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Synthesis and Reactions of Some Uracil and 5-Halouracil Nucleosides of 2-Acetamido-2-deoxy-D-glucose

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Silylated uracils react with 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-D-glucose (**5**) under trimethylsilyl trifluoromethanesulfonate catalysis to give the nucleosides **6**, **8**, **10** and **12**, respectively, as well as the diglycoside **14**. Deblocking with sodium methoxide in methanol afforded the free nucleosides **7**, **9**, **11** and **13**, respectively. Alternatively, the free nucleosides **11** and **13** were obtained directly by halogenation of **7** with *N*-bromosuccinimide or iodine monochloride, respectively. The structures of the synthesized compounds were confirmed by their ^{1}H NMR, UV and mass spectra and elemental analyses.

Modified nucleosides have been used among other compounds as broad spectrum antiviral, antibacterial or antitumor agents.[1] Several 5-halouracil nucleosides of chemical and biochemical interest[2] have been investigated extensively as antineoplastic and antiviral agents.[3] Some 5-chlorouracil nucleosides, which are less cytotoxic, exhibit selective anti-HIV activity.[4] 5-Fluoro-2′-deoxyuridine exhibits antileukemic activity, while its 5′-phosphate (FDUMP) is a potent inhibitor of the enzyme thymidylate synthase, and an active antitumor and antifungal agent.[5–7] On the other hand, 5-fluoro-2-thio-2′-deoxyuridine (S^4FDUMP) and its 2-thiocytosine analogue[8] proved to be effective inhibitors of proliferation of several mammalian tumor cell lines.[9] Ollapally *et al.*[10] have recently reported antiviral and *in vitro* antineoplastic activities of some keto unsaturated nucleosides of L-rhamnose carrying 6-azauracil and 5-fluorouracil. Some iodo analogues have been proved to be effective against viral infections, for example 5-iodo-2′-deoxyuridine (IDDU)[11] and the new, promising antiherpetic agent (2*S*′)-2′-methyl-5-iodouridine (SMIU).[12] In addition, halogenated nucleosides have also been used as synthons for the synthesis of many biologically active nucleosides.[13–18] We report now the synthesis of a new type of 5-halouracil nucleosides carrying a 2-acetamido-2-deoxy-D-glucosyl moiety at N-1 as promising antiviral, antimutagenic, antineoplastic agents or enzyme inhibitors. There is broad biochemical interest in D-glucosamine[19–21] and 5-fluorouracil itself possesses antileukemic properties.[22]

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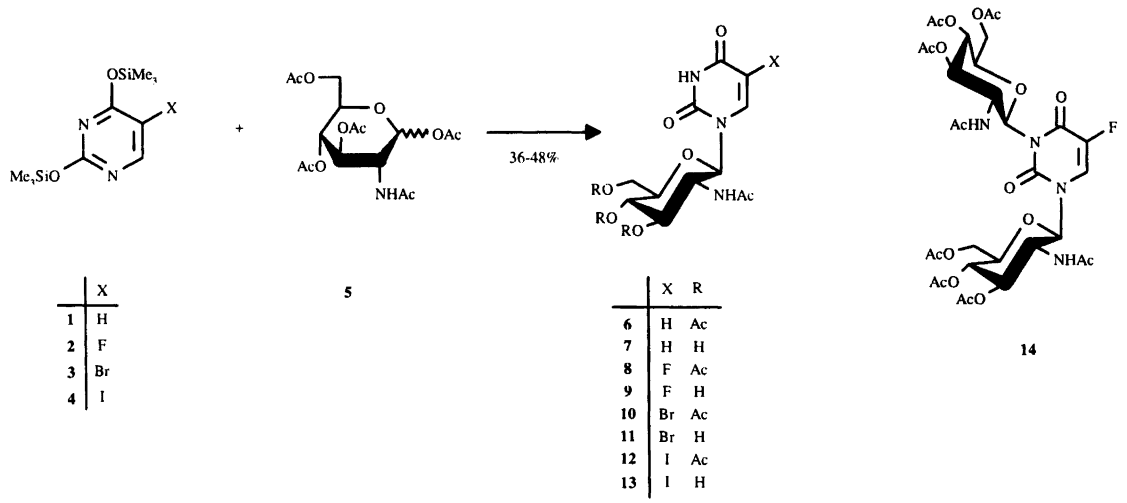
Result and discussion

