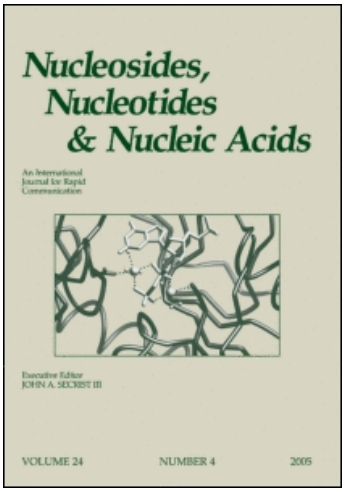


Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Aminopyrimidines and Derivatives. 15[1]. Synthesis of 3-Glycosyl-vic-Triazolo-(4,5-d) Pyrimidines[2]

R. Asenjo Asenjo[a]; M. Melgarejo Sampedro[a]; M. No-gueras Montiel[b]; M. Rodríguez Alonso[a]; C. Rodríguez Melgarejo[a]; A. Sánchez Rodrigo[b]
[a] Departamento de Química Orgánica, Facultad de Ciencias, Granada, Spain [b] Departamento de Química Orgánica, Colegio Universitario "Santo Reino", Jaén, Spain

To cite this Article Asenjo, R. Asenjo , Sampedro, M. Melgarejo , Montiel, M. No-gueras , Alonso, M. Rodríguez , Melgarejo, C. Rodrí-guez and Rodrigo, A. Sánchez(1984) 'Aminopyrimidines and Derivatives. 15[1]. Synthesis of 3-Glycosyl-vic-Triazolo-(4,5-d) Pyrimidines[2]', Nucleosides, Nucleotides and Nucleic Acids, 3: 2, 207 — 219
To link to this Article: DOI: 10.1080/07328318408079431
URL: http://dx.doi.org/10.1080/07328318408079431

NUCLEOSIDES AND NUCLEOTIDES, 3(2), 207-219 (1984)

AMINOPYRIMIDINES AND DERIVATIVES. 15[1]. SYNTHESIS OF 3-GLYCOSYL-VIC-TRIAZOLO-(4,5-d) PYRIMIDINES[2]

R. Asenjo Asenjo[+], M. Melgarejo Sampedro[+*], M. Nogueras Montiel[++], M. Rodríguez Alonso[+], C. Rodríguez Melgarejo[+] and A. Sánchez Rodrigo[++].

+Departamento de Química Orgánica. Facultad de Ciencias. Universidad de Granada. Granada. Spain.++Departamento de Química Orgánica. Colegio Universitario "Santo Reino". Jaén. Spain.

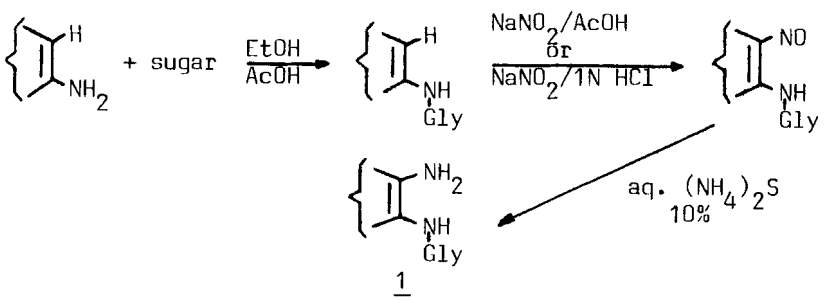
Abstract: A series of 3-glycosyl-vic-triazolo-(4,5-d) pyrimidines 2 and their O-acetyl derivatives 3 were prepared. Desulphurization of some of them has led to the 9-glycosyl-8-azahypoxantines 4.

Vic-triazolo-(4,5-d) pyrimidines (8-azapurines) are natural products present in the fermentation products of a variety of "S albus" (vasocidine and patocidine)[3]. Some synthetic derivatives of 5-amino-7-hydroxy-vic-triazolo-(4,5-d) pyrimidine have been reported to have antitumoral activity[4] and derivatives of 8-azahypoxantine show antiallergic activity.

