(12) F. v. Arlt, *Monatsh. Chem.*, **22**, 144 (1901); L. J. Haynes and F. H. Newth, *Advan. Carbohyd. Chem.*, **10**, 207 (1955).
(13) B. R. Baker, R. E. Schaub, and H. M. Kissman, *J. Amer. Chem. Soc.*, **77**, 5911 (1955).
(14) Y. Furakawa and M. Honjo, *Chem. Pharm. Bull. (Tokyo)*, **16**, 1076 (1968).
(15) H. Vorbrüggen and U. Niedballa, *Angew. Chem., Int. Ed. Engl.*, **10**, 657 (1971); H. Vorbrüggen, K. Krolikiewicz, and U. Niedballa, submitted for publication in *Justus Liebigs Ann. Chem.*
(16) (a) M. Muraoka, A. Takada, and T. Ueda, *Chem. Pharm. Bull. (Tokyo)*, **18**, 261 (1970); (b) E. H. Hamamura, K. Sato, and J. G. Moffatt, *J. Med. hem.*, **15**, 1061 (1972).
(17) T. Ueda and H. Nishino, *J. Amer. Chem. Soc.*, **90**, 1678 (1968).
(18) S. Nishimura in "Progress in Nucleic Acid Research and Molecular Biology," Vol. 12, J. N. Davidson and W. Cohn, Ed., Academic Press, New York–London, 1972, p 49.
(19) M. Prystaš and F. Šorm, *Collect. Czech. Chem. Commun.*, **29**, 2956 (1964).
(20) R. D. Guthrie and S. C. Smith, *Chem. Ind. (London)*, 547 (1968).
(21) P. Roy-Durman "Analogues of Nucleic Acid Compounds," Springer Verlag, Berlin–Heidelberg–New York, 1970, pp 42–45.
(22) The presence and formation of methyl pyranosides is discussed by R. J. Ferrier, *Fortschr. Chem. Forsch., Topics Curr. Chem.*, **14**, 389 (1970); R. E. Deriaz, W. G. Overand, M. Stacey, and L. F. Wiggins, *J. Chem. Soc. (London)*, 2836 (1949).
(23) M. Hoffer, *Chem. Ber.*, **93**, 2777 (1960).
(24) M. P. Kotick, C. Szantay, and Th. J. Bardos, *J. Org. Chem.*, **34**, 3806 (1969).
(25) M. Swierkowski and D. Shugar, *J. Med. Chem.*, **12**, 533 (1969).
(26) The free nucleoside has been described by J. Farkas, J. Beránek, and F. Šorm, *Collect. Czech. Chem. Commun.*, **31**, 4002 (1966); J. Beránek and F. Šorm, *ibid.*, **33**, 913 (1968).
(27) M. J. Robins and R. K. Robins, *J. Amer. Chem. Soc.*, **87**, 4934 (1965).
(28) For comparison the nmr spectra of the two anomeric 1-*p*-nitrobenzoates of 2,3,5-tribenzyl-D-arabinofuranoside [compare R. Baker and H. G. Fletcher, Jr., *J. Org. Chem.*, **26**, 4605 (1961)] were measured: $H_{1'}$ (β-1-*p*-nitrobenzoate), δ 4,57 ppm (J = 3, 5 Hz); $H_{1'}$ (α-1-*p*-nitrobenzoate), δ 4,57 ppm (J = 1 Hz).
(29) B. R. Baker, J. P. Joseph, R. E. Schaub, and J. H. Williams, *J. Org. Chem.*, **19**, 1786 (1954); J. J. Fox and I. Wempen, *Advan. Carbohyd. Chem.*, **14**, 283 (1959); H. G. Fletcher, *Trans. N.Y. Acad. Sci.*, **30**, 649 (1968). On reactions of peracylated sugars with silylated pyrimidines and $SnCl_4$, $TiCl_4$, or $AlCl_3$ as yet no nucleoside with a rearranged sugar could be isolated [compare H. Paulsen, *Advan. Carbohyd. Chem. Biochem.*, **26**, 127 (1971)].
(30) *Chem. Abstr.*, **71**, 30436e (1969); S. Hiller, M. Lidaks, R. A. Zhuk, A. Berzina, K. Pecs, I. N. Getsova, and E. J. Bruk, *Khim. Geterotsikl. Soedin.*, 375 (1969). For further silyl Hilbert-Johnson reactions of 2-chlorotetrahydrofurans and 2-chlorotetrahydropyrans, compare R. Brossmer and V. Eschenfelder, *Justus Liebigs Ann. Chem.*, **762**, 160 (1972); R. A. Earl and L. B. Townsend, *J. Heterocycl. Chem.*, **9**, 1141 (1972).
(31) J. J. Ritter and P. P. Minieri, *J. Amer. Chem. Soc.*, **70**, 4045 (1948); L. I. Krimen and D. J. Cota, *Org. React.*, **17**, 213 (1969).
(32) For leading references for such rearrangements with $HgBr_2$ or $HgCl_2$, compare D. Heller and G. Wagner, *Pharmazie*, **26**, 290 (1971); T. Rogers, R. S. Shadbolt, and T. L. V. Ulbricht, *J. Chem. Soc. C*, 207 (1969).
(33) H. Ohrui, H. Kuzuhara, and S. Emoto, *Tetrahedron Lett.*, 4267 (1971).
(34) K. A. Watanabe, I. M. Wempen, and J. J. Fox, *Carbohyd. Res.*, **21**, 148 (1972).
(35) D. H. Warnock, K. A. Watanabe, and J. J. Fox, *Carbohyd. Res.*, **18**, 127 (1971).
(36) G. Kowollik, G. Demirow, M. Schütt, and P. Langen, *Z. Chem.*, **12**, 106 (1972).
(37) D. S. Wise and L. B. Townsend, *J. Heterocycl. Chem.*, **9**, 1461 (1972).
(38) A. H. Haynes, *Tetrahedron*, **29**, 2807 (1973). Compare also G. H. Ransford, R. P. Glinski and M. B. Sporn, Abstracts of Papers of the 165th National Meeting of the American Chemical Society, Dallas, Texas, April 1973, CARB 17.
(39) G. Quinkert, B. Wegemund, F. Homburg, and G. Cimbollek, *Chem. Ber.*, **97**, 958 (1964); compare ref 8b for the use of two-phase tlc systems.
(40) E. F. Recondo and H. Rinderknecht, *Helv. Chim. Acta*, **42**, 1171 (1959).
(41) P. A. Levene and R. St. Tipson, *J. Biol. Chem.*, **92**, 109 (1931); H. Zinner, *Chem. Ber.*, **83**, 153 (1950).
(42) S. Tejima and H. G. Fletcher, Jr., *J. Org. Chem.*, **28**, 2999 (1963); C. P. J. Glaudemans and H. G. Fletcher, Jr., *ibid.*, **28**, 3004 (1963).
(43) J. Gut, *Collect. Czech. Chem. Commun.*, **23**, 1588 (1958).
(44) For a typical procedure compare the methanolysis of **21b**.
(45) J. Beranek and J. Šorm, German Patent 1445602 (1969).
(46) T. E. Johnson and E. F. Schröder, *J. Amer. Chem. Soc.*, **53**, 1989 (1931).

