# Syntheses of 2′-Deoxypseudouridine, 2′-Deoxyformycin B, and 2′,3′-Dideoxyformycin B by Palladium-Mediated Glycal–Aglycon Coupling

Han-Cheng Zhang and G. Doyle Daves, Jr.*

*Department of Chemistry, Rensselaer Polytechnic Institute, Troy, New York 12180*

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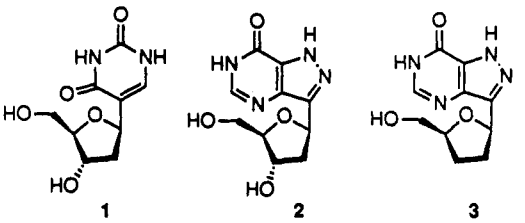
5-Iodouracil and the ribofuranoid glycal 1,4-anhydro-2-deoxy-3-*O*-[(1,1-dimethylethyl)diphenylsilyl]-D-*erythro*-pent-1-enitol underwent regio- and stereospecific coupling in the presence of catalytic palladium acetate and either triphenylphosphine or triphenylarsine ligands. The resulting *C*-glycosyl product was converted to 2′-deoxypseudouridine, 5-(2′-deoxy-β-D-ribofuranosyl)-2,4(1*H*,3*H*)-pyrimidinedione (63% overall yield). In a similar way, 2′-deoxyformycin B, 3-(2′-deoxy-β-D-ribofuranosyl)pyrazolo[4,3-*d*]pyrimidin-7-one, and 2′,3′-dideoxyformycin B, 3-(2′,3′-dideoxy-β-D-ribofuranosyl)pyrazolo[4,3-*d*]pyrimidin-7-one, have been synthesized by reaction sequences in which the key step is a palladium-mediated regio- and stereospecific *C*-glycosyl bond forming reaction between this furanoid glycal and a bis(tetrahydropyranyl)-protected 3-iodopyrazolo[4,3-*d*]pyrimidine aglycon derivative.

The intensive effort to find effective therapeutic agents for the treatment of acquired immunodeficiency syndrome (AIDS) and, particularly, the focus on discovery of agents which function as inhibitors of human immunodeficiency virus (HIV) reverse transcriptase[1-3] have reaffirmed the need for efficient general synthetic methods for the preparation of nucleosides and nucleoside analogs. Our research has involved the development of palladium-mediated coupling reactions of pyranoid and furanoid glycals (1,2-unsaturated carbohydrates) with appropriate aglycon derivatives for regio- and stereospecific formation of *C*-glycosyl bonds.[4-9] In the present report, we describe extensions of this powerful reaction and demonstrate for the first time its utility for nucleic acid constituent *C*-nucleoside analog synthesis.

We have succeeded in achieving the first palladium-mediated coupling of a glycal with a nitrogen heterocycle with unprotected NH groups.[10] This accomplishment is illustrated with an efficient synthesis of 2′-deoxypseudouridine[11] (1). Further, we have succeeded in achieving palladium-mediated glycal–aglycon coupling with a bicyclic, purine analog nitrogen heterocycle (albeit NH protected). This accomplishment has led to syntheses of 2′-deoxyformycin B[12] (2) and 2′,3′-dideoxyformycin B (3).



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In our studies of palladium-mediated glycal–aglycon coupling reactions,[4-8] we have used pyrimidine derivatives[13-17] NH-protected in order to achieve solubility in acetonitrile.[18a] We have now turned our attention to the preparation of nitrogen heterocyclic nucleic acid constituent *C*-nucleoside analogs which require that ring nitrogens be unprotected. Unprotected heterocyclic aglycon derivatives do not undergo palladium-mediated coupling with glycals under reaction conditions which are highly effective for anthracyclic aglycons[5,8,9,19] presumably because of nitrogen complexation with palladium.

**Palladium-Mediated Coupling Reactions of 5-Iodouracil.** Palladium-mediated coupling reactions of 2,4-dimethoxy-5-iodopyrimidine[17] (4) with 2,3-dihydrofuran (5) were carried out under a variety of reaction conditions (Table I, entries 1–4). When 4 and 2,3-dihydrofuran (5) were mixed in acetonitrile[18a] in the presence of catalytic palladium acetate, no reaction occurred (entry 1). Change of reaction solvent from acetonitrile[18a] to dimethyl sulfoxide (entry 2) or dimethylformamide[5,8,9,19,20] (entry 3) and introduction into the reaction mixture of tetra-*n*-butylammonium chloride[8,9,20,21] (entry 4) afforded increasingly

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(10) Cross-coupling reactions of vinylstannanes or acetylenic stannanes with 5-iodouracil have been reported. (See, for example: Farina, V.; Hauck, S. I. *Synlett.* **1991**, 157–159. Robins, M. J.; Barr, P. J. *Tetrahedron Lett* **1981**, *22*, 421–424. Robins, M. J.; Barr, P. J. *J. Org. Chem.* **1983**, *48*, 1854–1862. Arcadi, A.; Cacchi, S.; Martinelli, F. *Tetrahedron Lett.* **1989**, *30*, 2581–2584.) Heck-type coupling involving 1,2-addition of "R-Pd-X" involving NH-containing compounds is rare (Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic Press: New York, 1985).
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(17) Prystas, M.; Sorm, F. *Collect. Czech. Chem. Commun.* **1964**, *29*, 121–130.
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**Table I. Coupling of 2,4-Dimethoxy-5-iodopyrimidine (4) and 5-Iodouracil (8) with 2,3-Dihydrofuran (5) in the Presence of 0.1 equiv of Palladium Acetate[a]**

| entry | RI | ligand or $n$-$Bu_4NCl$ (equiv) | solvent | temp (°C) | time (h) | product(s) (yield, %) |
|---|---|---|---|---|---|---|
| 1 | 4 | | $CH_3CN$ | 25 | 24 | no reaction |
| 2 | 4 | | DMSO[b] | 25 | 48 | 6 (13), 7 (19) |
| 3 | 4 | | DMF[c] | 25 | 48 | 6 (26), 7 (39) |
| 4 | 4 | $n$-$Bu_4NCl$ (0.5) | DMF | 25 | 6 | 6 (26), 7 (55) |
| 5 | 8 | $n$-$Bu_4NCl$ (0.5) | DMF | 50 | 2 | no reaction |
| 6 | 8 | $PPh_3$ (0.2) | DMF | 50 | 12 | 9:10 (4:3, 68) |
| 7 | 8 | $AsPh_3$ (0.2) | DMF | 50 | 3 | 9:10 (3:2, 58) |

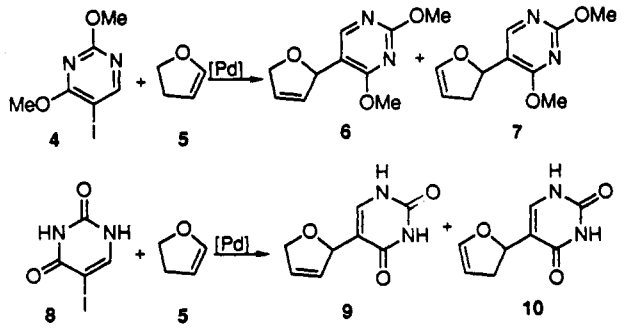
[a] Reaction mixtures contained 2.5 equiv of 2,3-dihydrofuran (5) and 1.5 equiv of tri-$n$-butylamine. Entries 1–5 also contained 1.0 equiv of sodium acetate. [b] Dimethyl sulfoxide. [c] Dimethylformamide.