The biological activity of 3-glycosyl-8-azapurines is well known, and they are being studied as antitumoral or antiviral agents[6,7,8]. Their synthesis can be achieved by three methods: firstly by reaction between the N-chloromercuric derivatives of 8-azapurines and acyl glycoside halides[9], its major disadvantage being the simultaneous formation of the 1- and 2-N-glycosyl isomers. Secondly, by the cyclization of 1-glycosyl-1,2,3-triazolo-4,5-dicarboxamides with hypobromite[10]. Again a mixture of isomers is likewise formed. Thirdly, by cyclization of 5-amino-4-glycosylamino pyrimidines with nitrous acid[11], yielding exclusively the 3-N-glycosyl isomer.

The interest in this class of compounds prompted us to synthesize some new 3-glycosyl-vic-triazolo-(4,5-d) pyrimidines. The third of the previously mentioned methods of synthesis has been employed.

 0732-8311/84/0302-0207$3.50/0



Scheme 1

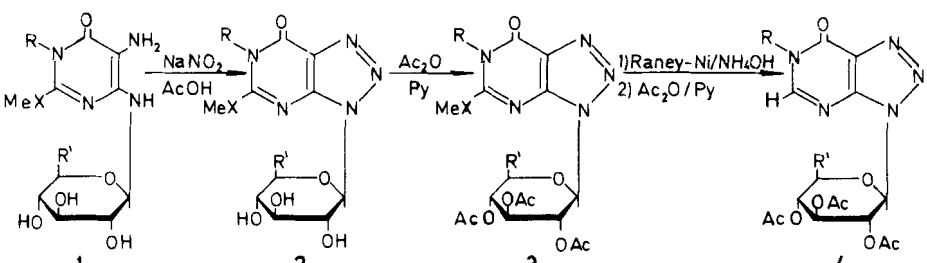
5-Amino-4-β-D-glycosylamino pyrimidines 1 used as starting material[1,12], were prepared as indicated in Scheme 1.

4-Amino-5-glycosylamino pyrimidines have been reported to mutarotate in water and to be hydrolized by acetic acid[13]; however the 4-aminoglycosides shown in Scheme 1 are both chemically and configurationally stable. Anomerization has not been observed after nitrosation reaction, and only traces of α-anomers have been detected in some of the compounds 1. This unusual stability has been attributed[1] to the low basicity of the amino group linked to the position four of the pyrimidine ring. Cyclizations 1 ⟶ 2 (Scheme 2) were carried out in aqueous solution with a double molar amount of nitrous acid, generated with sodium nitrite and acetic acid or 1N HCl. Crystallization of 2b and 2c could not be achieved. α-Anomers have not been detected in crystalline products 2.

O-acetyl derivatives 3 were formed by reaction of 2 with acetic anhydride and pyridine at room temperature. The acetylation of the dry reaction crude of 2b and 2c yielded crystalline products. The use of perchloric acid as catalyst in this reaction led to the cleavage of the glycosidic bond.

In order to prepare glycosyl derivatives similar to the natural ones, with increased biological potential, desulphurization reactions with Raney-Ni in ammonium hydroxide on the 3-glycosyl-5-methyl-8-azapurines 3d, 3e, 3f and 3g were attempted. The reaction took place with good results for 3d and 3e, yielding 9-β-D-xylopyranosyl-8-azahypoxantine (4d) and 9-β-D-glucopyranosyl-8-azahypoxantine (4e) respectively.

In the IR spectra of series 2, 3 and 4 the stretching bands of the carbonyl group at C-7 are shifted towards wavenumber values higher



1	R	X	R'
a	H	O	CH_2OH
b	Me	O	H
c	Me	O	CH_2OH
d	H	S	H
e	H	S	CH_2OH
f	Me	S	H
g	Me	S	CH_2OH

2	R	X	R'
a	H	O	CH_2OH
(b)	Me	O	H
(c)	Me	O	CH_2OH
d	H	S	H
e	H	S	CH_2OH
f	Me	S	H
g	Me	S	CH_2OH

3	R	X	R'
a	H	O	CH_2OAc
b	Me	O	H
c	Me	O	CH_2OAc
d	H	S	H
e	H	S	CH_2OAc
f	Me	S	H
g	Me	S	CH_2OAc

4	R	R'
d	H	H
e	H	CH_2OAc

Scheme 2

than those corresponding to the same bond in both series 1 and their 4-glycosylamino pyrimidine precursors. A similar, though less pronounced shift has already been observed in the IR spectra of 4-glycosylamino-5-nitroso pyrimidines in relation to their 4-glycosylamino pyrimidine precursors[1].

The singlets for Me-N_6 and Me-X as well as the doublets for anomeric protons in the ^{1}H-NMR of series 2, 3 and 4 (Tables 1,2 and 3) are shifted downfield as compared with the equivalent signals for their previously mentioned precursors.

