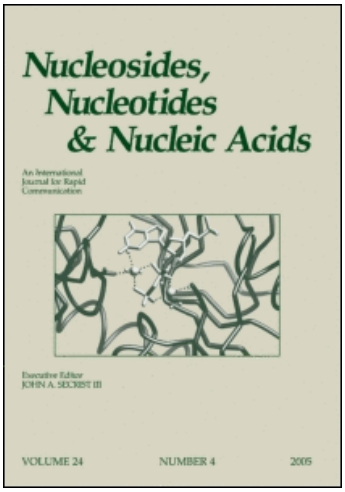


Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Nucleosides, XLVI[1] Syntheses and Reactions of 6- and 7-p-Chlorophenyllumazine Nucleosides

Najim A. Al-masoudi[a]; Wolfgang Pfleiderer[b]
[a] Dept. of Chemistry, College of Science, University of Basrah, Basrah, Iraq [b] Fakultät für Chemie, Universität Konstanz, Konstanz, West Germany

To cite this Article Al-masoudi, Najim A. and Pfleiderer, Wolfgang(1989) 'Nucleosides, XLVI[1] Syntheses and Reactions of 6- and 7-p-Chlorophenyllumazine Nucleosides', Nucleosides, Nucleotides and Nucleic Acids, 8: 8, 1485 — 1498
To link to this Article: DOI: 10.1080/07328318908048856
URL: http://dx.doi.org/10.1080/07328318908048856

NUCLEOSIDES & NUCLEOTIDES, 8(8), 1485-1498 (1989)

NUCLEOSIDES, XLVI[1]

SYNTHESES AND REACTIONS OF 6- AND 7-p-CHLOROPHENYLLUMAZINE NUCLEOSIDES

Najim A. Al-Masoudi[+] and Wolfgang Pfleiderer[*]

[+] Dept. of Chemistry, College of Science, University of Basrah, Basrah / Iraq;

[*] Fakultät für Chemie, Universität Konstanz, Postfach 5560, D-7750 Konstanz / West Germany

Abstract. The syntheses of 6-(4) and 7-p-chlorphenyl-1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-lumazine (6), was well as the debenzoylation to the corresponding free nucleosides 5 and 7, were improved. Thiation of 4 and 6 by P_4S_{10} led in excellent yields to 4-thiolumazine nucleosides (8,10) which could be deblocked to 9 and 11 and converted on treatment with ammonia into the isopterin-N-1- ribofuranosides 13 and 14. 2,2'-Anhydro-nucleoside formation worked well with 5 and 7 respectively to give 15 and 16, which formed on acid hydrolysis the 6- and 7-substituted 1-β-D-arabinofuranosyl-lumazines 18 and 19. The new nucleosides have been characterized by UV and ^{1}H-NMR spectra.

