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SYNTHESIS AND PROPERTIES OF 2,2′-ANHYDRO-*N*-3-LUMAZINE NUCLEOSIDES*,†

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ABSTRACT

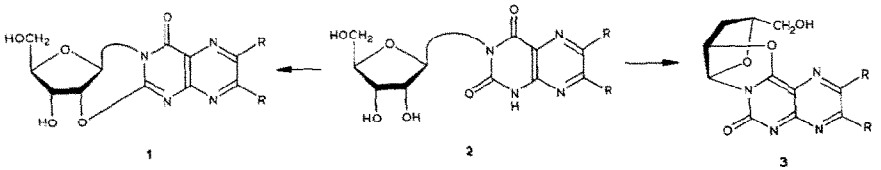
The reaction of 3-β-D-ribofuranosyllumazine, and its 6,7-dimethyl and diphenyl derivatives was studied for anhydronucleoside formation with adjacent carbonyl groups of the aglycon. Various conditions led to selective 2,2′-cyclization but no products possessing the less favored 4,2′-structure were obtained. The best yields of 2,2′-anhydro-3-β-D-arabinofuranosyllumazines were obtained from 3-(2,3-*O*-carbonyl-5-*O*-trityl-β-D-ribofuranosyl)lumazines in an imidazole-catalyzed reaction at elevated temperatures. Base hydrolysis of the 2,2′-bond allowed the synthesis of 3-β-D-arabinofuranosyllumazines.

INTRODUCTION

In a continuation of our investigations on the formation of anhydrolumazine nucleosides[2,3], we focussed our attention on the chemical behavior and reactivity of 3-β-D-ribofuranosyllumazines (**2**). The site of the ribofuranosyl residue at N-3 theoretically opens up two possibilities of cyclizations with both of the adjacent carbonyl groups to form the corresponding 2,2′-(**1**) and 2,4′-anhydrolumazine nucleosides (**3**), respectively.

RESULTS AND DISCUSSION

The starting materials, 3-β-D-ribofuranosyllumazine (**10**) and its 6,7-dimethyl (**16**) and 6,7-diphenyl derivatives (**17**) were prepared as previously described[4,5], *via* a modified Hilbert–Johnson–Birkofer[6] reaction, by treatment of the



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*Dedicated to Professor Raymond U. Lemieux.
†Nucleosides Part XXXIX. For Part XXVIII, see ref. 1.

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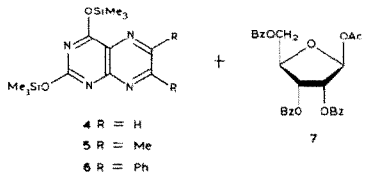
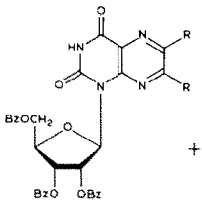


4 R = H
5 R = Me
6 R = Ph

7



8 R = H
9 R = Me
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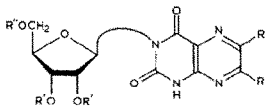
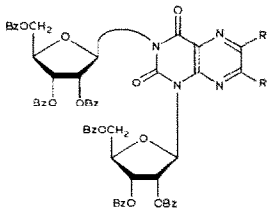
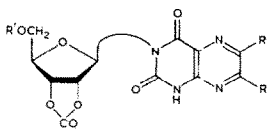


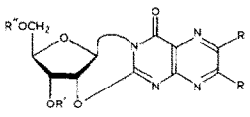
	R	R'	R''
11	H	Bz	Bz
12	Me	Bz	Bz
13	Ph	Bz	Bz
14	Ph	Ac	Ac
15	H	H	H
16	Me	H	H
17	Ph	H	H
18	H	H	Tr
19	Me	H	Tr
20	Ph	H	Tr
21	Ph	Ms	Ms



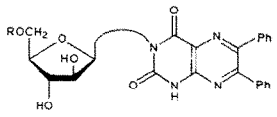
22 R = H
23 R = Me
24 R = Ph



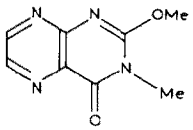
	R	R'
25	H	Tr
26	Me	Tr
27	Ph	Tr
28	Ph	Tr



	R	R'	R''
29	H	H	Tr
30	Me	H	Tr
31	Ph	H	Tr
32	H	H	H
33	Me	H	H
34	Ph	H	H
35	Ph	Ac	Ac
36	Ph	Ac	H
37	Ph	Ms	Ms
38	Ph	H	Ms



39 R = H
40 R = Tr



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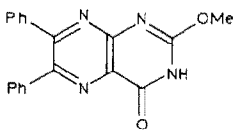

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trimethylsilylated lumazines **4–6** with 1-*O*-acetyl-2,3,5-tri-*O*-benzoylribofuranose (**7**) under boron trifluoride etherate catalysis in benzene to favor N-3 ribosylation. Whereas 6,7-diphenyl-2,4-bis(trimethylsilyloxy)pteridine (**6**) afforded a mixture of 6,7-diphenyl-**3** (**13**) and 6,7-diphenyl-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-lumazine (**10**), as well as 6,7-diphenyl-1,3-bis(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)lumazine (**24**) in 65, 11, and 7% yield, respectively, much less regioselectivity was found with 2,4-bis(trimethylsilyloxy)pteridine (**4**) and its 6,7-dimethyl derivative **5**. Compounds **4** and **5** led under analogous conditions to mixtures of more equal amounts of the three ribosides **8**, **11**, and **22**, and 9, **12**, and **23**, respectively, which could be separated by preparative silica gel column chromatography to give a 20–30% yield of each. A more convenient preparation of the 3-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)lumazines **14**, **12**, and **13** was then achieved by the acid cleavage of one glycosidic linkage of the easily available 1,3-diribosides **22**, **23**, and **24** in boiling trifluoroacetic acid to give equal amounts of the corresponding N-1 and N-3-monoribosides. Another approach to the preparation of **13** was achieved by boron trifluoride-catalyzed rearrangement in **10** or a ribosyl exchange between 6,7-diphenyl-2,4-bis(trimethylsilyloxy)pteridine (**6**) and the diriboside **24**. Both reactions led again, however, to mixtures of the two monoribosides **10** and **13**, and the diriboside **24**, which have to be separated chromatographically. Debenzoylation to give the free 3-β-D-ribofuranosyllumazines **15–17** was done by Zemplén's method[7] with sodium methoxide in methanol.