The signal shifts observed both in IR and NMR have been attributed to the electron withdrawing effect performed on the pyrimidine ring by the nitrous group in one case and by the vic-triazolo cycle in the other.

The β-pyranosyl configuration of the sugar moieties has been demonstrated by periodate titration and by the value of the coupling constants $J_{1',2'}$ of the anomeric protons (Tables 1,2 and 3).

EXPERIMENTAL

Melting points were determined in a Melting Point Apparatus Gallemkamp and are uncorrected. Proton nuclear magnetic resonance spectra

TABLE 1. ^{1}H-NMR data of compounds 2

COMP.	SOLVENT	δ (ppm), multiplicity and intensity						
						Sugar protons		
		H-6	Me-6	MeO-5	MeS-5	H-1' ($J_{1,2'}$)	others	HO-
2a	DMSO-d_6	12.40 s broad	---	4.00 s	---	5.60 d (9 Hz)	3.20-3.95 m 6H	3.20-4.00 m 4H
	D_2O	---	---	4.15 s	---	6.60 d (9 Hz)	3.60-4.00 m 6H	---
2d	DMSO-d_6	11.00 s broad	---	---	2.60 s	5.65 d (9 Hz)	3.20-3.80 m 5H	3.00-4.50 m 2H 5.20 m 1H
2e	DMSO-d_6	12.00 s broad	---	---	2.60 s	5.70 d (9 Hz)	3.30-3.85 m 6H	3.00-3.90 m 4H 4.00-5.40 m 2H
	D_2O	---	---	---	2.60 s	6.00 d (9 Hz)	3.60-4.10 m 6H	---
2f	DMSO-d_6	---	3.50 s	---	2.65 s	5.65 d (9 Hz)	3.30-3.80 m 5H	3.20-3.80 m 2H 3.90 m 1H 4.30 m 1H 5.28 m 1H
	D_2O	---	3.55 s	---	2.70 s	5.90 d (9 Hz)	3.50-4.20 m 5H	---
2g	DMSO-d_6	---	3.50 s	---	2.70 s	5.70 d (9 Hz)	3.20-4.00 m 6H	3.20-4.00 m 4H 5.00-5.50 m 2H
	D_2O	---	3.50 s	---	2.70 s	6.00 d (9 Hz)	3.60-4.10 m 6H	---

Protons H-6 and HO- exchangeable by D.

were recorded with a Hitachi Perkin-Elmer R-600 Spectrometer, 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 (KBr pellets). The analysis of C, H and N have been performed in "Instituto Nacional de Química Orgánica" in Madrid.

General Method of Cyclization to vic-triazolo-(4,5-d) Pyrimidines.

To an aqueous solution of 1, were added a double molar amount of $NaNO_2$ and acetic acid. The reaction mixtures were stirred for 15 minutes, evaporated in a rotary evaporator until half volume and kept in a refrigerator for 12 hours. The solids were filtered and washed with cold water. Evaporation of mother liquors afforded new crops. The solids were recrystallized in water. Compound 2d precipitated directly from the reaction mixture. The cyclization of 1a was carried out in 1N HCl instead of acetic acid, as the presence of acetate would have avoided the crystallization of 2a. Compounds 2b and 2c could not be isolated in solid state.

6,7-dihydro-5-methoxy-3-β-D-glucopyranosyl-7-oxo-vic-triazolo-(4,5-d) pyrimidine (2a). To a solution of 5-amino-1,6-dihydro-2-methoxy-4-N-β-D-glucopyranosyl-6-oxo pyrimidine (1a)[1,12] (0.85 g, 2.53 mmol) in 30 mL of water at 80 ºC, 0.35 g of sodium nitrite (5 mmol) and 4.93 mL of 1N HCl (5 mmol) were added. The mixture was concentrated and the water eliminated by adding methanol and evaporating several times. Boiling ethanol (70 mL) was then added and NaCl filtered off. The final solution was evaporated and the solid recrystallized in methanol yielding 2a (0.53 g, 63.7%); m.p. 174 ºC; $[\alpha]^{29}_{589,578 \text{ and } 546\ nm} = 0.0º$ (c 1, DMSO); UV (c 6.9×10^{-5}M, water): λ_{max} 253 (ε 11300) and 202 nm (17300); IR: ν 3500-3250 s broad, 1725 s, 1595 s, 1530 m and 1085 s cm^{-1}; ^{1}H-NMR: see Table 1.

