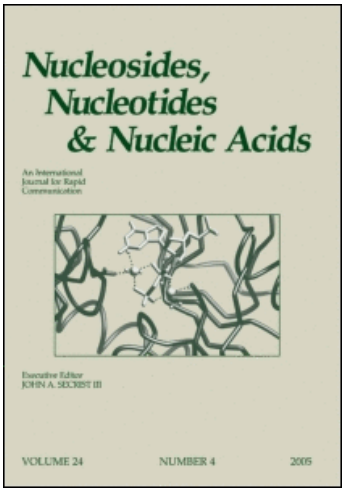

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Aminopyrimidines and Derivatives. 20. On the Acetylations of 5-Amino-4-Glycosylmino Pyrimidines

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AMINOPYRIMIDINES AND DERIVATIVES.20. ON THE ACETYLATIONS OF 5-AMINO-4-GLYCOSYLAMINO PYRIMIDINES.

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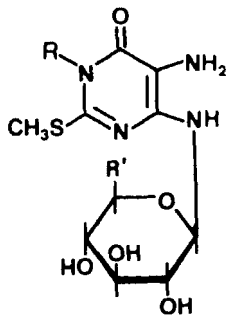
Abstract: The acetylation of 5-amino-4-glycosylamino pyrimidines afforded a wide variety of compounds, depending on the reaction conditions. A systematic study has been carried out and some conclusions with synthetic utility are proposed.

5-Amino-4-glycosylamino pyrimidines[1] are excellent starting materials for the syntheses of condensed heterocyclic systems, such as glycosylpurines[2], glycosylpteridines[3], glycosyltriazolopyrimidines[4] or glycosyloxazolopyrimidines[5]. All these products are nucleoside analogs, and their interest lies on their potential biological action, which covers a wide range of activities[6].

The interest of the title compounds prompted us to try their acetylation as a part of a wider study on the reactivity of these versatile products. We have found that a considerable number of products are formed, depending on the reaction conditions. In some cases an acetolysis of the glycosidic bond takes place, and many of the acetolysis products have been identified.

The acetylations have been performed on the products shown in Scheme 1[1]. The reaction products are shown in Scheme 2, and the results in the Table.



1

Comp	R	R'
1a	H	H
1b	H	CH_2OH
1c	CH_3	H
1d	CH_3	CH_2OH

SCHEME 1

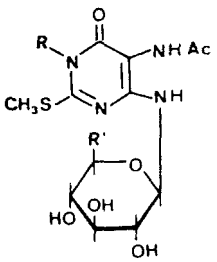
RESULTS AND DISCUSSION

5-Amino-4-glycosylamino pyrimidines **1** present three active sites for nucleophilic attack, aside from the sugar hydroxyls. The selective acetylation with acetic anhydride-methanol leads to the formation of 5-N-monoacetyl derivatives **2** as a consequence of the pronounced basic character of the 5-amino group in **1**[7].

When the acetylation is performed in acetic anhydride-pyridine at 0ºC, 5-N-monoacetyl derivatives **3c** and **d** are obtained from **1c** and **d**, whereas 5-N-diacetyl derivatives **4a** and **b** are obtained from **1a** and **b**.

The acetylation with acetic anhydride-pyridine at 80ºC on **1c** and **d** yields the 5-N-diacetyl derivatives **4**, but also produces an extensive hydrolysis of the glycosidic bond on **1a** and **b**, as well as a diminution in the yield of **4a** and **b**. The stability of the glycosidic bond seems to be increased by the N_1-Me substituent.

The possibility of cyclization to oxazolopyrimidines (on **1a** and **b**) together with a more extensive acetolysis of the glycosidic bond account for the formation of complex mixtures when the acetylation is carried out with Ac_2O under reflux or with acid catalysis. In fact, acid media seem to favour the cyclization to oxazolopyrimidines[5,8]. The total amount of oxazolopyrimidines obtained under the above mentioned conditions is in the order of 35-50% of the overall yield, against 30-25% of N-acetyl pyrimidines. The only exception is the acetylation of **1b** with $Ac_2O/HClO_4$. Only 25% of oxazolopyrimidines were obtained in this case, although 35% of them correspond to products of acetolysis of the glycosidic bond.