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

U. Niedballa and H. Vorbrüggen*

Research Laboratories of Schering A. G., Department Allgemeine Synthetische Chemie, 1 Berlin 65, Muellerstrasse 170–172, Germany

Received March 29, 1974

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.

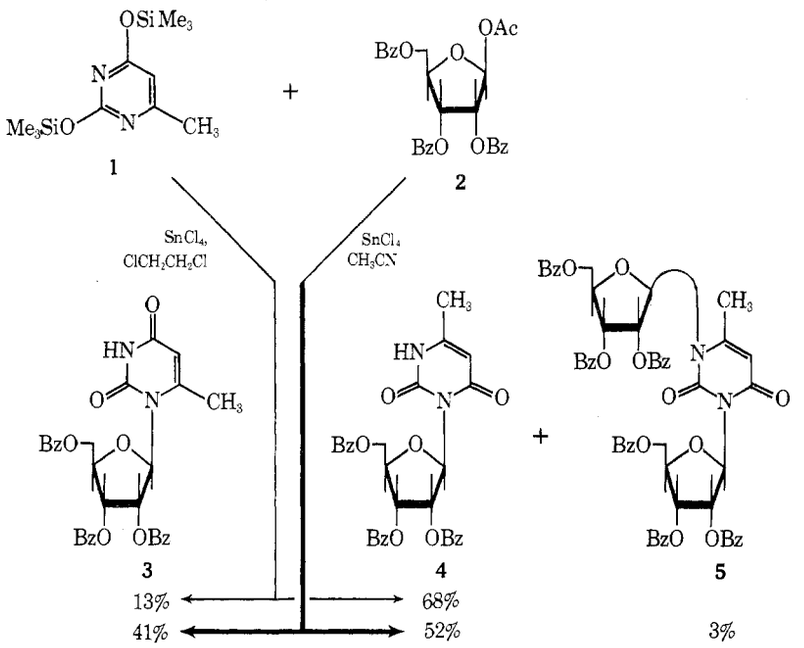
Since the Hilbert-Johnson reaction of silylated pyrimidines with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**2**) and $SnCl_4$ had given exclusively the natural β-N_1-pyrimidine nucleosides (compare part I of this series), we were curious how silylated 6-methyl- as well as 5,6-dimethyluracil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