Anal. Calcd. for $C_{11}H_{15}N_5O_7$: C, 40.12; H, 4.59; N, 21.27. Found: C, 40.05; H, 4.72; N, 21.23.

6,7-dihydro-5-methylthio-3-β-D-xylopyranosyl-7-oxo-vic-triazolo-(4,5-d) pyrimidine (2d). Obtained from 5-amino-1,6-dihydro-2-methylthio-4-N-β-D-xylopyranosyl-6-oxo-pyrimidine (1b)[1,12] (4.08 g, 13.4 mmol), $NaNO_2$ (1.85 g, 26.8 mmol) and acetic acid (1.61 g, 26.8 mmol) in 350 mL of water at 80ºC. Yield 3.14 g (74%); m.p. dec.; $[\alpha]^{29}_D$ = -24.6º (c 1, DMSO);

TABLE 2. ^{1}H-NMR data of compounds 3

COMP.	SOLVENT	δ (ppm), multiplicity and intensity						
		H-6	Me-6	MeO-5	MeS-5	Sugar protons		
						H-1' ($J_{1;2'}$)	others	AcO-
3a	DMSO-d_6	---	---	4.05 s	---	6.50 d (9 Hz)	4.00-4.80 m 3H 5.20 m 1H 5.45-6.25 m 2H	1.80 s 3H 2.00 s 9H
	Cl_3CD	Not observed	---	4.20 s	---	6.10 m	4.20 m 2H 5.40 m 3H 6.15 m 1H	1.90 s 3H 2.10 s 9H
3b	DMSO-d_6	---	3.30 s	4.20 s	---	6.45 d (9 Hz)	4.20 m 2H 5.10 m 1H 5.40-6.20 m 2H	1.80 s 3H 2.05 s 6H
	Cl_3CD	---	3.50 s	4.20 s	---	6.15 m	3.75 m 1H 4.20 m 1H 5.40 m 2H 6.15 m 1H	1.85 s 3H 2.10 s 6H
3c	DMSO-d_6	---	3.40 s	4.20 s	---	6.60 d (9 Hz)	4.15 m 2H 4.50 m 1H 5.20 m 1H 5.50-6.20 m 2H	1.80 s 3H 2.00 s 6H 2.05 s 3H
	Cl_3CD	---	3.50 s	4.20 s	---	6.20 m	4.20 m 3H 5.40 m 2H 6.20 m 1H	1.80 s 3H 2.05 s 6H 2.10 s 3H

3d	DMSO-d_6	13.10 s broad	---	---	2.60 s	6.40 d (9 Hz)	4.00 m 2H 5.10 m 1H 5.80 m 2H	1.80 s 3H 2.00 s 6H
3e	DMSO-d_6	---	---	---	2.70 s	6.65 d (9 Hz)	4.20 m 2H 4.50 m 1H 5.20 m 1H 5.5-6.2 2H	1.80 s 3H 2.00 s 6H 2.05 s 3H
	Cl_3CD	11.60 s broad	---	---	2.75 s	6.10 m	4.20 m 3H 5.50 m 2H 6.10 m 1H	1.80 s 3H 2.10 s 9H
3f	DMSO-d_6	---	3.50 s	---	2.75 s	6.50 d (9 Hz)	4.10 m 2H 5.10 m 1H 5.65 m 1H 6.05 m 1H	1.80 s 3H 2.00 s 3H 2.05 s 3H
	Cl_3CD	3.50 s 2H (H_2O)	3.60 s	---	2.80 s	6.20 m	3.95 m 1H 4.40 m 1H 5.45 m 2H 6.20 m 1H	1.85 s 3H 2.10 s 6H
3g	DMSO-d_6	---	3.50 s	---	2.75 s	6.65 d (9 Hz)	4.20 m 2H 4.50 m 1H 5.20 m 1H 5.5-6.2 2H	1.80 s 3H 2.00 s 6H 2.05 s 3H
	Cl_3CD	---	3.60 s	---	2.75 s	6.20 m	4.20 m 3H 5.35 m 2H 6.20 m 1H	1.80 s 3H 2.05 s 9H

Protons H-6 exchangeable by D.

