Anal. Calcd for $C_{15}H_{18}N_6O_8$: C, 43.88; H, 4.38; N, 20.47. Found: C, 44.01; H, 4.29; N, 20.21.

2,5-Diamino-1-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)imidazole-4-carboxamide (8). Raney Ni (500 mg) was added to a solution of **7** (80 mg) in 50% aqueous ethanol. The mixture was shaken under 40 psi of H_2 for 1 hr at 70°. The catalyst was removed by filtration and the filtrate was evaporated to dryness under reduced pressure. The material was purified by preparative thin-layer chromatography (20 cm × 20 cm × 2 mm silica gel plate) using an ethyl acetate–methylene chloride–methanol (6:3:1) system. Compound **8** was obtained as hygroscopic amorphous solid: 32 mg (40%); nmr (Me_2SO-d_6) δ 7.28 (s, 2, 2-NH_2); (Me_2SO-d_6–D_2O) δ 5.94 (s, 1, $J_{1',2'}$ = 6 Hz, H-1'); $\lambda_{max}^{pH\ 1}$ 276 mμ (ε 9700); $\lambda_{max}^{pH\ 11}$ 284 (12,600).

Anal. Calcd for $C_{15}H_{21}N_5O_8$: C, 45.11; H, 5.30; N, 17.54. Found: C, 45.02; H, 5.46; N, 17.38.

6-Methoxy-7-β-D-ribofuranosylimidazo[4,5-*d*]-*v*-triazin-(3*H*)4-one (9). Compound **5** (142 mg, 0.3 mmol) was refluxed with freshly prepared 0.35 *M* methanolic sodium methoxide (6 ml) for 2 hr. After 16 hr at room temperature it was treated with Dowex 50 (H^+ form) to remove the sodium, filtered, and evaporated to dryness to yield an amorphous product, 78 mg (62%): mp 114–116°; nmr (Me_2SO-d_6) δ 5.87 (d, 1, $J_{1',2'}$ = 6 Hz, H-1'), 4.22 (s, 3, OCH_3); $\lambda_{max}^{pH\ 1}$ 306 mμ (ε 10,500); $\lambda_{max}^{pH\ 11}$ 299 (12,200).

Anal. Calcd for $C_{10}H_{13}N_5O_6$: C, 40.07; H, 4.34; N, 23.33. Found: C, 40.16; H, 4.19; N, 23.11.

5-Amino-2-methoxy-1-β-D-ribofuranosylimidazole-4-carboxamide (10). Raney Ni (500 mg) was added to a solution of **9** (299 mg, 1 mmol) in H_2O (10 ml). It was hydrogenated at 30 psi and 25° for 40 hr. The catalyst was removed by filtration and the filtrate was evaporated to dryness under reduced pressure. The residue was triturated with EtOH, giving a crystalline product which was recrystallized from EtOH–H_2O giving 171 mg (59%) of **10**: mp 182–184°; nmr (D_2O) δ 5.66 (d, 1, $J_{1',2'}$ = 6 Hz, H-1'), 4.00 (s, 3, OCH_3); $\lambda_{max}^{pH\ 1}$ 272 mμ (ε 11,800); $\lambda_{max}^{pH\ 11}$ 281 (14,400).

Anal. Calcd for $C_{10}H_{16}N_4O_6$: C, 41.66; H, 5.59; N, 19.44. Found: C, 41.42; H, 5.79; N, 19.25.

7-β-D-Ribofuranosylimidazo[4,5-*d*]-*v*-triazine-4,6-dione (11). Compound **5a** (174 mg, 0.5 mmol) was treated with 6 ml of 3% NaOH for 16 hr at 4°, then passed through a column (1 × 15 cm) of Amberlite IRC 50 ([H^+], 100–200 mesh). The column was washed with H_2O (30 ml) and the combined eluates were evaporated to a small volume (1 ml) *in vacuo* and then applied to a column (2 × 30 cm) of microcrystalline cellulose (Avicel). The product was eluted with H_2O. A colorless, amorphous solid, 98 mg (67%), was obtained by lyophilizing the fractions containing the product: nmr (Me_2SO-d_6) δ 5.95 (d, 1, $J_{1',2'}$ = 5 Hz, H-1'); $\lambda_{max}^{pH\ 1}$ 297 mμ (ε 3560); $\lambda_{max}^{pH\ 11}$ 305 (5700).

Anal. Calcd for $C_9H_{11}N_5O_6$: C, 37.92; H, 3.86; N, 24.56. Found: C, 38.10; H, 3.77; N, 24.33.

6-Thio-7-β-D-ribofuranosylimidazo[4,5-*d*]-*v*-triazin-(3*H*)4-one (12). Compound **5a** (348 mg, 1 mmol) was added to a freshly prepared 2 *M* aqueous solution of NaSH (5 ml), stirred at 4° for 16 hr, and then diluted with H_2O (5 ml) and MeOH (15 ml). The pH of the solution was brought to 4 with Dowex 50 (H^+ form), the resin was removed by filtration, and the filtrate was evaporated to dryness. The product was recrystallized from aqueous EtOH to yield 261 mg (75%): mp 228–231°; nmr (Me_2SO-d_6) δ 5.90 (d, 1, $J_{1',2'}$ = 6.0 Hz, H-1'); $\lambda_{max}^{pH\ 1}$ 283 mμ (ε 9600), 341 (3600); $\lambda_{max}^{pH\ 11}$ 334 (7500).

Anal. Calcd for $C_9H_{11}N_5O_5S \cdot H_2O$: C, 33.83; H, 4.08; N, 21.95. Found: C, 33.91; H, 4.08; N, 21.98.

Registry No.—**1,** 2627-69-2; **1a,** 23274-21-7; **2,** 36519-16-1; **3,** 52906-34-0; **3a,** 52906-35-1; **4,** 52906-36-2; **4a,** 52906-37-3; **5,** 52906-38-4; **5a,** 52906-39-5; **6,** 52906-40-8; **7,** 52906-41-9; **8,** 52906-42-0; **9,** 52951-30-1; **10,** 52906-43-1; **11,** 52906-44-2; **12,** 52906-45-3.

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A General Synthesis of N-Glycosides. I.[1] Synthesis of Pyrimidine Nucleosides

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Reaction of silylated hydroxy-, amino-, and mercaptopyrimidines as well as 6-azapyrimidines (1,2,4-triazines) with protected 1-*O*-acetyl as well as 1-*O*-methyl sugars in the presence of Friedel–Crafts catalysts gave the corresponding pyrimidine nucleosides, generally in excellent yields. The scope and limitations of this new synthetic procedure are discussed.

