for $C_{14}H_7N_2F_9$: C, 44.94; H, 1.89; N, 7.49. Found: C, 45.66; H, 1.70; N, 7.68.

Preparation of 5a. **3a** (0.65 g, 1.6 mmol), sodium carbonate (0.50 g, 4.7 mmol), and 1,4-dioxane (5 mL) were placed in a 50-mL flask and heated at 100 °C with stirring until **3a** could not be detected by GLC (it required one day). The salts were filtered off, and the solvent was removed. The concentrate was distilled under reduced pressure to give white granules, which were purified by silica gel chromatography (hexane) and recrystallization from hexane (0.22 g, 43%): mp 74.6–77.7 °C; ^{1}H NMR ($CDCl_3$) δ 7.28–7.67 (5 + 1 H, m); ^{19}F NMR ($CDCl_3$) 57.4 ppm (6 F, dtq, J_{FF} = 13.3, 9.6, 2.4 Hz), 84.0 (6 F, q, J_{FF} = 2.4 Hz), 112.6 (4 F, qd, J_{FF} = 9.6 Hz, J_{HF} = 7.5 Hz), 120.2 (2 F, q, J_{FF} = 13.3 Hz); mass spectrum, m/e 632 (M^+), 361 ($C_{13}H_6N_2F_9^+$); IR 1620, 1510 cm^{-1}. Anal. Calcd for $C_{19}H_6N_4F_{18}$: C, 36.09; H, 0.96; N, 8.86. Found: C, 36.06; H, 0.77; N, 8.97.

Preparation of 5b. The technique used in this preparation and purification was the same as that for **5a**. Treatment of **3b** (1.00 g, 2.4 mmol) with sodium carbonate (1.28 g, 12.1 mmol) gave white granules (0.17 g, 22%): mp 63.6–66.6 °C; ^{1}H NMR ($CDCl_3$) δ 6.87–7.00 (2 H, m), 7.44–7.60 (3 H, m); ^{19}F NMR ($CDCl_3$) 57.5 ppm (6 F, dt, J_{FF} = 14.1, 9.2 Hz), 84.0 (6 F, s), 112.2 (4 F, q, J_{FF} = 9.2 Hz), 113.4 (2 F, q, J_{FF} = 14.1 Hz); mass spectrum, m/e 646 (M^+), 631 ($M^+ - CH_3$), 375 ($C_{14}H_8N_2F_9^+$); IR 1620, 1510 cm^{-1}. Anal. Calcd for $C_{20}H_8N_4F_{18}$: C, 37.17; H, 1.25; N, 8.67. Found: C, 37.15; H, 1.02; N, 8.81.

Preparation of 6a. Methanol (3 mL) was placed in a 30-mL flask, and sodium metal (11 mg, 0.48 mmol) was dissolved in it with stirring. A solution of **5a** (100 mg, 0.16 mmol) in methanol (2 mL) was added dropwise at room temperature until **5a** was consumed and not detected by GLC (about 3 h). The solution was neutralized with 10% aqueous HCl. The product was extracted with benzene and purified by silica gel chromatography (hexane) and recrystallized from hexane to give white granules (82 mg, 79%): mp 68.2–73.0 °C; ^{1}H NMR ($CDCl_3$) δ 3.91 (6 H, s), 7.25–7.54 (5 H, m), 7.70 (1 H, s); ^{19}F NMR ($CDCl_3$) 55.5 ppm (6 F, t, J_{FF} = 10.8 Hz), 83.9 (6 F, s), 112.0 (4 F, q, J_{FF} = 10.8 Hz); mass spectrum, m/e 656 (M^+), 373 ($C_{14}H_9N_2OF_8^+$); IR 1590, 1520 cm^{-1}. Anal. Calcd for $C_{21}H_{12}N_4O_2F_{16}$: C, 38.43; H, 1.84; N, 8.54. Found: C, 38.48; H, 1.53; N, 8.66.