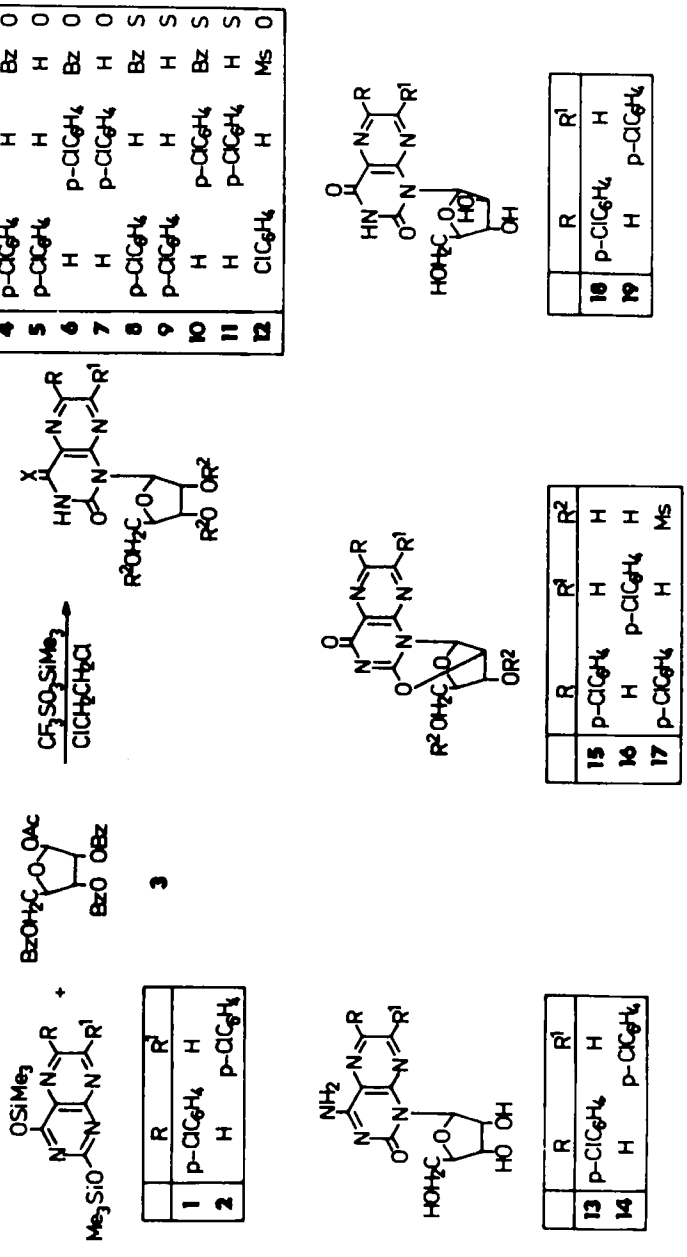
The AIDS problem and recently intensified antiviral research has acted as a stimulus to revive pteridine nucleoside chemistry, which has so far had little success as far as biological activity of this group of compounds is concerned. The fact that lumazine N-1 nucleosides[2-5] show a pronounced structural relationship to uridine, thymidine, and their synthetic analogs, such as the antivirally active 5-iodo-[6], 5-trifluoromethyl-[7], and E-5-(2-bromovinyl)-2'-deoxyuridine[8] as well as the 1-β-D-arabinofuranosylthymine[9], suggests that there is still the possibility that a new pattern of substituting on the pteridine nucleus will generate some bioactiv-

ity. We have glycosylated lumazine[2,10], its 6,7-dimethyl-[2], 6,7-diphenyl [2-5,11], 6-phenyl-[5], and 7-phenyl derivatives.[5] The use of a phenyl/substituent is always pharmacologically interesting, but its para-position may be further substituted to counteract enzymatic hydroxylation and deactivation. Because 6- and 7-p-chlorophenyl-1-β-D-ribofuranosyllumazine[5] are the only compounds known in this series to date, we decided to extend this group of compounds.

S Y N T H E S E S

Our previous work[5] applying the Hilbert-Johnson-Birkofer[12] procedure for the ribosylation of trimethylsilylated 6- (1) and 7-p-chlorophenyllumazine (2) with 1-O-acetyl-2,3,-5-tri-O-benzoyl-β-D-ribofuranose (3) was reinvestigated and improved by trimethylsilyl trifluoromethylsulfonate catalysis[13] and changing the solvent to 1,2-dichloroethane. 6-(4) and 7-p-chlorophenyl-1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-lumazine (6) could be isolated in improved 84 and 71 % yield, respectively. It was also found that debenzoylation of 4 and 6 under moderate basic conditions, using a catalytic amount of potassium carbonate in MeOH at room temperature, afforded the free nucleosides 5 and 7 in almost quantitative yields of 96 % and 95 %, respectively.

The thiation of the protected lumazine nucleosides 4 and 6 proceeded smoothly with P_4S_{10} in boiling dioxane and gave excellent yields of the corresponding yellow-colored 4-thio-derivatives 8 and 10. Their structures were assigned on the basis of comparison of their UV spectra, with 1-methyl-6,7-diphenyl-4-thiolumazine[14], and knowledge of the highly selective O^4-thiation of the lumazine system.[14,15] The 4-thio function is very light-sensitive and is easily photooxidized back to the starting lumazine derivative. Furthermore a high chemical reactivity was noticed, which afforded side products on debenzoylation under Zemplen's condition[16] using sodium methoxide, but worked very well with catalytic amounts of K_2CO_3 in MeOH to form 7 and 9 in 90 % and 83 % yield respec-



	R	R¹
1	p-ClC6H4	H
2	H	p-ClC6H4

	R	R¹	R²	X
4	p-ClC6H4	H	Bz	O
5	p-ClC6H4	H	H	O
6	H	p-ClC6H4	Bz	O
7	H	p-ClC6H4	H	O
8	p-ClC6H4	H	Bz	S
9	p-ClC6H4	H	H	S
10	H	p-ClC6H4	Bz	S
11	H	p-ClC6H4	H	S
12	ClC6H4	H	Ms	O