In recent years, Stevens *et al.*[23] described the chemical synthesis, physical properties and antitumor activity of 1-(2-acetamido-2-deoxy-β-D-glucopyranosyl)uracil (**7**). This compound was prepared from glycosylation of 1-chloro-2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-D-glucose with 2,4-dimethoxypyrimidine according to the Hilbert–Johnson procedure[24] followed by deprotection under acidic conditions. The structural assignment of the β-configuration of **7** was based on its specific rotation only. In the present work, the nucleoside **7** is proposed as a useful intermediate for the synthesis of some potentially biological active 5-halouracil nucleosides. The easy accessibility and the biochemical interest of 2-acetamido-2-deoxy-D-glucose prompted us to use this aminosugar as a starting material in glycosylation reactions of the Hilbert–Johnson–Birkofer type.[25] Thus, trimethylsilylated derivatives of uracil, 5-fluorouracil, 5-bromouracil and 5-iodouracil (**1**–**4**), respectively, were condensed with 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-D-glucose (**5**) in the presence of trimethylsilyl triflate as catalyst[26] in dry 1,2-dichloroethane. The reaction proceeded at boiling temperature to give the desired 1-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)uracil (**6**) and its 5-halo analogues **8**, **10** and **12** in yields of 45, 36, 48 and 45%, respectively. These reactions are thermodynamically controlled and form, by neighboring group participation of the 2-acetamido group, almost exclusively the β-anomers. Deacetylation proceeded smoothly with sodium methoxide in dry methanol at room temperature to give the known free



	X
1	H
2	F
3	Br
4	I

5

	X	R
6	H	Ac
7	H	H
8	F	Ac
9	F	H
10	Br	Ac
11	Br	H
12	I	Ac
13	I	H

14

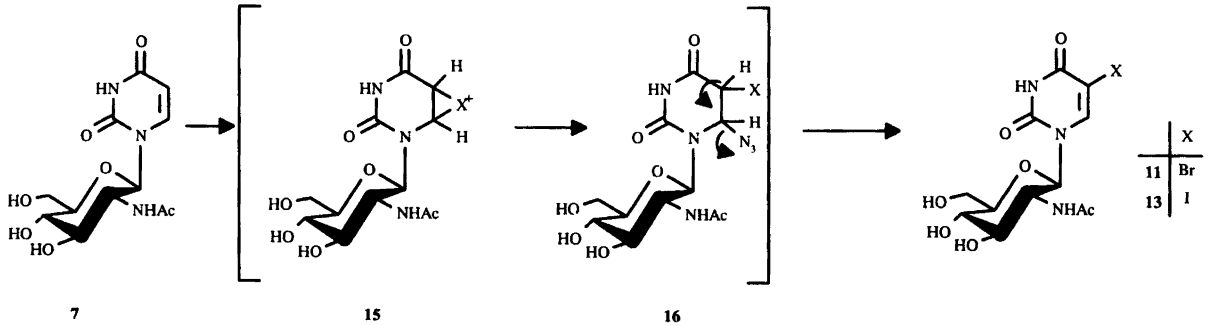
Scheme 1.

nucleoside **7** (76% yield),[23] **9** (63%), **11** (60%) and **13** (77%). The diglycoside **14** was obtained, in addition to the monoglycoside **8**, from the reaction of the silylated 5-fluorouracil with **5**, as a minor component in 5% yield (Scheme 1).

An attempt to synthesize the free 5-halonucleosides from the parent uracil derivative **7**, using the method of Knaus *et al.*,[27] has been examined. The reaction of **7** with *N*-bromosuccinimide or iodine monochloride, in the presence of sodium azide at 35 and 25 °C, gave the 5-bromo- and 5-iodo-uracil nucleosides **11** and **13** in 56 and 50% yield, respectively. The formation of these products was assumed to occur via a 5-halo-6-azido-5,6-dihydro intermediate, followed by elimination of HN_3 (Scheme 2).