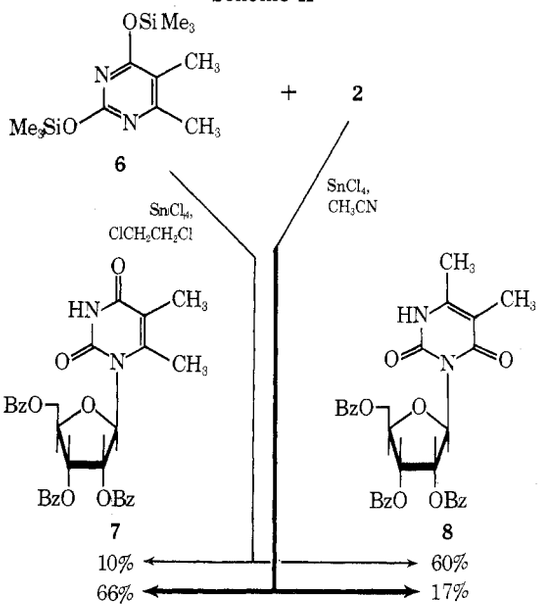
The structures of the N_1- as well as the N_3-nucleosides were established by the typical bathochromic shift of the uv spectra of the N_3-nucleosides in alkaline medium.[8] Furthermore the N_3-β-D-ribofuranosides show a characteristic downfield shift of the H-1′ proton of up to 1 ppm which is due to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

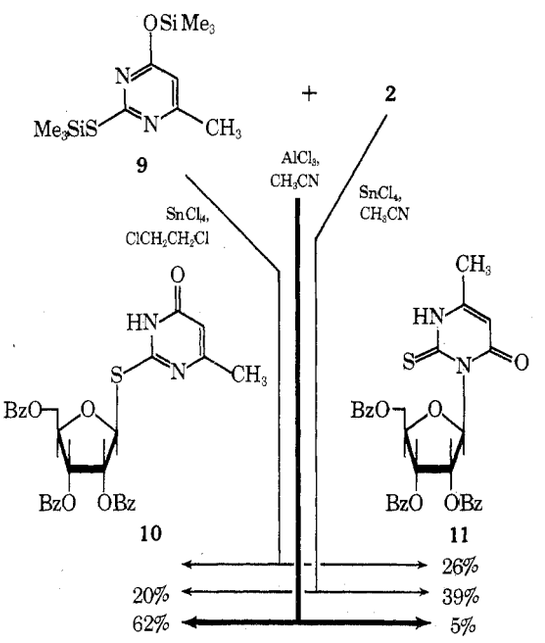
Scheme I



Scheme II



Scheme III



chloroethane were nearly reversed using acetonitrile as a solvent. There was obtained in this instance 66% **7** and 17% **8**, both of which crystallized.

Saponification of the benzoylated N_1-ribosides **3** and **7** gave the known[4,5] corresponding crystalline 6-methyl- and 5,6-dimethyluridines which were identified by their physical data. Saponification of the benzoylated N_3-ribosides **4** and **8** gave the corresponding free N_3-ribosides, which could not be obtained in crystalline form.

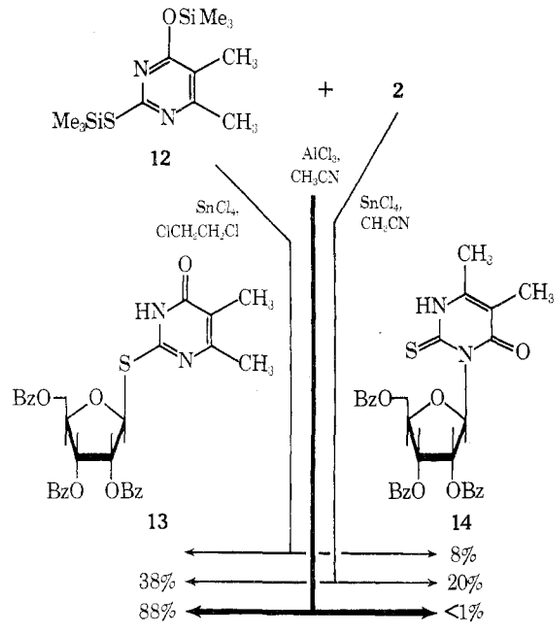
When we tried to prepare 6-methyluridine in larger amounts we encountered difficulties. It turned out that the yield of the benzoylated N_1-riboside **3** was extremely dependent on the purity of the solvents and reagents. As already emphasized in the preceding paper[1] the acetonitrile had to be distilled twice over phosphorus pentoxide, the $SnCl_4$ had to be fresh or to be redistilled, and the 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**2**) had to be recrystallized from 2-propanol or ethanol and subsequently dried carefully in high vacuum.