**Table II. Palladium-Catalyzed Coupling of 1,4-Anhydro-2-deoxy-3-*O*-[(1,1-dimethylethyl)diphenylsilyl]-D-*erythro*-pent-1-enitol[25] (11) with 3-Iodopyrazolo[4,3-*d*]pyrimidine Aglycon Derivative 19[a]**

| entry | [Pd] (0.1 equiv) | ligand or $n$-$Bu_4NCl$ (equiv) | solvent | temp (°C) | time (h) | yield (%) 20 | 21 | 22 |
|---|---|---|---|---|---|---|---|---|
| 1 | $Pd(OAc)_2$ | $n$-$Bu_4NCl$ (0.5) | DMF[b] | 25 | 24 | | no reaction | |
| 2 | $Pd(OAc)_2$ | $PPh_3$ (0.2) | DMF | 80 | 72 | 5 | 19 | 28 |
| 3 | $Pd(OAc)_2$ | $AsPh_3$ (0.2) | DMF | 80 | 72 | 19 | 27 | 32 |
| 4 | $Pd(OAc)_2$ | $AsPh_3$ (0.2) | $CH_3CN$ | 80 | 72 | 28 | 18 | 30 |
| 5 | $Pd(dba)_2$[c] | $AsPh_3$ (0.2) | DMF | 80 | 72 | 39 | 18 | 21 |
| 6 | $Pd(dba)_2$ | $AsPh_3$ (0.2) | *d* | 80 | 72 | 36 | 23 | 23 |
| 7 | $Pd(dba)_2$ | $AsPh_3$ (0.2) | $CH_3CN$ | 80 | 20 | 62 | 10 | 18 |

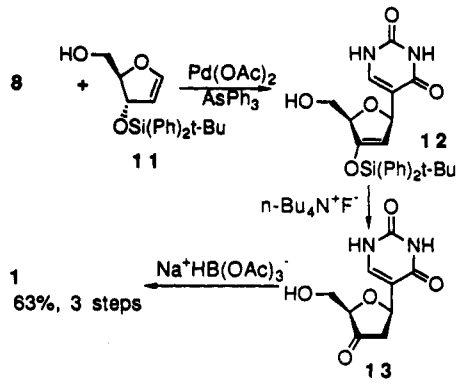
[a] Reaction mixtures contained 1.5 equiv of furanoid glycal 11[25] and 1.5 equiv of $n$-$Bu_3N$; entry 1 contained 1.0 equiv of NaOAc. [b] Dimethylformamide. [c] Bis(dibenzylidineacetone)–palladium(0). [d] *N*-Methylpyrrolidone.

effective reaction conditions for palladium-mediated coupling to form a bond between the $\alpha$-carbon[22] of the cyclic enol ether and the iodo-bearing carbon of the pyrimidine. Decomposition of the intermediate $\sigma$-organopalladium adduct afforded a mixture of double bond isomers 6 and 7.[18]




Experiments to define effective reaction conditions for palladium-mediated coupling of 5-iodouracil[23] (8) with 2,3-dihydrofuran (5) are summarized by entries 5–7 in Table I. The reaction conditions which effected coupling of protected iodopyrimidine 4 (entries 2–4) did not effect coupling of 5-iodouracil (8) (e.g., entry 5) even at 50 °C. Coupling and formation of a mixture of double bond isomers 9 and 10[18] was achieved by introduction of 2 equiv of triphenylphosphine per palladium (entry 6). Use of triphenylarsine as ligand for palladium[24] increased the rate of palladium-mediated coupling (entry 7).

**Synthesis of 2′-Deoxypseudouridine (1).** These reaction conditions (entry 7) were incorporated in an efficient three-step synthesis of 2′-deoxypseudouridine[11] (1) in 63% overall yield. The key step was the palladium-mediated coupling of 5-iodouracil[23] (8) with 1,4-anhydro-2-deoxy-3-*O*-[(1,1-dimethylethyl)diphenylsilyl]-D-*erythro*-pent-1-enitol[25] (11), a ribofuranoid glycal designed for stereospecific formation of $\beta$ *C*-glycosyl bonds. The coupling reaction formed $\beta$ *C*-nucleoside 12 which, without isolation, was desilylated with fluoride ion to form the 2′-deoxy-3′-keto *C*-nucleoside 13. Finally, sodium triacetoxyborohydride[8,9,25,26] was used to effect stereospecific reduction of the 3′-keto group from the $\beta$-face of the furanosyl ring forming 2′-deoxypseudouridine[11] (1).




**Formycin B Analogs.** The antibiotic *C*-nucleosides formycin and formycin B,[27] isomers of adenosine and inosine, respectively, exhibit interesting and important biological properties.[28] All reported syntheses of *C*-nucleosides of the formycin series[29] which involve formation

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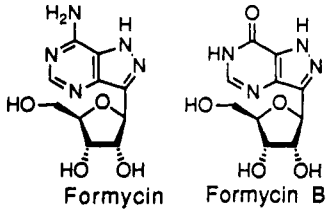
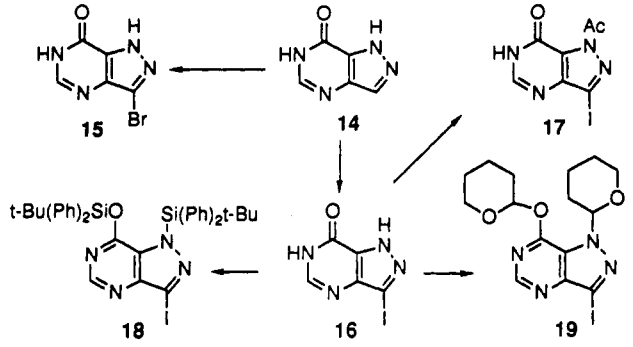
(28) Hacksell, U.; Daves, G. D., Jr. *Prog. Med. Chem.* **1985**, *22*, 1–65. Daves, G. D., Jr.; Cheng, C. C. *Prog. Med. Chem.* **1976**, *13*, 303–349.

of the C-glycosyl linkage have been accomplished by construction of the pyrazolo[4,3-*d*]pyrimidine aglycon ring system onto a C-1 carbon-substituted ribofuranosyl moiety. Many new C-nucleosides have been prepared by modification of natural formycin in either the nitrogen heterocyclic aglycon or carbohydrate.[12,27,30] Noteworthy is the preparation of 2',3'-dideoxyformycin by deoxygeneration of formycin.[30b,31]

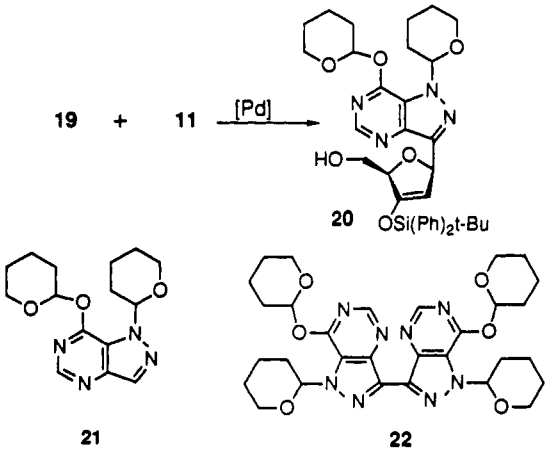



The aglycon pyrazolo[4,3-*d*]pyrimidin-7-one[32] (**14**) was treated with bromine in water and with *N*-iodosuccinimide in dimethylformamide to afford the corresponding 3-bromo (**15**[33]) and 3-iodo (**16**) derivatives. Iodo aglycon **16** was derivatized by acetylation[34] to form **17**, by bis-silylation to form **18**, and by bis-tetrahydropyranylation to form **19**.[35]

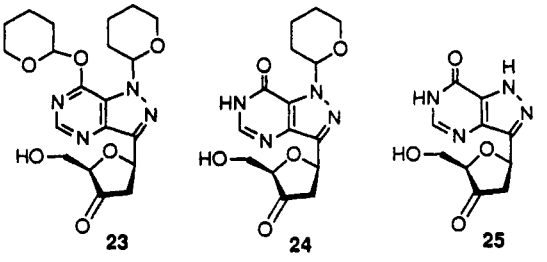



The utility of halopyrazolo[4,3-*d*]pyrimidine derivatives **15–19** in palladium-mediated coupling reactions with furanoid glycal **11**[25] were assessed. No reaction conditions were found which effected coupling of glycal **11** with aglycon derivatives **15–18**. Aglycon derivatives **15** and **16**, which possess readily accessible nitrogen centers, appear to inactivate the catalyst since the black color characteristic of palladium-catalyzed reactions failed to develop. Under various reaction conditions, the acetyl (**17**) and silyl (**18**) protective groups proved labile; 3-iodopyrazolo[4,3-*d*]pyrimidine (**16**) was isolated from these reaction mixtures.