2′,X-Anhydronucleoside formation was first investigated with 6,7-diphenyl-3-β-D-ribofuranosyllumazine (**17**) according to the approach of Hampton and Nichol[8] described in the pyrimidine nucleoside series. Treatment of **17** with diphenylcarbonate and sodium hydrogencarbonate in *N,N*-dimethylformamide led to a complex mixture of products from which the expected 2,2′-anhydro-3-β-D-arabinofuranosyl-6,7-diphenyllumazine (**34**) could be isolated chromatographically in 31% yield. In order to increase the solubility of the lumazine nucleosides in organic solvents and to reduce side reactions involving 5′-OH, **17** was tritylated to give 6,7-diphenyl-3-(5-*O*-trityl-β-D-ribofuranosyl)lumazine (**20**). Since cyclic 2′,3′-carbonates can be regarded as the reactive intermediates in the 2,2′-anhydronucleoside formation[8–11], **20** was converted by treatment with *N,N*-carbonyldiimidazole at room temperature in oxolane, in 91% yield, into 3-(2,3-di-*O*-carbonyl-5-*O*-trityl-β-D-ribofuranosyl)-6,7-diphenyllumazine (**27**). Heating in boiling *N,N*-dimethylformamide in the presence of sodium hydrogencarbonate afforded two anhydro products, from which 2,2′-anhydro-6,7-diphenyl-3-(5-*O*-trityl-β-D-arabinofuranosyl)lumazine (**31**) was isolated in 67% yield. The structure of the second component obtained in small amounts has not yet been elucidated; u.v., n.m.r., and mass spectral data indicate, however, that it is not the 4,2′-anhydronucleoside isomer. During the melting point determination of **27** it was observed that the substance melted with gas evolution at 180° to form **31**, as evidenced by t.l.c. This reaction also took place in preparative scale and yielded, on heating of **27** to 210°, 75% of **31** and 12% of the detritylated product **34**. Finally it was found that heating **27**

in melting imidazole to 120° for 15 min afforded an even better anhydro nucleoside formation with an 80% yield of isolated product. Detritylation of **31** and **27** to give **34** and **28**, respectively, proceeded as expected in good yields on heating in 80% acetic acid. Heating of **28** in boiling *N,N*-dimethylformamide containing sodium hydrogencarbonate for 30 min led almost exclusively to **34**, which was isolated chromatographically pure in 93% yield, and in crystalline form in 81% yield. Since the cyclizations of β-D-ribofuranosyllumazine 2′,3′-carbonates so far described lead to 2,2′-anhydrolumazine nucleosides in a more or less regiospecific manner, other methods have been attempted to achieve (at least in part) a reaction with the other carbonyl group of the lumazine component to give the structurally more interesting 4,2′-anhydronucleosides. Treatment of 6,7-diphenyl-3-β-D-ribofuranosyllumazine (**17**) with boron trifluoride etherate and acetic anhydride in acetonitrile, under conditions similar to those of Kondo and Inoue[12], afforded a complex mixture of five products, from which 2,2′-anhydro-3-(3,5-di-*O*-acetyl-β-D-arabinofuranosyl)-6,7-diphenyllumazine (**35**) and 6,7-diphenyl-3-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-lumazine (**14**) could be separated and isolated in 44% and 11% yield, respectively. The structures of both compounds were proven by acylation of **34** and **17**, respectively, with acetic anhydride–pyridine, as well as by mild deacylation with methanolic ammonia at room temperature of **35** to give **34**. Reaction of **17** with 2-acetoxybenzoyl chloride according to the method of Reichmann *et al.*[13], which may be regarded as an extension of the procedure of Greenberg and Moffatt[14] using α-acetoxyisobutyryl chloride, was again not very promising and led to another complex mixture of at least six chromatographically detectable compounds. As the main product, 3-(3-*O*-acetyl-β-D-arabinofuranosyl)-2,2′-anhydro-6,7-diphenyllumazine (**36**) was isolated in 38% yield, whereas a second pure compound turned out to be **35** (15%).

Further studies dealt with the synthesis and reactivity of 6,7-diphenyl-3-(2,3,5-tri-*O*-mesyl-β-D-ribofuranosyl)lumazine (**21**), which could be obtained from **17** with mesyl chloride in pyridine in good yield. The processing and purification of **21** was quite difficult owing to its high tendency to form 2,2′-anhydro-3-(3,5-di-*O*-mesyl-β-D-arabinofuranosyl)-6,7-diphenyllumazine (**37**), even in solution at room and slightly elevated temperature. Heating of **21** in *N,N*-dimethylformamide (and in the presence of sodium hydrogencarbonate) gave **37** in 73% yield and, in 14% yield, 2,2′-anhydro-3-(5-*O*-mesyl-β-D-arabinofuranosyl)-6,7-diphenyllumazine (**38**), which has only been characterized by u.v. and ^{1}H-n.m.r. spectral data. Structural proof for **37** was obtained by its synthesis in 71% yield by treatment of **34** with mesyl chloride in pyridine. The aforementioned results indicate that 6,7-diphenyl-3-β-D-ribofuranosyllumazine (**17**) and its derivatives react along a selective pathway to yield exclusively 2,2′-anhydrolumazine nucleosides owing to the preservation of the heteroaromatic character of the pyrazine component of the molecule, whereas the formation of a 4,2′-anhydro structure (**3**) would create a thermodynamically less-favored, *ortho*-quinonoid-type electron distribution.