TABLE 3. ^{1}H-NMR data of compounds 4

COMP.	SOLVENT	δ (ppm), multiplicity and intensity				
		H-6	H-5	Sugar protons		
				H-1' ($J_{1;2'}$)	others	AcO-
4d	DMSO-d_6	13.00 s broad	8.40 s	6.50 d (9 Hz)	4.10 m 2H 5.20 m 1H 5.80 m 2H	1.80 s 3H 2.05 s 6H
4e	DMSO-d_6	Not observed	8.40 s	6.70 d (9 Hz)	4.10 m 2H 4.60 m 1H 5.20 m 1H 5.90 m 2H	1.80 s 3H 2.00 s 9H

Protons H-6 exchangeable by D.

UV (c 6.66x10^{-5}M, water): λ_{max} 240 (ε 11130) and 277 nm (15180); IR: ν 3450 s, 3270 m broad, 1710 s, 1690 s, 1520 m, 1290 m and 1065 s cm^{-1}: ^{1}H-NMR: see Table 1.

Anal. Calcd. for $C_{10}H_{13}N_5O_5S$: C, 38.09; H, 4.15; N, 22.21. Found: C, 37.95; H, 3.84; N, 22.50.

6,7-dihydro-5-methylthio-3-β-D-glucopyranosyl-7-oxo-vic-triazolo-(4,5-d) pyrimidine (2e). Obtained from 5-amino-1,6-dihydro-2-methylthio-4-N-β-D-glucopyranosyl-6-oxo pyrimidine (1e)[1,12] (1.50 g, 4.26 mmol), $NaNO_2$ (0.59 g, 8.52 mmol) and acetic acid (0.51 g, 8.52 mmol) in 40 mL of water at 80ºC. Yield 1.3 g (84%); m.p. 270-5ºC (d); $[\alpha]^{29}_{436\ nm}$ = -7.5º (c 1, DMSO); UV (c 4.68x10^{-5}M, water): λ_{max} 240 (ε 10810) and 278 nm (14320); IR: ν 3460 s, 3400 s broad, 1720 s, 1695 s, 1630 w, 1535 m, 1260 w, 1080 m and 655 w cm^{-1}; ^{1}H-NMR: see Table 1.

Anal. Calcd. for $C_{11}H_{15}N_5O_6S.H_2O$: C, 36.36; H, 4.72; N, 19.27. Found: C, 36.40; H, 4.41; N, 19.25.

6,7-dihydro-6-methyl-5-methylthio-3-β-D-xylopyranosyl-7-oxo-vic-triazolo-(4,5-d) pyrimidine (2f). Obtained from 5-amino-1,6-dihydro-1-methyl-2-methylthio-4-N-β-D-xylopyranosyl-6-oxo pyrimidine (1f)[1,12] (4.5 g, 13.4 mmol), $NaNO_2$ (1.85 g, 26.8 mmol) and acetic acid (1.61 g, 26.8 mmol) in 350 mL of water at 80ºC. Yield 4.16 g (89%); m.p. 244ºC (d); $[\alpha]^{29}_{D}$ = -26.3º (c 1, DMSO); UV (c 7.2x10^{-5}M, water): λ_{max} 235 (ε 12580) and 278 nm (16000); IR: ν 3480 s, 3440 m, 3390 m, 3250 m broad, 1710 s, 1650 w broad, 1525 m, 1285 m, 1230 m, 1060 s and 665 w cm^{-1}; ^{1}H-NMR: see Table 1.

Anal. Calcd. for $C_{11}H_{15}N_5O_5S.H_2O$: C, 38.03; H, 4.93; N, 20.16. Found: C, 37.93; H, 5.03; N, 20.11.

6,7-dihydro-6-methyl-5-methylthio-3-β-D-glucopyranosyl-7-oxo-vic-triazolo-(4,5-d) pyrimidine (2g). Obtained from 5-amino-1,6-dihydro-1-methyl-2-methylthio-4-N-β-D-glucopyranosyl-6-oxo-pyrimidine (1g)[1,12] (4 g, 10.4 mmol), $NaNO_2$ (1.44 g, 20.8 mmol) and acetic acid (1.25 g, 20.8 mmol) in 350 mL of water at 80ºC. Yield 3.45 g (88%); m.p. 223-4ºC; $[\alpha]_{436}^{29}$ = -7.6º (c 1, DMSO); UV (c 5.30x10^{-5}M, water): λ_{max} 235 (ε 12740) and 278 nm (16340); IR: ν 3450 s, 3350 s broad, 1720 s, 1685 s, 1520 s, 1290 m, 1065 s, 1040 s and 645 w cm^{-1}; ^{1}H-NMR: see Table 1.