Traces of acetic acid or 2-propanol in **2** or humidity in the solvents resulted in a dramatic lowering of the yield of the desired benzoylated N_1-riboside **3** and a corresponding increase of the yield of the benzoylated N_3-riboside **4** and N_1,N_3-diriboside **5**. The yield of **3** also decreased on addition of ethereal HCl to the reaction mixture. Furthermore pretreatment of $SnCl_4$ in acetonitrile with small amounts of acetic acid and subsequent addition of **1** and **2** did not give any protected N_1-nucleoside **3** but only a 80% yield of the benzoylated N_3-nucleoside **4**.

When the optimal reaction time of ~3–5 hr was exceeded, the yield of the N_1 product **3** decreased in favor of less polar products. Replacement of $SnCl_4$ by fresh $AlCl_3$ did not improve the yield of **3**. Thus products and yields are dependent on very subtle changes in the reaction conditions and care has to be exercised in order to insure that the reactions proceed optimally.

The reaction of silylated 2-thio-6-methyluracil (**9**)

Scheme IV



(Scheme III) with **2** and $SnCl_4$ or $AlCl_3$ in 1,2-dichloroethane and acetonitrile did not give any of the desired benzoylated N_1-riboside. Instead, only the crystalline benzoylated S-riboside **10** as well as the crystalline benzoylated N_3-riboside **11**[9] were obtained in varying amounts. With increasing polarity of the solvent and strength of the Friedel–Crafts catalyst surprisingly[10] more S-riboside **11** was formed.

The reaction of silylated 2-thio-5,6-dimethyluracil (**12**) with **2** (Scheme IV) gave analogously only the benzoylated S-nucleoside **13** as well as some N_3-nucleoside **14**.

S-Alkylation of silylated 2-thiouracils has been observed before[10] and might be especially favored here because of the steric hindrance of the N_1 position by the 6-methyl group. Thus steric hindrance not only blocks the rearrangement of the S-nucleoside to the N_1-nucleoside, but even the rearrangement to the sterically favored N_3-nucleoside seems to be impeded and dependent on the catalyst–solvent complex.

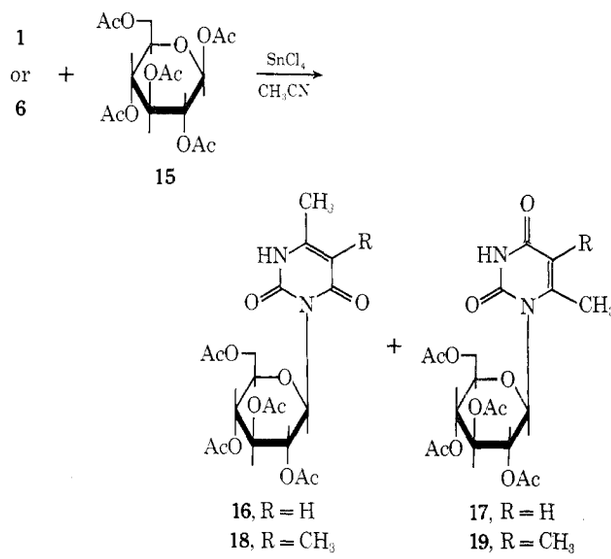
The structures of **10** as well as **13** were proved by cleavage with H_2S–pyridine[10,11] to 6-methyl-2-thiouracil as well as 5,6-dimethyl-2-thiouracil. The benzoylated S-riboside **10** rearranged furthermore on treatment with $HgBr_2$[12] in boiling toluene in moderate yield to the protected N_3-riboside **11**.

Since steric factors seem to determine the formation of either N_1- or N_3-nucleosides in the case of a 6-methyl substituent, we studied the reactions of the silylated uracils **1** and **6** with 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose (**15**)[13] which was expected to give a more bulky cation than **2** (Scheme V).

On reaction of **1** with **15** and $SnCl_4$ in acetonitrile we isolated in 42.3% yield the crystalline N_3-glucoside[6,14] **16** but no N_1-glucoside **17** could be detected. However, **6** gave with **15** in acetonitrile besides 1.2% N_3-glucoside **18** a 22.4% yield of the crystalline N_1-glucoside **19**.