	R	R¹
13	p-ClC6H4	H
14	H	p-ClC6H4

	R	R¹	R²
15	p-ClC6H4	H	H
16	H	p-ClC6H4	H
17	p-ClC6H4	H	Ms

	R	R¹
18	p-ClC6H4	H
19	H	p-ClC6H4

tively. Ammonolysis of 8 and 10 with conc. ammonia resulted in a nucleophilic displacement of the sulfur and simultaneous removal of the benzoyl groups from the sugar moiety forming the isopterin-N-1-β-D-ribofuranosides 13 and 14.

2,2'-Anhydro-nucleoside formation was investigated using diphenyl carbonate in DMF at 160°C.[4,17] Compounds 5 and 7 gave respectively 6- (15) and 7-p-chlorophenyl-2,2'-anhydro-1-β-D-arabinofuranosyllumazine (16) in 62 % and 93 % yield isolated as crystalline materials. Another 2,2'-anhydro nucleoside (17) was obtained from 6-p-chlorophenyl-2-(2,3,5-tri-O-mesyl-β-D-ribofuranosyl)-lumazine (12) on analogous treatment with a catalytic amount of $NaHCO_3$ in boiling DMF. The hydrolysis of 15 and 16 to 6- (18) and 7-p-chlorophenyl-1-β-D-arabinofuranosyllumazine (19) respectively was best achieved in acetone by boiling with 0.1 N H_2SO_4.

PHYSICAL PROPERTIES

Structural assignments for the newly synthesized pteridine nucleosides were based on UV and ^{1}H-NMR spectral comparisons with known structural analogs. The determinations of pK_a values indicate that changes in the configuration of the sugar moiety affect the acidity of the aglycone very little, as expected. The 1-β-D-arabinofuranosides 18 and 19 are therefore similar to the corresponding 1-β-D-ribofuranosides 5 and 7. Introduction of a thio function into the 4-position, however, caused a dramatic bathochromic shift in the long wavelength absorption band and increased the acidity of the molecules, close to one pK unit in the case of compound 11 (Table 1). It is furthermore concluded from the UV data that the 7-p-chlorophenyl substituent exhibits a stronger mesomeric interaction with the nucleus than its 6-substituted counterpart, as expressed by the differences in extinction. This observation may help to differentiate between 6- and 7-phenyl-substituted pteridines.

Other fine structural features can be depicted from the ^{1}H-NMR spectra (Table 2). The small coupling constants for

Table 1 - Physical Data of Pteridine-N-1-Nucleosides

	pK_a in H_2O	UV Absorption Spectra λ_{max} (nm)					log ε					pH Solvent	Molecular Form
5	8.28	222	277			351	4.17	4.40			3.98	6.0	o
		220	268			355	4.11	4.44			4.06	11.0	-
7	8.79	228	[256]	283		350	4.32	[3.92]	3.86		4.35	6.0	o
		230	[252]	[284]		353	4.28	[4.06]	[3.92]		4.32	11.0	-
8		229	254	[273]	296 [330]	395	4.67	4.33	[4.23]	4.36 [3.70]	4.02	MeOH	o
9		[228]	256		292	396	[4.20]	4.33		4.38	3.98	MeOH	o
	7.99	[222]	258		287	393	[4.23]	4.25		4.34	3.00	5.0	o
		238	264		[282] 353	[400]	4.30	4.36		[4.31] 4.06	[3.82]	12.0	-
10		229		273	[296] [325]	397	4.70		4.08	[4.03] [3.94]	4.32	MeOH	o
11		229		[270]	295 [334]	398	4.20		[3.98]	3.96 [3.87]	4.18	MeOH	o
	7.89	[226]	[250]		301 324	398	[4.23]	[3.89]		3.93 3.92	4.29	5.0	o
		[216]	259		[286] 356	395	[4.40]	4.07		[3.94] 4.20	4.13	11.0	-
12		[219]		277		351	[4.25]		4.50		4.10	MeOH	o
13		230		275		365	4.01		4.55		4.00	MeOH	o
14		[230]	[259]		[289] [302]	362	[4.28]	[4.05]		[4.03] [4.31]	4.35	MeOH	o
15		[216]	[248]	270	[297]	350	[4.21]	[4.25]	4.39	[4.09]	4.05	MeOH	o
16		231	[252]		287	346	4.31	[4.04]		3.91	4.35	MeOH	o
17		[217]	242	271		350	[4.32]	4.36	4.49		4.16	MeOH	o
18		[217]		280		353	[4.29]		4.40		3.98	MeOH	o
	8.62	[216]		278		352	[4.20]		4.40		3.99	6.0	o
		[220]		270	[298]	356	[4.11]		4.40	[4.11]	4.04	11.0	-
19		230		[280]		353	4.37		[3.97]		4.32	MeOH	o
	8.32	229	[256]	283		359	4.30	[3.87]	3.84		4.31	6.0	o
		231	[254]	[288]		354	4.29	[4.07]	[3.94]		4.32	11.0	-