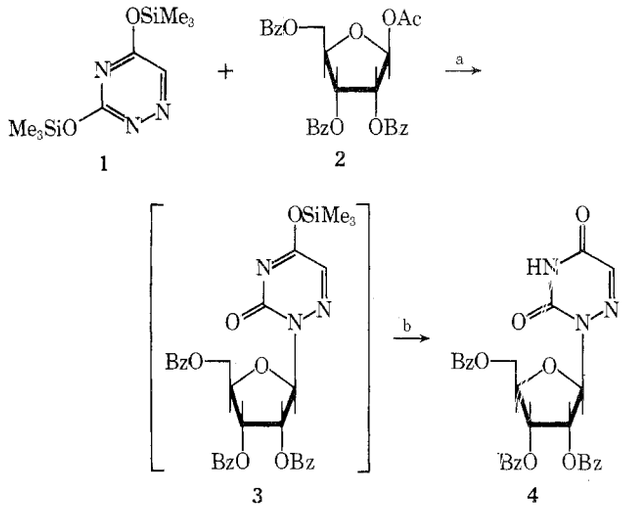
Because we wanted to prepare larger quantities of 6-azauridine, we investigated and compared the known methods for the preparation of pyrimidine nucleosides,[2] especially the silyl Hilbert–Johnson reaction.[3-8] After early synthetic studies by different groups,[9] Cristescu[10] and Wittenburg[11] had prepared 6-azauridine 2′,3′,5′-tri-*O*-benzoate in 60% yield by the benzenemercuric salt modification of the silyl Hilbert–Johnson reaction. Using this procedure we obtained varying yields of a rather impure substance which had to be purified by column chromatography. However the resulting crystalline product was still contaminated by mercuric compounds.

Since the Hilbert–Johnson reaction involves an attack of a sugar cation on the aromatic pyrimidine ring, we carried out the reaction in the presence of Friedel–Crafts catalysts, which are known[12] to convert acylated 1-acyloxy sugars into their corresponding acylated glycosyl halides.

Friedel–Crafts catalysts have been used by Baker[13] and later by Furukawa and Honjo[14] for the synthesis of purine nucleosides, but, strangely enough, the more obvious use of

Friedel–Crafts catalysts in the Hilbert–Johnson reaction had never been critically investigated.[7]

The reaction of 2,4-bis(trimethylsilyloxy)-6-azauracil (1) with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (2) and $SnCl_4$ in 1,2-dichloroethane gave even on a 10-kg scale, after hydrolysis of the reactive intermediate **3**, 93% recrystallized 6-azauridine 2′,3′,5′-tri-*O*-benzoate (**4**).

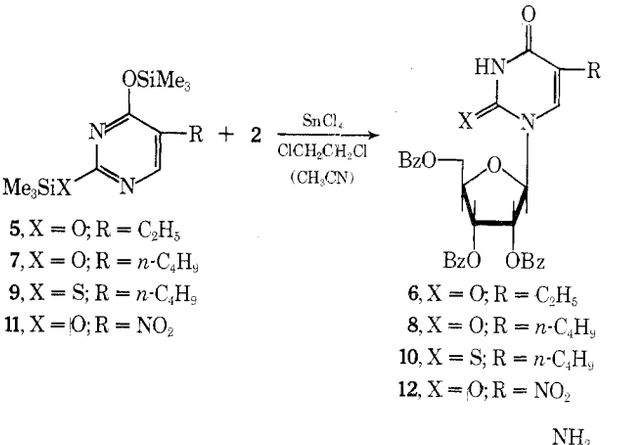


a, $SnCl_4/ClCH_2CH_2Cl$, 4 hr, 22°
b, $H_2O/NaHCO_3$

Investigation of the scope of this reaction showed that silylated uracils and cytosines as well as their silylated 2-thio[8] and 6-aza analogs react as readily as 1 with acylated sugars to form the corresponding acylated nucleosides in excellent yields.

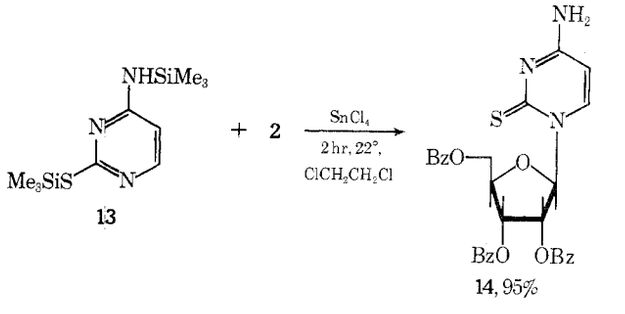
In this reaction all silylated uracils give intermediates like **3** with a reactive 4-trimethylsilyloxy group[5] which can either be hydrolyzed to uridines or be converted by excess ammonia or primary and secondary amines into their corresponding cytidines.[15]

The following examples are typical for the Friedel–Crafts-catalyzed silyl Hilbert–Johnson reaction. 5-Ethyluridine 2′,3′,5′-tri-*O*-benzoate (**6**)[16a] is formed in 95% yield after 20 hr at 22° in 1,2-dichloroethane starting from silylated 5-ethyluracil (**5**). Silylated 5-*n*-butyluracil (**7**) reacted very slowly with **2** in 1,2-dichloroethane, but gave 5-*n*-butyluridine 2′,3′,5′-tri-*O*-benzoate (**8**)[16] in 95% yield after addition of acetonitrile and an additional amount of $SnCl_4$. The corresponding silylated 5-*n*-butyl-2-thiouracil (**9**), however, afforded the 2-thio analog **10**[16b] after 5 hr in acetonitrile in 83% yield. Surprisingly the reaction of silylated 5-nitrouracil (**11**) was complete in 0.5 hr at 22° in 1,2-dichloroethane–acetonitrile to give 5-nitrouridine 2′,3′,5′-tri-*O*-benzoate (**12**) in 98% yield.



5, X = O; R = C_2H_5
7, X = O; R = *n*-C_4H_9
9, X = S; R = *n*-C_4H_9
11, X = O; R = NO_2

6, X = O; R = C_2H_5
8, X = O; R = *n*-C_4H_9
10, X = S; R = *n*-C_4H_9
12, X = O; R = NO_2



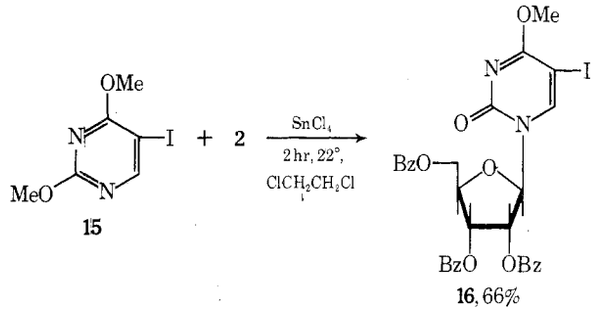
13

14, 95%

Persilylated 2-thiocytosine (**13**)[8] reacted with **2** to afford in 95% yield 2-thiocytidine 2′,3′,5′-tri-*O*-benzoate (**14**),[8,17] which gave with methanolic ammonia in excellent yield 2-thiocytidine, a rare nucleoside from t-RNA.[18]

These results indicate a complex relationship between the structure of the silylated bases and their rate of nucleoside formation in 1,2-dichloroethane and acetonitrile in the presence of $SnCl_4$ (compare also papers II and IV of this series).