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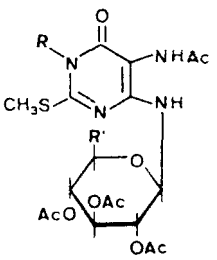
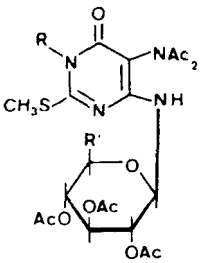


3

Comp	R	R'
2a	H	H
2b	H	CH_2OH
2c	CH_3	H
2d	CH_3	CH_2OH
3b	H	CH_2OAc
3c	CH_3	H
3d	CH_3	CH_2OAc
4a	H	H
4b	H	CH_2OAc
4c	CH_3	H
4d	CH_3	CH_2OAc
5a	--	H
5b	--	CH_2OAc
6a	--	H
6b	--	CH_2OAc



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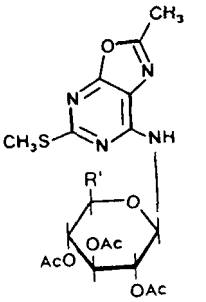

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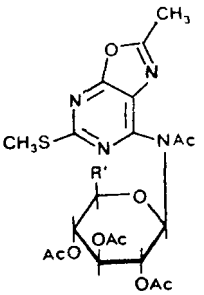

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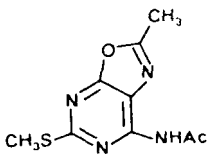

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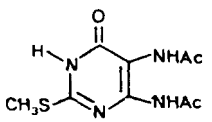

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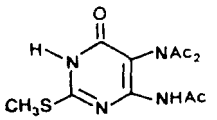

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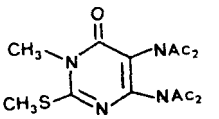

10

SCHEME 2

TABLE

ACETYLATION OF 1: REACTION PRODUCTS AND YIELDS (%)

	Ac_2O/MeOH	Ac_2O/Py, 0°C	Ac_2O/Py, 80°C	Ac_2O, reflux	$Ac_2O/HClO_4$
1a	2a (90)	4a (92)	4a (40) 6a (8)*	4a (34) 5a (14) 6a (20)*	6a (52)*
1b	2b (80)	4b (80)	4b (30)*	3b (2) 7(1) 4b (18) 9(14)* 5b (25) 6b (10)	3b (9) 8(12.5)* 5b (11) 6b (6) 7 (8.5)
1c	2c (70)	3c (80)	4c (100)	4c (64)	3c (32) 10 (35) 4c (30)
1d	2d (71)	3d (80)	4d (88)	4d (88)	3d (4) 10 (40) 4d (44)

*: Unidentified products of acetolysis of the glycosidic bond have also been detected in 25-40%.

However, when the acetylation of **1a** and **b** is performed in basic medium, oxazolopyrimidines are not practically formed. A 5-acetamido derivative must be rapidly formed because of the high nucleophilicity of the 5-amino group. The subsequent pathway must differ, according to the type of catalysis employed. Acid catalysts must decrease the nucleophilicity of C_5-N and increase the electrophilicity of the 5-acetamido carbonyl carbon, and therefore its attack on the polarized C_6-O group would have to take place more readily than the entry of a second acetyl group into nitrogen. In fact, in an independent experiment it has been found that the treatment of the 5-acetamido derivative **3b** with $POCl_3$ afforded quantitatively the oxazolopyrimidine **5b**. On the other hand, basic catalysts must stabilize a phenoxide anion on C_6, and its attraction on the C_5-NHAc proton must allow the entry of a second acetyl group on nitrogen. On C_5 unsubstituted analogs, the acetylation with Ac_2O/Py yielded the corresponding phenol esters[9]. Finally, when the acetylation is carried out without catalyst (Ac_2O under reflux), the total amount of both oxazolopyrimidines and N-acetyalmino pyrimidines are about the same.

The low nucleophilicity of the 4-amino group seems to be additionally weakened by its sugar substituent, because not even traces of purines (which should have been eventually formed by electrophilic attack of the C_5-acetamido carbonyl carbon on C_4-N) have been observed. The formation of purines have been reported in non-glycosidic similar instances[8].

The oxazole ring decreases the de-activation of the C_4 of the condensed system, allowing the acetylation of the corresponding 4-amino group (product **6**).

Products **7**, **8**, **9** and **10** presumibly must come from the acetolysis of the glycosidic bonds, due to the strong conditions used.