[ ] = Shoulder; o = neutral form; - = monoanion.

Table 2 - ^{1}H-NMR Data for the Pteridine-N-1 Nucleosides

	N-H	^{1}H-NMR Spectra in D_6-DMSO or $CDCl_3$* (δ-values in ppm against TMS)											
	NH_2	1'-H	2'-H	3'-H	4'-H	5'-H	5"-H	2'-OH	3'-OH	5'-OH	6-Subst.	7-Subst.	Sugar Benzoyl Mesyl
		$J_{1',2'}$	$J_{2',3'}$	$J_{3',4'}$	$J_{4',5'}$	$J_{4',5'}$	$J_{5',5"}$	$J_{2',OH}$	$J_{3',OH}$				
8*	10.10s	6.99d <0.5	6.32pt 6.7	6.24pt 7.95	4.76m	4.89dd 5.2	4.66dd 11.9	-	-	-	7.0-7.9m 4H	8.88s	7.0-7.9m 15H
9	13.44s	6.54d <0.5	4.59pt 5.5	4.25pq	3.76m	3.68dd 5.8	3.51dd 11.9	5.14d 5.9	4.96d 6.70	4.66t	8.23d 7.63d	9.40s	-
10*	10.04s	7.19d <0.5	6.34d 5.5	6.15pt 5.2	- 4.82m -		4.68dd	-	-	-	9.01s	7.0-7.9m 4H	7.0-7.9m 15H
11	13.39s	6.71d <0.5	4.65pt	4.23pq	3.77dd	3.67m	3.46m	5.16d 4.9	5.00d 6.4	4.65t	9.27s	8.24d 7.70d	-
12	12.32s	6.90d 6.0	5.88dd 3.0	5.67pt	4.97pt	- 4.46 -		-	-	-	8.24d 7.65d	9.39s	3.41s;3.36s; 3.26s
13	8.57d	6.57d 3.4	4.65pd 12.8	4.26dd 2.05	3.76dd 3.0	3.63dt 6.0	3.48m 11.9	5.05d 4.9	4.88d 6.4	4.69	8.43d 7.59d	9.39s	-
14	8.51d	6.57d 3.7	4.63dd 12.2	4.26dd 0.5	3.75dd 3.0	3.65dt 6.0	3.48m 11.5	5.06d 5.2	4.88d 6.4	4.86	9.39s	8.46d 7.29d	-
15	-	6.76d 5.8	5.36d 0	4.48d 0	4.15s 0	3.48 - 3.24m		-	5.96d 4.0	4.93t	8.22d 7.65d	9.43s	-
16	-	6.85d 5.8	5.37d 0	4.50s 0	4.17pt 0	3.30 - 3.39m		-	5.96d 0.5	5.37pt	9.44	8.33d 7.69d	-
17	-	6.90d 5.8	5.83d 0	5.63d 2.7	4.78m 3.5	4.33dd 6.0	4.24dd 12.0	-	-	-	8.24d 7.65d	9.46s	3.47s;3.08s
18	12.04s	6.91d 7.6	4.33s 0	4.55pt 5.0	-	3.69m	-	5.35d 4.9	5.26d 5.5	4.33m	8.21d 7.63d	9.36s	-
19	11.89s	7.19d 7.9	4.39m 0	4.52s	4.26m	- 3.67m -		5.32d 4.9	5.25d 5.2	4.39m	9.23s	8.33d 7.69d	-

s = Singlet; d = doublet; dd = doublet of doublet; t = triplet; pt = pseudotriplet; pq = pseudoquartet; m = multiplet.