Preparation of 6b. Treatment of **5b** (100 mg, 0.15 mmol) with sodium methoxide (sodium metal 11 mg, 0.48 mmol) by the same procedure as that for **6a** gave white granules (86 mg, 83%): mp 102.4–104.3 °C; ^{1}H NMR ($CDCl_3$) δ 2.63 (3 H, s), 3.55 (6 H, s), 6.88–7.08 (2 H, m), 7.35–7.52 (3 H, m); ^{19}F NMR ($CDCl_3$) 55.6 ppm (6 F, t, J_{FF} = 10.9 Hz), 83.8 (6 F, s), 111.6 (4 F, q, J_{FF} = 10.9 Hz); mass spectrum, m/e 670 (M^+), 655 ($M^+ - CH_3$), 387 ($C_{15}H_{11}N_2OF_8^+$); IR 1590, 1570, 1520 cm^{-1}. Anal. Calcd for $C_{22}H_{14}N_4O_2F_{16}$: C, 39.42; H, 2.11; N, 8.36. Found: C, 39.53; H, 1.84; N, 8.33.

Registry No. 1, 1584-03-8; **2a**, 5281-18-5; **2b**, 13466-30-3; **3a**, 97674-42-5; **3b**, 97674-43-6; **4a**, 97674-44-7; **4b**, 97674-45-8; **4c**, 97674-46-9; **5a**, 97674-47-0; **5b**, 97674-48-1; **6a**, 97674-49-2; **6b**, 97674-50-5.

Pd(0)-Catalyzed C-Glycosylation: A Facile Alkylation of Trifluoroacetylglucal[1]

T. V. RajanBabu

Central Research & Development Department, E328/208, Experimental Station, E. I. du Pont de Nemours & Co., Wilmington, Delaware 19898

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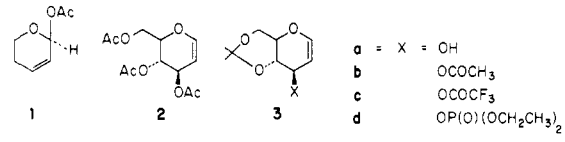
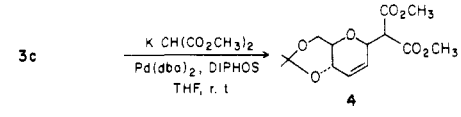
C-Glycosides are an important class of compounds receiving increasing attention from synthetic organic chemists recently.[2] The high stereochemical control accompanying transition-metal-mediated transformations[3] has prompted several groups[4-6] to employ such methods for C-glycosylations. Coupling of organomercury compounds with carbohydrate-derived enol ethers in the presence of stoichiometric amount of $Pd(OAc)_2$ has been reported.[4] Also a few β-dicarbonyl compounds in the presence of $Pd(CH_3CN)_2Cl_2$ and $BF_3{\cdot}Et_2O$ are known to add to various acylated glycals.[5] However, various other carbanions derived from, for example, dimethyl malonate and cyclohexane-1,3-dione fail to undergo this reaction. A Pd(0)-catalyzed reaction of acetoxydihydropyran **1** with tertiary carbanions like diethyl sodioformamidomalonate has been reported to proceed under more drastic (70 °C, 18 h, DMF) conditions.[6]



1 2 3

Conspicuously absent in these studies is the Pd(0)-catalyzed addition of the more useful malonate type carbon nucleophiles to glycals like **2** or **3**. The apparent lack of reactivity of electron-rich allylic acetates having oxygen conjugation has been observed before, and it is not surprising that further activation with Lewis acids[5] (for example $BF_3{\cdot}Et_2O$), and/or higher temperatures[6,7] are needed for the alkylation of these substrates. *Here we report a general solution to the problem by appropriately choosing the leaving group and the catalyst.* This is illustrated in a new C-glycosylation reaction via Pd(0)-catalyzed addition of stabilized carbon nucleophiles to a trifluoroacetylglucal.

We find that 4,6-isopropylidene-3-(trifluoroacetyl)-D-glucal **3c** reacts with potassium dimethyl malonate in the presence of 2–5 mol % bis(dibenzylideneacetone)–Pd(0) and bis(diphenylphosphino)ethane[8] to give **4** in 56% yield.