In summary, the most suitable conditions for the syntheses of the products shown in the Table are as follows. For 5-acetamido-4-glycosylamino pyrimidines (**2**, free sugar hydroxyls): Ac_2O/MeOH (70-90% overall yield). For 5-acetamido-4-glycosylamino pyrimidines (**3**, O-acetyl sugar): Ac_2O/Py at 0ºC (80% overall yield only for **3c** and **d**; not suitable for **3a** and **b**). For 5-N,N-diacetylamino-4-glycosylamino pyrimidines (**4**): Ac_2O/Py at 0ºC for **4a** and **b** (80-90% overall yield) and Ac_2O/Py at 80ºC for **4c** and **d** (90-100% overall yield). For xylopyrano-

syl oxazolopyrimidines (**5a** and **6a**): $Ac_2O/HClO_4$ (50% overall yield). -- For glucopyranosyl oxazolopyrimidines (**5b** and **6b**): Ac_2O under reflux - (35% overall yield).

EXPERIMENTAL

Melting points were determined in a Melting point Apparatus Gallemkamp and are uncorrected. Proton nuclear magnetic resonance spectra were recorded with a Bruker WH400, a Bruker WP80SY and a Hitachi - Perkin-Elmer R600 using Me_4Si as internal standard. Specific rotation values were determined with a polarimeter Perkin-Elmer 141. Ultraviolet-visible spectra were recorded with a Model 25 spectrophotometer -- Beckman. Infrared spectra with a spectrophotometer Beckman 4250 and a Perkin-Elmer 782 (KBr pellets). The elemental analyses were determined with a Carlo Erba elemental analyser Mod. 1106.

The following acetylation methods have been employed:

Acetylation with acetic anhydride-methanol:

a) To a suspension of **1a** or **b** (10 mmol) in 75 ml of methanol, Ac_2O (5 ml) was added. The suspension was stirred at room temperature for 30 min. The reaction took place in suspension. The solid was filtered -- and washed with cold methanol. By evaporating the mother liquors and - crystallizing the solid in the minimal amount of ethanol, a second --- crop was obtained.

b) To a stirred suspension of **1c** or **d** (10 mmol) in 75 ml of methanol, Ac_2O (5 ml) was added. The suspension was heated at 40ºC until all the solids dissolved. The solvents were completely removed under reduced - pressure by adding methanol and evaporating several times. The temperature was allways kept below 40°C. The resulting solid was crystallized from ethanol.

Acetylation with acetic anhydride-pyridine, 0°C: Over a solution of Ac_2O (60 ml) and pyridine (60 ml) at 0°C, **1** (10 mmol) was added. All the solids dissolved in 10-15 min. The solution was kept at 0ºC for 24 hours. Methanol was added in cold, and the solvents were completely removed as described in the former paragraph. The solid was recrystallized from absolute ethanol.

Acetylation with acetic anhydride-pyridine, 80ºC: Over a solution of Ac_2O (45 ml) and pyridine (45 ml) at 80°C, the glycoside **1** (10 mmol) was added. The solids dissolved inmediately, and the solution was kept

at 80°C for 24 hours. The solvents were removed as usual, and the solid worked-up as follows: when the acetylation was performed on **1a** or **b**, the solid was fractionated by column chromatography on silica gel, using a mixture of ethyl acetate/ethanol/hexane (2:1:7) as eluent. The oxazole **6** was recovered first, and then the diacetylamino derivative **4**. When the reaction was performed on **1c** or **d**, direct crystallization of the solid in absolute ethanol resulted in excellent yields in **4c** and **d** respectively.

Acetylation with acetic anhydride under reflux: A suspension of **1** (10 mmol) in Ac_2O (95 ml) was stirred under reflux. All the solids dissolved in 10-15 min. The reflux was kept for 3 hours and the solution worked-up as follows:

a) When the acetylation was performed on **1a**, methanol was added, and the solution was evaporated under reduced pressure. The solvents were completely removed in the usual way. The resulting solid was fractionated by column chromatography on silica gel, using ethyl acetate/ethanol/hexane (2:1:7) as eluent. The order of elution was **6a**, **5a** and **4a**.

b)[10]: When the acetylation was performed on **1b** or **d**, the solution was poured on 150 g of ice containing 163 grams (1.94 mmol) of $NaCO_3H$.[11] The resulting mixture was washed with 3x100 ml of $CHCl_3$. The chloroform solution was dried with Na_2SO_4, and the solvents removed in rotary evaporator. The remaining solid was fractionated by column chromatography as indicated in paragraph a). For the reaction mixture obtained from **1b**, the order of elution was **7**, **5b**, **6b**, **9**, **4b** and **3b**.

c) When the acetylation was performed on **1c**, ethanol was added to the solution, and the solvents completely removed in the usual way. The resulting solid was directly crystallized from absolute ethanol.