The bis(tetrahydropyranyl) derivative **19**[35] is stable under all reaction conditions investigated. Experiments to define conditions for palladium-mediated coupling reactions of aglycon derivative **19**[35] with furanoid glycal **11**[25] are summarized in Table II. Reaction conditions developed for C-glycosyl bond formation to protected pyrimidine **4** and anthracycline aglycons[8,9] (entry 1) were ineffective. Introduction of triphenylphosphine (2 equiv per palladium) as a ligand and raising the reaction temperature to 80 °C led to C-glycosyl bond formation (5%) yielding C-nucleoside **20** together with larger quantities of deiodinated aglycon **21** and aglycon dimer **22** (entry 2). Use of triphenylarsine[24] was more effective (entry 3) and use of acetonitrile rather than dimethylformamide as reaction solvent further increased the yield of **20** (entry 4). A Pd(0) catalyst rather than Pd(II) (entries 5 and 6) increased C-glycosyl bond formation further. Finally, use of a palladium(0) catalyst with triphenylarsine as ligand in acetonitrile (entry 7) resulted in regio- and stereospecific[4-8] formation of C-nucleoside **20** in 62% isolated yield.




The aglycon moieties of C-nucleosides derived from **19**, e.g. **20**, possess racemic tetrahydropyranyl groups and consist of a complex mixture of isomers owing to these groups and to the presence of both N-1 and N-2 alkylation.[35] This stereochemical ambiguity is ultimately inconsequential since the tetrahydropyranyl groups will be removed. Following desilylation of C-nucleoside **20**, a study was made to find conditions for removal of the tetrahydropyranyl groups from the resulting 3'-keto C-nucleoside **23**.




Treatment of **23** with *p*-toluenesulfonic acid in methanol–water at 40 °C effected removal of both tetrahydropyranyl groups but led to a mixture of two C-nucleosides, **25** and the corresponding α C-nucleoside anomer. The $^1$H nuclear magnetic resonance (NMR) spectrum of the isomer mixture exhibited signals for the anomeric hydrogen (H-1') at δ 5.54 (dd) and at δ 5.81 (dd) assigned to the β (**25**) and α anomers, respectively. Trifluoroacetic acid was also

(29) Rosowsky, A.; Ghoshal, M.; Solan, V. C. *Carbohydr. Res.* **1988**, *176*, 47–58. Buchanan, J. G.; Smith, D.; Wightman, R. H. *J. Chem. Soc. Perkin Trans. 1* **1986**, 1267–1271. Acton, E. M.; Ryan, K. J. *J. Org. Chem.* **1984**, *49*, 528–536. Buchanan, J. G.; Edgar, A. R.; Hutchison, R. J.; Stobie, A.; Wightman, R. H. *J. Chem. Soc., Chem. Commun.* **1980**, 237–238. Buchanan, J. G.; Stobie, A.; Wightman, R. H. *Can. J. Chem.* **1980**, *58*, 2624–2627. Kalvoda, L. *Collect. Czech. Chem. Commun.* **1978**, *43*, 1431–1437. Acton, E. M.; Fujiwara, A. N.; Goodman, L.; Henry, D. W. *Carbohydr. Res.* **1974**, *33*, 135–151. Farkas, J.; Sorm, F. *Collect. Czech. Chem. Commun.* **1972**, *37*, 2798–2803. Acton, E. M.; Ryan, K. J.; Henry, D. W.; Goodman, L. *J. Chem. Soc. D* **1971**, 986–988. Acton, E. M.; Ryan, K. J.; Goodman, L. *J. Chem. Soc. D* **1970**, 313–314. Bobek, M.; Farkas, F.; Sorm, F. *Tetrahedron Lett.* **1970**, 4611–4614. Sprinzl, M.; Farkas, J.; Sorm, F. *Tetrahedron Lett.* **1969**, 289–292.

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(31) Serafinowski, P. *Synthesis* **1990**, 411–415.

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(33) Cassidy, F.; Olsen, R. K.; Robins, R. K. *J. Heterocycl. Chem.* **1968**, *5*, 461–465.

(34) Townsend, L. B.; Tipson, R. S. *Nucleic Acid Chemistry*; John Wiley and Son, Inc.: New York, 1987; Part 1, p 112.

(35) Nuclear magnetic resonance (NMR) spectrometry ($^1$H, 500 MHz, see the Experimental Section) showed the product **19** to consist of a mixture (10:1) of N-1 and N-2 alkylated isomers (see: Stone, T. E.; Eustace, E. J.; Pickering, M. V.; Daves, G. D., Jr. *J. Org. Chem.* **1979**, *44*, 505–509).

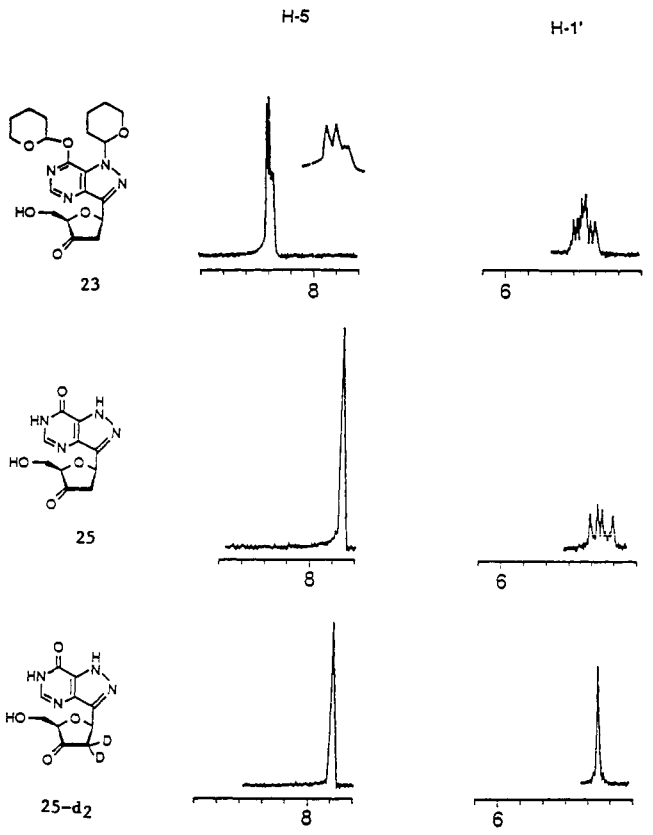
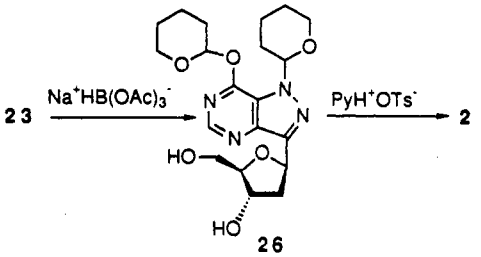