The conversion of 3-β-D-ribofuranosyllumazine (**15**) and its 6,7-dimethyl de-

rivative (**16**) into the corresponding 2,2′-anhydro-3-β-D-arabinofuranosyllumazines **32** and **33**, respectively, was then performed on the basis of our experiences in the 6,7-diphenyl series. In the first step of the synthesis, **15** and **16** were tritylated to give **18** and **19**, which gave the 2′,3′-cyclic carbonates **25** and **26** in 84%

TABLE I

U.V. DATA FOR LUMAZINE NUCLEOSIDES

Comp.	*pK_a*	*Solvent*	*U.v. absorption spectra*[a]							
	(water; 25°)		*λ_{max} (nm)*				*lg ε*			
8		MeOH	231			315	4.72			3.84
9		MeOH	229			326	4.75			4.01
10		MeOH	228	272		358	4.84	4.35		4.16
11		MeOH	230	274	281	325	4.71	3.60	3.61	3.90
12		MeOH	229	[272]	[281]	330	4.68	[3.54]	[3.51]	3.98
13		MeOH	229	273		364	4.83	4.30		4.21
14		MeOH	222	272		363	4.46	4.26		4.17
15	7.87 ±0.1	pH 4.0	234			327	4.07			3.90
		pH 11.0	[212]	245	272	366	[4.05]	4.08	4.10	3.78
		MeOH	235			326	4.07			3.84
16	8.30 ±0.1	pH 4.0	235			330	3.92			3.91
		pH 11.0	[214]	244	275	365	[4.08]	4.01	4.05	3.75
		MeOH	237			330	4.07			3.99
17	7.86 ±0.06	pH 1.0	[220]	272		363	[4.43]	4.19		4.19
		pH 11.0	[220]	[240]	292	388	[4.41]	[4.28]	4.39	4.07
		MeOH	[222]	272		364	[4.41]	4.17		4.18
18		MeOH	[228]			326	[4.28]			3.87
19		MeOH	[228]	[247]		331	[4.28]	[4.06]		3.99
20		MeOH	[220]	272		364	[4.64]	4.26		4.20
21		MeOH	222	276		363	4.52	4.27		4.21
22		MeOH	229			315	4.95			3.96
23		MeOH	229			323	5.02			4.09
24		MeOH	229	273		360	4.98	4.32		4.13
25		MeOH	[228]			326	[4.28]			3.85
26		MeOH	[229]	[245]		330	[4.24]	[3.99]		3.97
27		MeOH	[220]	277		366	[4.61]	4.22		4.15
28		MeOH	222	276		363	4.41	4.18		4.13
29		MeOH	[225]	260		319	[4.26]	3.95		3.76
30		MeOH	[229]	262		322	[4.25]	3.98		3.84
31		MeOH	[220]	246	282	357	[4.58]	4.25	4.22	4.09
32		MeOH	230	260		319	4.04	3.97		3.78
33		MeOH	232	262		322	4.03	3.96		3.84
34		MeOH	[220]	245	280	357	[4.50]	4.32	4.28	4.15
35		MeOH	[220]	246	280	357	[4.44]	4.27	4.25	4.12
36		MeOH	220	245	280	357	4.48	4.29	4.27	4.13
37		MeOH	220	246	280	357	4.44	4.26	4.22	4.10
39		MeOH	[220]	272		363	[4.50]	4.21		4.20
40		MeOH	[222]	271		365	[4.56]	4.20		4.16
41		MeOH	237	261		321	4.28	4.20		3.79
42		MeOH	222	245	277	362	4.33	4.21	4.23	4.05

[a]Shoulder values are given in brackets.

TABLE II

^{1}H-N.M.R DATA FOR LUMAZINE NUCLEOSIDES[a]

Comp.	*Solvent*	*H-1'*	$J_{1',2'}$	*H-2'*	*H-3'*	*H-4''*	H_2-5''
11	$CDCl_3$	6.80s		6.27m		4.76bs	
12	$CDCl_3$	6.88s		6.38m		4.84bs	
13	$CDCl_3$	6.89s		6.2–6.5m		4.5–5.1m	
14	$CDCl_3$	6.56d	1.8	5.90m	5.70m	4.1–4.6	
15	$(C^2H_3)_2SO/D_2O$	6.22d	3.5	4.40q	4.21t	3.4–3.8m	
16	$(C^2H_3)_2SO/D_2O$	6.21d	3.0	4.56q	4.23t	3.6–3.8m	
17	$(C^2H_3)_2SO/D_2O$	6.32d	3.1	4.67q	4.32t	3.3–4.1m	
18	$(C^2H_3)_2SO/D_2O$	6.32d		4.52q	4.5	4.00m	3.28bs
19	$(C^2H_3)_2SO/D_2O$	6.26d		4.5–4.2m		3.98bs	3.3m
20	$(C^2H_3)_2SO/D_2O$	6.30d		4.6–3.8m		3.1–3.4m	
21	$CDCl_3$	6.76s		5.80m		4.2–4.6m	
25	$(C^2H_3)_2SO$	6.72s		5.70d	5.34q	4.20m	3.20m
26	$CDCl_3$	6.76s		5.3–5.6m		4.35m	3.48m
27	$CDCl_3$	6.84s		5.2–5.6m		4.38q	3.46m
28	$(C^2H_3)_2SO$	6.63d	1.8	5.84d	5.40q	4.30m	3.68m
29	$(C^2H_3)_2SO$	6.64d	6.0	5.74d	4.48bs		3.1m
30	$CDCl_3$	6.62d	6.0	5.40d	4.71bs	4.46bs	3.10d
31	$CDCl_3$	6.78d	6.0	5.42d	4.56bs	4.50bs	3.04bs
32	$(C^2H_3)_2SO$	6.58d	6.0	5.30d	4.46bs	4.14bs	3.36bs
33	$(C^2H_3)_2SO$	6.54d	6.0	5.26d	4.46bs	4.12bs	3.36bs
34	$(C^2H_3)_2SO$	6.70d	6.0	5.40d	4.56bs	4.24bs	3.44bs
35	$CDCl_3$	6.78d	6.0	5.52d	5.40bs	3.70bs	4.2dq
36	$(C^2H_3)_2SO$	6.73d	6.0	5.63d	5.48bs	4.40bs	3.50bs
37	$(C^2H_3)_2SO/CDCl_3$	6.84d	6.0	5.87d	5.64d	4.80q	4.40bd
39	$(C^2H_3)_2SO$	6.64d	7.0	4.34bs		3.72m	
40	$(C^2H_3)_2SO$	6.70d	7.0	4.0–4.40m		3.6–3.9m	

[a] δ Values from signal of internal standard, Me_4Si, *J* values in Hz; s, singlet; bs, broad singlet; d, doublet; t, triplet; q, quartet; and m, multiplet.

and 88% yield, respectively, on treatment with *N,N*-carbonyldiimidazole. Heating **25** and **26** in toluene for 1 h under reflux in the presence of imidazole gave **29** (91%) and **36** (93%), respectively, in crystalline form. Subsequent detritylation in 80% acetic acid then gave **32** and **33**. Finally 2,2'-anhydro-3-β-D-arabinofuranosyl-6,7-diphenyllumazine (**34**) was cleaved with aqueous alkali to give 3-β-D-arabinofuranosyl-6,7-diphenyllumazine (**39**), which could also be obtained by alkaline hydrolysis of **31** followed by detritylation.