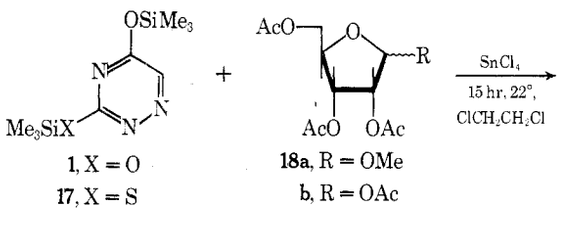
A "classical" Hilbert–Johnson reagent like 5-iodo-2,4-dimethoxypyrimidine (**15**) reacted, as expected, as the 2,4-bissilyl compound did with **2** in the presence of $SnCl_4$ to give 1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-5-iodo-4-methoxy-1,2-dihydropyrimidin-2-one (**16**)[19] in 66% yield.



15

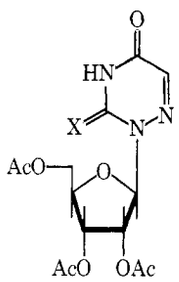
16, 66%

In the following examples we have investigated the influence of the sugar moiety on nucleoside formation in the presence of $SnCl_4$.



1, X = O
17, X = S

18a, R = OMe
b, R = OAc

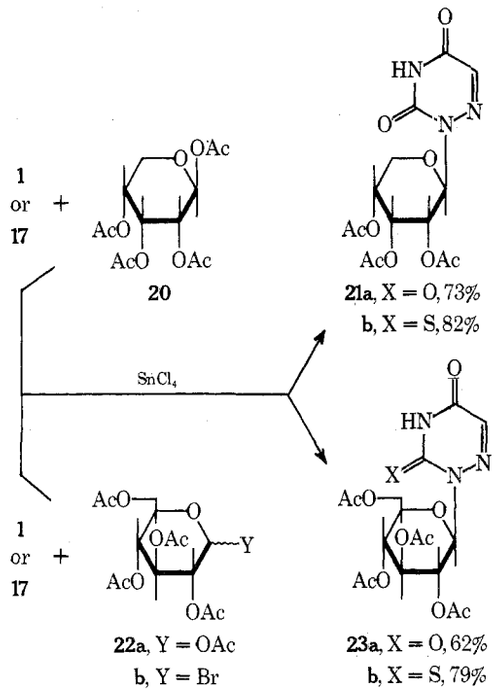


19a, X = S
b, X = O

Persilylated 2-thio-6-azauracil (**17**) reacted with syrupy, redistilled methyl 2,3,5-tri-*O*-acetyl-D-ribofuranoside (**18a**)[20] as well as with crystalline **18b**[20] to give an ~73% yield of recrystallized 2-thio-6-azauridine 2′,3′,5′-tri-*O*-acetate (**19a**). The direct conversion of **1** with **18a** or **18b** into the therapeutically important[21] 6-azauridine 2′,3′,5′-tri-*O*-acetate (**19b**) proceeds in high yields. However, crude **19b**

crystallizes poorly and very slowly even in the presence of only a small amount of impurities.

Reaction of the persilylated 6-azauracil (1) as well as the analogous 2-thio derivative (17) with 1,2,3,4-tetra-*O*-acetyl-β-D-ribopyranose (**20**) and 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose (**22a**) afforded the corresponding new ribopyranosides (**21a** and **21b**) and glucopyranosides (**23a** and **23b**) in 62–82% yields, which were saponified to the free nucleosides.



In our initial reactions with crude **20** and **22a** in 1,2-dichloroethane heating to 50–60° was required to complete the reactions, but, when 1,2,3,4-tetra-*O*-acetyl-β-D-ribopyranose (**20**) and 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose (**22a**) were finely powdered and dried at 80° (0.001 mm) to remove traces of solvents, their reaction with **1** afforded **21a** and **23a** within 3 hr at 22°. The reaction of **1** with acetobromoglucose (**22b**) at 22° required 3 hr using 1,2-dichloroethane, but was complete in ~30 min in the more polar solvent acetonitrile (compare General Discussion).

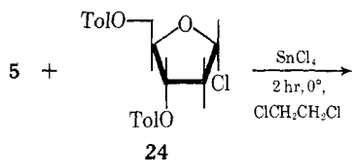
In the case of the preparation of the 2-thio analogs (**21b** and **23b**), heating in 1,2-dichloroethane as well as acetonitrile for 3 hr at 50° or 2 hr at 80° was necessary to complete the reaction in a reasonable time.

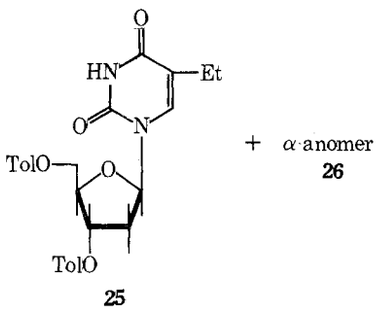
Monitoring this reaction at 22° with tlc showed besides **23b** the presence of additional products as possible intermediates which disappeared on heating the reaction mixture in either solvent with the formation of **23b.** We are at present investigating the structure of these unknown products.

In all the examples discussed above and investigated only the β anomer of the N_1-nucleosides could be detected and isolated in the presence of a 2α-acyloxy substituent in the sugar moiety, but, as expected, in the case of acylated 2-deoxy-D-ribose as well as benzylated D-arabinose derivatives without a 2-participating group both anomeric nucleosides were formed.

Crude acylated methyl 2-deoxy-D-ribofuranoside gave with **5** a complex mixture of products[22] and was therefore converted into the commonly used crystalline 1α-chloro-2-deoxy-3,5-bis(*p*-toluoyl)-α-D-ribofuranosyl chloride (**24**).[23]

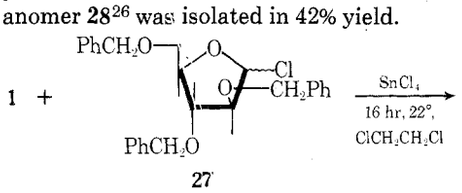
Reaction of the silylated pyrimidine (**5**) with **24** gave at 0° a 92% yield of the anomeric mixture of nucleosides from which 42% crystalline β anomer **25** could be readily separated by crystallization from the α anomer **26.** In a number of experiments, we always found a nearly constant ratio of anomers α/β ≈1 which apparently could not be influenced by variation of the reaction conditions.[24]

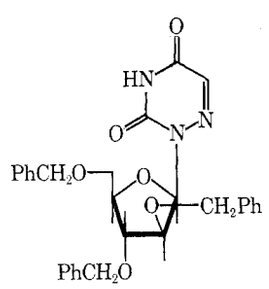




It should be emphasized here that the use of the 3,5-bis(*p*-toluoyl) sugar derivative (**24**) has proved quite superior to other acyl derivatives[25] in the preparation of **25** and analogs, because of the ease of separation of the β anomer during crystallization.

