REACTIONS OF 5,6-DIAMINO-1,3-DIMETHYLURACIL WITH D-XYLOSE. SYNTHESIS OF 7-XYLOPYRANOSYLXANTHINE

Rodrigo Rico Gomez
Departamento de Quimica Organica, Universidad de Malaga, Malaga, Spain

Abstract — 6-Amino- and 6-acetylamino-5-(xylopyranosyl)acetylamino-1,3-dimethyluracils are synthetised from 4-amino-5-xylosylidenimino-1,3-dimethyluracil. Cyclisation to 7-xylopyranosylxanthine is carried out from both 6-amino- and 6-acetylamino derivatives.

5,6-Diaminopyrimidines are intermediates in the synthesis of purines. The preparation of purines has been carried out by a great variety of methods since Traube's synthesis.[1] Nucleosides have been obtained from 6-(N-glycosyl)amino-5-thioformylaminopyrimidines.[2]

The synthesis of 7-gluco- and 7-galactopyranosylxanthines from 4-acetylamino-5-(N-glycopyranosyl)acetylaminouracils was reported in a previous paper.[3]

In the present paper, reactions with xylose are studied in relation to our synthetic studies of nucleosides analogues.

The products of condensation between 5,6-diamino-1,3-dimethyluracil (1) and aldehydic sugar were formulated as N-glycosides.[4,5] However, other authors gave them the Schiff base structures.[6,7]

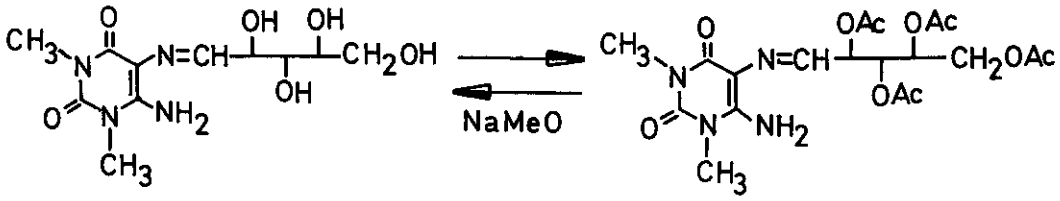
Condensation of (1) with D-xylose gives the xylosylidenimino derivative (2), on which mutarotation was observed. Acetylation with acetic anhydride and pyridine gave the corresponding tetraacetate (3) [mp 124°C; $[\alpha]_D^{23}$ = + 1.3° (c 1, $CHCl_3$)], which was treated with sodium methoxide to yield compound (2) again.

Heating (2) with a mixture of acetic anhydride and perchloric acid at 40°C for 8 h gave 6-amino-5-(N-β-D-2′,3′,4′-tri-O-acetyl-xylopyranosyl)acetylamino-1,3-dimethyluracil (4) [mp 160°C; $[\alpha]_D^{24}$ = + 30° (c 1, $CHCl_3$)].

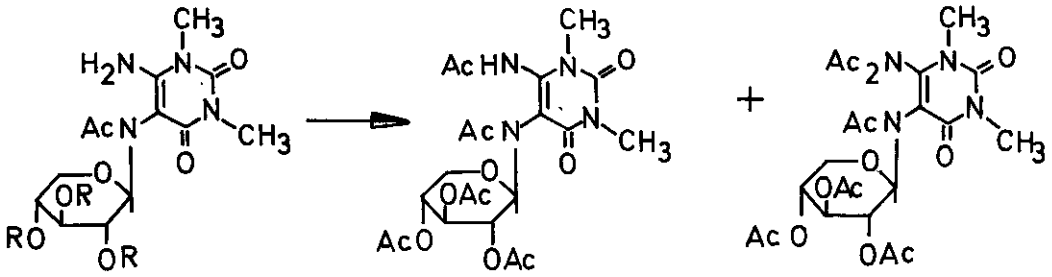
5,6-Diacetylamino-1,3-dimethyluracil was also isolated from the reaction mixture. This compound is formed by acetolysis of the starting material.

According to a previous paper,[5b] cyclisation to pyranosyl derivatives occurs by attack of acylating agent on the N at 6-position as the first step of the reaction, and then attack of the OH of C-5′ on C-1′. No furanosyl derivatives were detected either in the case of xylo- or gluco- and galacto-.