4

Reaction of the corresponding acetate **3b** or the phosphate[9] **3d** failed to yield any addition products even under conditions recommended[7] for relatively unreactive substrates. Triacetylglucal **2** was similarly recovered unchanged after heating for 7 h in toluene at 100 °C in the presence of $(Ph_3P)_4Pd$, DBU, and dimethyl malonate.

In the formation of **4** the reaction proceeds with remarkable stereospecificity as expected by the double inversion mechanism usually associated with these types of reactions.[3] The high-field (360 MHz) ^{1}H NMR spectra of the adducts are completely consistent with the assigned

(1) Contribution 3668 from Central Research & Development Department.

(2) See, for example: Lewis, M. D.; Cha, J. K.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 4976. Reed, L. A.; Ito, Y.; Masamune, S.; Sharpless, K. B. *J. Am. Chem. Soc.* **1982**, *104*, 6468 and references cited therein. Giese, B.; Dupuis, J. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 622.

(3) For examples in the Pd-catalyzed reactions, see: Tsuji, J. "Organic Synthesis with Pd Compounds"; Springer-Verlag: West Berlin, 1980. Trost, B. M. *Tetrahedron* **1977**, *33*, 2615. Heck, R. *Acc. Chem. Res.* **1979**, *12*, 146.

(4) (a) Hacksell, U.; Daves, G. D., Jr. *J. Org. Chem.* **1983**, *48*, 2870 and references cited therein. (b) Czernecki, S.; Gruy, F. *Tetrahedron Lett.* **1981**, *22*, 437. (c) See also ref 6 for a related reaction.

(5) Yougai, S.; Miwa, T. *J. Chem. Soc., Chem. Commun.* **1983**, 68.

(6) Dunkerton, L. V.; Serino, A. J. *J. Org. Chem.* **1982**, *47*, 2812.

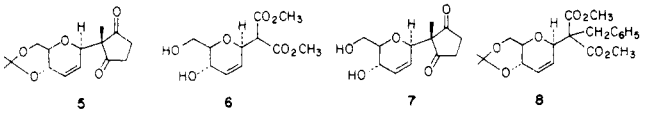
(7) Trost, B. M.; Gowland, F. W. *J. Org. Chem.* **1979**, *44*, 3448 and ref 3.

(8) Fiaud, J. C.; Malleron, J. L. Tetrahedron Lett. **1980**, *21*, 4437.

(9) Tanigawa, Y.; Nishimura, K.; Kawasaki, A.; Murahashi, S. I. *Tetrahedron Lett.* **1982**, *23*, 5549.

0022-3263/85/1950-3642$01.50/0

β-configuration of the anomeric carbon. In addition to the expected coupling patterns, $J_{4,5}$, characteristic of the conformationally stable β-anomer with all groups in the quasi-equatorial position, is 10 Hz in **4** and 8 Hz each in **5** and **7**.[10] The confirmation of these assignments come



5 **6** **7** **8**

from difference nuclear Overhauser effect (NOE) spectra of **4** and **7**. Upon irradiation of H_1 (δ 4.90) significant (~15%) enhancement of the H_5 signal (δ 3.45) is observed in **4**. An amplitude enhancement of similar magnitude is observed for the H_1 signal upon irradiation of H_5. Similarly, in **7**, prepared by the hydrolysis of **5**, irradiation of either H_1 or H_5 shows significant NOE on each other's resonance. In these cases such enhancements are possible only if H_1 and H_5 both are α. Mechanistic rationale[3] together with these experiments conclusively prove the stereochemical assignments. The reaction is also regiospecific, and capture of the malonate anion at C-3 was not observed. In the absence of Pd(0), the reaction does not proceed even at higher temperatures, thus confirming the role of the catalyst and ruling out the intermediacy of a stabilized glucal carbonium ion formed by an uncatalyzed dissociation of the trifluoroacetate.