The characterization of the newly synthesized compounds was best achieved by u.v. and ^{1}H-n.m.r. spectroscopy. The u.v. spectra (Table I) revealed small but distinct differences between the 1- and 3-monoribosyllumazine series, which allowed accurate structural assignments. The 1-*N*-ribofuranosyllumazines absorb, in general, at lower wavelengths than their N-3 counterparts, and from the properties of the fully deblocked analogs **15–17** it was noticed that the NH-1 group is more acidic and that monoanion formation was associated with a stronger bathochromic shift of the longer wavelength band. This behavior is in full agreement with obser-

vations made with the simpler 1- and 3-methyllumazine derivatives[15]. Various substitutions of the sugar residue expectedly did not change the spectrum of the basic molecule significantly, but influenced the extinctions, especially at lower wavelength, according to their absorbance. The 2,2′-anhydro-3-β-D-arabinofuranosyllumazines possess a new chromophor group in the aglycon residue, which is reflected in an additional absorption band as observed already in the model compounds[15] 2-methoxy-3-methyl-4-oxodihydropteridine[15] (**41**) and 2-methoxy-4-oxo-6,7-diphenyldihydropteridine (**42**).

More detailed information on the fine structure of the various compounds was obtained from the ^{1}H-n.m.r. spectra (Table II). The ^{1}H-n.m.r. spectra of the benzoylated 3-β-D-ribofuranosyllumazines **11–13** showed a singlet for the anomeric H-1′, which can be taken as proof of the existence of a β-D-glycosylic linkage between sugar and heterocyclic aglycon residue. The other proton signals of the D-ribose residue were not well resolved and appeared as two sets of multiplets containing the H-2′ and -3′, as well as H-4′ and -5′, respectively. Deacylation to the free nucleosides **15–17** led to a splitting of the H-1′ signal to a doublet with the non-diagnostic J ~3 Hz, and an additional signal separation of H-2′ and -3′. Tritylation of OH-5′ to give **18–20** did not alter the spectrum much, but bridging OH-2′ and -3′ to a cyclic carbonate group (**25–27**) resulted in a more rigid conformation of the carbohydrate residue, which was reflected in a somewhat better separation of the sugar proton signals. The best resolved spectra, however, were provided by the 2,2′-anhydro-3-β-D-arabinofuranosyllumazines **29–37**. The rigidity of the system led to clearly different chemical shifts of the sugar protons with decreasing δ values according to increasing numbering. H-1′ and -2′ coupled with 6 Hz and gave raise to characteristic doublets, whereas little magnetic interaction was observed for H-3′. Finally, H_2-5′ of **35** appeared in a well-resolved double quartet, which is seldom seen so clearly.

EXPERIMENTAL

Melting points are not corrected. U.v.-spectra were recorded with a Cary-Recording spectrometer, model 118, and ^{1}H-n.m.r. spectra with JEOL-JNM-100 and Bruker WM-250 spectrometers. T.l.c. was performed on thin-layer sheets of Silica gel F 1500 LS 254 and Cellulose F 1440/LS 254 of Schleicher and Schüll, column chromatography on silica gel (0.05–0.2 mm), and preparative thick-layer plates with Silica gel PF_{254} (Merck). Large-scale column chromatography was performed with the low-pressure equipment Jobin–Yvon Chromatospac prep of ISA Division d'Instruments using 1.5 kg of Silica gel 60 PF_{254} (Merck) at a pressure of 0.8–1.2 MPa. Substances were dried in an oven at 100° or in the vacuum oven Büchi–TO 50 in the presence of phosphorus pentaoxide.

*1-(2,3,5-Tri-*O*-benzoyl-β-*D*-ribofuranosyl)lumazine* (**8**), *3-(2,3,5-tri-*O*-benzoyl-β-*D*-ribofuranosyl)lumazine* (**11**), *and 1,3-bis(2,3,5-tri-*O*-benzoyl-β-*D*-ribofuranosyl)lumazine* (**22**). — (*a*) *From* **4**. Lumazine (3.8 g, 23.2 mmol) was tri-

methylsilylated to give 2,4-bis(trimethylsilyloxy)pteridine (**4**) by boiling under reflux in hexamethyldisilazane (50 mL) in the presence of some crystals of ammonium sulfate for 48 h. The excess of hexamethyldisilazane was distilled off, and then the reaction product was distilled in high vacuum according to an earlier procedure[16]. The colorless distillate (5.2 g) was dissolved in abs. benzene (300 mL). After addition of BF_3-etherate (6 mL), a solution of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**7**, 6.0 g) in abs. benzene (150 mL) was added dropwise with stirring within 2 h. Stirring was continued for another h at room temp., and the mixture then treated with an aqueous solution of $NaHCO_3$ for neutralization. The organic layer was separated, dried (Na_2SO_4), and evaporated to dryness. The residue was applied to a silica gel column (30 × 7 cm) to give, on chromatography with chloroform, **22** (2.6 g, 20%), **8** (2.2 g, 30%), and **11** (1.5 g, 19%).

(*b*) *From* **22**. A solution of **22** (ref. 16) (38.2 g, 36 mmol) in trifluoroacetic acid (120 mL) was boiled under reflux for 15 h. Evaporation *in vacuo* led to a dark residue that was dissolved in dichloromethane (600 mL). The solution was washed with aqueous $NaHCO_3$, dried (Na_2SO_4), and evaporated to a small volume for chromatography on a silica gel column (20 × 9 cm) in 4:1 dichloromethane–ethyl acetate. The main fraction consisting of **8** (ref. 16) and **11** was collected and evaporated to dryness (23.1 g). Separation was achieved by preparative flash-chromatography in a Jobin–Yvon Chromatospac prep with 21:1 dichloromethane–ethyl acetate (14 L). The first fraction (4 L) contained contaminants, and from the second (4–7 L) **11** (10.3 g, 46%) and the last fraction (8–14 L) **8** (9.8 g, 44%) could be isolated. Reprecipitation of **11** from a little benzene into cyclohexane gave a colorless material, m.p. 128–130°.

