. M.; Oh, T.; Overman, L. E. *J. Org. Chem.* **1987**, *52*, 4130–4133.

(12) Synthesis of trans-2,5-arylated tetrahydrofurans by palladium-mediated arylation of 2,3-dihydrofuran with double-bond migration followed by a second palladium-mediated olefin arylation has been reported (Larock, R. C.; Gong, W. H. *J. Org. Chem.* **1990**, *55*, 407–408).

(13) Takano, S.; Yonaga, M.; Ogasawara, K. *Synthesis* **1981**, 265–266.

(14) Prystas, M.; Sorm, F. *Collect. Czech. Chem. Commun.* **1964**, *29*, 121–130.

(15) Daves, G. D., Jr.; Hallberg, A. *Chem. Rev.* **1989**, *89*, 1433–1445.

(16) Tolman, C. A.; Seidel, W. C.; Gerlach, D. H. *J. Am. Chem. Soc.* **1972**, *94*, 2669–2676.

(17) Farina, V.; Krishnan, B. *J. Am. Chem. Soc.* **1991**, *113*, 9585–9595.

Table III. Optical Rotation, Combustion Analysis, and Mass and ^{1}H Nuclear Magnetic Resonance Spectrometric Data for Glycals and C-Nucleosides

compd	$[\alpha]^{24}_D$	MS, *m/z* (MH^+)	anal. (HRMS) calcd	anal. (HRMS) found	^{1}H NMR spectra $H_{1'}$	$H_{2'}$	$H_{3'}$	$H_{4'}$	$H_{5'}$	H_6	OMe	CPh_3
2a	+66.0° (*c* = 1.5, $CHCl_3$)	343										
2b	−66.7° (*c* = 1.5, $CHCl_3$)	343	C, 84.18 H, 6.48	C, 83.85 H, 6.34	6.33 (q)	4.86 (q)	2.34 (et) 2.64 (dt)	4.73 (m)	3.10 (dd) 3.26 (dd)			7.22–7.51(m)
3a	−43.5° (*c* = 0.85, dioxane)	483										
3b	+44.7° (*c* = 0.85, dioxane)	483	(483.2284)	(483.2263)	5.10 (t)	1.65–2.45 (m)	1.65–2.45 (m)	4.41 (m)	3.13 (dd) 3.21 (dd)	8.29 (s)	3.99 (s)	7.22–7.51(m)
4a	+10.8° (*c* = 1.0, dioxane)	483	(483.2284)	(483.2305)	5.00 (t)	1.62–2.40 (m)	1.62–2.40 (m)	4.24 (m)	3.16 (dd) 3.33 (dd)	8.32 (s)	3.95 (s) 3.97 (s)	7.22–7.51(m)
4b	−9.9° (*c* = 1.0, dioxane)	483										
8a	−209.2° (*c* = 1.2, $CHCl_3$)	481										
8b	+211.7° (*c* = 1.2, $CHCl_3$)	481	C, 74.98 H, 5.87 N, 5.83	C, 74.83 H, 5.78 N, 5.76	5.09–6.01 (m)	5.09–6.01 (m)	5.09–6.01 (m)	5.15 (q)	3.20 (dd) 3.27 (dd)	8.22 (s)	3.98 (s) 4.01 (s)	7.22–7.51(m)
10a	−54.2° (*c* = 1.2, $CHCl_3$)	481										
10b	+52.5° (*c* = 1.2, $CHCl_2$)	481	C, 74.98 H, 5.87 N, 5.83	C, 74.74 H, 5.80 N, 5.79	5.65 (dd)	2.49 (dddd) 3.13 (dddd)	5.0 (m)		3.68 (s)	8.30 (s)	3.99 (s) 4.00 (s)	7.23–7.52(m)