Potassium salt of 2-methyl cyclopentane-1,3-dione, a more hindered, relatively unreactive carbanion, also undergoes a regio- and stereospecific addition to give a single compound **5**. Both **4** and **5** can be converted into the corresponding free sugars **6** and **7**, respectively, without isomerization at the anomeric center by acidic hydrolysis of the acetonide.

The C-3 isomeric trifluoroacetate, 3-(trifluoroacetyl)-4,6-*O*-benzylidene-1,2-dideoxy-D-*ribo*-hex-1-enopyranoside[11] is remarkably more unstable than **3c** and failed to undergo addition reactions under a variety of conditions.

Finally, adducts of the type of **4** are useful for further elaboration of the side chain as illustrated by the benzylation of its potassium salt to give **8**. It should be noted that the products **4–8** carry sufficient latent functionality for the reconstruction of a variety of pyranose sugars.

Experimental Section

Infrared spectra were determined on a Perkin-Elmer Model 21 double-beam Acculab 8 or Nicolet Model 7199 FT spectrometer. NMR spectra were obtained on a Varian EM-390, IBM NR 80, or Nicolet 360WB spectrometer and were recorded in $CDCl_3$ with tetramethylsilane as the standard. All reagents and solvents except the Pd(0) catalysts and DIPHOS were purified prior to use, and reactions were carried out under nitrogen. The catalysts and DIPHOS were purchased from Aldrich Chemical Co. Unless otherwise indicated all chromatographic separations were done on silica gel support.

3-(Trifluoroacetyl)-1,2-dideoxy-4,6-*O*-isopropylidene-D-*arabino*-hex-1-enopyranose (3c). A flame-dried 100-mL flask was charged with 3.45 g (18.55 mmol) of 1,2-dideoxy-4,6-*O*-isopropylidene-D-*arabino*-hex-1-enopyranose (**3a**),[12] 2.27 mL (19.50 mmol) of 2,6-lutidine, and 0.23 g (1.95 mmol) of (dimethylamino)pyridine in 60 mL of dry methylene chloride. The mixture was cooled to 0 °C, and from a syringe was added 2.75 mL (19.50 mmol) of distilled trifluoroacetic anhydride. As soon as the addition was complete, the cold bath was removed, and the mixture was stirred for 15 min. TLC (30% ethyl acetate/hexane) showed complete conversion to **3c**. Water (40 mL) was added, and the methylene chloride layer was separated. The aqueous layer was extracted further with methylene chloride (50 mL × 3). The combined organic layer was washed with saturated potassium hydrogen phosphate (30 mL × 2) and water (30 mL). The organic layer was dried and concentrated to get 4.68 g (96%) of the trifluoroacetate **3c**, which was used for the next step without further purification: ^1H NMR (80 MHz) δ 1.43 (s, 3 H), 1.53 (s, 3 H), 3.60–4.40 (m, 4 H) 4.73 (d, d, J = 5, 2 Hz, 1 H), 5.57 (d, t, J = 6.7, 2 Hz, 1 H), 6.43 (d, d, J = 5, 1 Hz, 1 H).