**Figure 1.** Top: $^1$H NMR resonances of *C*-nucleoside **23** for H-5 of the aglycon and H-1′, the anomeric resonance of the carbohydrate. The resonance for H-5 consists of four singlets owing to the racemic nature of the tetrahydropyranyl asymmetric centers. Middle: Following removal of the tetrahydropyranyl groups to produce **25**, the resonance for H-5 appears as a singlet indicative that the molecule is now a single stereoisomer. Bottom: Deuterium exchange of the hydrogens at C-2′ of **25** removed the coupling with H-1′ and produced a spectrum in which both the resonances for H-5 and for H-1′ are singlets, indicative that the *C*-nucleoside is a single isomer and that no stereoisomerization has occurred during the deprotection reaction.

effective in removing the tetrahydropyranyl groups; however, again anomerization occurred. Acetic acid did not affect the anomeric center of the carbohydrate moiety but removed only one of the tetrahydropyranyl groups forming *C*-nucleoside **24**. Finally, treatment of **23** with pyridinium *p*-toluenesulfonate[36] in methanol–water at 50 °C for 2 days removed both tetrahydropyranyl groups without affecting the anomeric center producing *C*-nucleoside **25**.

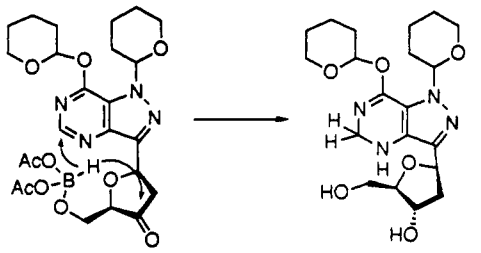
The $^1$H NMR data shown in Figure 1 illustrate the stereochemical complexity of 3′-keto *C*-nucleoside **23** and its inconsequential nature in synthesis of formycin analogs. In the $^1$H NMR spectrum of **23**, H-5 of the aglycon appears as four singlets (Figure 1, top). The $^1$H NMR spectrum of **25**, which lacks the tetrahydropyranyl groups, exhibits a single resonance for H-5 (Figure 1, middle). Finally, deuterium exchange of the hydrogens at C-2′ of **25** produced an analog **25-d$_2$** for which the resonances for both H-5 and H-1′ are singlets (Figure 1, bottom), attesting to the stereochemical integrity of the chiral centers of 3′-keto *C*-nucleoside **25**.

The palladium-mediated coupling reaction[4-8] leading to *C*-nucleoside **20** formed a β *C*-glycosyl bond as expected for reactions of glycal **11**.[25] This carbohydrate stereochemistry, that of the formycin series, was rigorously established by conversion of **20** (via 3′-keto *C*-nucleoside **23**) into the known 2′-deoxyformycin B[12] (**2**). In addition, 2′,3′-dideoxyformycin B (**3**) was synthesized from this intermediate.




2′-Deoxyformycin B (**2**), previously prepared from formycin,[12] was obtained from *C*-nucleoside **20** in three steps. Following desilylation of the silylenol ether (**20** → **23**), stereospecific reduction of the keto group[25] (triacetoxyborohydride,[26] **23** → **26**) and removal of the tetrahydropyranyl groups (pyridinium *p*-toluenesulfonate[36]) yielded 2′-deoxyformycin B (**2**) indistinguishable from an authentic sample.[12]

The ketone reduction using triacetoxyborohydride[26] proved unexpectedly difficult. When the reaction was carried out at room temperature as is usual,[8,9,25,26] significant quantities of a second product was formed in addition to **26**. Only by carrying out the reduction at −22 °C was an acceptably high yield of **26** obtained. On the basis of mass and $^1$H NMR spectra, structure **27** was assigned to the second product. We rationalize its formation as resulting from the proximity of the hydride to aglycon carbon C-5 in the activated complex **23A**.[26] In support of this mechanism we note that *C*-nucleosides of the formycin family are predominantly of syn conformation around the *C*-glycosyl bond in solution[37] although formycin B in the crystalline state is anti.[38] No reduction occurred when the aglycon derivative **21** was treated with triacetoxyborohydride, indicative that activation of the reagent by reaction with the carbohydrate hydroxyl was necessary.[25,26]




Transformation of 2′-deoxy *C*-nucleoside **26** into 2′,3′-dideoxyformycin B (**3**), a potential HIV reverse transcriptase inhibitor,[1-3] was accomplished in five steps in 52% overall yield. The primary hydroxyl at C-5′ was selectively silylated to form **28** followed by derivatization of the C-3′ hydroxyl using *O*-phenyl chlorothionoformate,[39] producing intermediate **29** which was deoxygenated at C-3′ using tri-*n*-butyltin hydride in the presence of 2,2′-azobis(2-methylpropionitrile) (AIBN). The resulting 2′,3′-dideoxy *C*-nucleoside **30** was deprotected by sequential treatment with fluoride ion (**30** → **31**) and pyridinium *p*-toluenesulfonate to produce 2′,3′-dideoxyformycin B (**3**).

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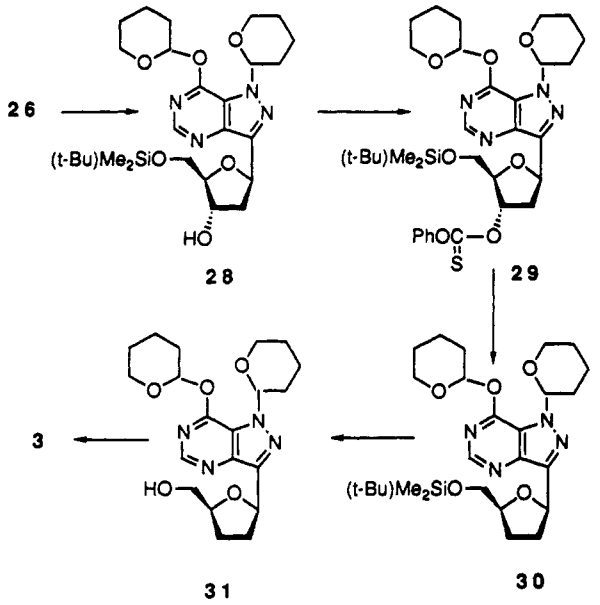
(38) Koyama, G.; Nakamura, H.; Umezawa, H.; Iitaka, Y. *Acta Crystallogr.* **1976**, *B32*, 813–820.
(39) Robins, M. J.; Wilson, J. S. *J. Am. Chem. Soc.* **1981**, *103*, 932–933.




## 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-cm² 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 Bruker AM-500 spectrometer and are referenced to tetramethylsilane. Mass spectra were obtained with a Hewlett-Packard 5987A GC/MS system. High-resolution mass spectrometry was performed by Dr. A. J. Alexander, Department of Chemistry, Cornell University. Melting points were determined with a Thomas-Hoover capillary melting point apparatus. Elemental analysis were carried out by Quantitative Technologies, Bound Brook, NJ.