Table IV. ^{13}C Nuclear Magnetic Resonance Data ($CDCl_3$) for Glycals and C-Nucleosides

compd	$C_{1'}$	$C_{2'}$	$C_{3'}$	$C_{4'}$	$C_{5'}$	C_2	C_4	C_5	C_6	OCH_3	CPh_3	Ph
2b	145.14	99.08	31.73	80.07	66.17							
3b	74.52	32.59[a]	28.62[a]	78.56	66.43	164.61	168.20	116.67	155.06	53.86 54.69	86.51	126.91, 127.75 128.75, 144.10
4b	74.53	32.06[a]	28.19[a]	78.64	66.07	164.44	167.89	116.37	155.10	53.68 54.56	86.39	126.82, 127.64 128.61, 143.90
8b	80.80	129.21[a]	128.79[a]	85.68	66.44	164.95	168.39	115.39	156.24	54.02 54.79	86.52	126.98, 127.79 128.76, 144.06
9b	76.25	37.01	96.25	154.94	59.80	164.85	168.02	116.34	154.91	53.97 54.77	87.16	127.10, 127.91 128.86, 143.81

[a] Assignments could be reversed.

vored. Use of a silver salt[11d,e,18] (procedure C) completely suppressed double-bond migration.

Hydrogenation of Carbohydrate Double Bonds. Hydrogenations of the carbohydrate double bonds of coupling products **8a**, **10a**, **8b**, and **10b** were accomplished readily using palladium on carbon and ammonium formate (Table II). Hydrogenations of the 3′,4′-unsaturated C-nucleosides **10a** and **10b** occurred selectively from the less hindered face of the furanoid ring yielding cis substituted products **4b** and **4a**, respectively, which involve inversion of the original glycal stereocenters and transformations between D and L series.

Spectrometric Comparison of C-Nucleoside Enantiomers and Diasteriomers. Characterizing data for glycal enantiomers **2a** and **2b** and C-nucleoside enantiomer pairs **3a** and **3b**, **4a** and **4b**, **8a** and **8b**, and **10a** and **10b** are contained in Tables III and IV and in Figure 1. The enantiomeric nature of each pair is confirmed by their indistinguishable mass, ^{1}H (Table III) and ^{13}C NMR (Table IV) spectra; in each case, only optical rotation (Table III) distinguishes the two enantiomers. Perhaps most striking are the circular dichroism spectra (Figure 1) which clearly demonstrate the enantiomeric nature of C-nucleoside pairs **3a** and **3b** and **4a** and **4b**. Similarly, diasteriomeric pairs **3a** and **4a** and **3b** and **4b** are identified by their differing spectrometric properties. Assignments of C-nucleosides as 1′,4′-cis and 1′,4′-trans substituted were confirmed by nuclear Overhauser enhancement (NOE) spectrometry.[19]

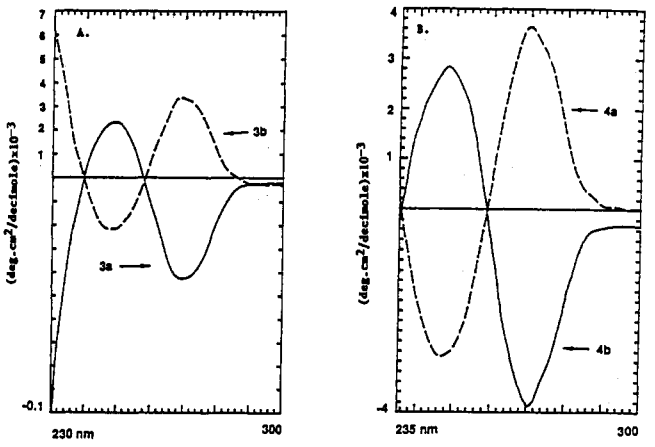


Figure 1. Circular dichroism spectra for enantiomer pairs **3a** and **3b** (A, left) and **4a** and **4b** (B, right).

For 1′,4′-cis compounds (e.g., **4a** and **4b**) irradiation of H-1′ led to an NOE effect at H-4′; no such effect was observed upon irradiation of H-1′ of 1′,4′-trans compounds (e.g., **3a** and **3b**).