1'-H in 8-11 is in agreement with the β-configuration of the glycosidic bond and a high population of the N-type conformation[18] of the sugar moiety. The additional brdiging of the sugar and aglycone in the 2,2'-anhydro-nucleosides causes a high degree of conformational restriction as seen from the distinct separation of the signals of the sugar protons.

E X P E R I M E N T A L

UV Spectra were recorded on a Perkin Elmer spectrophotometer Lambda 5; ^{1}H-NMR spectra were measured with a Bruker WM-250 high resolution spectrometer with tetramethylsilane as an internal standard and on a δ-scale in ppm. The pK_a values were determined spectrophotometrically.[19] Thin layer chromatography was performed on silica-gel sheets F 1550 LS 254 of Schleicher & Schüll. Drying of the substances was achieved in a vacuum desiccator or in a Büchi-TO 50 drying oven under vacuum at room temp. Melting points are not corrected.

6-(p-Chlorophenyl)-1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl) lumazine (4).[5] Improved synthesis. A mixture of 6-(p-chlorphenyl)-lumazine (5.0 g, 18.2 mmol) and dry hexamethyldisilazane (100 ml) was heated under reflux for 20 h with a catalytic amount of ammonium sulphate. After cooling, the solution was evaporated to dryness under anhydrous condition to give the silylated derivative 1, which was dissolved in 60 ml of dry dichloroethane. To this was added a solution of 1-O-acetyl-2,3,5-tri-O-benzoyl-β-D-ribofuranose (3) (9.17 g, 18.2 mmol) dissolved in dry dichloroethane (30 ml) and then the mixture treated with trimethylsilyl trifluoromethanesulfonate (2.34 ml, 18.2 mmol) as catalyst. After stirring for 3 h at room temperature, the solution was evaporated and the residue was partitioned between $CHCl_3$ and aqueous sodium bicarbonate. The organic layer was dried (Na_2-

SO_4), filtered and evaporated to give a crude product (15.0g). Recrystallization from chloroform gave compound 4 (11.0 g, 84 %, m.p. 229-230°C, lit.[5], 66 % yield, m.p. 230-231°).

6-(p-Chlorophenyl)-1-β-D-ribofuranosyllumazine (5).[5] Compound 4 (1.98 g, 2.75 mmol) was stirred in abs. MeOH (150 ml) and potassium carbonate (0.72 g) for 20 h at room temperature. Evaporation of solvent under vacuum gave a colorless solid, which was dissolved in hot water and neutralized with 2N AcOH to pH 5. The precipitate was filtered off and afforded on recrystallization from MeOH compound 5 as colorless crystals (1.08 g, 96 %), m.p. 278°C (decomp.), lit.[5], m.p. 280°C.

7-(p-Chlorophenyl)-1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-lumazine (6).[5] Improved Synthesis. A mixture of 7-(p-chlorophenyl)-lumazine (10 g, 3.64 mmol) and a trace amount of ammonium sulfate was heated in anhydrous hexamethyldisilazane (300 ml) under reflux for 18 h. After cooling, the solution was evaporated under anhydrous condition to dryness to give the silylated lumazine 2. To a solution of this residue in anhydrous dichloroethane (200 ml) was added a solution of 1-O-acetyl-2,3,5-tri-O-benzoyl-β-D-ribofuranose (3) (18.36 g, 3.64 mmol) in anhydrous dichloroethane (50 ml) followed by dropwise addition of the catalyst trimethylsilyl trifluoromethanesulfonate (6.55 ml, 3.64 mmol). After stirring for 3 h at room temperature, chloroform (200 ml) was added and the mixture partitioned with a cold solution of sodium bicarbonate. The organic extract was dried (Na_2SO_4), filtered and evaporated to a solid residue (30 g). Recrystallization from $CHCl_3$/MeOH gave the pure colorless nucleoside 6 (18.5 g, 71 %, m.p. 246-248°C, lit.[5], 61 % yield, m.p. 246-247°C).

7-(p-Chlorophenyl)-1-β-D-ribofuranosyllumazine (7). A solution of 6 (7.5 g, 10.4 mmol) in abs. MeOH (150 ml) and

potassium carbonate (2.74 g) was stirred for 20 h at room temperature. MeOH was evaporated and the solid was dissolved in boiling H_2O, followed by neutralization with 2N AcOH to pH 5 to yield a colorless precipitate. Recrystallization from hot MeOH gave compound 7 (4.2 g, 95 %, m.p. 257°C dec., lit.[5], 88 % yield, m.p. 260°C dec.).