**Palladium-Mediated Coupling of 2,4-Dimethoxy-5-iodopyrimidine[17] (4) with 2,3-Dihydrofuran (5).** 2,4-Dimethoxy-5-iodopyrimidine[17] (4) (267 mg, 1 mmol), 2,3-dihydrofuran (5) (189 μL, 2.5 mmol), tri-*n*-butylamine (357 μL, 1.5 mmol), sodium acetate (82 mg, 1 mmol), and tetra-*n*-butylammonium chloride hydrate (148 mg, 0.5 mmol) were dissolved in dimethylformamide (DMF) (10 mL). Palladium acetate (22 mg, 0.1 mmol) was added, and the resulting mixture was stirred under nitrogen at room temperature for 6 h. The reaction mixture was then filtered through Celite and the volatiles were removed. Preparative TLC of the resulting residue using hexane–$CH_2Cl_2$–ethyl acetate (1:1:1) afforded 115 mg (55%) of 5-(2′,3′-dihydrofuran-2′-yl)-2,4-dimethoxypyrimidine (7) and 54 mg (26%) of 5-(2′,5′-dihydrofuran-2′-yl)-2,4-dimethoxypyrimidine (6) as colorless oils.

For 7: $^1$H NMR ($CDCl_3$) δ 2.37–2.48, 2.94–3.08 (m, 2 H, H-3′, H-3″), 3.97, 4.05 (2 s, 6 H, $OCH_3$), 4.92 (m, 1 H, H-4′), 5.53 (dd, 1 H, H-2′), 6.38 (m, 1 H, H-5′), 8.19 (s, 1 H, H-6); $^{13}$C NMR ($CDCl_3$) δ 36.09 (C-3′), 53.91, 54.69 ($OCH_3$), 75.66 (C-2′), 99.22 (C-4′), 115.99 (C-5), 144.91 (C-5′), 154.87 (C-6), 164.78, 168.05 (C-2, C-4).

Anal. Calcd for $C_{10}H_{12}N_2O_3$: C, 57.7; H, 5.81; N, 13.4. Found: C, 57.6; H, 5.75; N, 13.1.

For 6: $^1$H NMR ($CDCl_3$) δ 3.98, 4.02 (2 s, 6 H, $OCH_3$), 4.78 (m, 2 H, H-5′, H-5″), 5.87–5.92, 5.99–6.03 (m, 3 H, H-2′, H-3′, H-4′), 8.18 (s, 1 H, H-6); $^{13}$C NMR ($CDCl_3$) δ 54.02, 54.78 ($OCH_3$), 75.55 (C-5′), 80.72 (C-2′), 115.54 (C-5), 127.37, 127.70 (C-3′, C-4′), 155.94 (C-6), 164.92, 168.38 (C-2, C-4).

Anal. Calcd for $C_{10}H_{12}N_2O_3$: C, 57.7; H, 5.81; N, 13.4. Found: C, 57.4; H, 5.74; N, 13.1.

**Palladium-Mediated Coupling of 5-Iodouracil[23] (8) with 2,3-Dihydrofuran (5).** Palladium acetate (13 mg, 0.06 mmol) and triphenylarsine (37 mg, 0.12 mmol) were dissolved in DMF (3 mL), and the mixture was stirred under nitrogen at room temperature for 20 min. Then a solution of 5-iodouracil[23] (8) (143 mg, 0.6 mmol), 2,3-dihydrofuran (5) (113 μL, 1.5 mmol), and tri-*n*-butylamine (214 μL, 0.9 mmol) in DMF (4 mL) was added. The resulting reaction mixture (in a sealed tube) was stirred at 50 °C for 3 h. Then the reaction mixture was filtered through Celite, and the volatiles were removed. The residue was separated by preparative TLC using $CH_2Cl_2$–ethyl acetate–acetone (1:1:1) to yield 63 mg (58%) of a mixture of **9** and **10** in a ratio of 3:2: $^1$H NMR (DMSO-$d_6$) δ 2.35–3.20 (m, 2 H, H-3′, H-3″ of **10**), 4.58 (m, 2 H, H-5′, H-5″ of **9**), 4.95 (m, 1 H, H-4′ of **10**), 5.24 (dd, 1 H, H-2′ of **10**), 5.52 (m, 1 H, H-2′ of **9**), 5.83–6.20 (m, 2 H, H-3′, H-4′ of **9**), 6.48 (m, 1 H, H-5′ of **10**), 7.15, 7.21 (2 s, 2 H, H-6 of **10** and **9**).

**5-(2′-Deoxy-β-D-ribofuranosyl)-2,4(1*H*,3*H*)-pyrimidinedione (2′-Deoxypseudouridine,[11] 1).** A mixture of palladium acetate (10 mg, 0.045 mmol) and triphenylarsine (28 mg, 0.09 mmol) in DMF (3 mL) was stirred under nitrogen at room temperature for 20 min. Then 5-iodouracil[23] (8) (107 mg, 0.45 mmol), 1,4-anhydro-2-deoxy-3-*O*-[(1,1-dimethylethyl)diphenylsilyl]-D-*erythro*-pent-1-enitol[25] (11) (240 mg, 0.68 mmol), and tri-*n*-butylamine (160 μL, 0.7 mmol) in DMF (3 mL) were added, and the resulting reaction mixture was stirred under nitrogen at 60 °C until the reaction was finished (15 h, based on TLC). The mixture was then cooled to 0 °C, and acetic acid (100 μL) was added followed by tetra-*n*-butylammonium fluoride (900 μL of a 1 M solution in tetrahydrofuran, 0.9 mmol). The desilylation reaction was complete in 10 min based on TLC. The mixture was filtered through Celite, the filtrate was evaporated, and the resulting residue was separated by preparative TLC using $CHCl_3$–acetone–methanol (2:2:1) to afford 69 mg of **13** as a colorless solid: $^1$H NMR (DMSO-$d_6$) δ 2.30–2.75 (m, 2 H, H-2′a, H-2′b), 3.50–3.70 (m, 2 H, H-5′a, H-5′b), 3.90 (dd, 1 H, $J_{4',5'a}$ = 2.9 Hz, $J_{4',5'b}$ = 2.6 Hz, H-4′), 4.94 (dd, 1 H, $J_{1',2'a}$ = 7.1 Hz, $J_{1',2'b}$ = 9.7 Hz, H-1′), 7.57 (s, 1 H, H-6).

This material, without further purification or characterization, was dissolved in acetic acid (10 mL) and acetonitrile (10 mL), the solution was cooled to 0 °C, and sodium triacetoxyborohydride (159 mg, 0.75 mmol) was added. The reaction was complete within 10 min at 0 °C based on TLC. The volatiles were removed, and the residue was separated by preparative TLC using $CHCl_3$–methanol (2:1) to yield 65 mg (63%, 3 steps from **8**) of 2′-deoxypseudouridine[11] (1) as a colorless solid which, after recrystallization from ethanol, exhibited mp 219–221 °C (lit.[11e] mp 221–223 °C) and spectrometric data indistinguishable from those exhibited by an authentic sample.

**Pyrazolo[4,3-*d*]pyrimidin-7-one (14).**[32] The following modified procedure leads to better yields than that originally reported.[32] To a solution of ethyl 4-nitropyrazole-3-carboxylate[32] (1.85 g, 10 mmol) in dry methanol (20 mL) was added 10% Pd/C (0.3 g) followed by ammonium formate (4.4 g, 70 mmol). The mixture was stirred under nitrogen at room temperature for 3.5 h at which time TLC analysis indicated that the reaction was complete. The catalyst was removed by filtration through Celite, and the solvent was removed. The resulting crude product was dissolved in 25 mL of 2-ethoxyethanol, and formamidine acetate (3.12 g, 30 mmol) was added. The mixture was heated under reflux under nitrogen for 2 h. The solution was concentrated and cooled, and the resulting solid was separated and suspended in 10 mL of hot water. A 1 N sodium hydroxide solution was added to effect solution. The solution was then treated with charcoal and filtered, and the hot filtrate was acidified with acetic acid and then cooled. Filtration afforded 1.05 g (77%) of **14**[32] as a light brown solid.