Acetylation with acetic anhydride-perchloric acid: The glycoside **1** (10 mmol)was suspended in Ac_2O (80 ml). The acid catalyst was prepared by adding 3 drops of $HClO_4$ to 15 ml of Ac_2O. After 10 min., the catalyst was added to the suspension, and the mixture was kept 24 hours at 115°C. Then the solution was cooled in an ice bath, and MeOH (50 ml) was added drop by drop. When the addition finished, the solution was kept 30 more minutes in the ice bath. The solvents were completely removed by the usual procedure. The solid was fractionated by column chromatography as described above. The order of elution for the mixtu-

re derived from **1b** was **8**, **7**, **5b**, **6b** and **3b**, and for the ones derived from **1c** and **d** was **10**, **4** and **3**.

The following products have been obtained:

5-Acetamido-1,6-dihydro-2-methylthio-4-β-D-xylopyranosylamino-6-oxo-pyrimidine (2a): m.p.:180°C (d); $|\alpha|_D^{22}$ = 8° (c 1.5, DMSO); u.v. (c 2.2×10^{-5}M, MeOH): λ_{max} 285 (ε 9900) nm; i.r.: ν 3360 (m), 3300 (m, broad), 2800-2980 (w, broad, several bands), 1660 (s) and 1520 (s) cm^{-1}; ^{1}H-nmr (DMSO-d_6): 12.2 (s, broad, 1H, exchangeable by D, N_1-H), 8.6 (s, 1H, exchangeable by D, C_5N-H), 6.8 (d, J= 9Hz, 1H, exchangeable by D, C_4N-H), 5.6-3.0 (m, 9H, sugar protons), 2.5 (s, 3H, S-Me), 2.0 (s, 3H, C_5N-Ac). Anal. Calcd. for $C_{12}H_{18}N_4O_6S$: C 41.62, H 5.20, N 16.18. Found: C 41.58, H 5.08, N 16.01.

5-Acetamido-1,6-dihydro-2-methylthio-4-β-D-glucopyranosylamino-6-oxo-pyrimidine (2b) : m.p.: 209-210°C; $|\alpha|_D^{22}$ = -10° (c 1, DMSO); u.v. (c 3.9×10^{-5}M, MeOH): λ_{max} 286 (ε 5800) nm; i.r.: ν 3460 (m), 3320 (s, broad),1705 (s), 1610 (s) and 1545 (s) cm^{-1}; ^{1}H-nmr (DMSO-d_6): 8.55 s, 1H, exchangeable by D), 6.75 (d, J= 9Hz, exchangeable by D, C_4-NH), 5.3-3.0 (m, 11H, sugar protons), 2.5 (s, 3H, S-Me), 2.0 (s, 3H, C_5N-Ac) Anal. Calcd. for $C_{13}H_{20}N_4O_7S$: C 41.49, H 5.32, N 14.89. Found: C 41.47 H 5.28, N 14.81.

5-Acetamido-1,6-dihydro-1-methyl-2-methylthio-4-β-D-xylopyranosylamino-6-oxo-pyrimidine (2c): m.p.: 170-175°C; $|\alpha|_D^{22}$ = 5° (c 1, DMSO); u.v. (c 7×10^{-5}M, MeOH): λ_{max} 286 (ε 4800) and 232 (12800) nm; i.r.: ν 3460 (m), 3360 (s, broad), 2920 (w), 1705 (s), 1655 (s) and 1545 (s) cm^{-1}; ^{1}H-nmr (DMSO-d_6): 8.65 (s, 1H, exchangeable by D, C_5N-H), 6.75 (d, J= 9Hz, 1H, exchangeable by D, C_4N-H), 5.5-3.0 (m, 9H, sugar protons), 3.4 (s, 3H, N_1-Me), 2.55 (s, 3H, S-Me), 2.0 (s, 3H, C_5N-Ac). Anal. Calcd. for $C_{13}H_{20}N_4O_6S$: C 43.33, H 5.55, N 15.55. Found: C 43.28 H 5.49, N 15.52.