Bärwolf, Kowollik, and Langen[15] discovered recently that silylated 6-fluorothymine reacted with acetobromoglucose in the presence of $SnCl_4$ to afford the N_1-nucleosides in excellent yields. Thus the size of the 6 substituent is critical since Pichat and Chatelain[16] found that silylated 6-chlorouracil gave with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl chloride on heating to 190° only the 6-chloro N_3-riboside in low yield. Analogously Winkley and Robins[17] allowed silylated 6-methylmercaptouracil and 1-bromo-2,3,5-tri-*O*-benzoyl-D-ribofuranose to react in acetonitrile and obtained only the corresponding 6-methylmercapto N_3-riboside in 75% yield, which could be desulfurized to 3-β-D-ribofuranosyluracil after saponification.

Scheme V



It can therefore be anticipated that silylated orotic acid or orotic esters will yield probably only the N_3-nucleosides thus limiting the chemical synthesis of orotidine at present to the efficient Ueda method[18] starting from 2′,3′-*O*-isopropylidene-5-bromouridine.

Experimental Section

For instruments and the purification of solvents as well as the work-up of the reaction mixtures compare part I.[1]

Column chromatography was performed on neutral alumina Woelm and silica gel Merck (Darmstadt). Tlc system: A [ethyl acetate–hexane (2:1)].

6-Methyl- and 5,6-dimethyluracil were purchased from EGA-Chemie KG, Steinheim a. Albuch. 2-Thio-6-methyl- and 5,6-dimethyluracil were prepared according to Draminski and Fiszer.[19]

3-(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)-6-methyl-1,2,-3,4-tetrahydropyrimidine-2,4-dione (4) and 1-(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)-6-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (3). To **1** (12 mmol) and **2** (5.04 g, 10 mmol) in CH_3CN (150 ml), $SnCl_4$ (1.5 ml, 12.9 mmol) in CH_3CN (100 ml) was added under stirring at 14° and stirred 4 hr at 22°. After work-up,[1] chromatography on neutral alumina (300 g, activity III) gave on elution with *n*-hexane–ethyl acetate (9:1) a mixture of unreacted sugar and N_1,N_3-diriboside **5** (400 mg). **5** was purified by preparative tlc on silica gel using the same solvent system and obtained as a white foam: mp 110–112°; yield 0.170 g (3.4%); nmr ($CDCl_3$) δ 6.64 [d, 1, J = 2 Hz, H-1′ (N_3)], 5.77 [s, 1, H-1′ (N_1)], 5.65 (s, 1, H-5), 2.30 (s, 3, 6-CH_3).

Anal. Calcd for $C_{57}H_{46}N_2O_{16}$ (1015.17): C, 67.44; H, 4.57; N, 2.78. Found: C, 67.54; H, 5.01; N, 2.74.

The less polar N_3-nucleoside was eluted from alumina with ethyl acetate–hexane (2:1) and crystallized from the same solvent giving 2.934 g (51.5%) of **4**, mp 108–109°, $[\alpha]^{20}D$ 31.9° (*c* 1, $CHCl_3$).

Anal. Calcd for $C_{31}H_{26}N_2O_9$ (570.53): C, 65.26; H, 4.59; N, 4.91. Found: C, 65.10; H, 4.96; N, 4.92.

The N_1-nucleoside **3** was eluted from alumina with ethyl acetate–methanol (9:1) and crystallized (CH_2Cl_2–pentane) giving 2.316 g (40.6%) of **3**, mp 126–129°, $[\alpha]^{20}D$ −5.0° (*c* 1, $CHCl_3$) (lit.[5] 125–128°).

Anal. Calcd for $C_{31}H_{26}N_2O_9$ (570.53): C, 65.26; H, 4.59; N, 4.91. Found: C, 65.07; H, 4.78; N, 4.88.

The analogous reaction in 1,2-dichloroethane (4 hr at 22°) gave 67% **4** and 13% **3**.

3-(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)-5,6-dimethyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (8) and 1-(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)-5,6-dimethyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (7). To **2** (7.56 g, 15 mmol) and **6** (18

mmol) in CH_3CN (250 ml), $SnCl_4$ (2.0 ml, 17.1 mmol) in CH_3CN (150 ml) was added under stirring at 0°. After stirring overnight at 22° and work-up,[1] the residue was chromatographed on neutral alumina (350 g, activity II). The less polar nucleoside **8** was eluted with *n*-hexane–ethyl acetate (1:1) and crystallized (ethanol) giving 1.46 g (16.7%) of platelets: mp 200–201°; $[\alpha]^{20}D$ 34.6° (*c* 1, $CHCl_3$); nmr ($CDCl_3$) δ 6.73 (d, 1, *J* ≈ 1 Hz, H-1′), 2.17 (s, 3, 6-CH_3), 1.90 (s, 3, 5-CH_3).

Anal. Calcd for $C_{32}H_{28}N_2O_9$ (584.56): C, 65.75; H, 4.83; N, 4.79. Found: C, 65.82; H, 4.87; N, 4.62.