Reaction of 3c with the Potassium Salt of Dimethyl Malonate in the Presence of Bis(dibenzylideneacetone)-Pd(0) (Pd(dba)$_2$). To a suspension of 0.804 g (20.05 mmol) of mineral oil free potassium hydride in 50 mL of anhydrous THF was added 2.276 mL (20 mmol) of dimethyl malonate dropwise at 0 °C. The mixture was stirred for 2 h at 0 °C and was transferred via a cannula into a solution of 4.350 g (16.60 mmol) of **3c**, 0.254 g (0.440 mmol) of Pd(dba)$_2$, and 0.162 g (0.407 mmol) of DIPHOS. The reaction was stirred until no more **3c** was visible on TLC (1:1 ethyl acetate/hexane). Saturated potassium hydrogen phosphate (20 mL) and water (10 mL) were added, and the product was extracted into methylene chloride. Concentration and flash chromatography[13] (1:1 ethyl acetate/hexane on silica) yielded 2.39 g (56%) of **4** in addition to 0.643 g of starting alcohol: $[\alpha]_D$ 43.4 ± 0.8° C 1, $CDCl_3$); IR (neat) 2990, 2950, 1750, 1740 cm^{-1}; ^1H NMR (360 MHz) δ 1.41 (s, 3 H, CH_3C), 1.51 (s, 3 H, CH_3C), 3.45 (ddd, $J_{4,5}$ = 10 Hz, $J_{5,6a}$ = 8 Hz, $J_{5,6e}$ = 5 Hz, H_5, 1 H), 3.53 (d, $J_{1,7}$ = 7 Hz, $HC(CO_2CH_3)_2$, H_7, 1 H), 3.75 (1 H, multiplicity unclear, H_{6a}, 1 H), 3.75 (s, OCH_3, 3 H), 3.76 (s, 3 H, OCH_3, 3 H), 3.87 (dd, $J_{6a,e}$ = 10 Hz, H_{6e}, 1 H), 4.20 (dm, H_4, 1 H), 4.90 (d, m, H_1, 1 H), 5.79 (ddd, $J_{2,3}$ = 10 Hz, $J_{1,2}$ = 3 Hz, $J_{2,4}$ = 2 Hz, H_2, 1 H), 5.95 (d br, 1 H, H_3) [assignments and coupling constants established by double irradiation and NOE experiments, see text]; ^{13}C NMR δ 18.95, 29.05, 52.50, 52.55, 56.44, 62.80, 66.94, 71.89, 73.83, 99.61, 127.09, 129.46, 166.72, 166.96; HRMS, 285.0962 (M^+ · – CH_3; calcd for $C_{13}H_{17}O_7$ 285.0974), 242.0791 (M^+ · – acetone; calcd 242.0790).

Reaction of 3c with the Potassium Salt of 2-Methylcyclopentane-1,3-dione. To a suspension of 0.377 g (9.4 mmol) of KH in 20 mL of THF was added 1.26 mL (11.02 mmol) of 2-methylcyclopentane-1,3-dione. When the gas evolution ceased, 5 mL of DMF and 10 mL of dry CH_3CN were added followed by 0.239 g (0.60 mmol) of DIPHOS and 0.275 g (0.48 mmol) of Pd(dba)$_2$. To the above mixture was added 2.62 g (10 mmol) of **3c**, and the mixture was stirred for 2 h at room temperature. The reaction was essentially complete. Saturated ammonium chloride (50 mL) was added, and the product was extracted into ether (200 mL × 4). The organic fraction was dried, concentrated, and chromatographed on silica with 30% ethyl acetate in hexane as the solvent to get 1.76 g (63%) of the product: $[\alpha]_D$ −28.5 ± 0.4° (c 2, $CDCl_3$); IR (neat) 1725, 1640 cm^{-1}; ^1H NMR (360 MHz) δ 1.10 (s, CH_3C, 3 H), 1.38 (s, CH_3C, 3 H), 1.47 (s, CH_3C, 3 H), 2.60–2.80 (m, CH_2CH_2, 4 H), 3.30 (ddd, $J_{5,6a}$ = 10 Hz, $J_{5,6e}$ = 5 Hz, $J_{4,5}$ = 8 Hz, H_5, 1 H), 3.60 (dd, $J_{6a,6e}$ = 10 Hz, $J_{6a,5}$ = 10 Hz, H_{6a}, 1 H), 3.81 (dd, H_{6e}, 1 H), 4.10 (dm, $J_{4,5}$ = 8 Hz, H_4, 1 H), 4.48 (m, H_1, 1 H), 5.79 (ddd, $J_{1,2}$ = 2 Hz, $J_{2,3}$ = 11 Hz, $J_{2,4}$ = 2 Hz, H_2, 1 H), 5.96 (d br, H_3, 1 H); ^{13}C NMR δ 14.97, 18.98, 29.08, 36.14, 36.50, 57.97, 62.75, 66.95, 71.83, 80.73, 99.77, 124.65, 130.19, 214.54, 215.86; HRMS, 280.1326 (M^+; calcd for $C_{15}H_{20}O_5$ 280.1315), 265.1062 (M^+ · – CH_3; calcd for $C_{14}H_{17}O_5$ 265.1076).