**3-Iodopyrazolo[4,3-*d*]pyrimidin-7-one (16).** **14** (1.02 g, 7.5 mmol) and *N*-iodosuccinimide (2.53 g, 11.3 mmol) in DMF (20 mL) was stirred under nitrogen at 60 °C for 5 h. The solvent was then concentrated to about 4 mL, and 20 mL of water was added. The resulting light yellow solid was collected and suspended in 20 mL of hot water. A 1 N aqueous sodium hydroxide solution was added to effect solution; the solution was treated with decolorizing carbon, and the resulting hot filtrate was acidified with acetic acid and cooled to give 1.77 g (90%) of **16** as a light yellow solid: mp >300 °C; $^1$H NMR (DMSO-$d_6$) δ 7.92 (s, 1 H, H-5); $^{13}$C NMR (DMSO-$d_6$) δ 93.25 (C-3), 128.62 (C-7a), 141.82 (C-3a), 143.19 (C-5), 153.22 (C-7); MS *m*/*z* 263 ($MH^+$).

Anal. Calcd for $C_5H_3N_4OI$: C, 22.9; H, 1.15; N, 21.4. Found: C, 23.2; H, 1.15; N, 21.3.

**3-Iodo-1-[(1,1-dimethylethyl)diphenylsilyl]-7-[[(1,1-dimethylethyl)diphenylsilyl]oxy]pyrazolo[4,3-*d*]pyrimidine (18).** (1,1-Dimethylethyl)diphenylsilyl chloride (390 μL, 1.5 mmol) was added to the mixture of **16** (131 mg, 0.5 mmol) and 1,8-dia-

zabicyclo[5.4.0]undecene (224 μL, 1.5 mmol) in acetonitrile (7 mL). The mixture was stirred at 80 °C for 3 h and then cooled. The resulting solid was collected and washed with cold acetonitrile to afford 299 mg (81%) of **18** as a colorless solid: mp 262–265 °C; $^1$H NMR ($CDCl_3$) δ 0.79, 1.19 (2 s, 18 H, $Si(CH_3)_3$), 6.63–6.67, 7.11–7.36 (m, 20 H, phenyl), 8.34 (s, 1 H, H5); $^{13}$C NMR ($CDCl_3$) δ 19.40, 20.65, 26.53, 28.22, 98.77, 127.19, 127.58, 128.52, 129.25, 130.10, 131.57, 132.65, 134.80, 135.03, 151.28, 151.49, 154.76; MS *m/z* 739 ($MH^+$).

Anal. Calcd for $C_{37}H_{39}N_4OISi_2$: C, 60.1; H, 5.32; N, 7.58. Found: C, 59.8; H, 5.22; N, 7.51.

**3-Iodo-1-(tetrahydropyran-2-yl)-7-[(tetrahydropyran-2-yl)oxy]pyrazolo[4,3-*d*]pyrimidine (19).** 3,4-Dihydro-2*H*-pyran (2.3 mL, 25 mmol) was added dropwise to a mixture of **16** (1.11 g, 4.2 mmol) and *p*-toluenesulfonic acid monohydrate (65 mg, 0.3 mmol) in dry DMF (2 mL) and dry ethyl acetate (18 mL). The reaction mixture was stirred under nitrogen at 50 °C until TLC indicated that the reaction was complete (about 2 d). Volatiles were then removed, and the resulting residue was crystallized from methanol–ethyl acetate to give 1.56 g (86%) of a 10:1 mixture of 3-iodo-1- and 3-iodo-2-(tetrahydropyran-2-yl)-7[(tetrahydropyran-2-yl)oxy]pyrazolo[4,3-*d*]pyrimidines as a colorless solid: $^1$H NMR ($CDCl_3$) δ 1.53–2.56 (12 H, tetrahydropyranyl), 3.66–3.76, 4.03–4.21 (4 H, tetrahydropyranyl), 5.85–5.90 (1 H, tetrahydropyranyl), 6.21–6.27 (1 H, tetrahydropyranyl), 8.17, 8.19 (2 s, 1:10 ratio, 1 H, H-5); $^{13}$C NMR ($CDCl_3$) δ 94.53 (C-3), 124.83 (C-7a), 142.55, 142.67 (C-3a, C-5), 151.38 (C-7); two tetrahydropyranyl residues 22.65, 22.84, 24.81, 24.89, 29.27, 32.58, 68.21, 69.50, 81.98, 86.13; MS *m/z* 431 ($MH^+$).

Anal. Calcd for $C_{15}H_{19}N_4O_3I$: C, 41.9; H, 4.45; N, 13.0. Found: C, 41.6; H, 4.21; N, 12.7.

**Palladium-Mediated Coupling of Aglycon Derivative 19 with Glycal 11 (Typical Procedure).** A mixture of bis(dibenzylideneacetone)palladium(0) (29 mg, 0.05 mmol) and triphenylarsine (31 mg, 0.1 mmol) in dry acetonitrile (4 mL) was stirred under nitrogen at room temperature for 20 min. This mixture was then transferred by syringe to a solution of **19** (215 mg, 0.5 mmol), 1,4-anhydro-2-deoxy-3-*O*-[(1,1-dimethylethyl)-diphenylsilyl]-D-*erythro*-1-enitol[25] (**11**) (266 mg, 0.75 mmol), and tri-*n*-butylamine (180 μL, 0.75 mmol) in dry acetonitrile (8 mL). The resulting light yellow solution was stirred under nitrogen at 80 °C for 20 h, at which time TLC indicated that the aglyon derivative **19** 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 (ethyl acetate–hexane, 1:1) to give 204 mg (62%) of (2′*R*)-*cis*-3-[2′,5′-dihydro-4′-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-5′-(hydroxymethyl)-2′-furanyl]-1-(tetrahydropyran-2-yl)-7-[(tetrahydropyran-2-yl)oxy]pyrazolo-[4,3-*d*]pyrimidine (**20**) as a colorless solid, 15 mg (10%) of 1-(tetrahydropyran-2-yl)-7-[(tetrahydropyran-2-yl)oxy]pyrazolo-[4,3-*d*]pyrimidine (**21**) as a colorless solid, and 27 mg (18%) of 1,1′-bis(tetrahydropyran-2-yl)-7,7′-bis[(tetrahydropyran-2-yl)-oxy]-3,3′-bis[pyrazolo[4,3-*d*]pyrimidine] (**22**) as a colorless solid.

For **20**[35] (a mixture of two pairs of diastereoisomers): $^1$H NMR ($CDCl_3$) δ 1.05 (9 H, $C(CH_3)_3$), 1.41–2.52 (12 H, tetrahydropyranyl), 3.58–4.24 (6 H, H-5′s, tetrahydropyranyl), 4.32–4.37 (1 H, H-4′), 4.72–4.82 (1 H, H-2′), 5.83–5.97 (2 H, H-1′, tetrahydropyranyl), 6.10–6.24 (1 H, tetrahydropyranyl), 7.10–7.80 (10 H, phenyl), 8.17–8.21 (4 s, 1 H, H-5); MS *m/z* 657 ($MH^+$).

For **21**:[35] $^1$H NMR ($CDCl_3$) δ 1.55–2.60 (12 H, tetrahydropyranyl), 3.62–3.81, 4.02–4.21 (4 H, tetrahydropyranyl), 5.87–5.95 (1 H, tetrahydropyranyl), 6.22–6.32 (1 H, tetrahydropyranyl), 7.95 (1 H, H-3), 8.11 (1 H, H-5); MS *m/z* 305 ($MH^+$).