Anal. Calcd. for $C_{12}H_{17}N_5O_6S.H_2O$: C, 28.19; H, 5.07; N, 18.56. Found: C, 38.31; H, 4.70; N, 18.95.

General Method of Acetylation of 3-glycosyl-vic-triazolo-(4,5-d) Pyrimidines.

Compounds 3 (except 3b and 3c whose synthesis will be described in detail below) were obtained in the following way: to a mixture of dry pyridine (10mL) and acetic anhydride (10 mL), compounds 2 (1.25 mmol) were added. The mixture was stirred at room temperature until all of the solids dissolved and was left for 24 hours. The solution was evaporated at reduced pressure (temperature below 60ºC). The excess of solvents was removed by dissolving in methanol and evaporating several times. The final product was crystallized either from ethanol or methanol, a mixture of the two, or finally in water, as will be indicated in each case.

6,7-dihydro-5-methoxy-3-β-D-(2',3',4',6'-tetra-O-acetyl)-glucopyranosyl-7-oxo-vic-triazolo-(4,5-d) pyrimidine (3a). Yield 0.44 g (71%); m.p. 142-4ºC (crystallized in water); $[\alpha]_D^{18}$ = -27.8º (c 1, DMSO); UV (c 5.23x10^{-5}M, water): λ_{max} 202 (ε 14110) and 260 nm (8110); IR: ν 3470 w broad, 1760 s broad, 1710 s, 1595 s, 1530 m, 1225 s broad and 1035 s cm^{-1}; ^{1}H-NMR: see Table 2.

Anal. Calcd. for $C_{19}H_{23}N_5O_{11}$: C, 45.87; H, 4.66; N, 14.08. Found: C, 45.72; H, 4.65; N, 14.10.

6,7-dihydro-5-methoxy-6-methyl-3-β-D-(2',3',4'-tri-O-acetyl)-xylopyranosyl-7-oxo-vic-triazolo-(4,5-d) pyrimidine (3b). To a solution of 5-amino-1,6-dihydro-2-methoxy-1-methyl-4-N-β-D-xylopyranosyl-6-oxo pyrimidine (1b) (0.48 g, 1.5 mmol) in 30 mL of water at 80ºC, $NaNO_2$ (0.21 g,

3.mmol) and acetic acid (0.18 g, 3 mmol) were added. The solution was left to cool until it reached room temperature and evaporated to dryness. The excess of water was carefully removed by dissolving in methanol and evaporating several times. The dry residue was directly acetylated by adding 10 mL of acetic anhydride and 10 mL of pyridine and stirring for 24 hours. The reaction mixture was processed in the usual way, yielding 0.32 g (49%) of 3b (crystallized in water); m.p. 129-30ºC; $[\alpha]_D^{18}$ = -61.6º (c 1, Cl_3CH); UV (c 5.50x10^{-5}M, water): λ_{max} 207 (ε 19600) and 258 nm (11040); IR: ν 1760 s broad, 1720 s, 1590 s, 1520 m, 1240 s, 1210 s and 1030 m; ^{1}H-NMR: see Table 2.

Anal. Calcd. for $C_{17}H_{21}N_5O_9$: C, 46.47; H, 4.82; N, 15.94. Found: C, 46.29; H, 4.63; N, 15.74.

6,7-dihydro-5-methoxy-6-methyl-3-β-D-(2',3',4',6'-tetra-O-acetyl)-glucopyranosyl-7-oxo-vic-triazolo-(4,5-d) pyrimidine (3c). 5-Amino-1,6-dihydro-2-methoxy-1-methyl-4-N-β-D-glucopyranosyl-6-oxo pyrimidine (1c) was cyclizated and acetylated as described for 3d, yielding 0.55 g (71.7%) of 3c (crystallized in ethanol); m.p. 205ºC; $[\alpha]_D^{18}$ = -56º (c 1, Cl_3CH); UV (c 4.69x10^{-5}M, water): λ_{max} 207 (ε 20600) and 258 nm (11660); IR: ν 1750 s, 1725 s, 1560 s broad, 1520 m, 1270-1200 s broad and 1040 s cm^{-1}; ^{1}H-NMR: see Table 2.

Anal. Calcd. for $C_{20}H_{25}N_5O_{11}$: C, 46.96; H, 4.93; N, 13.69. Found: C, 46.68; H, 4.71; N, 13.83.