Reaction of 3c with Potassium Dimethyl Malonate in the Absence of Pd(0) Catalyst. A mixture of 0.322 g (1.14 mmol) of **3c** and 0.170 g (1.56 mmol) of potassium dimethyl malonate in 10 mL of THF was refluxed for 3 days, and the products were isolated. No trace of alkylation product **4** was recovered. However, 0.184 g (65%) of alcohol resulting from hydrolysis of the trifluoroacetate was isolated by column chromatography.

Attempted Alkylation of Triacetylglucal (2). The reaction of triacetylglucal with dimethyl malonate was carried out according

(10) (a) For several examples of such assignments, see: Achmatowicz, O.; Burkowski, P. *Rocz. Chem.* **1973**, *47*, 99. (b) Fraser-Reid, B.; Dawe, R. D.; Tulshian, D. B. *Can. J. Chem.* **1979**, *57*, 1746. See also: Dawe, R. D.; Froser-Reid, B. *J. Org. Chem.* **1984**, *49*, 522. (c) Herscovici, J.; Muleka, K.; Antonakis, K. *Tetrahedron Lett.* **1984**, *25*, 5653.

(11) For the preparation of the corresponding alcohol, see: Tsuda, N.; Yokota, S.; Kudo, T.; Mitsunobu, O. *Chem. Lett.* **1983**, 289.

(12) Fraser-Reid, B.; Walker, D. L.; Tam, S. Y.-K.; Holder, N. L. *Can. J. Chem.* **1973**, *51*, 3950.

(13) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

to a procedure recommended for relatively unreactive allyl acetate.[7] A mixture of 1.36 g (5 mmol) of **2**, 0.76 mL (5 mmol) of dimethyl malonate, 0.40 mL (2.6 mmol) of DBU, and 0.490 g (0.42 mmol) of $Pd(Ph_3P)_4$ in 13 mL of toluene was stirred at room temperature for 18 h and was further maintained at 100 °C for 7 h. High-resolution NMR spectrum of the crude product and TLC revealed no incorporation of malonate into the sugar residue. Unconverted starting material was recovered mostly intact.

The reaction was repeated under modified conditions reported in this paper as follows: to 1.2 g (4.41 mmol) of triacetylglucal, 0.0376 g (0.065 mmol) of $Pd(dba)_2$, and 0.026 g of DIPHOS in 5 mL of THF was added 0.83 g (4.88 mmol) of potassium dimethyl malonate in 10 mL of THF. The mixture was stirred at room temperature for 3 days and further refluxed for 12 h. TLC revealed only unconverted starting material.

3-Acetyl-1,2-dideoxy-4,6-*O*-isopropylidene-D-*arabino*-hex-1-enopyranose (3b). The acetoxy derivative **3b** was prepared according to the procedure reported above for **3c** except substituting acetic anhydride for trifluoroacetic anhydride. Chromatography on silica gave the pure compound: ^1H NMR (80 MHz) δ 1.40 (s, 3 H), 1.50 (s, 3 H), 2.07 (s, 3 H), 3.87 (m, 4 H), 4.73 (dd, J = 6, 2 Hz, 1 H), 5.33 (d, J = 7 Hz, 1 H), 6.33 (dd, J = 6, 2 Hz, 1 H); HRMS, 228.0981 (M^+·; calcd for $C_{11}H_{16}O_5$ 228.0997).

Attempted Alkylation of 3b. Potassium salt of dimethyl malonate was prepared from 0.20 g (4.98 mmol) of potassium hydride and 0.65 mL (12.7 mmol) of dimethyl malonate in 10 mL of anhydrous THF, and this solution was added to 0.628 g (2.71 mmol) of **3b** dissolved in 5 mL of THF. To this were added 0.0376 g of $Pd(dba)_2$ and 0.026 g of DIPHOS. The mixture was stirred for 3 days at room temperature and subsequently was refluxed for 12 h. The reaction was worked up, and the product was analyzed by TLC and high-resolution ^1H NMR. No trace of coupling product **4** was detected.