The structures of the synthesized uracil nucleosides were determined on the basis of their UV, ^{1}H NMR, ^{13}C NMR and mass spectra which were found to be consistent with the assigned structures. The formation of N-1 nucleosides was confirmed by UV spectral comparison with known structures of glycopyranoside analogues and 1 (5-thio-β-D-xylopyranosyl)pyrimidines.[28]

The ^{1}H NMR spectra of **6**, **8**, **10** and **12** showed the anomeric protons as doublets at δ 5.64, 5.71, 5.74 and 5.40 with *J* coupling of 9.5, 9.2, 9.5 and 10.0 Hz, respectively, corresponding to a diaxial orientation of H-1′ and H-2′ protons which are indicative of the β-configuration. The large coupling constants $J_{2',3'}$, $J_{3',4'}$ and $J_{4',5'}$ (9.0–10.0 Hz) confirmed the $^4C_1$ conformation of the sugar moiety. The four acetyl groups appeared as three singlets at δ 1.92–2.08, while signals appearing at δ 1.68–1.94 were attributed to the acetamido groups. Similarly, the free nucleosides **7**, **9**, **11** and **13** showed, in their ^{1}H NMR spectra, the signals from anomeric protons as doublets at δ 5.57, 5.35 5.39 and 5.38, 5.57 with large $J_{1',2'}$ coupling constants (10.0, 9.7, 9.5 and 9.5, respectively) clearly indicating that these compounds have also the β-configuration. The assignments of the hydroxy groups in these compounds were determined from D_2O exchange. The ^{1}H NMR spectrum of **14** showed large $J_{H,H}$ coulpings [$J_{(1',2')a}$, $J_{(1',2')b}$ 9.5 Hz; $J_{(4',5')a}$, $J_{(4',5')b}$ 9.5 Hz] indicative of the β-form with the $^4C_1$ conformation of the sugar moieties at N-1 and N-3. In the ^{13}C NMR spectrum of **14** the signals at δ 171.6–169.2 were attributed to the ester carbonyl carbon atoms, while that at δ 148.2, to the C-5 atom of the nucleobase. A signal at δ 124.1 was assigned to the C-6 atom. The anomeric carbon atoms C-1′$_a$ and C-1′$_b$ appeared at δ 81.2 and 80.8, respectively. Another ten signals at δ 75.1–49.5 were assigned to C-2′, C-3′, C-4′, C-5′ and C-6′ of both sugar moieties at N-1 and N-3, while signals at δ 23.2–20.5 were attributed to the acetoxy methyl carbons.



7 15 16

Scheme 2.

In summary, we have achieved a regiospecific synthesis of 5-halouracil nucleosides by the direct glycosylation of 5-halouracil with peracylated D-glucosamine and via the halogenation of the uracil nucleoside **7** by an electrophilic halogen reagent and sodium azide under mild conditions. These nucleosides will be utilized for the biological evaluation studies.

Experimental

General. ^{1}H NMR and ^{13}C NMR spectra were measured with Bruker WM 250 and Bruker AC 250 spectrometers (unless otherwise stated) with tetramethylsilane as an internal standard and on a δ scale in ppm. UV spectra were recorded on a Perkin–Elmer spectrophotometer Lambda 5. Thin layer chromatography was performed on silica gel sheets F 1550 LS 254 from Scheicher & Schüll. Silica gel 60 (Merck) was used for column chromatography. EI and FAB mass spectra were recorded on a MAT 312 mass spectrometer using 3-nitrophenol (NBOH) or glycerol as matrix. Some molecular ions were detected by doping the samples with Na^+ ion. The melting points were determined with a Dr. Tottli melting point apparatus and are not corrected.

*5-Halouracil nucleosides of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-*D*-glucose* (**6**), (**8**), (**10**) and (**12**). *General method.* A suspension of 5-fluoro-, 5-bromo- or 5-iodo-uracils (3.84 mmol) in hexamethyldisilazane (20 ml) containing a few crystals of $(NH_4)_2SO_4$ was heated under reflux for 8 h. After cooling, the solutions were evaporated to dryness to give crude **1**–**4**. These were dissolved in dry 1,2-dichloroethane (20 ml), and a solution of the sugar **5** (3.84 mmol) was added, followed by trimethylsilyl trifilate catalyst (0.70 mmol). The solutions were heated under reflux for 3 h and then cooled and evaporated to dryness. The residues were chromatographed on silica gel (50 g) using a gradient of MeOH (0–0.5%) in $CHCl_3$.