6,7-dihydro-5-methylthio-3-β-D-(2',3',4'-tri-O-acetyl)-xylopyranosyl--7-oxo-vic-triazolo-(4,5-d) pyrimidine (3d). Crystallized in ethanol-methanol (1:1). Yield 0.21 g (38%); m.p. 280ºC; $[\alpha]_D^{18}$ = -48.9 (c 1, DMSO); UV (c 8x10^{-5}M, methanol): λ_{max} 203 (ε 11875), 232 (8375) and 273 nm (13750); IR: ν 3280 m, 3260 m, 3230 m, 1750 s broad, 1720 s broad, 1550 m, 1510 m, 1290 m, 1255 s, 1235 s, 1055 s and 605 w cm^{-1}; ^{1}H-NMR: see Table 2.

Anal. Calcd. for $C_{16}H_{19}N_5O_8S$: C, 43.53; H, 4.34; N, 15.87. Found: C, 43.57; H, 4.46; N, 15.69.

6,7-dihydro-5-methylthio-3-β-D-(2',3',4',6'-tetra-O-acetyl)-glucopyranosyl-7-oxo-vic-triazolo-(4,5-d) pyrimidine (3e). Crystallized in ethanol. Yield 0.47 g (74%); m.p. 172ºC; $[\alpha]_D^{18}$ = -70.7º (c 1, Cl_3CH); UV (c 3.89x10^{-5}M, water): λ_{max} 236 (ε 9850) and 277 nm (17870); IR: ν 3200 w broad, 1760 s broad, 1705 s, 1565 s, 1540 s, 1260-1210 s, 1040 s and 650 w cm^{-1}; ^{1}H-NMR: see Table 2.

Anal. Calcd. for $C_{19}H_{23}N_5O_{10}S$: C, 44.44; H, 4.52; N, 13.64. Found: C, 44.13; H, 4.50; N, 13.45.

6,7-dihydro-6-methyl-5-methylthio-3-β -D-(2',3',4'-tri-O-acetyl)-xylopyranosyl-7-oxo-vic-triazolo-(4,5-d) pyrimidine (3f). Crystallized in methanol-water (4:1). Yield 0.50 g (85%); m.p. 150ºC; $[\alpha]_D^{18}$ = -102.7º (c 1, Cl_3CH); UV (c 6.12x10^{-5}M, water): λ_{max} 236 (ε 9870) and 280 nm (13100); IR: ν 3520 w broad, 1770 s, 1755 s, 1730 s, 1580 m, 1485 m, 1245 s, 1210 s, 1065 s, 1045 s and 680 w cm^{-1}; ^{1}H-NMR: see Table 2.

Anal. Calcd. for $C_{17}H_{21}N_5O_8S.H_2O$: C, 43.12; H, 4.90; N, 14.79. Found: C, 43.67; H, 4.92; N, 14.72.

6,7-dihydro-6-methyl-5-methylthio-3-β -D-(2',3',4',6'-tetra-O-acetyl)-glucopyranosyl-7-oxo-vic-triazolo-(4,5-d) pyrimidine (3g). Crystallized in methanol. Yield 0.51 g (79%); m.p. 171ºC; $[\alpha]_D^{18}$ = -55º (c 1, Cl_3CH); UV (c 4.36x10^{-5}M, water): λ_{max} 236 (ε 11080) and 280 nm (14800); IR: ν 1750 s, 1735 s, 1720 s, 1575 m, 1490 m, 1270 m, 1250 s, 1050 s and 620 w cm^{-1}; ^{1}H-NMR: see Table 2.

Anal. Calcd. for $C_{20}H_{25}N_5O_{10}S$: C, 45.53; H, 4.78; N, 13.28. Found: C, 45.25; H, 4.77; N, 13.13.

Desulphurization Reaction.

6,7-dihydro-3-β -D-(2',3',4'-tri-O-acetyl)-xylopyranosyl-7-oxo-vic-triazolo-(4,5-d) pyrimidine (4d). A suspension of 3d (4.42 g, 0.95 mmol) in a mixture of 2 g of Raney-Ni and 40 mL of 2M NH_4OH was refluxed for 1 hour. The mixture was filtered and the solution evaporated. The water was removed by dissolving in ethanol and evaporating several times. The residue was re-acetylated with acetic anhydride (10 mL) and pyridine (10 mL), stirring at room temperature for 24 hours. After removing the solvents 0.2 g (53%) of 4d (crystallized from methanol) were obtained; m.p. 268-9ºC (d); $[\alpha]_D^{18}$ = -52º (c 1, DMSO); UV (c 8x10^{-5}M, methanol): λ_{max} 205 (ε 13375) and 233 nm (8375); IR: ν 3110 w broad, 1755 s broad, 1715 s, 1580 m, 1500 m, 1270 m, 1080 s and 1035 s cm^{-1}; ^{1}H-NMR: see Table 3.