5-Acetamido-1,6-dihydro-1-methyl-2-methylthio-4-β-D-glucopyranosylamino-6-oxo-pyrimidine (2d): m.p.: 190-195°C; $|\alpha|_D^{22}$ = -20° (c 1.5, DMSO); u.v. (c 1.92×10^{-5}M, MeOH): λ_{max} 285 (ε 19400) and 233 (50000) nm; i.r.: ν 3460-3360 (w, broad), 2980 (w), 1690 (s), 1630 (s) and 1550 (s) cm^{-1}; ^{1}H-nmr (DMSO-d_6): 8.6 (s, 1H, exchangeable by D, C_5N-H), 6.7 (d, J= 9Hz, 1H, exchangeable by D, C_4N-H), 5.3-3.0 (m, 11H, sugar protons), 3.3 (s, 3H, N_1-Me), 2.55 (s, 3H, S-Me), 2.0 (s, 3H, C_5N-Ac).

Anal. Calcd. for $C_{14}H_{22}N_4O_7S$: C 43.08, H 5.64, N 14.36. Found: C 43.02 H 5.61, N 14.27.

5-Acetamido-1,6-dihydro-2-methylthio-4-(2 ,3 ,4 ,6 -tetra-O-acetyl-β--D-glucopyranosylamino)-6-oxo-pyrimidine (3b): m.p.: 220-221°C; $|\alpha|_D^{25}$ = -18° (c 1, $CHCl_3$); u.v. (c 9x10^{-5}M, MeOH): λ_{max} 284 (ε 8000) and 232 (14200) nm; i.r.: ν 3410 (w), 3270 (w, broad), 3000(w, broad), 1765 (s), 1675 (s), 1615 (s) and 1575 (m) cm^{-1}; ^{1}H-nmr ($CDCl_3$): 7.95 (s, 1H, exchangeable by D, C_5N-H), 6.45 (d, J= 9Hz, 1H, exchangeable by D, C_4N-H), 4.85-5.55 (m, 4H, H-1 ,2 ,3 and 4), 4.00-4.25 (m, 2H, H-6), 3.65-3.90 (m, 1H, H-5), 2.50 (s, 3H, S-Me), 2.00-2.10 (m, 15H, C_5N-Ac and sugar-O-acetyls). Anal. Calcd. for $C_{21}H_{28}N_4O_{11}S$: C 46.32, H 5.15, N 10.29. Found: C 46.28, H 5.01, N 10.12.

5-Acetamido-1,6-dihydro-1-methyl-2-methylthio-4-(2 ,3 ,4 -tri-O-acetyl-β-D-xylopyranosylamino)-6-oxo-pyrimidine (3c): m.p.: 205-7°C, $|\alpha|_D^{22}$ = 11° (c 1, $CHCl_3$); u.v. (c 2.79x10^{-5}M, MeOH): λ_{max} 285 (ε 9400) nm; i.r.: ν 3375 (w), 2970-2900 (w, broad), 1740 (s), 1640 (m), 1595 (s) and 1510 (m) cm^{-1}; ^{1}H-nmr ($CDCl_3$): 7.80 (s, broad, 1H, exchangeable by D, C_5N-H), 6.42 (d, J= 9Hz, 1H, exchangeable by D, C_4N-H), 5.30 (pt, 2H, H-1 and 3), 4.80-5.20 (m, 2H, H-2 and 4), 4.12 (dd, 1H, H-5 e) 3.43 (s, 4H, N_1-Me and H-5 a), 2.55 (s, 3H, S-Me), 2.15 (s, 3H, C_5N-Ac) 2.05 (s, 9H, sugar-O-acetyls). Anal. Calcd. for $C_{19}H_{26}N_4O_9S$: C 46.91, H 5.35, N 11.52. Found: C 46.79, H 5.10, N 11.36.

5-Acetamido-1,6-dihydro-1-methyl-2-methylthio-4-(2 ,3 ,4 ,6 -tetra-O--acetyl-β-D-glucopyranosylamino)-6-oxo-pyrimidine (3d): m.p.: 199°C; $|\alpha|_D^{22}$ = -9° (c 1, $CHCl_3$); u.v. (c 2.5x10^{-5}M, MeOH):λ_{max} 285 (ε 6800) nm; i.r.: ν 3400 (w, broad), 3260 (w, broad), 3040-2920 (w, broad), 1745 (s), 1655 (m), 1610 (s) and 1530 (m) cm^{-1}; ^{1}H-nmr ($CDCl_3$): 7.40 (s, 1H, exchangeable by D, C_5N-H), 6.50 (d, J= 9Hz, exchangeable by D, C_4N-H), 5.38 (dd, 2H, H-1 and 3), 5.06-5.13 (m, 2H, H-2 and 4), 4.24 (dd, 1H, H-6), 4.10 (dd, 1H, H-6), 3.77 (m, 1H, H-5), 3.46 (s, 3H, N_1-Me), 2.58 (s, 3H, S-Me), 2.18 (s, 3H, C_5N-Ac) and 2.06-2.09 (m, 12H, sugar-O-acetyls); Anal. Calcd. for $C_{22}H_{30}N_4O_{11}S$: C 47.31, H 5.38, N 8.60. Found: C 47.26, H 5.29, N 8.49; m.s.: see ref.12.