*1-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-*D*-glucopyranosyl)uracil* (**6**). Yield: 0.76 g (45%); R_f ($CHCl_3$–MeOH 9:1) 0.48, m.p. 161–165 °C decomp. (from EtOAc). UV: λ_{max} (MeOH) 273 (log ε 4.06). ^{1}H NMR: δ 11.43 (s,1 H, NH), 8.08 (d, 1 H, H-6), 7.89 (d, 1 H, NHAc, $J_{2',NH}$ 7.7 Hz), 5.76 (d, 1 H, H-5, $J_{5,6}$ 7.8 Hz), 5.64 (d, 1 H, H-1′, $J_{1',2'}$ 9.5 Hz), 5.24 (t, 1 H, H-3′, $J_{3',4'}$ 9.8 Hz), 5.12 (dd, 1 H, H-4′, $J_{4',5'}$ 9.0 Hz), 4.51 (q, 1 H, H-2′, $J_{2',3'}$ 9.8 Hz), 4.20–3.89 (m, 3 H, H-5′, H-6′, H-6″), 2.01, 1.99, 1.93 (3 s, 9 H, 3 OAc), 1.77 (s, 3 H, NHAc). Found: C 47.75; H 5.19; N 9.81. Calc. for $C_{18}H_{23}N_3O_{10}$: C 48.00; H 5.30; N 9.50; MS: *m/z* (EI > 0) 442 $(M+H)^+$.

*1-(Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-*D*-glucopyranosyl)-5-fluorouracil* (**8**). Yield: 0.68 g (36%); R_f ($CHCl_3$–MeOH 9:1) 0.34, m.p. 115–120 °C, decomp. at 205 °C. UV: λ_{max} (MeOH) 263 (log ε 3.86). ^{1}H NMR: δ 11.88 (s, 1 H, NH), 8.36 (s, 1 H, H-6, $J_{6,F}$ 7.3 Hz), 8.10 (d, 1 H, NHAc, $J_{2',NH}$ 9.3 Hz), 5.71 (d, 1 H, H-1′, $J_{1',2'}$ 9.2 Hz), 5.24 (t, 1 H, H3′, $J_{3',4'}$ 9.6 Hz), 5.12 (t, 1 H, H-4′, $J_{4',5'}$ 9.4 Hz), 4.25 (q, 1 H, H-2′, $J_{2',3'}$ 9.7 Hz), 4.06–3.31 (m, 3 H, H-5′, H-6′, H-6″), 2.00, 1.97, 1.92 (3 s, 9 H, 3 OAc), 1.71 (s, 3 H, NHAc). Found: C 46.86; H 4.78; N 9.29. Calc. for $C_{18}H_{22}FN_3O_{10}$: C 47.06; H 4.83; N 9.15.