6-(p-Chlorophenyl)-1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-4-thiolumazine (8). A mixture of 6-(p-chlorophenyl)-1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-lumazine (4) (8.0 g, 11.0 mmol) and diphosphorous pentasulfide (8.9 g, 20 mmol) was boiled in abs. dioxane (200 ml) under reflux for 1.5 h. The suspension was cooled, filtered and the orange filtrate was evaporated to dryness. The residue was partitioned between brine solution and $CHCl_3$, the organic layer was dried (Na_2SO_4), filtered and evaporated to a yellow amorphous solid. Recrystallization from $CHCl_3$/MeOH gave 8 as a yellow solid (7.85 g, 96 %, m.p. 252-253°C).

Anal. calc. for $C_{38}H_{27}ClN_4O_8S$ (735.2): C, 62.08; H, 3.70; N, 7.62. Found: C, 62.06; H, 3.73; N, 7.51.

6-(p-Chlorophenyl)-1-β-D-ribofuranosyl-4-thiolumazine (9). (a) Compound 8 (2.0 g, 2.7 mmol) was added to a methanolic sodium methoxide solution (7.5 mg of Na in 200 ml of abs. MeOH) and then stirred for 20 h at room temperature. Water (35 ml) was added and then the solution was extracted with ether. Acidification of the aqueous layer with 2N AcOH to pH 5 afforded a yellow precipitate. Recrystallization from DMF/H_2O gave a yellow solid (0.95 g, 83 %, m.p. 265°C dec.).

Anal. calc. for $C_{17}H_{15}ClN_4O_5S$ (422.8): C, 48.29; H, 3.57; N, 13.25. Found: C, 48.32; H, 3.46; N, 13.25.

(b) A mixture of 8 (1.0 g, 1.36 mmol) and potassium carbonate (0.36 g) in dry MeOH (100 ml) was stirred at room temperature for 24 h. The solvent was evaporated and the re-

sidue was dissolved in hot H_2O, followed by acidification of the solution with 2N AcOH to pH 5 to give a yellow precipitate (0.52 g, 90 %, m.p. 265°C), which had the same analytical data as the preceding sample.

7-(p-Chlorophenyl)-1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-4-thiolumazine (10). A suspension of 7-(p-chlorophenyl)-1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-lumazine (6) (7.0 g, 9.7 mmol) and diphosphorous pentasulfide (7.8 g, 17.5 mmol) in dry dioxane (250 ml) was refluxed for 2 h. After cooling, the suspension was filtered, and the filtrate was evaporated to dryness. The residue was partitioned between $CHCl_3$ and brine solution. The organic extract was dried (Na_2SO_4), filtered and evaporated to dryness to give a crude yellow material. Recrystallization from $CHCl_3$/MeOH gave 10 as yellow crystals (6.56 g, 93 %, m.p. 260-262°C).

Anal. calc. for $C_{38}H_{27}ClN_4O_8S$ (737.2): C, 62.08; H, 3.70; N, 7.62. Found: C, 61.98; H, 3.78; N, 7.62.

7-(p-Chlorophenyl)-1-β-D-ribofuranosyl)-4-thiolumazine (11). Compound 10 (1.0 g, 1.36 mmol) was stirred at room temperature in a solution of dry MeOH (150 ml) and potassium carbonate (0.36 g) for 10 h. The solution was evaporated to dryness, the residue dissolved in hot H_2O and then acidified with 2N AcOH to pH 5 to yield a yellow precipitate of 11 (0.5 g, 83 %, m.p. 250°C dec.):

Anal. calc. for $C_{17}H_{15}ClN_4O_5S$ (422.8): C, 48.29; H, 3.57; N, 13.25. Found: C, 48.19; H, 3.60; N, 13.13.

6-(p-Chlorophenyl)-1-(2,3,5-tri-O-methanesulfonyl-β-D-ribofuranosyl)-lumazine (12). A mixture of 5 (1.8 g, 4.43 mmol) and methanesulfonyl chloride (2.03 g, 17 mmol. 1.39 ml) in dry pyridine (50 ml) was stirred for 10 h at room temperature. $CHCl_3$ (100 ml) was added, then washed with 5 %

sulfuric acid, a diluted solution of sodium bicarbonate, and finally with H_2O. The organic extract was dried (Na_2SO_4), filtered and evaporated to a pale yellowish crystalline product, which afforded on recrystallization from EtOH compound 12 as colorless crystals (2.2 g, 78 %, m.p. 183-186°C).