The N_1-nucleoside **7** was eluted with ethyl acetate. Crystallization (CH_2Cl_2–pentane) gave 5.77 g (65.9%) of **7** in needles: mp 176–178°; $[\alpha]^{20}D$ −10.3° (*c* 1, $CHCl_3$); nmr ($CDCl_3$) δ 5.81 (d, 1, *J* < 1 Hz, H-1′), 2.29 (s, 3, 6-CH_3), 1.99 (s, 3, 5-CH_3).

Anal. Calcd for $C_{32}H_{28}N_2O_9$ (584.56): C, 65.75; H, 4.83; N, 4.79. Found: C, 65.50; H, 4.99; N, 4.71.

The analogous reaction in 1,2-dichloroethane (addition of $SnCl_4$ at 0°, then 6 hr at 22°) gave 60.3% **8** and 10.3% **7**.

3-(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)-6-methyl-2-thio-1,2,3,4-tetrahydropyrimidin-4-one (11) and 2-[(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)thio]-6-methyl-3,4-dihydropyrimidin-4-one (10). To **2** (12.6 g, 25 mmol) and 6-methyl-2,4-*S*,*O*-bis(trimethylsilyl)pyrimidine (**9**, 30 mmol) in CH_3CN (300 ml) $SnCl_4$ (10 ml, 85.6 mmol) in CH_3CN (300 ml) was added under stirring at 0°. After 3 hr at 22° and work-up[1] chromatography on neutral alumina (500 g, activity III) gave on elution with ethyl acetate the N_3-nucleoside **11**. The S-riboside **10** was eluted with methanol–H_2O (2:1). **11** crystallized (ethanol) to give 5.75 g (39.3%): mp 192–193°; $[\alpha]^{20}D$ 32.8 (*c* 1, $CHCl_3$); nmr ($CDCl_3$) δ 7.27 (m, 1, H-1′), 5.75 (s, 1, H-5), 2.11 (s, 3, 6-CH_3).

Anal. Calcd for $C_{31}H_{26}N_2O_8S$ (568.62): C, 63.50; H, 4.47; N, 4.77; S, 5.46. Found: C, 63.15; H, 4.48; N, 4.65; S, 5.68.

10 crystallized (ethanol–ether) to give 2.89 g (19.7%): mp 151–153°; $[\alpha]^{20}D$ −22.8° (*c* 1, $CHCl_3$); uv^{20} (CH_3OH) λ_{max} 275 nm (ε 9620), 281 (sh, 8980); nmr ($CDCl_3$) δ 6.45 (d, 1, *J* = 2.5 Hz, H-1′), 6.04 (s, 1, H-5), 2.21 (s, 3, 6-CH_3).

Anal. Calcd for $C_{31}H_{26}N_2O_8S$ (586.62): C, 63.50; H, 4.47; N, 4.77; S, 5.46. Found: C, 63.23; H, 4.37; N, 4.81; S, 5.67.

The analogous reaction with $SnCl_4$ in 1,2-dichloroethane (4 hr, 22°) gave 26% **11**. In CH_3CN–$AlCl_3$ (addition of 1.5 equiv of $AlCl_3$ at 0°, 5 hr at 22°) 62% **10** and ~5% **11** were obtained.

3-(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)-5,6-dimethyl-2-thio-1,2,3,4-tetrahydropyrimidin-4-one (14) and 2-[(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)thio]-5,6-dimethyl-3,4-dihydropyrimidin-4-one (13). To **2** (5.04 g, 10 mmol) and **12** (12.0 mmol) in CH_3CN (200 ml) $SnCl_4$ (3.2 ml, 27.4 mmol) in CH_3CN (80 ml) was added at 14°. After 20 hr at 22° and work-up[1] the residue (5.3 g) was chromatographed on silica gel (260 g). The products were eluted with hexane–ethyl acetate (6:4). The less polar **14** was crystallized (ethanol) giving 1.20 g (20%) of **14**: mp 191–193°; $[\alpha]^{20}D$ −22.7° (*c* 1, $CHCl_3$); nmr ($CDCl_3$) δ 7.50 (d, 1, *J* = 3 Hz, H-1′), 2.12 (s, 3, 6-CH_3), 1.89 (s, 3, 5-CH_3).

Anal. Calcd for $C_{32}H_{28}N_2O_8S$ (600.56): C, 63.99; H, 4.70; N, 4.66; S, 5.30. Found: C, 63.74; H, 5.10; N, 4.88; S, 5.32.