Anal. Calc. for $C_{32}H_{24}N_4O_9$ (608.5): C, 63.15; H, 3.96; N, 9.21. Found: C, 63.17; H, 4.08; N, 9.22.

*6,7-Dimethyl-1-(2,3,5-tri-*O*-benzoyl-β-*D*-ribofuranosyl)lumazine* (**9**), *6,7-dimethyl-3-(2,3,5-tri-*O*-benzoyl-β-*D*-ribofuranosyl)lumazine* (**12**), *and 6,7-dimethyl-1,3-bis(2,3,5-tri-*O*-benzoyl-β-*D*-ribofuranosyl)lumazine* (**23**). — (*a*) *From* **5**. 6,7-Dimethyllumazine (3.84 g, 22 mmol) was trimethylsilylated to give 2,4-bis(trimethylsilyloxy)pteridine (**5**) in the usual manner[16] and, after evaporation, the residue dissolved in abs. benzene (300 mL). BF_3-etherate (10 mL) and a solution of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**7**) (10 g, 20 mmol) in abs. benzene (100 mL) were added and the mixture was processed as described under (*a*). The separation of the mixture of products could be achieved by column chromatography(30 × 5 cm) on silica gel with 29:1 chloroform–ethyl acetate to yield **23** (5.62 g, 26%), **9** (3.18 g, 25%), and from the last fraction **12** (2.45 g, 19%). Compound **12** did not crystallize, but an amorphous powder was obtained from ethanol–water, m.p. of 129–135°.

Anal. Calc. for $C_{34}H_{28}N_4O_9$ (636.6): C, 64.14; H, 4.43; N, 8.80. Found: C, 63.84; H, 4.55; N, 8.52.

(*b*) *From* **23**. A solution of **23** (1.08 g, 1 mmol) in trifluoroacetic acid (10 mL) was boiled under reflux for 8.5 h. The dark-colored solution was evaporated to dry-

ness, the residue dissolved in chloroform (50 mL), and the solution washed with aqueous $NaHCO_3$. The organic layer was dried (Na_2SO_4), and evaporated to dryness, and the residue fractionated by preparative thick-layer chromatography on 40 × 20 × 0.2-cm plates in 49:1 chloroform–methanol (two developments). From the faster-running band was isolated **12** (0.22 g, 34%) and from the slower-moving **9** (0.245 g, 38%).

*6,7-Diphenyl-1-(2,3,5-tri-*O*-benzoyl-β-*D*-ribofuranosyl)lumazine*[16] (**10**), *6,7-diphenyl-3-(2,3,5-tri-*O*-benzoyl-β-*D*-ribofuranosyl)lumazine*[5] (**13**), *and 6,7-diphenyl-1,3-bis(2,3,5-tri-*O*-benzoyl-β-*D*-ribofuranosyl)lumazine*[16] (**24**). — (*a*) *From* **24**. A solution of **24** (refs. 5, 16) (54.2 g, 45 mmol) in trifluoroacetic acid (175 mL) was heated under reflux for 18 h. Trifluoroacetic acid was distilled off *in vacuo,* and the residual solvent coevaporated with chloroform several times. After dissolution of the residue in chloroform, the mixture of compounds was separated on a silica gel column (20 × 9 cm) by chromatography first with 29:1 dichloromethane–ethyl acetate to give **13** and then with 9:1 dichloromethane–ethyl acetate to give **10** (15.1 g, 44%). The first fraction (**13**) was purified further by preparative low-pressure, flash chromatography with dichloromethane–ethyl acetate to yield pure **13** (14.8 g, 43%) as an amorphous solid.

(*b*) *From* **6**. 6,7-Diphenyllumazine (3.18 g, 10 mmol) was converted[16] into 6,7-diphenyl-2,4-bis(trimethylsilyloxy)pteridine (**6**). This was dissolved in abs. benzene (250 mL), and **24** (12 g, 10 mmol) and BF_3-etherate (5 mL) were added. The mixture was boiled under reflux for 12 h under elimination of any moisture, and then made neutral with aqueous $NaHCO_3$. A precipitate was filtered off, and the organic layer dried (Na_2SO_4) and then evaporated to give a crude mixture (13.2 g). Separation of the components was achieved by silica gel column (35 × 2.5 cm) chromatography with a 49:1 to 19:1 gradient of dichloromethane–ethyl acetate (7 L) to yield **24** (6.8 g, 56%), **13** (2.6 g, 17%), and **10** (3.0 g, 20%).

(*c*) *From* **10**. A solution of **10** (ref. 16) (14.0 g, 11.6 mmol) in toluene (100 mL), abs. 1,4-dioxane (150 mL), and hexamethyldisilazane (50 mL) was boiled under reflux for 3 days. The mixture was evaporated to dryness *in vacuo,* the residue dissolved in abs. benzene, and the solution slowly added dropwise to a boiling solution of BF_3-etherate (20 mL) in abs. benzene (200 mL). After 1 h another portion of BF_3-etherate (30 mL) was added and boiling continued for 24 h. The solution was made neutral with aqueous $NaHCO_3$ or triethylamine, and the organic layer dried (Na_2SO_4) and then evaporated. The residue was fractionated chromatographically as described under (*b*) to yield **24** (2.3 g, 33%), **13** (2.2 g, 16%), and **10** (1.9 g, 14%).

*6,7-Diphenyl-3-(2,3,5-tri-*O*-acetyl-β-*D*-ribofuranosyl)lumazine* (**14**). — A mixture of 6,7-diphenyl-3-β-D-ribofuranosyllumazine (**17**) (0.2 g, 0.45 mmol) and 1:1 pyridine–acetic anhydride (7 mL) was stirred at room temp. for 1 h. Evaporation to dryness and chromatography on a preparative silica gel plate in 10:1 chloroform–methanol, followed by crystallization from 1:2 methanol–water yielded colorless crystals (0.18 g, 70%), m.p. 132–134°.

Anal. Calc. for $C_{29}H_{26}N_4O_9$ (574.6): C, 60.63; H, 4.56; N, 9.75. Found: C, 60.50; H, 4.49; N, 9.62.