Anal. Calcd. for $C_{15}H_{17}N_5O_8$: C, 45.57; H, 4.33; N, 17.72. Found: C, 45.45; H, 4.12; N, 17.40.

6,7-dihydro-3-β -D-(2',3',4',6'-tetra-O-acetyl)-glucopyranosyl-7-oxo-vic-triazolo-(4,5-d) pyrimidine (4e). A suspension of 3e (0.3 g, 0.58 mmol) in a mixture of 1.5 g of Raney-Ni and 30 mL of 2M NH_4OH was refluxed for 1 hour. The reaction was carried out as described for 4d yiel-

ding 0.11 g (40%) of 4e (crystallized in water); m.p. 250ºC (d); $[\alpha]_D^{18}$ = -29.8º (c 1, DMSO); UV (c 10^{-4}M, methanol): λ_{max} 205 (ε 10000) and 233 nm (5900); IR: ν 3100 w broad, 1745 s broad, 1720 s, 1580 m, 1535 m, 1245 s, 1220 s and 1035 s cm^{-1}; ^{1}H-NMR: see Table 3.

Anal. Calcd. for $C_{18}H_{21}N_5O_{10}$: C, 46.25; H, 4.53; N, 14.98. Found: C, 46.13; H, 4.39; N, 14.90.

REFERENCES

1. For Part 14 see M. Nogueras Montiel, A. Sánchez Rodrigo, R. Asenjo Asenjo, M.Melgarejo Sampedro, M.Rodríguez Alonso and C.Rodríguez Melgarejo. An. Quim., in press.
2. This paper has been presented, in part, in the II National Meeting of Therapeutical Chemistry. Madrid. 1982.
3. R.J.Suhadolnik. "Nucleoside Antibiotics". Wiley Intescience. New York 1970.
4. R.C.Parks and K.C.Agarwal. Handb. Exp. Pharmacol. 38, 47 (1975).
5. K.R.H.Wooldridge and col. J. Medicin. Chem. 18, 1117 (1975).
6. W.Hutzenlaub, R.L.Tolman and R.K.Robins. J. Medicin. Chem. 15, 879 (1972).
7. C.W.Smith, R.W.Sidwell, R.K.Robins and R.L.Tolman. J. Medicin. Chem. 15, 883 (1972).
8. Proc. 4th Internat. Symp. Quantum Chem. and Biochem., ed. E.D.Bergman and B.Pullman, Jerusalem 1972.
9. J.Davoll. J. Chem. Soc., 1593 (1958). J.Davoll and Lowy. J. Am. Chem. Soc., 73, 1650 (1951). J.Davoll and Lowy. J. Am. Chem. Soc., 74, 1563 (1952).
10. J.Baddiley, J.G.Buchanan and G.O.Osborne. J. Chem. Soc., 3606 (1958). Ibid. 1651 (1958).
11. S.Gabriel and J.Colman. Ber., 34, 1234 (1901). J.Davoll, J. Chem. Soc., 1593 (1958). W.Pfleiderer and E.Bühler. Chem. Ber., 99, 3022 (1966).
12. R.Asenjo Asenjo, M.Melgarejo Sampedro, C.Rodríguez Melgarejo, M.Nogueras Montiel and A. Sánchez Rodrigo. Part 13 of this series. An. Quim., in press.
13. M.Melgarejo Sampedro and R.Rico Gómez. An. Quim., 72, 998 (1976). M.Melgarejo Sampedro, C.Rodríguez Melgarejo and A.Sánchez Rodrigo. Ibid., 77 C, 126 (1981). M.Melgarejo Sampedro and R.Rico Gómez.

Ibid., 77 C, 130 (1981). M.Melgarejo Sampedro, C.Rodríguez Melgarejo, M.Nogueras Montiel and A.Sánchez Rodrigo, Ibid., 78 C, 399 (1982).

Received April 2, 1984