5-(N,N-diacetylamino)-1,6-dihydro-2-methylthio-4-(2 ,3 ,4 -tri-O-ace--tyl-β-D-xylopyranosylamino)-6-oxo-pyrimidine (4a): m.p. : 120-122°C; $|\alpha|_D^{25}$ = 30° (c 1, $CHCl_3$); u.v. (c 4.36x10^{-5}M, MeOH): λ_{max} 284 (ε 8950) and 232 (18400) nm; i.r.: ν 3370 (w), 3020 (w), 2920 (w), 1760 (s),

1670 (m), 1615 (m) and 1565 (m) cm^{-1}; ^{1}H-nmr ($CDCl_3$): 6.05 (d, J= 9Hz, 1H, exchangeable by D, C_4N-H), 5.30 (m, 2H, H-1 and 3), 5.0 (m, 2H, H-2 and 4), 4.15 (dd, 1H, H-5 e), 3.35 (pt, 1H, H-5 a), 2.55 (s, 3H, S-Me), 2.50 (s, 3H, C_5N-Ac), 2.20 (s, 3H, C_5N-Ac), 2.05 (s, 9H, sugar--O-acetyls). Anal. Calcd. for $C_{20}H_{26}N_4O_{10}S$: C 46.69, H 5.06, N 10.89. Found: C 46.57, H 5.01, N 10.80; m.s.: see ref. 12.

5-(N,N-diacetylamino)-1,6-dihydro-2-methylthio-4-(2 ,3 ,4 ,6 -tetra--O-acetyl- β-D-glucopyranosylamino)-6-oxo-pyrimidine (4b): m.p.: 145-6 °C; $|\alpha|_D^{25}$ = 21° (c 1, $CHCl_3$); u.v. (c 3.48x10^{-5}M, MeOH): λ_{max} 284 (ε 9800) and 232 (19600) nm; i.r.: ν 3380 (w, broad); 3030 (w), 2940 (w), 1770 (s), 1675 (m), 1610 (s) and 1570 (m) cm^{-1}; ^{1}H-nmr ($CDCl_3$): 6.00 (d, J= 9Hz, 1H, exchangeable by D, C_4N-H), 5.60-4.90 (m, 4H, H-1 , 2 , 3 and 4), 4.05-4.55 (m, 1H, H-5), 2.55 (s, 3H, S-Me), 2.50 (s, 3H, C_5N-Ac), 2.25 (s, 3H, C_5N-Ac), 2.05 (s, 12H, sugar-O-acetyls). Anal. Calcd. for $C_{23}H_{30}N_4O_{12}S$: C 47.10, H 5.12, N 9.56. Found: C 46.98, H 5.08, N 9.49.

5-(N,N-diacetylamino)-1,6-dihydro-1-methyl-2-methylthio-4-(2 ,3 ,4 ---tri-O-acetyl-β -D-xylopyranosylamino)-6-oxo-pyrimidine (4c): m.p.: --251-3°C; $|\alpha|_D^{22}$ = 60° (c 1, $CHCl_3$); u.v. (c 4x10^{-5}M, MeOH): λ_{max} 285 (ε 8550) and 233 (20400) nm; i.r: ν 3410 (w), 2990 (w), 2960 (w), 2940 (w), 2920 (w), 1750 (s), 1735 (s), 1715 (s), 1655 (s), 1605 (s) and 1530 (s) cm^{-1}; ^{1}H-nmr ($CDCl_3$): 5.73 (d, J= 9Hz, exchangeable by D^{13} , C_4N-H), 5.36 (pt, 1H, H-3), 5.25 (dd, 1H, H-1), 5.00 (m, 1H, H-4), 4.91 (pt, 1H, H-5 e), 3.38 (pt, 1H, H-5 a), 3.48 (s, 3H, N_1-Me), 2.60 (s, 3H, S-Me), 2.55 (s, 3H, C_5N-Ac), 2.21 (s, 3H, C_5N-Ac), 2.05 (s, 9H, sugar-O-acetyls). Anal. Calcd. for $C_{21}H_{28}N_4O_{10}S$: C 47.73, H 5.30, N 10.61. Found: 47.67, H 5.22, N 10.60.; m.s.: see ref.12.