*1,3-Bis(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-*D*-glucopyranosyl)-5-fluorouracil* (**14**). Yield: 0.15 g (5%); R_f ($CHCl_3$–MeOH 9:1) 0.62, m.p. 204–206 °C (decomp.). UV: λ_{max} (MeOH) 268 (log ε 3.82). ^{1}H NMR (600 MHz): δ 7.45 (d, 1 H, H-6, $J_{6,F}$ 5.5 Hz), 6.18 (d, 1 H, NHAc, $J_{2',NH}$ 9.2 Hz), 5.90 (d, 1 H, NHAc, $J_{2',NH}$ 9.0 Hz), 5.87 (d, 1 H, H-1′, $J_{1',2'}$ 9.7 Hz), 5.81 (d, 1 H, H-1′, $J_{1',2'}$ 9.5 Hz), 5.27 (t, 1 H, H-3′, $J_{3',4'}$ 9.7 Hz), 5.17 (t, 1 H, H-3′, $J_{3',4'}$ 9.5 Hz), 5.13 (t, 1 H, H-4′, $J_{4',5'}$ 9.7 Hz), 5.07 (t, 1 H, H-4′, $J_{4',5'}$ 9.5 Hz), 4.30 (q, 1 H, H-2′, $J_{2',3'}$ 9.7 Hz), 4.21 (q, H-2′, $J_{2',3'}$ 9.5 Hz), 4.19 (dd, 1 H, H-6′, $J_{5',6''}$ 2.0 Hz), 4.18 (dd, 1 H, H-6″, $J_{6',6''}$ 2.0 Hz), 4.17 (dd, 1 H, H-6′, $J_{5',6''}$ 2.0 Hz), 4.10 (dd, 1 H, H-6″, $J_{6',6''}$ 12.0 Hz), 3.86 (ddd, 1 H, H-5′, $J_{5',6'}$ 4.2 Hz), 3.77 (ddd, 1 H, H-5′, $J_{5',6'}$ 4.0 Hz), 2.09, 2.08, 2.07, 2.04, 2.03, 2.02 (6 s, 18 H, 6 OAc), 1.94, 1.77 (2 s, 6 H, 2 NHAc). ^{13}C NMR: δ 171.6, 171.5, 171.4, 171.3, 170.7, 170.6 (2), 169.2 (C=O), 148.2 (C-5), 124.1 (C-6), 81.2 (C-1′), 80.8 (C-1′), 75.1 (C-2′), 75.0 (C-2′), 73.2 (C-3′), 73.1 (C-3′), 67.6 (C-4′), 67.5 (C-4′), 62.1 (C-6′), 61.6 (C-6′), 51.6 (C-5′), 49.5 (C-5′). Found: C 48.51; H 5.12; N 7.02. Calc. for $C_{32}H_{41}FN_4O_{18}$: C 48.73; H 5.24; N 7.10. MS: *m/z* (EI < 0) 668 $(M^+ - 2\,HOAc)$.

*1-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-*D*-glucopyranosyl)-5-bromouracil* (**10**). Yield: 0.96 g, (48%); R_f ($CHCl_3$–MeOH 9:1) 0.41, m.p. 255–258 °C (decomp.). (from EtOAc). UV: λ_{max} (MeOH) 273 (log ε 4.06). ^{1}H NMR: δ 8.47 (s, 1 H, H-6), 8.03 (d, 1 H, NHAc, $J_{2',NH}$ 9.5 Hz), 5.74 (d, 1 H, H-1′, $J_{1',2'}$ 9.5 Hz), 5.25 (t, 1 H, H-3′, $J_{3',4'}$ 9.5 Hz), 5.18 (t, 1 H, H-4′, $J_{4',5'}$ 9.5 Hz), 4.53 (q, 1 H, H-2′, $J_{2',3'}$ 9.0 Hz), 4.02 (m, 3 H, H-5′, H-6′, H-6″), 2.02, 1.98, 1.93 (3 s, 9 H, 3 OAc), 1.71 (s, 3 H, NHAc). Found: C 41.32; H 4.12; N 8.19. Calc. for $C_{18}H_{22}BrN_3O_{10}$: C 41.55; H 4.26; N 8.08. MS: *m/z* (EI) 520 (519/521 bromine isotopes) (M^+).

*1-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-*D*-glucopyranosyl)-5-iodouracil* (**12**). Yield: 0.98 g (45%); R_f ($CHCl_3$–MeOH 7:3) 0.76, m.p. 177–181 °C (from EtOH). UV: λ_{max} (MeOH) 279 (log ε 3.72). ^{1}H NMR: δ 7.92 (s, 1 H, H-6), 6.76 (s, H, NHAc, $J_{2',NH}$ 8.0 Hz), 5.40 (d, 1 H, H-1′, $J_{1',2'}$ 10.0 Hz), 5.27 (t, 1 H, H-3′, $J_{3',4'}$ 10.0 Hz), 5.14 (t, 1 H, H-4′, $J_{4',5'}$ 10.0 Hz), 4.48 (q, 1 H, H-2′, $J_{2',3'}$ 10.0 Hz), 4.26 (dd, 1 H, H-6′, $J_{5',6''}$ 5.0 Hz), 4.15 (dd, 1 H, H-6″, $J_{6',6''}$ 12.0 Hz), 3.96 (ddd, 1 H, H-5′, $J_{5',6'}$ 4.0 Hz), 2.10, 2.08, 2.06 (3 s, 9 H, 3 OAc), 1.94 (s, 3 H, NHAc). Found: C 38.01; H 3.86; N 7.52. Calc. for $C_{18}H_{22}IN_3O_{10}$: C 38.11; H 3.91; N 7.41. MS: *m/z* (FAB > 0) 568 $(M+H)^+$.