Reaction of persilylated 6-azauracil (1) with 2,3,5-tri-*O*-benzyl-D-arabinosyl chloride (**27**) gave a 74.3% overall yield of a nucleoside mixture from which the crystalline β anomer **28**[26] was isolated in 42% yield.



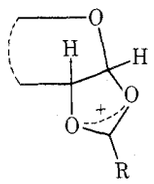


The β configuration of the acylated nucleosides **25** and **28** was clearly established by their nmr spectra. The $H_{1'}$ proton in **25** showed the expected triplet[27] at δ 6.31 ppm (J = 5.5 Hz) for the β anomer and the $H_{1'}$ proton in **28** the expected doublet[28] at δ 6.32 ppm (J = 6 Hz) for the cis coupling with the $H_{2\alpha'}$ proton.

The rapid reaction of 2-deoxy-3,5-bis(*p*-toluoyl)-α-D-ribofuranosyl chloride (**24**) with the silylated 5-ethyluracil (**5**) at 0° (compare formation of **6**) posed the question which factors determine the rate of the nucleoside formation.

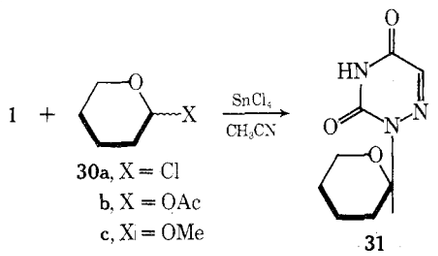
Since the reaction of silylated 6-azauracil (**1**) with D-glucopyranose pentaacetate (**22a**) as well as acetobromoglucose (**22b**) to give **23a** proceeded at room temperature at roughly the same rate, the rather stable 1,2-α-acyloxonium salt (**29**)[29] formed from 2-α-acyloxy sugars seems not only to determine the exclusive formation of β anomers but consequently also to decrease the reactivity of these electrophiles.

To eliminate the influence of a 2-acyloxy group as well as of any residual substituents in the pyranose derivatives we



29

finally investigated the reaction of silylated 6-azauracil (**1**) with the tetrahydropyranyl derivatives **30** as the most simple model of such sugar pyranosides. The sensitive 2-chloro derivative **30a** as well as the more stable **30b** and **30c** gave the crystalline *dl*-pyranoside **31**[30] rapidly at 0° in yields of up to 92%.



30a, X = Cl
b, X = OAc
c, X = OMe

31

The reaction of **1** with dihydropyran in the presence of acetonitrile gave besides a 20% yield of **31** a number of additional products, which will be described in a separate publication.

In Table I the already discussed reaction of silylated 6-azauracil (**1**) with 1-*O*-acetyl-2,3,5-tribenzoyl-β-D-ribofuranose (**2**) to give 6-azauridine 2′,3′,5′-tri-*O*-benzoate (**4**) has been performed under a variety of conditions with different Friedel–Crafts catalysts and in different solvents. Most of these experiments were only done once and therefore some of the depicted yields can certainly be raised.

Table I
Variation of Reaction Conditions

Solvent	Catalyst	Amount[a]	Time, hr	t, °C	Yield in % Crude	Yield in % Crystalline
1,2-Dichloroethane	$SnCl_4$	0.720	4	20	97	93
Acetonitrile	$SnCl_4$	0.720	4	20	97	82.5
Dioxane	$SnCl_4$	0.720	4	101	77	72
Tetrahydrofuran	$SnCl_4$	0.720	3	65	98	75
Dimethylformamide	$SnCl_4$	0.720	4	153	77.5	68.5
Benzene	$SnCl_4$	0.720	6	80	80.5	66
Toluene	$SnCl_4$	0.720	6	111	86	66
Carbon disulfide	$SnCl_4$	0.720	4	46	87	67
Carbon tetrachloride	$SnCl_4$	0.720	4	77	93	73
1,2-Dichloroethane	$ZnCl_2$	1.440	5	84	100	83
1,2-Dichloroethane	$TiCl_4$	0.800	30	20	65	40
Chlorobenzene	$AlCl_3$	1.440	6	132	63	40
Tetrachloroethane	$FeCl_3$	1.456	5	146	44	25
Carbon disulfide	BF_3–Et_2O	1.390	6	46	70	60

[a] Mole of catalyst/mole of sugar component 2.

General Discussion

Although all Friedel–Crafts catalysts tried gave in most aprotic solvents generally good yields of 6-azauridine 2′,3′,5′-tri-*O*-benzoate (**4**), the combination 1,2-dichloroethane–$SnCl_4$ seems to be most simple and practical, since 1,2-dichloroethane is more easily purified and more stable than absolute methylene chloride or chloroform. Furthermore the use of 1,2-dichloroethane gives the opportunity to raise the reaction temperature to 83° if necessary. As catalyst, liquid $SnCl_4$ can be readily measured and administered. Fresh $SnCl_4$ can be used as such, older samples should be purified by distillation.

Besides 1,2-dichloroethane, acetonitrile as a solvent sometimes results in a more rapid reaction owing to its higher polarity and can give different products compared to 1,2-dichloroethane. In part II of this series, the reactions of silylated 6-methyluracils with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**2**) and $SnCl_4$ are described to give strikingly varying ratios of N_1- and N_3-nucleosides when acetonitrile is used instead of 1,2-dichloroethane.

As yet no 1-acetylamino sugars could be detected as products formed by a Ritter reaction[31] between the 1-*O*-acyl sugars and acetonitrile in the presence of $SnCl_4$.

In view of the simpler purification of 1,2-dichloroethane and especially the simpler work-up after the reactions, 1,2-dichloroethane should be generally preferred to acetonitrile.

The amount of Friedel–Crafts catalysts depends on the components; *e.g.*, on using the sensitive and reactive 1-halo sugars ~0.25 equiv of catalyst is usually sufficient whereas with 1-*O*-methyl or 1-*O*-acetyl sugars 0.75 to 1.5 equiv of catalyst is necessary. If the silylated pyrimidine (or any other hydroxy N-heterocycle) has not been distilled *in vacuo*, hexamethyldisilazane (HMDS) or pyridine as a silylation solvent might still be present, which inactivate the catalyst.

The catalyst is furthermore inactivated by traces of solvents in the sugar moiety like ethanol, 2-propanol, or acetic acid (compare preparation of **21a** and **23a**). The hydrogen halide liberated by the reaction of alcohols and acetic acid with $SnCl_4$ can cleave the disaccharide linkage in reactions with peracylated cellubiose, lactose, and maltose or might lead to formation of N_3-nucleosides as well as $N_{1,3}$-bisglycosides (compare part III of this series). The liberated hydrogen halide can also destroy sensitive groups like azides. Therefore the solid acylated 1-*O*-alkyl or 1-*O*-acyl sugar derivatives should always be powdered and dried at ~50–80° (0.001 mm) or distilled under high vacuum as in the case of the liquid methyl 2,3,5-tri-*O*-acetyl-D-ribofuranoside (**18a**).