Preparation and Attempted Pd(0)-Catalyzed Alkylation of the Phosphate 3d. The diethyl phosphate **3d** was prepared by treating the alcohol **2** with diethyl chlorophosphate in the presence of triethylamine and (dimethylamino)pyridine in methylene chloride. A mixture of 0.464 g (1.44 mmol) of **3d**, 0.166 g (0.144 mmol) of $Pd(Ph_3P)_4$, and 0.244 g (1.43 mmol) of potassium dimethyl malonate in 10 mL of THF was stirred at room temperature for 2 days. No alkylation products were detected by comparison of TLC's of this reaction mixture with those of an authentic sample of **4**.

Hydrolysis of 4 and 5. A solution of 0.73 g of **4** in 2 mL of THF and 1 mL of methanol was stirred with 1 mL of 2 N HCl for 3 h. Methylene chloride (30 mL) and 10 mL of saturated sodium bicarbonate were added, and the organic layer was separated. Further extraction with methylene chloride, drying, and concentration yielded an oil, which was purified by column chromatography (3% methanol/CH_2Cl_2, silica) to get 0.55 g (88%) of **6**: $[\alpha]_D$ 50.1 ± 0.4° (*c* 2 $CDCl_3$); IR (neat) 3200–3550 (br), 1730 cm^{-1}; ^1H NMR (360 MHz) δ 3.39 (m br, H_5 and OH, 2 H), 3.55 (d, $J_{1,7}$ = 8 Hz, $HC(CO_2Me)_2$, 1 H), 3.75 (s, 3 H), 3.76 (s, 3 H), 3.70–3.80 (m br, $H_{6,6}$ and OH, 3 H), 4.15 (d br, $J_{4,5}$ = 7 Hz, H_4, 1 H), 4.77 (dm, $J_{1,7}$ = 8 Hz, H_1, 1 H), 5.78–5.95 (m, $H_{2,3}$, 2 H); ^{13}C NMR δ 52.69, 52.73, 56.49, 62.60, 63.38, 72.76, 78.82, 127.30, 131.30, 166.94, 167.33; HRMS, 211.0596 (M^+· – (CH_3O + H_2O); calcd for $C_{10}H_{11}O_5$ 211.0607).

With the identical procedure, **7** was prepared from **5** in 77% yield: $[\alpha]_D$ –19.2 ± 0.8° (c 1 $CDCl_3$); IR (KBr) 3250–3330 (br), 1724 cm^{-1}; ^1H NMR (360 MHz) δ 1.10 (s, CH_3, 3 H), 2.20–2.40 (s br, OH, 1 H), 2.40–2.60 (s br, OH, 1 H), 3.33 (ddd, $J_{4,5}$ = 8 Hz, $J_{5,6a}$ = 4 Hz, $J_{5,6e}$ = 4 Hz, H_5, 1 H), 3.65–3.80 (m, H_6, 2 H), 4.10 (d, m $J_{4,5}$ = 8 Hz, H_4, 1 H), 4.37 (s br, H_1, 1 H), 5.87–5.97 (m, $H_{2,3}$, 2 H) [assignments and coupling constants established by double irradiation and NOE experiments]; ^{13}C NMR δ 14.58, 36.32, 36.51, 58.41, 62.85, 63.64, 78.96, 79.54, 124.84, 131.98, 214.70, 216.48; HRMS, 240.1007 (M^+·; calcd for $C_{12}H_{16}O_5$ 240.0997).