Free nucleosides of 2-acetamido-2-deoxy-D-glucose (**7**), (**9**), (**11**) and (**13**). *General deprotection procedure.* A solution of the acylated nucleosides (**6**, **8**, **10** and **12**, 0.35 mmol) in 0.3 M sodium methoxide solution (10 ml) was stirred at room temperature for 3 h. After neutralization with Dowex resin (IR 84-H^+ form), the solution was filtered and the resin was washed with MeOH. The combined extracts were evaporated and the residue was partitioned between water and ether. The aqueous phase was evaporated to dryness and lyophilized from water. The residue was co-evaporated with silica gel (1 g) and placed on top of a column of silica gel (10 g). Elution with a gradient of MeOH (0–20%) in $CHCl_3$ afforded the desired nucleosides.

1-(2-Acetamido-2-deoxy-β-D-glucopyranosyl)uracil (**7**). Yield: 120 mg (78%); R_f ($CHCl_3$–MeOH 3:2) 0.10, m.p. 213–215 °C decomp. (lit.[23] 216–217°C decomp.). UV: λ_{max} (MeOH) 259 (log ε 3.94). ^1H NMR : δ 7.92 (d, 1 H, NHAc, $J_{2',NH}$ 8.5 Hz), 7.10 (d, 1 H, H-6), 5.57 (d, 1 H, H-1', $J_{1',2'}$ 10.0 Hz), 5.30–5.14 (m, 3 H, 3 OH), 5.19 (d, 1 H, H-5, $J_{5,6}$ 7.6 Hz), 3.83 (q, 1 H, H-2', $J_{2',3'}$ 10.0 Hz), 3.64 (dd, 1 H, H-3', $J_{3',4'}$ 9.0 Hz), 3.48–3.39 (m, H-4', H-5'), 3.29–3.08 (m, 2 H, H-6', H-6''), 1.68 (s, 3 H, NHAc). Found: C 45.42; H 5.52; N 13.08. Calc. for $C_{12}H_{17}N_3O_7$: C 45.71; H 5.44; N 13.33. MS: *m/z* (FAB>0) 338 $(M+Na)^+$.

1-(2-Acetamido-2-deoxy-β-D-glucopyranosyl)-5-fluorouracil (**9**). Yield: 73 mg (63%); R_f ($CHCl_3$–MeOH 3:2) 0.17, m.p. 210–212 °C (decomp.). UV: λ_{max} (MeOH) 264 (log ε 3.70). ^1H NMR: δ 8.05 (d, 1 H, H-6, $J_{6,F}$ 7.0 Hz), 7.95 (d, 1 H, NHAc, $J_{2',NH}$ 8.6 Hz), 5.35 (d, 1 H, H-1', $J_{1',2'}$ 9.7 Hz), 5.04 (2 d, C_2'-OH, C_4'-OH, *J* 5.0, 6.5 Hz), 4.57 (t, 1 H, C_6'-OH, *J* 5.5 Hz), 3.81 (q, 1 H, H-2', $J_{2',3'}$ 9.7 Hz), 3.70 (t, 1 H, H-3', $J_{3',4'}$ 9.8 Hz), 3.46–3.22 (m, 4 H, H-4', H-5', H-6', H-6''), 1.74 (s, 3 H, NHAc). Found: C 43.12; H 4.78; N 12.48. Calc. for $C_{12}H_{16}FN_3O_7$: C 43.25; H 4.84; N 12.61. MS: *m/z* (FAB>0) 356 $(M+Na)^+$.