5-(N,N-diacetylamino)-1,6-dihydro-1-methyl-2-methylthio-4-(2 ,3 ,4 ,6 -tetra-O-acetyl-β -D-glucopyranosylamino)-6-oxo-pyrimidine (4d): m.p.: 130-1°C; $|\alpha|_D^{22}$ = 25° (c1, $CHCl_3$); u.v. (c 4x10^{-5}M, MeOH): λ_{max} 284 (ε 8100) and 232 (20000) nm; i.r.: ν 3420 (w, broad), 3060 (w), 2970 (w), 1780 (s), 1690 (m), 1630 (s), 1560 (s) and 1500 (m) cm^{-1}; ^{1}H-nmr ($CDCl_3$): 6.10 (d, J= 9Hz, 1H, exchangeable by D, C_4N-H), 5.80-5.00 (m, 4H, H-1 , 2 , 3 and 4), 4.15-4.35 (m, 2H, H-6), 3.55 (s, 3H, N_1-Me) 3.80-3.22 (m, 1H, H-5), 2.60 (s, 3H, S-Me), 2.55 (s, 3H, C_5N-Ac), 2.25 (s, 2H, C_5N-Ac), 2.05 (s, 12H, sugar-O-acetyls). Anal. Calcd. for $C_{24}H_{32}N_4O_{12}S$: C 48.00, H 5.33, N 9.33. Found: C 47.93, H 5.29, N 9.17.

2-Methyl-6-methylthio-4-(2 ,3 ,4 -tri-O-acetyl- β-D-xylopyranosylamino -oxazolo|5,4-d|pyrimidine (5a)[14]: m.p.: 186-188°C; $|\alpha|_D^{25}$ = 2° (c 1 -- $CHCl_3$); u.v. (c 3.5x10^{-5}M, MeOH): λ_{max} 277 (ε 15600) and 240 (14900) nm; i.r.: ν 3360 (w), 2990 (w), 2910 (w), 1775 (s), 1650 (s) and 1605 (w) cm^{-1}; ^{1}H-nmr: see ref. 5. Anal. Calcd. for $C_{18}H_{22}N_4O_8S$: C 47.58, H 4.85, N 12.33. Found: C 47.49, H 4.82, N 12.27; m.s.: see ref. 12.

2-Methyl-6-methylthio-4-(2 ,3 ,4 ,6 -tetra-O-acetyl- β-D-glucopyrano-- sylamino)-oxazolo|5,4-d|pyrimidine (5b)[14]: m.p.: 160-1°C; $|\alpha|_D^{25}$ = -- -27° (c 1, $CHCl_3$); u.v. (c 7.8x10^{-5}M, MeOH): λ_{max} 277 (ε 17000) and 241 (15000); i.r.: ν 3410 (w), 2930 (w), 1747 (s), 1623 (s), 1581 (m) and 1518 (m) cm^{-1}; ^{1}H-nmr: see ref. 5. Anal. Calcd. for $C_{21}H_{26}N_4O_{10}S$: C 47.91, H 4.94, N 10.65. Found: C 47.82, H 4.89, N 10.60; m.s.: see ref. 12.

4-Acetamido-2-methyl-6-methylthio-4-N-(2 ,3 ,4 -tri-O-acetyl- β-D-xy-- lopyranosyl)-oxazolo|5,4-d|pyrimidine (6a)[14]: m.p.: 156-7°C; $|\alpha|_D^{25}$ = = -12° (c 1, $CHCl_3$); i.r.: ν 2990 (w), 2970 (w), 2950 (w), 2930 (w), 2880 (w), 1760 (s), 1690 (m), 1610 (s) and 1555 (m) cm^{-1}; ^{1}H-nmr: see ref. 5. Anal. Calcd. for $C_{20}H_{24}N_4O_9S$: C 48.39, H 4.84, N 11.29. Found: C 48.28, H 4.37, N 11.21; m.s.: see ref. 12.

4-Acetamido-2-methyl-6-methylthio-4-N-(2 ,3 ,4 ,6 -tetra-O-acetyl-β - -D-glucopyranosyl)-oxazolo|5,4-d|pyrimidine (6b)[14]: m.p.: 119-120°C; - $|\alpha|_D^{25}$ = 26° (c1, $CHCl_3$); u.v. (c13.4x10^{-5}M, MeOH): λ_{max} 311 (ε 6000) and 263 (1900) nm; i.r.: ν 3010 (w), 2960 (w), 1765 (s), 1755 (s), 1720 (m), 1625 (s) and 1570 (m) cm^{-1}; ^{1}H-nmr: see ref. 5. Anal. Calcd. for $C_{23}H_{28}N_4O_{11}S$: C 48.59, H 4.93, N 9.86. Found: C 48.55, H 4.86, N 9.80; m.s.: see ref. 12.