The more polar **13** crystallized (ethanol–ethyl acetate) giving 2.30 g (38.4%) of **13**: mp 135–137°; $[\alpha]^{20}D$ −20.5° (*c* 1, $CHCl_3$); uv^{20} (CH_3OH) λ_{max} 276 nm (10,600), 280 (sh, 10,300); nmr ($CDCl_3$) δ 6.42 (d, 1, *J* = 2.5 Hz, H-1′), 2.23 (s, 3, 6-CH_3), 1.99 (s, 3, 5-CH_3).

Anal. Calcd for $C_{32}H_{28}N_2O_8S$ (600.56): C, 63.99; H, 4.70; N, 4.66; S, 5.30. Found: C, 64.03; H, 5.21; N, 4.99; S, 5.55.

The analogous reaction with $SnCl_4$ in 1,2-dichloroethane (5 hr at 22°) gave 7.7% **14**, whereas with $AlCl_3$ in CH_3CN (2 hr, 20°) 88% **14** and ~1% **13** were obtained.

Treatment of the S-Ribosides with H_2S–Pyridine. A slow stream of H_2S gas was bubbled through **10** (2.0 g, 3.41 mmol) in dry pyridine (30 ml) and stirred for 2 hr at 22°. After evaporation *in vacuo* the residue was extracted with ethyl acetate and the insoluble material crystallized (ethanol) to give 6-methyl-2-thiouracil (440 mg, 90.8%) with mp 300°, which was identical with an authentic sample.[19]

The analogous treatment of **13** (600 mg, 1 mmol) in dry pyridine (30 ml) with H_2S for 3 hr at 40° gave after evaporation and pouring the ethanolic solution into pentane a precipitate, which afforded after crystallization (ethanol) and sublimation [130° (0.001 mm)] 5,6-dimethyl-2-thiouracil (115 mg, 73.7%), mp 225°, which was identical with an authentic sample.[19]

Rearrangement of 2-[(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)thio]-6-methyl-3,4-dihydropyrimidin-4-one (10) with $HgBr_2$. **10** (400 mg, 0.684 mmol) was heated for 2 hr at 100° under argon in benzene–toluene (50 ml, 1:2) with $HgBr_2$ (1.8 g, 4.98 mmol). After filtering and washing with benzene, the filtrate was extracted with KI solution (30%), dried ($MgSO_4$), and evaporated. Tlc (system A) showed that **10** had disappeared and that, beside a sugar derivative, only **11** could be detected in ~10% yield.

3-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-6-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (16). To **15** (13.2 g, 33.9 mmol) in CH_3CN (100 ml) and **1** (200 ml, 40 mmol) in CH_3CN, $SnCl_4$ (5.3 ml, 45.3 mmol) in CH_3CN (200 ml) was added. After 3 hr at 22° and work-up[1] the crude nucleoside (8.5 g) was crystallized (ethanol) with charcoal to give 6.54 g (42.3%) of **16**: mp 153–154°; $[\alpha]^{23}D$ −10.1° (*c* 0.595, $CHCl_3$); nmr ($CDCl_3$) δ 6.30 (d, 1, *J* = 9 Hz, H-1′).

Anal. Calcd for $C_{19}H_{24}N_2O_{11}$ (456.42): C, 49.98; H, 5.30; N, 6.14. Found: C, 49.72; H, 5.44; N, 6.11.

1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-5,6-dimethyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (19) and 3-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-5,6-dimethyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (18). To **15** (3.89 g, 10 mmol) and **6** (12 mmol) in dry CH_3CN (120 ml), $SnCl_4$ (2 ml, 17.1 mmol) in CH_3CN (100 ml) was added at 15°. After 15 hr at 22° and work-up[1] the residue (3.84 g) was dissolved in ethyl acetate and poured into *n*-hexane (1.2 l.). The precipitate was collected and the procedure was repeated twice to give 2.83 g of product, which was chromatographed in ethyl acetate on silica gel (150 g). The first eluate fractions afforded **19** which crystallized (ethanol) to give 1.053 g (22.4%): mp 202–204°; $[\alpha]^{23}D$ 20.1 (*c* 1.02, $CHCl_3$); nmr ($CDCl_3$) δ 6.35 (d, 1, *J* = 9 Hz, H-1′), 2.48 (s, 3, 6-CH_3), 2.06 (s, 3, 5-CH_3).

Anal. Calcd for $C_{20}H_{26}N_2O_{11}$ (470.60): C, 51.05; H, 5.57; N, 5.99. Found: C, 51.06; H, 5.57; N, 6.17.

Following **19** impure **18** (56.4 mg, 1.2%) was eluted: uv (CH_3OH + H_2O) λ_{max} (pH 1) 270 nm, λ_{min} (pH 1) 242 nm, λ_{max} (pH 13) 299 nm, λ_{min} (pH 13) 253 nm; nmr ($CDCl_3$) δ 6.18 (d, 1, *J* = 7 Hz, H-1′).