For **22**:[35] $^1$H NMR ($CDCl_3$) δ 1.50–2.60 (24 H, tetrahydropyranyl), 3.60–3.80, 4.05–4.21 (8 H, tetrahydropyranyl), 5.89–5.95, 6.27–6.35 (4 H, tetrahydropyranyl), 8.21 (s, 2 H, H-5, H-5′); MS *m/z* 607 ($MH^+$).

**3-(β-D-*glycero*-Pentofuran-3′-ulos-1′-yl)-1-(tetrahydropyran-2-yl)-7-[(tetrahydropyran-2-yl)oxy]pyrazolo[4,3-*d*]pyrimidine (23).** To a solution of **20** (488 mg, 0.74 mmol) in tetrahydrofuran (10 mL) at 0 °C was added acetic acid (180 μL, 3 mmol) followed by 1.5 mL of a 1 M solution of tetra-*n*-butylammonium fluoride in tetrahydrofuran (1.5 mmol). The desilylation reaction was complete in 10 min based on TLC. The volatiles were removed, and the residue was separated by column chromatography (ethyl acetate–hexane, 1.5:1) to afford 295 mg (95%) of **23** (a mixture of two pairs of diastereoisomers) as a colorless solid: $^1$H NMR ($CDCl_3$) δ 1.40–2.46 (12 H, tetrahydropyranyl), 2.86–2.93 (2 H, H-2′s), 3.69–4.20 (7 H, H-4′, H-5′s, tetrahydropyranyl), 5.59–5.69 (1 H, H-1′), 5.85–5.91 (1 H, tetrahydropyranyl), 6.20–6.28 (1 H, tetrahydropyranyl), 8.17–8.20 (4 s, 1 H, H-5); $^{13}$C NMR ($CDCl_3$) δ (all signals multiplets) 44.06 (C-2′), 62.75 (C-5′), 72.92 (C-4′), 81.33 (C-1′), 125.90 (C-7a), 134.49 (C-3a), 142.76 (C-5), 145.61 (C-3), 151.73 (C-7), 213.48 (C-3′), 22.70, 22.81, 24.84, 24.95, 29.55, 32.67, 68.45, 69.49, 82.16, 85.87 (two tetrahydropyranyl resonances); MS *m/z* 419 ($MH^+$).

Anal. Calcd for $C_{20}H_{26}N_4O_6$: C, 57.4; H, 6.26; N, 13.4. Found: C, 57.4; H, 6.36; N, 12.9.

**3-(β-D-*glycero*-Pentofuran-3′-ulos-1′-yl)pyrazolo[4,3-*d*]-pyrimidin-7-one (25).** A mixture of **23** (30 mg, 0.07 mmol) and pyridinium *p*-toluenesulfonate (9 mg, 0.036 mmol) in methanol (4 mL) and water (0.5 mL) was stirred at 50 °C for 2 d. The volatiles were then removed, and the residue was separated by preparative TLC (methanol–ethyl acetate–$CH_2Cl_2$, 1:3:3) to yield 15 mg (84%) of **25** as a colorless solid: mp 234 °C dec; $^1$H NMR (DMSO-$d_6$) δ 2.86–3.11 (dd's, 2 H, $J_{1',2'a}$ = 6.4 Hz, $J_{1',2'b}$ = 10.2 Hz, $J_{2'a,2'b}$ = 17.8 Hz, H-2′s), 3.64 (m, 2 H, H-5′s), 4.07 (t, 1 H, $J_{4',5'a} = J_{4',5'b}$ = 2.7 Hz, H-4′), 5.58 (dd, 1 H, H-1′), 7.86 (s, 1 H, H-5); MS *m/z* 251 ($MH^+$).

Two drops of $D_2O$ was added to a solution of **25** in DMSO-$d_6$; after standing for 2 days at room temperature the $^1$H NMR spectrum obtained exhibited no signals in the region δ 2.8–3.1 assignable to H-2′s and the H-1′ resonance at δ 5.56 now appeared as a singlet; 4.13 (t, 1 H, $J_{4',5'a} = J_{4',5'b}$ = 2.8 Hz, H-4′), 3.73 (m, 2 H, H-5′s), 7.88 (s, 1 H, H-5).

**3-(2′-Deoxy-β-D-ribofuranosyl)-1-(tetrahydropyran-2-yl)-7-[(tetrahydropyran-2-yl)oxy]pyrazolo[4,3-*d*]pyrimidine (26).** To a solution of **23** (100 mg, 0.24 mmol) in acetonitrile (8 mL) and acetic acid (8 mL) at −22 °C was added sodium triacetoxyborohydride (68 mg, 0.32 mmol). The reaction was complete within 40 min based on TLC. Volatiles were then removed, and the resulting residue was separated by preparative TLC (1:3:3, methanol–ethyl acetate–hexane) to give 86 mg (86%) of **26** (a mixture of two pairs of diastereoisomers) as a colorless solid: $^1$H NMR ($CDCl_3$) δ 1.50–2.60 (14 H, H-2′s, tetrahydropyranyl), 3.60–4.23 (7 H, H-4′, H-5′s, tetrahydropyranyl), 4.63–4.71 (1 H, H-3′), 5.50–5.61 (1 H, H-1′), 5.82–5.93 (1 H, tetrahydropyranyl), 6.17–6.30 (1 H, tetrahydropyranyl), 8.14–8.16 (4 s, 1 H, H-5); MS *m/z* 421 ($MH^+$).

When the reduction was carried out at room temperature a second product was isolated: MS *m/z* 423 ($MH^+$); $^1$H NMR ($CDCl_3$) δ 1.40–2.40 (14 H, H-2′s, tetrahydropyranyl), 3.50–4.20 (7 H, H-4′, H-5′s, tetrahydropyranyl), 4.38–4.65 (3 H, H-5s, H-3′), 5.25–5.40, 5.50–5.62 (2 H, H-1′, tetrahydropyranyl), 6.07–6.17 (1 H, tetrahydropyranyl). The addition of two hydrogens, the absence of a resonance near δ 8.15 assignable to H-5 of the pyrazolo[4,3-*d*]pyrimidine aglycon and the appearance of new resonances in the region δ 4.38–4.65 (m, 2 H) permitted the assignment of structure **27**. When **21** was subjected to the reduction conditions at room temperature no reaction occurred.

**3-(2′-Deoxy-β-D-ribofuranosyl)pyrazolo[4,3-*d*]pyrimidin-7-one (2′-Deoxyformycin B, 2).** A mixture of **26** (62 mg, 0.15 mmol) and pyridinium *p*-toluenesulfonate (18 mg, 0.07 mmol) in methanol (4.5 mL) and water (0.5 mL) was maintained at 50 °C for 3 days. The volatiles were then removed, and the resulting residue was separated by preparative TLC (acetone–ethyl acetate–$CHCl_3$, 1.5:1:1) to give 31 mg (83%) of **2** as a colorless solid which, after recrystallization from water, exhibited mp 241 °C dec (lit.[12] 240–243 °C) and was indistinguishable from an authentic sample.

**3-[2′-Deoxy-5′-*O*-[(1,1-dimethylethyl)dimethylsilyl]-β-D-ribofuranosyl]-1-(tetrahydropyran-2-yl)-7-[(tetrahydropyran-2-yl)oxy]pyrazolo[4,3-*d*]pyrimidine (28).** A solution of (1,1-dimethylethyl)dimethylsilyl chloride (80 mg, 0.53 mmol) and imidazole (75 mg, 1.1 mmol) in dry DMF (3 mL) was added to **26** (185 mg, 0.44 mmol) in dry DMF (3 mL) at 0 °C. The mixture was warmed to room temperature and stirred for 12 h. The solvent was removed, and the residue was separated by preparative TLC (ethyl acetate–hexane, 1:2) to afford 187 mg (79%) of **28** (a mixture of two pairs of diastereoisomers) as a colorless solid: $^1$H NMR ($CDCl_3$) δ 0.10 (6 H, Si-Me's), 0.82 (9

H, Si-t-Bu), 1.50–2.60 (14 H, H-2's, tetrahydropyranyl), 3.53–4.21 (7 H, H-4', H-5's, tetrahydropyranyl), 4.52–4.67 (1 H, H-3'), 5.45–5.62 (1 H, H-1'), 5.72–5.90 (1 H, tetrahydropyranyl), 6.10–6.27 (1 H, tetrahydropyranyl), 8.11–8.14 (4 s, 1 H, H-5).