3-β-D-Ribofuranosyllumazine (**15**). — Compound **11** (2.5 g, 4.1 mmol) was stirred at room temp. in a solution of sodium (0.15 g) in abs. methanol (150 mL) for 18 h. The mixture was then diluted with water (50 mL), made acid with acetic acid to pH 4–5, and evaporated to dryness *in vacuo*. The residue was triturated several times with ether and then purified by chromatography on a silica gel column (15 × 4 cm) with 4:1 chloroform–methanol. The main fraction was collected, evaporated, and gave on crystallization from 1:1 ethanol–water (120 mL) colorless crystals (0.95 g, 78%), m.p. 145–149°.

Anal. Calc. for $C_{11}H_{12}N_4O_6$ (296.2): C, 44.60; H, 4.08; N, 18.91. Found: C, 44.55; H, 4.15; N, 19.10.

6,7-Dimethyl-3-β-D-ribofuranosyllumazine (**16**). — Compound **12** (3.5 g, 5 mmol) was treated as described for the preparation of **15**. Compound **16** could not be obtained in crystalline form and, therefore, was reprecipitated from little ethanol into hexane to yield a colorless, amorphous solid (1.21 g, 74%), m.p. 158°.

Anal. Calc. for $C_{13}H_{16}N_4O_6$ (324.3): C, 48.15; H, 4.97; N, 17.28. Found: C, 47.99; H, 4.90; N, 17.06.

6,7-Diphenyl-3-β-D-ribofuranosyllumazine[16] (**17**). — Compound **13** (11.4 g, 15 mmol) was stirred in a solution of sodium (0.4 g) in abs. methanol (280 mL) for 16 h at room temp. On dilution with water (100 mL) and acidification with acetic acid to pH 4–5, a precipitate separated. Methanol was distilled off in a flash evaporator, and then the precipitate collected. Crystallization from 1:5 1-propanol–water (200 mL) yielded yellowish crystals (5.83 g, 88%), m.p. 170–172° (lit.[16] m.p. 168–172°).

3-(5-O-Trityl-β-D-ribofuranosyl)lumazine (**18**). — Compound **15** (3.56 g, 12 mmol) and chlorotriphenylmethane (4.0 g, 13.6 mmol) were stirred in abs. pyridine (150 mL) for 6 days at room temp. The mixture was concentrated to half of its volume and then added dropwise to ice–water (600 mL) with vigorous stirring. The precipitate was collected, dried in a vacuum desiccator, and then precipitated from 9:1 chloroform–methanol (50 mL) into hexane (1.8 L) to yield an amorphous powder (5.23 g, 82%), which was pure enough for further reactions. An analytical sample was obtained by chromatography of 1.8 g on a silica gel column (15 × 4 cm) in 9:1 chloroform–methanol. The main fraction was evaporated and yielded, on crystallization from ethanol (80 mL), colorless crystals (1.2 g), m.p. 205–206°.

Anal. Calc. for $C_{30}H_{26}N_4O_6$ (538.6): C, 66.91; H, 4.87; N, 10.40. Found: C, 67.12; H, 4.78; N, 10.68.

6,7-Dimethyl-3-(5-O-trityl-β-D-ribofuranosyl)lumazine (**19**). — Compound **16** (1.0 g, 3 mmol) and chlorotriphenylmethane (0.9 g) were treated in abs. pyridine (30 mL) as described for the preparation of **18**. The crude reaction product was purified by column chromatography on silica gel in 29:1 chloroform–methanol, and crystallization of the main fraction from 2:1 ethanol–2-propanol (30 mL) yielded colorless crystals (1.31 g, 75%), m.p. 168–170°.

Anal. Calc. for $C_{32}H_{30}N_4O_6$ (566.6): C, 67.38; H, 5.34; N, 9.89. Found: C, 67.23; H, 5.31; N, 9.56.

6,7-Diphenyl-3-(5-O-trityl-β-D-ribofuranosyl)lumazine (**20**). — A mixture of **17** (4.5 g, 10 mmol) and chlorotriphenylmethane (3.0 g, 10.8 mmol) in abs. pyridine (80 mL) was stirred at room temp. for 2 days. In order to complete the reaction, the mixture was boiled under reflux for 4 h, and then added slowly to vigorously stirred ice–water (900 mL) to form a colorless precipitate. After filtration and drying in a vacuum desiccator, purification was achieved by chromatography on a silica gel column (40 × 4 cm) with a gradient (30:1 to 10:1) of chloroform–methanol. The main fraction was collected and evaporated, and the residue crystallized from ethanol (110 mL) to yield yellowish crystals (5.53 g, 79%), m.p. 205°.

Anal. Calc. for $C_{42}H_{34}N_4O_6$ (690.8): C, 73.03; H, 4.96; N, 8.11. Found: C, 73.20; H, 4.87; N, 8.11.

6,7-Diphenyl-3-(2,3,5-tri-O-mesyl-β-D-ribofuranosyl)lumazine (**21**). — A mixture of **17** (1.79 g, 4 mmol) and methanesulfonyl chloride (2.2 g, 19 mmol) in abs. pyridine (30 mL) was stirred for 2 h at room temp. The solution was then poured under vigorous stirring into ice–water saturated with $NaHCO_3$ (300 mL). The precipitate was collected and yielded, on crystallization from ethanol–cyclohexane, colorless crystals (2.38 g, 87%), which were chromatographically pure and used for further reactions. For analysis, a sample (0.2 g) was further purified by preparative thick-layer chromatography on a silica gel plate (40 × 20 × 0.2 cm) in 10:1 chloroform–methanol. The main band was eluted with methanol and then precipitated by slow addition of water to yield colorless material (0.13 g), m.p. 137–139°. Heating time for recrystallization was short since anhydronucleoside formation takes place easily at elevated temperatures.

Anal. Calc. for $C_{26}H_{26}N_4O_{12}S_3$ (682.7): C, 45.74; H, 3.84; N, 8.21; S, 14.09. Found: C, 46.31; H, 3.90; N, 7.93; S, 13.71.