1-(2-Acetamido-2-deoxy-β-D-glucopyranosyl)-5-bromouracil (**11**). *(a) From deprotection experiment.* Yield: 83 mg (60%), R_f ($CHCl_3$–MeOH) 3:2) 0.18, m.p. 278–282 °C (decomp.) (from EtOH–ether). UV: λ_{max} (MeOH) (268) (log ε 3.70). ^1H NMR: δ 11.82 (s, 1 H, NH), 8.15 (d, 1 H, H-6), 7.73 (d, 1 H, NHAc, $J_{2',NH}$ 8.9 Hz), 5.39 (d, 1 H, $J_{1',2'}$ 9.5 Hz), 4.66–4.41 (m, 3 H, 3 OH), 3.86 (q, 1 H, H-2', $J_{2',3'}$ 10.0 Hz), 3.85 (t, 1 H, H-3', $J_{3',4'}$ 10.0 Hz), 3.49–3.37 (m, 2 H, H-4', H-5'), 3.29–3.05 (m, 2 H, H-6', H-6''), 1.72 (s, 3 H, NHAc). Found: C 36.69; H 4.13; N 10.42. Calc. for $C_{12}H_{16}BrN_3O_7$: C 36.57; H 14.09; N 10.66. MS: *m/z* (EI) 394 (393/395 bromine isotopes) (M^+).

(b) From reaction of **7** *with* N-*bromosuccinimide.* *N*-Bromosuccinimde (NBS, 0.20 g, 1.1 mmol) was added at 35 °C to a suspension prepared by mixing a solution of **7** (0.31 g, 1.0 mmol) in 1,2-dimethoxyethane (25 ml) and DMF (5 ml) with a solution of sodium azide (0.26 g, 4.0 mmol) in water (1 ml). The reaction mixture was stirred for 3 h at 35 °C, after which the solvent was removed *in vacuo* and the residue was purified by silica gel chromatography using a gradient of MeOH (0–20%) in $CHCl_3$ to give **11** (0.22 g, 56%) as a solid. The ^1H NMR and mass spectra, m.p. and mixed m.p. were identical with those for the compound prepared in experiment (a).

1-(2-Acetamido-2-deoxy-β-D-glucopyranosyl)-5-iodouracil (**13**). *(a) From deprotection experiment.* Yield: 153 mg (77%); R_f ($CHCl_3$–MeOH 7:3) 0.30, m.p. 185–188 °C (decomp.). UV: λ_{max} (MeOH) 275 (log ε 3.80). ^1H NMR: δ 7.98 (s, 1 H, H-6), 7.94 (d, 1 H, NHAc, $J_{2',NH}$ 10.0 Hz), 5.38 (d, 1 H, H-1', $J_{1',2'}$ 9.5 Hz), 3.90 (q, 1 H, H-2', $J_{2',3'}$ 9.5 Hz), 3.71–3.25 (m, 8 H, H-3', H-4', H-5', H-6', H-6'', 3 OH), 1.71 (s, 3 H, NHAc). Found: C 32.31; H 3.51; N 9.42. Calc. for $C_{12}H_{16}IN_3O_7$: C 32.67; H 3.66; N 9.52. MS: *m/z* (FAB>0) 442 $(M+H)^+$, 464 $(M+Na)^+$.

(b) From reaction of **7** *with iodine monochloride.* Iodine monochloride (ICl, 0.40 g, 2.5 mmol) was added slowly over a 5 min period to a suspension of sodium azide (0.26 g, 4.0 mmol) in acetonitrile (30 ml) at ice-bath temperature and the stirring was continued for another 5 min. To this, a solution of **7** (0.31 g, 1.0 mmol) in acetonitrile (30 ml) and DMF (3 ml) was added and the reaction mixture was warmed to 25 °C and stirred for 24 h. The solvent was evaporated off and the residue was poured onto a column of silica gel. Elution with a gradient of MeOH (0–20%) in $CHCl_3$ afforded **13** (0.22 g, 50%). The ^1H NMR and mass spectra, m.p. and mixed m.p. were identical with those for the compound prepared in experiment (a).

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