If a reaction monitored by tlc is not proceeding, either a further amount of catalyst should be added, the temperature raised, or both. Furthermore, if 1,2-dichloroethane is used as a solvent, addition of acetonitrile might accelerate the reaction as mentioned above and exemplified by the formation of **8**.

It is principally advisable to follow the reactions by tlc since the nucleoside formation can proceed rather rapidly; *e.g.*, in the case of silylated 2-mercaptopyrimidine (compare part IV of this series), a longer reaction time might lead to the destruction of already formed product.

A slight (5–10%) excess of the silylated pyrimidine is often advantageous to effect a complete conversion of the usually more precious sugar component and to simplify the reaction work-up, because the hydrolyzed pyrimidines can usually be much more easily removed than unreacted sugar derivatives.

Although normally nucleosides (N-glycosides) are formed in the presence of $SnCl_4$, O- or S-glycosides can also be isolated in certain cases (compare parts II and IV of this

series), which might be mistaken for nucleosides. Thus, when new types of silylated hydroxy or mercapto N-heterocycles are employed and doubts arise about the structure of the new products, a small scale experiment should be performed in refluxing 1,2-dichloroethane or acetonitrile–$SnCl_4$. Under these conditions the O- or S-glycosides are either rearranged[32] or decomposed, whereas the nucleosides are usually stable.

In the last years following our preliminary publication[1] a number of groups have applied successfully our standard reaction conditions (1-*O*-acetyl sugars, $SnCl_4$ or $TiCl_4$ in 1,2-dichloroethane or methylene chloride) to give acylated N_1-nucleosides in generally high yields.[16b,33-37]

It is interesting to note that Ohrui, Kuzuhara, and Emoto[33] observed that on using a very small amount of $SnCl_4$ the α-nucleoside was also formed.

Furthermore, Haynes[38] described the formation of the N_3-riboside in addition to the desired N_1-riboside by reaction of silylated uracil with 1-*O*-acetyl-3,5-di-*O*-benzoyl-2-*O*-methyl-β-D-ribofuranose (compare part II of this series).

In paper IV of this series further applications of the Friedel–Crafts-catalyzed Hilbert–Johnson reaction to a variety of silylated hydroxy N-heterocycles are described and analogous applications by other groups reviewed.

Experimental Section

All melting points were taken on a Kofler melting point microscope and are uncorrected. The uv spectra were recorded on a Cary Model 14 spectrometer, the nmr spectra were determined on Varian A-60 and HR-100 instruments and the mass spectra on an Atlas CH4 instrument.

The thin layer chromatography was performed on Merck silica gel plates GF_{254}. For the protected nucleosides the following system was especially efficient: (A) toluene–acetic acid–H_2O (5:5:1).[8b,39]

The solvents were carefully purified: 1,2-dichloroethane was refluxed for 2 hr over P_2O_5 and distilled. Acetonitrile was refluxed for 2 hr over P_2O_5 and distilled, the procedure was repeated, and finally it was stored over 3 Å molecular sieves.

$SnCl_4$ (Riedel-deHaen) was usually redistilled at normal pressure. 1-*O*-Acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**2**), mp 131–132°, was prepared by a slightly modified procedure according to Recondo and Rinderknecht[40] in ~75% yield starting from D-ribose (Papierwerke Waldhof-Aschaffenburg AG). Methyl 2,3,5-tri-*O*-acetyl-D-ribofuranoside (**18a**) and 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose (**18b**), mp 82–83°, were prepared in ~95 and 50% yield according to Guthrie and Smith.[20] 1,2,3,4-Tetra-*O*-acetyl-β-D-ribopyranose (**20**), mp 110–112°, was obtained in ~70% yield according to Levene and Tipson[41] and 1,2,3,4,6-penta-*O*-acetyl-β-D-glucose (**22a**), mp 131–132°, according to standard procedures. The crystalline peracetylated sugar derivatives were carefully powdered and dried at 70–80° (0.001 mm). Meanwhile methyl 2,3,5-tri-*O*-acetyl-D-ribofuranoside (**18a**) was distilled in a Kugelrohr apparatus at 140° (0.01 mm). Finally 1-α-chloro-2-deoxy-3,5-bis(*p*-toluoyl)-D-ribofuranose (**24**) was prepared according to Hoffer[23] and 2,3,5-tri-*O*-benzyl-D-arabinofuranosyl chloride (**27**) according to Tejima, Glaudemans, and Fletcher.[42]

Silylation. The silylations of the corresponding uracils and cytosines were performed according to standard methods. Therefore only few silylations are described (compare the preparation of **1**). Since silylated 2-thiouracils and 2-thiocytosines are generally less stable,[8b] the distillation of these compounds should be done at the lowest temperature possible (high vacuum Kugelrohr distillation).

Work-Up. The work-up was usually performed as described for the preparation of **4**. For reactions in CH_3CN it is often advantageous to remove part of the CH_3CN *in vacuo* at 22° before dilution with 1,2-dichloroethane or methylene chloride.

3,5-Bis(trimethylsilyloxy)-1,2,4-triazine (1). 2,3,4,5-Tetrahydro-1,2,4-triazine-3,5-dione (6-azauracil)[43] (120.0 g, 1.06 mol) was suspended in hexamethyldisilazane (HMDS) (600 ml) (Dow Chemical Co.), trimethylchlorosilane (10 ml) was added, and the mixture was refluxed with exclusion of humidity. Ammonia was vigorously evolved and NH_4Cl deposited in the reflux condenser. After 2 hr the solid had dissolved and the excess HMDS was removed at ~50-mm pressure (collected for reuse after redistillation) at 90° and finally at 12-mm vacuum. The residue was distilled at 140° (0.1 mm) to give 264.4 g (97%) of **1**.

2-(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)-2,3,4,5-tetrahydro-1,2,4-triazine-3,5-dione (4, 6-Azauridine Tribenzoate). To a solution of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**2**, 378 g, 0.75 mol) in 1,2-dichloroethane (4.5 l) a solution of 3,5-bis(trimethylsilyloxy)-1,2,4-triazine (**1**, 204.0 g, 0.79 mol) in dichloroethane (500 ml) was added. The mixture was cooled with ice and redistilled $SnCl_4$ (63 ml, 0.54 mol) in 1,2-dichloroethane (300 ml) was added with vigorous stirring and exclusion of humidity. The yellow homogenous solution was kept for 4 hr at 22° when tlc (system A, R_f 0.5) indicated the completion of the reaction. After dilution with 1,2-dichloroethane (2.0 l.), the reaction mixture was shaken with saturated $NaHCO_3$ solution (3.0 l.) and the resulting emulsion filtered over a layer of sand–Celite. The filtering aid was carefully washed with 1,2-dichloroethane (1.0 l.); the organic phase was separated, dried (Na_2SO_4), and evaporated under reduced pressure. The slightly yellowish crystalline residue (407.3 g) was recrystallized from acetone–ethanol to give 388.2 g (93%) of pure **4**, mp 192–194°), as colorless needles, $[\alpha]^{23}D$ −71° (*c* 0.5, $CHCl_3$).