3-(2,3-O-Carbonyl-5-O-trityl-β-D-ribofuranosyl)lumazine (**25**). — A mixture of **18** (4.0 g, 7.4 mmol) and *N,N*-carbonyldiimidazole (3.0 g, 18.5 mmol) in abs. oxolane (200 mL) was stirred for 3 h at room temp. The solution was evaporated to dryness, the residue dissolved in chloroform (200 mL), and the solution washed five times with water. The organic layer was dried (Na_2SO_4), evaporated to a small volume, and applied to a silica gel column (15 × 9 cm) for chromatography in 29:1 chloroform–methanol. The main fraction was evaporated to give chromatographically pure material. For analysis, a sample (1.2 g) was further purified by chromatography on a silica gel column (15 × 3 cm) eluted first with 99:1 (300 mL) and then 49:1 chloroform–methanol (1.2 L) to elute the main product. Crystallization from 5:1 ethanol–water yielded colorless crystals (0.91 g), m.p. 165° (dec.).

Anal. Calc. for $C_{31}H_{24}N_4O_7$ (564.6): C, 65.95; H, 4.29; N, 9.92. Found: C, 66.02; H, 4.27; N, 9.95.

3-(2,3-O-Carbonyl-5-O-trityl-β-D-ribofuranosyl)-6,7-dimethyllumazine (**26**). — A mixture of **19** (1.0 g, 1.76 mmol) and *N,N*-carbonyldiimidazole (1.0 g) in abs. oxolane (30 mL) was stirred for 3 h at room temp. After evaporation to dryness,

the residue was dissolved in chloroform (50 mL) and the solution washed several times with water. The organic layer was dried (Na_2SO_4) and evaporated to a small volume for chromatography on a silica gel column (10 ×3 cm) in chloroform. The main fraction was collected and evaporated, and the residue precipitated from a little chloroform into pentane with stirring to yield a colorless material (0.924 g, 88%), m.p. 163° (dec.).

Anal. Calc. for $C_{33}H_{28}N_4O_7$ (592.6): C, 66.88; H, 4.76; N, 9.45. Found: C, 66.55; H, 4.88; N, 9.34.

3-(2,3-O-Carbonyl-5-O-trityl-β-D-ribofuranosyl)-6,7-diphenyllumazine (**27**). — A mixture of **20** (5.5 g, 7.9 mmol) and of 1,1-dicarbonyl-2,2'-di-imidazole (1.78 g, 10 mmol) in abs. oxolane (100 mL) was stirred for 3 h at room temp. The solution was evaporated, the residue dissolved in dichloromethane (160 mL), and the solution washed five times with water. The organic layer was dried ($MgSO_4$) and evaporated to dryness, and the residue dissolved in little chloroform for chromatography on a silica gel column (40 × 4 cm) 40:1 chloroform–methanol. The main fraction was collected and evaporated, and the residue precipitated from hot methanol into water with stirring to yield a colorless amorphous material (5.13 g, 91%), m.p. 180° (dec.).

Anal. Calc. for $C_{43}H_{32}N_4O_7$ (716.8): C, 72.06; H, 4.50; N, 7.82. Found: C, 72.12; H, 4.54; N, 7.62.

3-(2,3-O-Carbonyl-β-D-ribofuranosyl)-6,7-diphenyllumazine (**28**). — A mixture of **27** (1.43 g, 2 mmol) in 4:1 acetic acid–water (20 mL) was heated under reflux for 20 min. Dilution with water (200 mL) afforded a colorless precipitate, which was purified by chromatography on a silica gel column (30 × 4 cm) in 20:1 chloroform–methanol. The main fraction was collected and yielded, after evaporation and purification by precipitation from methanol–water, colorless, amorphous material (0.63 g, 67%), m.p. 285°.

Anal. Calc. for $C_{24}H_{18}N_4O_7$ (474.4): C, 60.76; H, 3.82; N, 11.81. Found: C, 60.54; H, 3.86; N, 11.83.

2,2'-Anhydro-3-(5-O-trityl-β-D-arabinofuranosyl)lumazine (**29**). — A mixture of **25** (0.564 g, 1 mmol) and imidazole (1.1 g) in abs. toluene (50 mL) was heated for 60 min to 120°. After evaporation to dryness, the residue was dissolved in chloroform (80 mL) and the solution washed several times with water. The organic layer was dried (Na_2SO_4) and evaporated, and the residue purified by chromatography on a silica gel column (15 × 3 cm) in 29:1 chloroform–methanol. The main fraction was collected and yielded, on evaporation and crystallization from ethanol (30 mL), colorless crystals (0.473 g, 91%), m.p. 246°.

Anal. Calc. for $C_{30}H_{24}N_4O_5$ (520.5): C, 69.22; H, 4.65; N, 10.76. Found: C, 68.98; H, 4.52; N, 10.59.

2,2'-Anhydro-6,7-dimethyl-3-(5-O-trityl-β-D-arabinofuranosyl)lumazine (**30**). — A mixture of **26** (0.8 g, 1.38 mmol) and imidazole (0.5 g) in abs. toluene (50 mL) was heated under reflux for 3 h. Work-up and chromatography in 24:1 chloroform–acetone were as described for the preparation of **29**. Crystallization

from 1:1 methanol–water (40 mL) yielded colorless crystals (0.71 g, 93%), m.p. 158–160°.

Anal. Calc. for $C_{32}H_{28}N_4O_5$ (548.6): C, 70.06; H, 5.15; N, 10.21. Found: C, 70.05; H, 5.25; N, 10.10.

2,2'-Anhydro-6,7-diphenyl-3-(5-O-trityl-β-D-arabinofuranosyl)lumazine (**31**). (*a*) — A mixture of **27** (1.43 g, 2 mmol) and $NaHCO_3$ (60 mg) in abs. *N,N*-dimethylformamide (10 mL) was heated for 15 min to 160°. The solvent was distilled off *in vacuo* and the residue dissolved in little chloroform for purification by preparative thick-layer chromatography on five silica gel plates (40 × 20 × 0.2 cm) in 8:1 chloroform–methanol. The main band was eluted and the substance crystallized from methanol (130 mL) to yield colorless crystals (0.91 g, 67%), m.p. 170–171°.

Anal. Calc. for $C_{42}H_{32}N_4O_5 \cdot 0.5\ H_2O$ (681.7): C, 73.99; H, 4.88; N, 8.22. Found: C, 73.90; H, 4.94; N, 8.00.