Benzylation of 4 to 8. To a suspension of 0.017 g (0.45 mmol) of potassium hydride in 2 mL of THF was added 0.136 g (0.45 mmol) of **4** dissolved in 2 mL of THF at 0 °C. The mixture was stirred for 30 min, and 0.072 mL (0.60 mmol) of benzyl bromide was added dropwise from a syringe. The mixture was warmed to room temperature and further stirred for 2 h. Saturated potassium hydrogen phosphate (10 mL) was added, and the product was extracted into methylene chloride. Concentration and isolation by preparative TLC yielded 0.092 g (52%) of **8**: IR (neat) 3080, 3060, 1735, 1605, 1585, 1500, 1200–1100 cm^{-1}; ^1H NMR (360 MHz) δ 1.42 (s, CH_3C, 3 H), 1.52 (s, CH_3C, 3 H), 3.19 (d, J = 14 Hz, PhC*H*, 1 H), 3.43 (ddd, $J_{5,6a}$ = 10 Hz, $J_{4,5}$ = 8 Hz, $J_{5,6e}$ = 5 Hz, H_5, 1 H), 3.60 (d, J = 14 Hz, PhC*H*, 1 H), 3.67 (s, OCH_3, 3 H), 3.70 (s, OCH_3, 3 H), 3.84 (dd, $J_{6a,6e}$ = 10 Hz, $J_{6a,5}$ = 10 Hz, H_{6a}, 1 H), 3.96 (dd, J = 10, 5 Hz, H_{6e}, 1 H), 4.10 (d, m, $J_{4,5}$ = 8 Hz, H_4, 1 H), 4.58 (m, 1 H, H_1), 5.81 (d, $J_{2,3}$ = 10 Hz, H_2, 1 H), 5.96 (ddd, $J_{1,3}$ = $J_{3,4}$ = 2 Hz, H_3, 1 H), 7.12 (m, Ar, 2 H), 7.25 (m, Ar, 3 H); HRMS, 390.1681 (M^+·; calcd for $C_{21}H_{26}O_7$ 390.1678).

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Registry No. **2**, 2873-29-2; **3a**, 51450-36-3; **3b**, 97747-17-6; **3c**, 97689-89-9; **3d**, 97689-91-3; **4**, 97689-95-7; **5**, 97689-90-2; **6**, 97689-92-4; **7**, 97689-93-5; **8**, 97689-94-6; DIPHOS, 1663-45-2; $Pd(dba)_2$, 32005-36-0; $Pd(Ph_3P)_4$, 14221-01-3; dimethyl malonate, 108-59-8; 2-methylcyclopentane-1,3-dione, 765-69-5; diethyl chlorophosphate, 814-49-3; potassium dimethyl malonate, 61111-62-4; benzyl bromide, 100-39-0.

Fluorocarbohydrates in Synthesis. An Efficient Synthesis of 1-(2-Deoxy-2-fluoro-β-D-arabinofuranosyl)-5-iodouracil (β-FIAU) and 1-(2-Deoxy-2-fluoro-β-D-arabinofuranosyl)thymine (β-FMAU)

Chou H. Tann,*[1] Paul R. Brodfuehrer, Steven P. Brundidge, Chester Sapino, Jr., and Henry G. Howell*[2]

Chemical Process Development, Bristol-Myers Pharmaceutical Research and Development Division, Syracuse, New York 13221-4755

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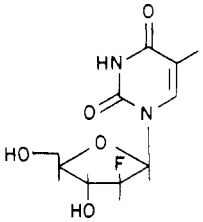
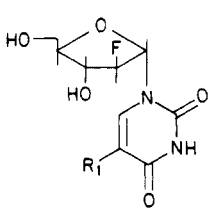
Recent literature[3,4] has indicated an interest in the preparation of nucleosides with antiviral and anticancer properties. The potent antiviral activity of 1-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-5-iodouracil (β-FIAU; **1a**, R_1 = I) and 1-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)thymine (β-FMAU; **2a**, R_1 = CH_3) made these compounds candidates for further synthetic development.



1a, R_1 = I
2a, R_1 = CH_3



1b, R_1 = I
2b, R_1 = CH_3

Results and Discussion

The most direct synthetic plan to reach **1a** and **2a** required the access to the fluorodeoxy sugar **6**. The latter would be accessible via an appropriately blocked riboside

(1) Present address: Schering Corporation, U-5A, Union, NJ 07083.
(2) Author to whom correspondence should be directed.
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