When the same reaction was done at higher temperature, only the products corre-

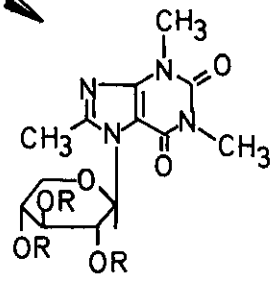


2 3



4, R = Ac
5, R = H

6 7



8, R = H ; 9, R = Ac

sponding to acetolysis were obtained.

This behaviour is different from that of the mentioned gluco- and galacto- derivatives, which gave 6-acetylamino-5-(N-β-D-2′,3′,4′,6′-tetra-O-acetyl-glycopyranosyl)acetylamino-1,3-dimethyluracils when the reaction was done at 80°C and 6-amino derivatives when the reaction temperature was 40°C.

6-Acetylamino-5-(N-β-D-2′,3′, 4′-tri-O-acetyl-xylopyranosyl)acetylamino-1,3-dimethyluracil (6) [mp 240°C; $[\alpha]_D^{23}$ = - 121.3° (c 1, $CHCl_3$)] was obtained from (4) by heating with a mixture of acetic anhydride and perchloric acid at 85°C for 10 h. 6-Diacetylamino-5-(N-β-D-2′,3′,4′-tri-O-acetyl-xylopyranosyl)acetylamino-1,3-dimethyluracil (7) [mp 206°C; $[\alpha]_D^{23}$ = + 57.3°(c 1, $CHCl_3$)] was also isolated from the reaction mixture.

Compound (3) was treated with a solution of 1.1 equivalents of sodium methoxide in dry methanol overnight at room temperature, yielding 6-amino-5-(N-β-D-xylopyranosyl)acetylamino-1,3-dimethyluracil (5) [mp 230°C; $[\alpha]_D^{23}$ = - 13.2° (c 1, H_2O)].

Heating (6) with a solution of 2.2 equivalents of sodium methoxide in dry methanol under reflux for 8 h gave 7-β-xylopyranosyl-1,3,8-trimethylxanthine (8) [mp 234°C; $[\alpha]_D^{23}$ = - 24.3° (c 1, H_2O)] in 90% yield.

A similar result was obtained with the gluco- and galacto- derivatives.

Moreover, (8) was prepared from (4) or (5) by the same means. In this case cyclisation occurs by loss of one molecule of water, instead of one molecule of acetic acid as was reported in the mentioned method.[3]

The nucleoside analogue (8) was acetylated with a mixture of acetic anhydride and pyridine to give 7-β-D-(2′,3′,4′-tri-O-acetyl)xylopyranosylxanthine (9) [mp 188°C; $[\alpha]_D^{23}$ = - 12.4° (c 1, $CHCl_3$)].

Acknowledgements The author wishes to thank the University of Alberta, Edmonton, Canada, for the 200-MHz-nmr-spectrum, the Microanalytical Laboratory of the Department of Quimica Organica, Universidad de Granada, Spain, for the microanalyses realized, and finally J. M. Vazquez Lasa and A. Palma Jimenez for their valuable help.

References

1. W. Traube, Chem. Ber., 1900, 33, 1371.
2. A. R. Todd, B. Lythgoe and G. W. Kenner, J. Chem. Soc., 1944, 652.
3. A. Fernandez Fernandez, M. Melgarejo Sampedro, R. Rico Gomez, R. Robles Diaz and A. Sanchez Rodrigo, J. Carbohydr. Nucleosides Nucleotides, 1981, 8 (4), 00.
4. G. M. Blackburn and A. W. Jonhson, J. Chem. Soc., 1960, 4358.
5. R. Granados, F. Marquez and M. Melgarejo Sampedro, An. Quim., 1962, 58, 115.

6. a) R. Rico Gomez, Tesis Doctoral. Universidad de Granada, 1973.
b) M. Melgarejo Sampedro and R. Rico Gomez, An. Quim., 1976, 72, 998.
c) M. Melgarejo Sampedro and R. Rico Gomez, An. Quim., 1981, 77 C, 130.
7. a) H. Ogura, H. Takahashi and M. Sakaguchi, Heterocycles, 1975, 3, 93.
b) H. Ogura, M. Sakaguchi and Y. Koyama, Japan Kokai, 75, 112,379 (C1, C07D, A61K, C09K); Chem. Abstr., 1976, 84, 59937y.

Received, 26th October, 1981