Anal. calc. for $C_{20}H_{21}ClN_4O_{12}S_3$ (640.1): C, 37.53; H, 3.31; N, 8.75. Found: C, 37.59; H, 3.09, N, 8.75.

4-Amino-6-(p-chlorophenyl)-1-β-D-ribofuranosyl-2-oxo-dihydropteridine (13). A mixture of compound 8 (2.25 g, 3.06 mmol) in 25 % methanolic ammonia (100 ml) was stirred at 80° in a pressure bottle for 20 h. The solution was filtered and the yellowish crude product was recrystallized from a mixture of DMF/MeOH 1:5 to give the nucleoside 13 as a yellow powder (0.79 g, 66 %, m.p. 256°C dec.).

Anal. calc. for $C_{17}H_{16}ClN_5O_5$ (405.8): C, 50.32; H, 3.97; N, 17.25. Found: C, 50.01; H, 3.90; N, 17.01.

4-Amino-7-(p-chlorophenyl)-1-β-D-ribofuranosyl-2-oxo-dihydropteridine (14). The preceding procedure used for ammonolysis of 10 (1.5 g, 20.4 mmol) was to afford a pale yellow crystalline product (0.46 g, 56 %, m.p. 220°C dec.).

Anal. calc. for $C_{17}H_{16}ClN_5O_5$ (405.8): C, 50.32; H, 3.79; N, 17.25. Found: C, 50.18; H, 3.81; N, 17.35.

2,2'-Anhydro-6-(p-chlorophenyl)-1-β-D-arabinofuranosyl-lumazine (15). Compound 5 (0.34 g, 0.83 mmol) was dissolved in dry DMF (25 ml), then diphenyl carbonate (0.22 g, 1mmol) and $NaHCO_3$ (7 mg) were added and the reaction mixture heated to 155-160° for 45 min. It was evaporated to dryness, the brownish residue boiled with ether for 30 min. and the solid collected by filtration. Recrystallization from MeOH gave the anhydro nucleoside 15 as a colorless solid (0.2 g, 62.5 %, m.p. 268-270°C dec.).

Anal. calc. for $C_{17}H_{13}ClN_4O_5$ (388.8): C, 52.52; H, 3.37; N, 14.41. Found: C, 52.37; H, 3.40; N, 14.28.

2,2'-Anhydro-7-(p-chlorophenyl)-1-β-D-arabinofuranosyllumazine (16). A mixture of 7-(p-chlorophenyl)-1-β-D-ribofuranosyllumazine (7) (3.0 g, 7.06 mmol), diphenyl carbonate (1.89 g, 8.8 mmol) and dry DMF (32 ml) containing a catalytic amount of $NaHCO_3$ (20 mg) was heated to 155-160°C for 30 min. After cooling, the brown solution was treated with ether (100 ml) to form a crude precipitate. Recrystallization from MeOH gave the anhydro derivative 16 as a pale yellow crystalline powder (2.35 g, 93 %, m.p. 280-281°C).

Anal. calc. for $C_{17}H_{13}ClN_4O_5$ (388.8): C, 52.52; H, 3.37; N, 14.41. Found: C, 52.14; H, 3.47; N, 14.29.

2,2'-Anhydro-6-(p-chlorophenyl)-1-(3,5-di-O-methanesulfonyl-β-D-ribofuranosyl)-lumazine (17). a) A mixture of 12 (0.2 g, 3.56 mmol) and $NaHCO_3$ (50 mg) in dry DMF (10 ml) was heated under reflux for 30 min. The solution was evaporated under vacuum to dryness and the residue was recrystallized from MeOH to afford colorless crystals of 17 (0.12 g, 63 %, m.p. 251-252°C).