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 column chromatography, silica gel 60 (230–400 mesh ASTM, E. Merck) was used. Nuclear magnetic resonance (NMR) spectra were obtained on either a Varian Associates XL-200 or a Varian Unity 500 spectrometer and are referenced to tetramethylsilane. Mass spectra were

(18) Karabelas, K.; Westerlund, C.; Hallberg, A. *J. Org. Chem.* **1985**, *50*, 3896–3900.
(19) Brakta, M.; Farr, R. N.; Chaguir, B.; Massiot, G.; Lavaud, C.; Anderson, W. R., Jr.; Sinou, D.; Daves, G. D., Jr. *J. Org. Chem.*, in press.

obtained with a Hewlett-Packard 5987A GC/MS system. Optical rotations were determined using a Perkin-Elmer 241 polarimeter, and circular dichroism spectrometry (JASCO J-720) was performed by Dr. Robert Maccoll, Wadsworth Laboratories, New York State Department of Health. High-resolution mass spectrometry was performed by Dr. Richard Kondrat, University of California at Riverside. Melting points were determined with a Thomas Hoover capillary melting point apparatus. Elemental analyses were carried out by Quantitative Technologies, Bound Brook, NJ. Characterizing data for new compounds are contained in Tables III and IV and in Figure 1.

(5*R*)-4,5-Dihydro-5-[(triphenylmethoxy)methyl]furan[4] (2b). To a solution of (5*R*)-5-[(triphenylmethoxy)methyl]-γ-butyrolactone[13] (**1b**) (5.0 g, 13.9 mmol) in dry CH_2Cl_2 (15 mL) cooled to −78 °C under nitrogen was added diisobutylaluminum hydride (20 mL, 1.0 M in tetrahydrofuran, 20 mmol). The resulting reaction mixture was stirred at −78 °C for 20 min, and then cold 0.4 N HCl was added. The mixture was extracted with ether. The combined ether extracts were washed with H_2O followed by aqueous $NaHCO_3$, dried over Na_2SO_4, and evaporated to give 4.5 g of crude lactol which exhibited the same R_f (= 0.34, ethyl acetate–hexane (1:3)) as the starting material but gave a different appearance upon spraying the TLC plate with acid.

The dried crude lactol was dissolved in dry CH_2Cl_2 (25 mL) and cooled to −22 °C under nitrogen. To this solution triethylamine (7.8 mL, 55.6 mmol) was added followed by methanesulfonyl chloride (1.4 mL, 18.1 mmol). The resulting mixture was stirred at −22 °C for 20 min, warmed to 40 °C, and then heated under reflux for 5 h. The reaction mixture was diluted with CH_2Cl_2, washed with H_2O, and dried over Na_2SO_4. The volatiles were removed, and the residue was separated by silica gel column chromatography using ethyl acetate–hexane–triethylamine (1:4:0.1) to afford 2.8 g (59%) of **2b**[4] as a colorless solid. Recrystallization from methanol–ethyl acetate gave colorless needles, mp 92.5–94 °C.

(5*S*)-4,5-Dihydro-5-[(triphenylmethoxy)methyl]furan[4] (2a). Similarly, from (5*S*)-5-[(triphenylmethoxy)methyl]-γ-butyrolactone[13] (**1a**), **2a**[4] was prepared, yield 63%, mp 93–94 °C.

Palladium-Mediated Coupling of 2,4-Dimethoxy-5-iodopyrimidine[14] (5) with 2,3-Dideoxyfuranoid Glycals 2a and 2b. Procedure A. To a mixture of 2,4-dimethoxy-5-iodopyrimidine (**5**) (399 mg, 1.5 mmol), sodium acetate (123 mg, 1.5 mmol), triethylamine (418 μL, 3.0 mmol), and tetra-*n*-butylammonium chloride·H_2O (222 mg, 0.75 mmol) in dimethylformamide (DMF) (10 mL) was added (5*R*)-4,5-dihydro-5-[(triphenylmethoxy)-methyl]furan (**2b**) (616 mg, 1.8 mmol) followed by palladium acetate (33.7 mg, 0.15 mmol). The resulting mixture was stirred under nitrogen at room temperature for 20 h and then filtered through Celite. The volatiles were removed in vacuo, and the resulting residue was separated by column chromatography using ethyl acetate–hexane (1:3) to yield 404 mg (56%) of 2,4-dimethoxy-(2′*R*)-*trans*-5-[2′,5′-dihydro-5′-[(triphenylmethoxy)-methyl]-2′-furanyl]pyrimidine (**8b**) and 223 mg (31%) of 2,4-dimethoxy-(2′*R*)-5-[2′,3′-dihydro-5′-[(triphenylmethoxy)methyl]-2′-furanyl]pyrimidine (**10b**) as colorless foams. **8b** was recrystallized from ethyl acetate–hexane to yield colorless crystals, mp 114–115 °C.