**3-[2'-Deoxy-5'-*O*-[(1,1-dimethylethyl)dimethylsilyl]-3'-*O*-[phenoxy(thiocarbonyl)]-β-D-ribofuranosyl]-1-(tetrahydropyran-2-yl)-7-[(tetrahydropyran-2-yl)oxy]pyrazolo[4,3-*d*]pyrimidine (29).** A solution of **28** (172 mg, 0.32 mmol) and pyridine (0.4 mL) in dry $CH_2Cl_2$ (6 mL) was cooled to 0 °C, and phenoxythiocarbonyl chloride (89 μL, 0.64 mmol) was added. The reaction mixture was stirred under nitrogen at room temperature for 5 h at which time TLC indicated that reaction was complete. $CHCl_3$ was then added, and the mixture was washed with cooled dilute hydrochloric acid followed by water and aqueous sodium bicarbonate. The organic phase was then dried over sodium sulfate, and the volatiles were removed. The resulting residue was separated by preparative TLC (ethyl acetate–hexane, 6:1) to give 201 mg (93%) of **29** (a mixture of two pairs of diastereoisomers) as a colorless oil: $^1$H NMR ($CDCl_3$) δ 0.12 (6 H, Si-Me's), 0.88 (9 H, Si-t-Bu), 1.50–3.21 (14 H, H-2's, tetrahydropyranyl), 3.59–4.48 (7 H, H-4', H-5's, tetrahydropyranyl), 5.44–5.62 (1 H, H-1'), 5.70–6.00 (2 H, H-3', tetrahydropyranyl), 6.20–6.38 (1 H, tetrahydropyranyl), 7.09–7.50 (5 H, phenyl), 8.11–8.17 (4 s, 1 H, H-5).

**3-[2',3'-Dideoxy-5'-*O*-[(1,1-dimethylethyl)dimethylsilyl]-β-D-ribofuranosyl]-1-(tetrahydropyran-2-yl)-7-[(tetrahydropyran-2-yl)oxy]pyrazolo[4,3-*d*]pyrimidine (30).** To a solution of **29** (94 mg, 0.14 mmol) and 2,2'-azobis(2-methylpropionitrile) (18 mg, 0.11 mmol) in dry toluene (5 mL) was added a solution of tri-*n*-butyltin hydride (188 μL, 0.7 mmol) in toluene (1 mL). The reaction mixture was heated at 80 °C for 15 h. The volatiles were then removed, and the residue was separated by preparative TLC (ethyl acetate–$CHCl_3$–hexane, 2:1:4) to afford 63 mg (86%) of **30** (a mixture of two pairs of diastereoisomers) as a colorless solid: $^1$H NMR ($CDCl_3$) δ 0.11 (6 H, Si-Me's), 0.85 (9 H, Si-t-Bu), 1.50–2.70 (16 H, H-2's, H-3's, tetrahydropyranyl), 3.60–4.30 (7 H, H-4', H-5's, tetrahydropyranyl), 5.19–5.34 (1 H, H-1'), 5.84–5.94 (1 H, tetrahydropyranyl), 6.18–6.28 (1 H, tetrahydropyranyl), 8.06–8.09 (4 s, 1 H, H-5).

**3-(2',3'-Dideoxy-β-D-ribofuranosyl)-1-(tetrahydropyran-2-yl)-7-[(tetrahydropyran-2-yl)oxy]pyrazolo[4,3-*d*]pyrimidine (31).** To a solution of **30** (89 mg, 0.17 mmol) in tetrahydrofuran (5 mL) was added a 1 M solution of tetra-*n*-butylammonium fluoride in tetrahydrofuran (0.33 mL, 0.33 mmol). The mixture was stirred at room temperature, and desilylation was complete in 30 min based on TLC. The solvent was removed and the residue was separated by preparative TLC (ethyl acetate–hexane, 1:1) to give 65 mg (94%) of **31** (a mixture of two pairs of diastereoisomers) as a colorless solid: $^1$H NMR ($CDCl_3$) δ 1.50–2.70 (16 H, H-2's, H-3's, tetrahydropyranyl), 3.62–4.30 (7 H, H-4', H-5's, tetrahydropyranyl), 5.16–5.28 (1 H, H-1'), 5.78–5.88 (1 H, tetrahydropyranyl), 6.14-6.25 (1 H, tetrahydropyranyl), 8.09–8.12 (4 s, 1 H, H-5).

**3-(2',3'-Dideoxy-β-D-ribofuranosyl)pyrazolo[4,3-*d*]pyrimidin-7-one (2',3'-Dideoxyformycin B, 3).** A mixture of **31** (41 mg, 0.10 mmol) and pyridinium *p*-toluenesulfonate (12 mg, 0.048 mmol) in methanol (4.5 mL) and water (0.5 mL) was stirred at 50 °C for 2 d. Volatiles were then removed, and the residue was separated by preparative TLC (1:1:1 acetone–ethyl acetate–$CH_2Cl_2$) to yield 21 mg (88%) of **3** as a colorless solid: $^1$H NMR (DMSO-$d_6$) δ 1.95–2.39 (m, 4 H, H-2's, H-3's), 3.40, 3.56 (dd's, 2H, $J_{4',5'a}$ = 4.4 Hz, $J_{4',5'b}$ = 3.9 Hz, $J_{5'a,5'b}$ = 11.5 Hz, H-5's), 4.01–4.12 (m, 1 H, H-4'), 5.13 (dd, 1 H, $J_{1',2'a}$ = 6.3 Hz, $J_{1',2'b}$ = 8.1 Hz, H-1'), 7.86 (s, 1 H, H-5); $^{13}$C NMR (DMSO-$d_6$) δ 27.94, 31.26 (C-2', C-3'), 64.27 (C-5'), 74.39, 80.16 (C-1', C-4'), 126.15 (C-7a), 136.24 (C-3a), 144.01, 144.61 (C-3, C-5), 155.70 (C-7); HRMS calcd for $C_{10}H_{12}N_4O_3$ + $H^+$ 237.0985, found 237.0990.

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# Synthesis of γ- and δ-Lactones by Free-Radical Annelation of *Se*-Phenyl Selenocarbonates

Mario D. Bachi* and Eric Bosch

*Department of Organic Chemistry, The Weizmann Institute Of Science, Rehovot 76100, Israel*

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A general method for the synthesis of γ- and δ-lactones through the intramolecular addition of alkoxycarbonyl radicals, formed by reaction of *Se*-phenylselenocarbonates with *n*-$Bu_3SnH$, onto carbon–carbon multiple bonds is described. This free-radical cyclization is characterized by high regioselectivity favoring exo addition and by a high ratio of cyclization to reduction. Monocyclic, fused bicyclic, and spirocyclic lactones are formed in good to excellent yield. Use of allyltri-*n*-butyltin as a chain-transfer agent in the place of *n*-$Bu_3SnH$ affords the corresponding 3-butenyl lactones.

The recent advances in synthetic free-radical chemistry are largely due to an increased understanding, and subsequent synthetic application, of the factors affecting the selectivity of free-radical reactions.[1,2] The reaction of

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