4-Acetamido-2-methyl-6-methylthio-oxazolo|5,4-d|pyrimidine (7): m.p.: 119°C; u.v. (c 4.45x10^{-5}M, $CHCl_3$): λ_{max} 297 (ε 10400), 266 (16600) and 244 (24400) nm; i.r.: ν 3446 (m, broad), 3121 (m), 3063 (m), 3031 (m), 1685 (s) and 1601 (s) cm^{-1}; ^{1}H-nmr ($CDCl_3$): 8.40 (s, broad, 1H, exchangeable by D, C_4N-H), 2.55 (m, 9H, C_2Me, S-Me and C_4 N-Ac), Anal. Calcd. for $C_9H_{10}N_4O_2S$: C 45.38, H 4.20, N 23.53. Found: C 45.29, H 4.12, N 23.20.

4,5-Diacetamido-1,6-dihydro-2-methylthio-6-oxo-pyrimidine (8): m.p.: 297°C; u.v. (c 4.7x10^{-5}M, MeOH): λ_{max} 291 (ε 5900) and 237 (24200) nm; i.r.: ν 3322 (m), 3141 (w), 3014 (w), 2941 (w), 2847 (w), 1684 (s), 1664 (s), 1597 (w), 1550 (s) and 1526 (s) cm^{-1}; ^{1}H-nmr ($CDCl_3$): 8.00

(s, broad, 1H, exchangeable by D), 7.60 (s, 1H, exchangeable by D), 2.50 (s, 3H, S-Me), 2.35 (s, 3H), 2.25 (s, 3H). Anal. Calcd. for $C_9H_{12}N_4O_3S$: C 42.19, H 4.69, N 21.88. Found: C 42.09, H 4.63, N 21.76.

4-Acetamido-5-(N,N-diacetylamino)-1,6-dihydro-2-methylthio-6-oxo-pyrimidine (9): m.p.: 129-130°C; u.v. (c 5.25×10^{-5}M, $CHCl_3$): λ_{max} 291 (ϵ 3600) and 239 (3800) nm; i.r.: ν 3217 (s, broad), 3141 (s, broad), 3015 (w), 2930 (m), 1692 (s), 1610 (s) and 1573 (m) cm^{-1} ; ^{1}H-nmr ($CDCl_3$): 8.70 (s, broad, 1H, exchangeable by D, C_4N-H), 2.60 (m, 12H, S-Me, C_5N-Ac_2, C_4N-Ac). Anal. Calcd. for $C_{11}H_{14}N_4O_4S$: C 44.30, H 4.70, N 18.79. Found: C 44.24, H 4.63, N 18.65.

4,5-(N,N,N',N'-tetraacetylamino)-1,6-dihydro-1-methyl-2-methylthio-6--oxo-pyrimidine (10): m.p.: 119-120°C; u.v. (c 4.84×10^{-5}M, $CHCl_3$): λ_{max} 305 (ϵ 12400) and 242 (8900) nm; i.r.: ν 3450 (w), 3400 (w), 3030 (w), 2950 (w), 1715 (s), 1600 (m) and 1520 (m) cm^{-1}; ^{1}H-nmr ($CDCl_3$): 3.60 (s, 3H, N_1-Me), 2.60 (s, 3H, S-Me), 2.45 (s, 12H, C_4N-Ac_2 and C_5N-Ac_2) Anal. Calcd. for $C_{14}H_{18}N_4O_5S$: C 47.46, H 5.08, N 15.82. Found: C 47.39 H 5.02, N 15.75.

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10. The purification of the reaction mixture prior to column chromatography is indicated in this case, as a very dark solid was obtained in the acetylation. On the other hand, the use of this method in the acetylation of **1a**, resulted in a relatively extensive acetolysis of the glycosidic bond of **6a**, in a decrease in the yield of **4a**, and in the formation of the corresponding 5-acetamido derivative **3**.
11. A decrease in the yield of **4** together with an increase in the yield of **3** have been observed when Na_2CO_3 was used instead of $NaCO_3H$.
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13. Trifluoroacetic acid ought to be added to induce the exchange.
14. The synthesis of this product has been reported already[5], although its physical data are not given therein.

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