Procedure B. A mixture of palladium acetate (22 mg, 0.1 mmol) and triphenylarsine (61 mg, 0.2 mmol) in dry acetonitrile (5 mL) was stirred under nitrogen at room temperature for 20 min. The mixture was then transferred to a solution of 2,4-dimethoxy-5-iodopyrimidine[14] (**5**) (266 mg, 1.0 mmol), **2b** (411 mg, 1.2 mmol), and triethylamine (279 μL, 2.0 mmol) in dry acetonitrile (8 mL). The resulting light yellow solution was stirred under nitrogen at 75 °C for 10 h, at which time TLC indicated that the iodoaglycon derivative **5** had been consumed from the now dark reaction mixture. The reaction mixture was then filtered through Celite, and the volatiles were removed. The resulting residue was separated by column chromatography using ethyl acetate–hexane (1:3) to give 87 mg (18%) of **8b** and 284 mg (59%) of **10b**.

Procedure C. A mixture of 2,4-dimethoxy-5-iodopyrimidine[14] (**5**) (98 mg, 0.37 mmol), (5*S*)-4,5-dihydro-5-[(triphenylmethoxy)-methyl]furan (**2a**) (151 mg, 0.44 mmol), triethylamine (103 μL, 0.74 mmol), triphenylphosphine (19 mg, 0.074 mmol), silver carbonate (204 mg, 0.74 mmol), and palladium acetate (8.3 mg, 0.037 mmol) in acetonitrile (8 mL) was stirred under nitrogen at 75 °C for 10 h. The reaction mixture was filtered through Celite, and the volatiles were removed. The resulting residue was separated by column chromatography to afford 71 mg (40%) of 2,4-dimethoxy-(2′*S*)-*trans*-5-[2′,5′-dihydro-5′-[(triphenylmethoxy)-methyl]-2′-furanylpyrimidine (**8a**) as a colorless foam which was recrystallized from ethyl acetate–hexane to give colorless crystals, mp 113.5–115 °C.

Hydrogenation of 2′,3′-Unsaturated C-Glycosides. To a solution of **8b** (144 mg, 0.3 mmol) in anhydrous ethanol (5 mL) was added 10% Pd–C (30 mg) followed by ammonium formate (132 mg, 2.1 mmol). The resulting mixture was stirred under nitrogen at room temperature for 3 h and then filtered through Celite. The ethanol was removed in vacuo, and the resulting residue was dissolved in ether, washed with H_2O, and dried with Na_2SO_4. After the ether was evaporated, the residue was purified by column chromatography using ethyl acetate–hexane (1:3) to yield 136 mg (94%) of 2,4-dimethoxy-(2′*R*)-*trans*-5-[tetrahydro-5′-[(triphenylmethoxy)methyl]-2′-furanyl]pyrimidine **3b** as a colorless foam.

Hydrogenation of 3′,4′-Unsaturated C-Glycosides. Procedure A. Compound **10b** (120 mg, 0.25 mmol) was reduced by the ammonium formate/Pd–C/ethanol system (see previous procedure). The reaction mixture was separated by preparative TLC using ether–CH_2Cl_2–benzene (1:4:6) to afford 103 mg (85%) of 2,4-dimethoxy-(2′*R*)-*cis*-5-[tetrahydro-5′-[(triphenylmethoxy)-methyl]-2′-furanyl]pyrimidine (**4a**) and 8.4 mg (7%) of **3b** as colorless foams.

Procedure B. A mixture of **10b** (144 mg, 0.3 mmol) and 10% Pd–C (15 mg) in anhydrous ethanol (8 mL) was shaken under 2 atm of hydrogen at room temperature for 4 h. The catalyst was then removed by filtration through Celite, and ethanol was evaporated in vacuo. The resulting residue was separated by preparative TLC to yield 125 mg (86%) of **4a** and 10 mg (7%) of **3b**.

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