The oily residue from the mother liquor contained mainly sugar derivatives and was discarded.

Anal. Calcd for $C_{29}H_{23}N_3O_9$: C, 62.47; H, 4.16; N, 7.54. Found: C, 62.53; H, 4.28; N, 7.55.

Methanolysis[44] gave the free nucleoside 2-[β-D-ribofuranosyl]-2,3,4,5-tetrahydro-1,2,4-triazine-3,5-dione (6-azauridine), mp 159–160° (lit.[9] 160°), which could be readily acetylated to the triacetate **13b**, mp 102–104° (lit.[45] 100–101°).

1-(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)-5-ethyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (6, 5-Ethyluridine Tribenzoate). To **2** (4.27 g, 8.47 mmol) in 1,2-dichloroethane (150 ml) 5-ethyl-2,4-bis(trimethylsilyloxy)pyrimidine (**5**) (3.0 g, 10.5 mmol) and $SnCl_4$ (0.71 ml, 6.0 mmol) in 1,2-dichloroethane (10 ml) were added. After 20 hr at 22° and work-up, crystallization gave 4.7 g (95%) of **6** as white prisms, mp 159–160° (lit.[16a] 154–155°), $[\alpha]^{23}D$ −96.7° (*c* 0.6, $CHCl_3$).

1-(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)-5-butyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (8). To 5-butyl-2,4-bis(trimethylsilyloxy)pyrimidine (**7**, 22 mmol) and **2** (10.08 g, 20 mmol) in 1,2-dichloroethane (150 ml), $SnCl_4$ (1.66 ml, 14.2 mmol) in 1,2-dichloroethane (100 ml) was added. After 5 hr at 22° according to tlc only a trace of nucleoside had formed. Therefore $SnCl_4$ (2 ml, 17.1 mmol) in CH_3CN (150 ml) was added and the mixture kept for 66 hr at 22° over the weekend. After work-up crystallization (ethanol) gave 11.70 g (95.4%) of **8** with mp 157–158° (lit.[16a] 156.5–157.5°), $[\alpha]^{23}D$ −106° (*c* 1.08, $CHCl_3$).

1-(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)-5-butyl-2-thio-1,2,3,4-tetrahydropyrimidin-4-one (10). To **2** (15.12 g, 30 mmol) in CH_3CN (200 ml) and 48 ml (30 mmol) of 5-butyl-2,4-*S,O*-bis(trimethylsilyl)pyrimidine (**9**) in CH_3CN, $SnCl_4$ (7 ml, 60 mmol) in CH_3CN (150 ml) was added. After 5 hr at 22° and work-up crystallization (ethanol) gave 15.80 g (83.7%) of **10** as white needles with mp 123–125° (lit.[16b] 122.5–124.5°), $[\alpha]^{24}D$ −88.2° (*c* 1.325, $CHCl_3$).

1-(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)-5-nitro-1,2,3,4-tetrahydropyrimidin-2,4-dione (12, 5-Nitrouridine Tribenzoate). To **2** (2.52 g, 5 mmol) in 1,2-dichloroethane (50 ml) 5-nitro-2,4-bis(trimethylsilyloxy)pyrimidine (**11**, 7.6 mmol) in CH_3CN (10 ml) and $SnCl_4$ (0.50 ml, 4.28 mmol) in 1,2-dichloroethane (10 ml) were added. After 0.5 hr at 22° and work-up crystallization (ethanol) gave 2.94 g (97.8%) of **12**, mp 184–185° (lit.[2b] 183–184°), $[\alpha]^{23}D$ −128.8° (*c* 0.75, $CHCl_3$).

1-(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)-4-amino-2-thio-1,2-dihydropyrimidine (14, 2-Thiocytidine Tribenzoate). To **2** (5.04 g, 10 mmol) in 1,2-dichloroethane (150 ml) a solution of 2,4-*S,N*-bis(trimethylsilyl)-2-thio-4-aminopyrimidine (**13**, 16.4 ml, 11 mmol) and $SnCl_4$ (1.68 ml, 14.4 mmol) in 1,2-dichloroethane (20 ml) was added. After 2 hr at 22° and work-up crystallization (methanol) gave 5.4 g (94.5%) of **14** as colorless crystals, mp 194–195° (lit.[17] 190–191°), $[\alpha]^{23}D$ −34.6° (*c* 1, $CHCl_3$).

For methanolysis of **14** to 2-thiocytidine compare **8b**.

1-(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)-5-iodo-4-methoxy-1,2-dihydropyrimidin-2-one (16). To **2** (2.52 g, 5 mmol) in 1,2-dichlororethane (100 ml) 5-iodo-2,4-dimethoxypyrimidine (**15**, 1.66 g, 6.25 mmol) and $SnCl_4$ (0.84 ml, 7.2 mmol) in 1,2-dichloroethane (10 ml) were added. After 4 hr at 22° and work-up the crude **19** (3.34 g) crystallized (ethanol) to give 2.32 g (66.6%) of **16** as white needles with mp 186–187° (lit.[19] 186–187°), $[\alpha]^{23}D$ −107.7° (*c* 0.20, $CHCl_3$), nmr ($CDCl_3$) δ 6.50 (d, 1, J = 5 Hz, $H_{1'}$).

Anal. Calcd for $C_{31}H_{25}IN_2O_9$ (696.46): C, 53.46; H, 3.62; N, 4.02; I, 18.22. Found: C, 53.44; H, 3.72; N, 4.03; I, 18.05.

2-(2,3,5-Tri-*O*-acetyl-β-D-ribofuranosyl)-3-thio-2,3,4,5-tetrahydro-1,2,4-triazin-5-one (19a, 2-Thio-6-azauridine Triacetate). To **18a** (7.8 g, 30 mmol) and 3,5-*S,O*-bis(trimethylsilyl)-1,2,4-triazine (**17**, 9.0 g, 33 mmol) in 1,2-dichloroethane (250 ml), $SnCl_4$ (3.7 ml, 31.2 mmol) in 1,2-dichloroethane (30 ml) was added. After 5 hr at 22° crystallization (benzene) and recrystallization (ether) gave 8.43 g (72.5%) long needles of **19a**, mp 101–104°, $[\alpha]^{23}D$ −44.8° (*c* 1, $CHCl_3$), nmr ($CDCl_3$) δ 7.15 (d, 1, *J* = 3 Hz, $H_{1'}$).

Anal. Calcd for $C_{14}H_{17}N_3O_8S$: C, 43.41; H, 4.; N, 10.85; S, 8.28. Found: C, 43.23; H, 4.71; N, 10.92; S, 8.35.

Methanolysis[8b] gave the free nucleoside with mp 201–203° which was identical with an authentic sample[8b] of 2-thio-6-azauridine and could be oxidized by alkaline H_2O_2[8b,46] to 6-azauridine.