Acknowledgment. We are indebted to Dr. G.-A. Hoyer and Dr. D. Rosenberg for the nmr spectra and Diplom-Ing. G. Huber for the analyses.

Registry No.—**1**, 31111-31-6; **2**, 6974-32-9; **3**, 23316-76-9; **4**, 24744-17-0; **5**, 25691-87-6; **6**, 31111-32-7; **7**, 25691-82-1; **8**, 52523-05-4; **9**, 32865-97-7; **10**, 52523-06-5; **11**, 29881-44-5; **12**, 52523-07-6; **13**, 52523-08-7; **14**, 52523-09-8; **15**, 604-69-3; **16**, 52554-31-1; **18**, 52523-10-1; **19**, 52523-11-2.

References and Notes

(1) Synthesis of Nucleosides No. 10. Part I: *J. Org. Chem.*, **39**, 3654 (1974).
(2) For the proof of the syn conformation compare nmr evidence [M. P. Schweizer, J. T. Witkowski, and R. K. Robins, *J. Amer. Chem. Soc.*, **93**, 277 (1971)]; X-ray analysis [D. Suck and W. Saenger, *ibid.*, **94**, 6520 (1972)] and dipole moments [I. Kulakowska, A. Rabczenko, and D. Shugar, *Biochem. Biophys. Res. Commun.*, **48**, 65 (1972)].
(3) For the biochemical and pharmacological effects compare, *e.g.*, A. M. Kapuler and S. Spiegelman, *Proc. Nat. Acad. Sci.*, **66**, 539 (1970); A. M. Kapuler, C. Monny, and A. M. Michelson, *Biochim. Biophys. Acta*, **217**, 18 (1970); S. S. Tavale and H. M. Sobell, *J. Mol. Biol.*, **48**, 109 (1970); S. S. Tavale and H. M. Sobell, *J. Mol. Biol.*, **48**, 109 (1970); A. R. Diwan, R. K. Robins, and W. H. Prusoff, *Experientia*, **25**, 98 (1969).
(4) M. W. Winkley and R. K. Robins, *J. Org. Chem.*, **33**, 2822 (1968).
(5) M. Prystaš and F. Šorm, *Collect. Czech. Chem. Commun.*, **34**, 2316 (1969).
(6) N. Yamaoka, E. Takahashi, and K. Tuzimura, *Carbohyd. Res.*, **19**, 262 (1971).
(7) E. Wittenburg, *Collect Czech. Chem. Commun.*, **36**, 246 (1971).
(8) J. J. Fox and D. Shugar, *Biochim. Biophys. Acta*, **9**, 199 (1952); **9**, 369 (1952); M. Sano, *Chem. Pharm. Bull. (Tokyo)*, **10**, 320 (1962). For a recent survey compare R. Shapiro and S. Kang, *Biochim. Biophys. Acta*, **232**, 1 (1971).
(9) T. Ueda and H. Tanaka, *Chem. Pharm. Bull. (Tokyo)*, **18**, 1491 (1970).
(10) Compare H. Vorbrüggen and P. Strehlke, *Chem. Ber.*, **106**, 3039 (1973).
(11) T. Ueda and H. Nishino, *J. Amer. Chem. Soc.*, **90**, 1678 (1968).
(12) For a recent review of such rearrangements compare G. Wagner, *Pharmazie*, **25**, 675 (1970).
(13) Compare ref 6 and 7 for the reaction of **1** with acetobromoglucose.
(14) The nmr spectra of the free N_3-glucoside have been discussed by N. Yamaoka, H. Sugiyama, and K. Tuzimura, *Bull Chem. Soc. Jap.*, **44**, 1442 (1971), and K. A. Watanabe, S. S. Saluja, B. A. Otter, and J. J. Fox, *Tetrahedron Lett.*, 3911 (1972).
(15) D. Bärwolf, G. Kowollik, and P. Langen, *Collect Czech. Chem. Commun.*, **39**, 1494 (1974).
(16) L. Pichat and G. Chatelain, *Bull. Soc. Chim. Fr.*, 1833 (1970).
(17) M. W. Winkley and R. K. Robins, *J. Chem. Soc.* C, 791 (1969).
(18) H. Inoue and T. Ueda, *Chem. Pharm. Bull. (Tokyo)*, **19**, 1743 (1971); S. Senda, K. Hirota, and T. Asao, *Tetrahedron Lett.*, 1647 (1973).
(19) M. Draminski and B. Fiszer, *Roczniki Chem.*, **45**, 211 (1971).
(20) For the uv spectra of S-alkylated 2-thiouracils compare ref 10.