Anal. calc. for $C_{19}H_{17}ClN_4O_9S_2$ (544.2): C, 41.93; H, 3.04; N, 10.28. Found: C, 42.02; H, 3.09; N, 9.95.

b) The anhydro nucleoside 15 (0.1 g, 0.26 mmol) was dissolved in dry pyridine (10 ml), then methanesulfonyl chloride (3 ml) was added at 0°C and the mixture left at room temperature for 20 h. Several drops of H_2O were added, followed by $CHCl_3$. The solution was partitioned with 5 % sulfuric acid, 5 % sodium bicarbonate and finally with H_2O. The organic extract was dried (Na_2SO_4), filtered and evaporated to dryness. The pale yellow compound was recrystallized from MeOH to give colorless crystals of 17 (0.13 g, 93 %, m.p. 251°C). The product was chromatographically and spectrophotometrically identical with an authentic sample.

6-(p-Chlorophenyl)-1-β-D-arabinofuranosyllumazine (18). Compound 15 (0.15 g, 0.38 mmol) was boiled with a mixture of acetone/0.1 N sulfuric acid 1:1 (20 ml) for 3.5 h. The solution was evaporated to dryness and the crude product was recrystallized from 50 % aqueous MeOH to give compound 18 as colorless crystals (0.13 g, 83 %, m.p. 260°C dec.).

Anal. calc. for $C_{17}H_{15}ClN_4O_6 \cdot 1/2\ H_2O$ (415.6): C, 49.11; H, 3.88; N, 13.48. Found: C, 49.15; H, 3.77; N, 13.71.

7-(p-Chlorophenyl)-1-β-D-arabinofuranosyllumazine (19). The anhydro compound 16 (0.43 g, 1.1 mmol) was heated under reflux with a 1:1 mixture of acetone/0.1 N sulfuric acid (50 ml) for 4 h. Acetone was evaporated and the residue was kept at 0°C overnight. The precipitate was collected by filtration and recrystallized from 50 % aqueous MeOH (40 ml) to afford the arabino nucleoside 19 as colorless crystals (0.32 g , 68 %, m.p. 214-216°C).

Anal. calc. for $C_{17}H_{13}ClN_4O_5 \cdot H_2O$ (424.8): C, 48.07; H, 4.03; N, 13.19. Found: C, 48.27; H, 3.86; N, 13.19.

ACKNOWLEDGEMENT

We thank the Alexander von Humboldt Foundation for a fellowship, the Fonds der Chemischen Industrie for financial support of these investigations, and Mrs. M. Bischler for the pK determinations and measurements of the UV spectra.

REFERENCES

1. Part XLV: L. Kiriasis and W. Pfleiderer, Nucleosides & Nucleotides 8, in press (1989).
2. G. Ritzmann and W. Pfleiderer, Chem.Ber. 106, 1401 (1973).

3. K. Kobayashi and W. Pfleiderer, Chem.Ber. 109, 3184 (1976).
4. W. Hutzenlaub, K. Kobayashi, and W. Pfleiderer, Chem. Ber. 109, 3217 (1976).
5. G. Ritzmann, K. Ienaga, and W. Pfleiderer, Liebigs Ann. Chem. 1217 (1977).
6. W.H. Prusoff and B. Goz, Fed.Proc.Am.Soc.Exp.Biol. 32, 1679 (1973).
7. E. DeClercq, J. Descamps, G.F. Huang, and P.F. Torrence, Mol.Pharmacol. 14, 422 (1978).
8. E. DeClercq, Arch.Int.Physiol.Biochim. 87, 353 (1979).
9. G.A. Gentry and J.F. Aswell, Virology 65, 294 (1975).
10. W. Pfleiderer, G. Ritzmann, K. Harzer, and J.C. Jochims Chem.Ber. 106, 2982 (1973).
11. K. Kobayashi and W. Pfleiderer, Chem.Ber. 109, 3194 (1976).
12. L. Birkofer and A. Ritter, Angew.Chem. 77, 414 (1965).
13. H. Vorbrüggen and G. Höfle, Chem.Ber. 114, 1256 (1981).
14. H. Lutz and W. Pfleiderer, Croatica Chem.Acta 59, 199 (1986).
15. T.E. Gorizdra, Khim.Geterosikl.Soedin. 5, 908 (1969).
16. G. Zemplen, A. Geres, and J. Hadacsy, Ber.Deut.Chem.Ges. 69, 1827 (1936).
17. A. Hampton and A.W. Nichols, Biochemistry 5, 2076 (1966).
18. C.A. Hona and M. Sundaralingam, J.Am.Chem.Soc. 95, 2333 (1973).
19. A. Albert and E.P. Serjeant in "The Determination of Ionization Constants", Chapman and Hall Ltd., London 1971, p. 44.

Received April 9, 1989.