2-(2,3,4-Tri-*O*-acetyl-β-D-ribopyranosyl)-2,3,4,5-tetrahydro-1,2,4-triazine-3,5-dione (21a). To 1,2,3,4-tetra-*O*-acetylribopyranose (**20**, 1.59 g, 5 mmol) in 1,2-dichloroethane (100 ml) 5.54 ml of **1** (6.25 mmol) in benzene and $SnCl_4$ (0.42 ml, 3.6 mmol) in 1,2-dichloroethane (5 ml) were added. After 3 hr at 22° and work-up crystallization (ethanol) gave 1.36 g (73.3%) of **21a** as white needles, mp 172–173° $[\alpha]^{23}D$ −25.7° (*c* 1, $CHCl_3$).

Methanolysis[44] afforded in 87.8% yield the free 2-(β-D-ribopyranosyl)-2,3,4,5-tetrahydro-1,2,4-triazine-3,5-dione, mp 221–222°, $[\alpha]^{23}D$ −60.0° (*c* 0.5, $C_2H_5OH + H_2O$ (1:1)).

2-(2,3,4-Tri-*O*-acetyl-β-D-ribopyranosyl)-3-thio-2,3,4,5-tetrahydro-1,2,4-triazin-5-one (21b). To **20** (9.5 g, 29.9 mmol) and **17** (10.2 g, 37.4 mmol) in 1,2-dichloroethane (300 ml) $SnCl_4$ (5.04 ml, 43.4 mmol) in 1,2-dichloroethane (500 ml) was added. After 3 hr at 50° and work-up **21b** was obtained as a slight yellowish foam, which was homogenous on tlc (system A): yield 9.46 g (81.8%); nmr ($CDCl_3$) δ 6.82 (d, 1, *J* = 9 Hz, $H_{1'}$), 7.63 (s, 1, H_5).

Anal. Calcd for $C_{14}H_{17}N_3O_8S$ (387.36): C, 43.41; H, 4.42; N, 10.85; S, 8.28. Found: C, 43.19; H, 4.62; N, 10.78; S, 8.36.

2-(β-D-Ribopyranosyl)-3-thio-2,3,4,5-tetrahydro-1,2,4-triazin-5-one. To **21b** (1.86 g, 4.8 mmol) in dry methanol (100 ml) a $NaOCH_3$ solution (8 ml, 7.2 mmol) was added. After 3 hr at 22°, filtration through a 1 × 20 cm column of Dowex 50 (H^+) resin and washing with 2:1, CH_3OH–H_2O the eluate was evaporated. Crystallization (methanol) gave 937 mg (74.8%) of free nucleoside with mp 239–241°, $[\alpha]^{23}D$ −37.8° [*c* 1.066, $CH_3OH + H_2O$ (8:2)], nmr (D_2O) δ 6.80 (d, 1, *J* = 9 Hz, $H_{1'}$).

Anal. Calcd for $C_8H_{11}N_3O_5S$ (261.26): C, 36.77; H, 4.24; N, 16.08; S, 12.27. Found: C, 36.69; H, 4.38, N, 16.14, S, 12.53.

2-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-2,3,4,5-tetrahydro-1,2,4-triazine-3,5-dione (23a). To 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose (**22a**, 27.3 g, 70 mmol) in 1,2-dichloroethane (600 ml) 77.5 ml of **1** (87.5 mmol) in benzene and $SnCl_4$ (5.9 ml, 50.4 mmol) in 1,2-dichloroethane (100 ml) were added. After 5 hr at 22° and work-up crystallization (ethanol) gave 19.2 g (61.6%) white needles of **23a**, mp 208–210°, $[\alpha]^{20}D$ −53.4° (*c* 1, $CHCl_3$), nmr ($CDCl_3$) δ 5.93 (d, 1, *J* = 9 Hz, $H_{1'}$).

Anal. Calcd for $C_{17}H_{21}N_3O_{11}$ (443.37): C, 46.05; H, 4.77; N, 9.48. Found: C, 45.85; H, 4.84; N, 9.55.

Methanolysis[44] gave in 85% yield the free 2-(β-D-glucopyranosyl)-2,3,4,5-tetrahydro-1,2,4-triazine-3,5-dione with mp 210–212°, $[\alpha]^{23}D$ −44.4° [*c* 0.5, EtOH + H_2O (1:1)], nmr (D_2O) δ 5.75 (d, 1, *J* = 9 Hz, $H_{1'}$).

Anal. Calcd for $C_9H_{13}N_3O_7$ (275.22): C, 39.27; H, 4.76; N, 15.27. Found: C, 39.40; H, 5.04; N, 15.35.

2-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-3-thio-2,3,4,5-tetrahydro-1,2,4-triazin-5-one (23b). To **22a** (15.6 g, 40 mmol) in 1,2-dichloroethane (400 ml) **17** (12.3 g, 45 mmol) and $SnCl_4$ (6.8 ml, 57.7 mmol) in 1,2-dichloroethane (40 ml) were added. After 3 hr at 50° and work-up crystallization (ethanol) gave 14.5 g (79%) of **23b** as white needles with mp 225–226°, $[\alpha]^{20}D$ + 18.5° (*c* 1, pyridine), nmr ($CDCl_3$) δ 6.74 (d, 1, *J* = 8.5 Hz, $H_{1'}$).

Anal. Calcd for $C_{17}H_{21}N_3O_{10}S$ (459.44): C, 44.43; H, 4.61; N, 9.14; S, 6.98. Found: C, 44.41; H, 4.87; N, 9.20; S, 7.07.

Methanolysis[44] gave in 87% yield the free 2-(β-D-glucopyranosyl)-3-thio-2,3,4,5-tetrahydro-1,2,4-triazin-5-one which crystallized (ethanol–H_2O) as the monohydrate (the yellow prisms changed to a glass above 130°), $[\alpha]^{23}D$ −139.2° [*c* 1.135, ethanol–H_2O (1:1)], nmr (D_2O) δ 6.61 (d, 1, *J* = 9.5 Hz, $H_{1'}$) 7.78 (s, 1, H_6).

Anal. Calcd for $C_9H_{13}N_3O_6S \cdot H_2O$ (309.31): C, 34.95; H, 4.89; N, 13.59; S, 10.37. Found: C, 34.79; H, 5.08; N, 13.64; S, 10.66.

1-[2-Deoxy-3,5-bis-*O*-*p*-toluoyl)-β-D-ribofuranosyl]-5-ethyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (25, 5-Ethyldeoxyuridine Ditoluoylate). To **24** (1.95 g, 5.0 mmol) and 5-ethyl-2,4-bis(trimethyl-silyloxy)pyrimidine (**5**, 1.78 g, 6.25 mmol) in 1,2-dichloroethane (50 ml) $SnCl_4$ (0.107 ml, 1.25 mmol) in 1,2-dichloroethane (25 ml) was added at 0°. After a few minutes the solution became clear and was kept for 2 hr at 0°. After work-up the crude nucleoside (2.8 g) gave on fractionated crystallization (ethanol) 1.41 g (57%) **25** with mp 197–198°, $[\alpha]^{23}D$ −90° (*c* 0.49, $CHCl_3$), nmr ($CDCl_3$) δ 6.44 (dd, 1, *J* = 7 + 7 Hz, $H_{1'}$).

Anal. Calcd for $C_{27}H_{28}N_2O_7$ (492.51): C, 65.84; H, 5.73; N, 5.69. Found: C, 65.59; H, 5.90; N, 5.71.

From the mother liquor the α anomer **26** was isolated as crystalls with mp 160–161°, $[\alpha]^{23}D$ −10.0° (*c* 1, $CHCl_3$), nmr ($CDCl_3$) δ 6.35 (dd, 1, *J* = 7 + 3.0 Hz, $H_{1'}$).

Methanolysis[44] of **25** gave the free 5-ethyl-2′-deoxyuridine with mp 149–151° (lit.[25] 152–153°).

2-(2,3,5-Tri-*O*-benzyl-β-D-arabinofuranosyl)-3,5-dioxo-2,3,4,5-tetrahydro-1,2,4-triazine (28). From 2,3,5-tri-*O*-benzyl-D-arabinofuranose (4.62 g, 11 mmol) the halo sugar **27**[42] was prepared and dissolved in 1,2-dichloroethane (100 ml), then **1** (7 ml, 11 mmol) in benzene and subsequently at 0° a solution of $SnCl_4$ (0.42 ml, 3.6 mmol) in 1,2-dichloroethane (2 ml) were added with stirring. After 16 hr at 22° and work-up crystallization (CH_2Cl_2–pentane) gave 2.40 g (42%) of **28** as long white needles with mp 123–124°, nmr ($CDCl_3$) δ 6.31 (d, 1, *J* = 5.5 Hz, $H_{1'}$).

Anal. Calcd for $C_{29}H_{29}N_3O_6$ (515.55): C, 67.56; H, 5.67;, N, 8.15. Found: C, 67.43; H, 5.76; N, 8.07.

1-(Tetrahydro-2-pyranyl)-2,3,4,5-tetrahydro-1,2,4-triazine-3,5-dione (31). A. **1** (13 ml, 20.8 mmol) in CH_3CN was diluted with CH_3CN (100 ml) and $SnCl_4$ (1.51 ml, 25 mmol) and finally 2-chlorotetrahydropyran (**30a**, 30 ml, 25 mmol) in 1,2-dichloroethane (50 ml) was added dropwise with stirring at 0° under an atmosphere of argon during 45 min. After 2 hr at 4° concentration *in vacuo* to ~30 ml, dilution with 1,2-dichloroethane (500 ml), and work-up gave crude **31** which crystallized (ethyl acetate) to give 3.6 g (92%) of **31** as colorless prisms with mp 163–164° (lit.[30] mp 160–162°).

Anal. Calcd for $C_8H_{11}N_3O_3$: C, 48.72; H, 5.62; N, 21.31. Found: C, 48.79; H, 6.00; N, 21.20.

B. Analogous reaction of **1** with **30b** and **30c** gave **31** in 85% and 72% yield, respectively.

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Registry No. **1**, 17331-61-2; **2**, 6974-32-9; **4**, 1627-29-8; **5**, 31167-05-2; **6**, 25692-02-8; **7**, 40110-78-9; **8**, 40110-83-6; **9**, 40110-77-8; **10**, 40110-82-5; **11**, 52522-97-1; **12**, 23392-16-7; **13**, 52522-98-2; **14**, 20649-48-3; **15**, 52522-99-3; **16**, 2880-93-5; **17**, 33088-44-7; **18a**, 52554-28-6; **19a**, 29725-42-6; **20**, 4049-34-7; **21a**, 52523-00-9; **21a** free nucleoside, 52523-01-0; **21b**, 52523-02-1; **21b** free nucleoside, 52523-03-2; **22a**, 83-87-4; **23a**, 31356-88-4; **23a** free nucleoside, 52523-04-3; **23b**, 29725-44-8; **23b** free nucleoside, 33156-22-8; **24**, 4330-21-6; **25**, 29900-44-5; **26**, 29900-45-6; **27**, 52554-29-7; **28**, 29725-46-0; **30a**, 3136-02-5; **31**, 52554-30-0; 6-azauracil, 461-89-2.

References and Notes

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A General Synthesis of N-Glycosides. II.[1] Synthesis of 6-Methyluridines

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The reaction of silylated 6-methyl- as well as 5,6-dimethyluracil with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose and 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose gave strikingly varying yields of N_1- and N_3-glycosides depending on the use of either 1,2-dichloroethane or acetonitrile as solvents. Silylated 2-thio-6-methyl- as well as 5,6-dimethyluracil afforded only mixture of S- and N_3-glycosides. The steric as well as mechanistic implications of these results are discussed.

The synthesis of the chemically[2] as well as biologically[3] interesting 6-methyl substituted pyrimidine nucleosides has recently been investigated by different groups.[4–7]

The data obtained by the previous workers[5,7] indicate that very subtle steric as well as energetic factors seem to determine whether the thermodynamically more stable N_1 or (in the presence of a 6 substituent) the sterically and, apparently kinetically, favored N_3 product is formed. Furthermore any excess of the halo sugar seems to lead to N_1,N_3-bisglycoside formation.

Since the Hilbert-Johnson reaction of silylated pyrimidines with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**2**) and $SnCl_4$ had given exclusively the natural β-N_1-pyrimidine nucleosides (compare part I of this series), we were curious how silylated 6-methyl- as well as 5,6-dimethyluracil would behave under these reaction conditions.

Our first results are summarized in Scheme I. In the less polar solvent 1,2-dichloroethane 6-methyl-2,4-bis(trimethylsilyloxy)pyrimidine (**1**) reacted with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**2**) and $SnCl_4$ to give only 13% crystalline benzoylated N_1-riboside **3** and 68% crystalline benzoylated N_3-riboside **4**, whereas in the more polar acetonitrile ~41% **3** and ~52% **4** were obtained as well as 3% benzoylated N_1,N_3-bisriboside **5**. As described earlier[5] the N_1- and N_3-nucleosides can be readily separated by column chromatography on alumina or silica gel.

The structures of the N_1- as well as the N_3-nucleosides were established by the typical bathochromic shift of the uv spectra of the N_3-nucleosides in alkaline medium.[8] Furthermore the N_3-β-D-ribofuranosides show a characteristic downfield shift of the H-1′ proton of up to 1 ppm which is due to the two neighboring lactam carbonyls compared to the N_1-nucleosides with only one neighboring lactam carbonyl group.

The difference in yields on changing the solvents is even more striking for the reactions of 5,6-dimethyl-2,4-bis(trimethylsilyloxy)pyrimidine (**6**) (Scheme II). The yields of 10% N_1-nucleoside **7** and 60% N_3-nucleoside **8** in 1,2-di-