(*b*). Compound **27** (0.65 g, 0.1 mmol) was heated in an oil bath to 210° for 10 min, whereby the substance melted with gas evolution. The material was dissolved in little chloroform and purified as described under (*a*) to give, on crystallization, colorless crystals (0.456 g, 75%), m.p. 170–171°.

2,2'-Anhydro-3-β-D-arabinofuranosyllumazine (**32**). — Compound **29** (1.56 g, 3 mmol) in 4:1 acetic acid–water (50 mL) was heated under reflux for 15 min. The solution was evaporated, and the residue treated with hot hexane and chloroform, and then crystallized from 2:1 ethanol–water (130 mL) to yield colorless crystals (0.536 g, 65%), m.p. 295° (dec.).

Anal. Calc. for $C_{11}H_{10}N_4O_5$ (278.2): C, 47.49; H, 3.62; N, 20.14. Found: C, 47.52; H, 3.50; N, 20.40.

2,2'-Anhydro-3-β-D-arabinofuranosyl-6,7-dimethyllumazine (**33**). — Compound **30** (0.274 g, 0.5 mmol) in 4:1 acetic acid–water (30 mL) was heated under reflux for 20 min. The solution was evaporated, and the residue extracted twice with hot ether and then crystallized from 1:1 ethanol–chloroform (30 mL) to yield colorless crystals (0.141 g, 91%), m.p. 285°.

Anal. Calc. for $C_{13}H_{14}N_4O_5 \cdot 0.5\ H_2O$ (315.3): C, 49.52; H, 4.79; N, 17.77. Found: C, 49.67; H, 4.75; N, 17.64.

2,2'-Anhydro-3-β-D-arabinofuranosyl-6,7-diphenyllumazine (**34**). — (*a*) *From* **17**. A mixture of **17** (0.9 g, 2 mmol), diphenyl carbonate (0.47 g, 2.2 mmol), and $NaHCO_3$ (10 mg) in abs. *N,N*-dimethylformamide (5 mL) was heated for 15 min in an oil-bath to 160°. After being cooled, the brown solution was treated with ether (50 mL) to form a precipitate. Crystallization from methanol (100 mL) yielded a crude material that was further purified by preparative thick-layer chromatography on three silica gel plates (40 × 20 × 0.2 cm) in 6:1 chloroform–methanol to give many bands. The second from the bottom was eluted and evaporation yielded, after crystallization from methanol (80 mL), colorless crystals (0.28 g, 31%), m.p. 274–275°.

Anal. Calc. for $C_{23}H_{18}N_4O_5$ (430.4): C, 64.18; H, 4.21; N, 13.03. Found: C, 64.04; H, 4.23; N, 13.00.

(*b*) *From* **28**. A mixture of **28** (0.3 g, 0.63 mmol) and $NaHCO_3$ (3 mg) in abs. *N,N*-dimethylformamide (2 mL) was heated under reflux for 30 min. *N,N*-Dimethylformamide was distilled off *in vacuo*, the residual solvent coevaporated several times with toluene, and the residue purified by preparative thick-layer chromatography on two silica gel plates (40 × 20 × 0.2 cm) in 5:1 chloroform–methanol. The main band yielded, on crystallization from methanol (70 mL), colorless crystals (0.221 g, 81%), m.p. 274–275°.

(*c*) *From* **35**. Compound **35** (80 mg, 0.115 mmol) was stirred in methanolic ammonia (5 mL) for 1.5 h at room temp. Evaporation to dryness and preparative thick-layer chromatography in 5:1 chloroform–methanol yielded from the main band colorless material (30 g, 45%), m.p. 275°.

(*d*) *From* **31**. Compound **31** (0.2 g, 0.3 mmol) was heated under reflux in 4:1 acetic acid–water for 15 min. Dilution with water (15 mL) gave a colorless precipitate that was purified by chromatography on a preparative silica gel plate (40 × 20 × 0.2 cm) in 5:1 chloroform–methanol. The main band was eluted and yielded, on crystallization from methanol (15 mL), colorless crystals (91 mg, 71%), m.p. 275°.

*2,2'-Anhydro-3-(3,5-di-*O*-acetyl-β-*D*-arabinofuranosyl)-6,7-diphenyllumazine* (**35**). — A solution of acetic anhydride (0.64 g, 6 mmol) in abs. acetonitrile (6 mL) was added dropwise within 10 min to a boiling solution of **17** (0.9 g, 2 mmol) and BF_3-etherate (0.8 mL) in abs. acetonitrile (10 mL). After being boiled under reflux for another 5 min, the solution was evaporated and the residue dissolved in chloroform and fractionated by preparative thick-layer chromatography on seven silica gel plates (40 × 20 × 0.2 cm) in 11:1 chloroform–methanol. Elution of the main band and crystallization from ethanol (30 mL) gave colorless needles (0.452 g, 44%), m.p. 152°.

Anal. Calc. for $C_{27}H_{22}N_4O_7$ (514.5): C, 63.03; H, 4.31; N, 10.89. Found: C, 63.01; H, 4.36; N, 10.79.

From the other strong band could be isolated 6,7-diphenyl-3-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)lumazine (**14**, 0.13 g, 11%).

(*b*). Compound **35** was obtained as a by-product in 15% yield on treatment of **17** with 2-acetoxybenzoyl chloride in acetonitrile, as described in the following procedure.

*3-(3-*O*-Acetyl-β-*D*-arabinofuranosyl)-2,2'-anhydro-6,7-diphenyllumazine* (**36**). — A mixture of **17** (0.9 g, 2 mmol) and 2-acetoxybenzoyl chloride (1.6 g, 7.4 mmol) in abs. acetonitrile (3 mL) was heated for 5 min to 40°. The solution was evaporated, the residue dissolved in 10:1 chloroform–methanol (10 mL), and the solution chromatographed on a silica gel column (10 × 3 cm) with chloroform (1 L). The first four fractions (100 mL each) contained the reagents and by-products, and the fluorescing material was eluted much later. The second part of the eluate (0.6 L) was evaporated, and the residue further fractionated by preparative thick-layer chromatography on seven silica gel plates (40 × 20 × 0.2 cm) in 6:1 chloroform–methanol. The residue of the eluted main band gave, on recrystallization from ethanol (170 mL), colorless crystals 0.33 g (35%), m.p. 266°.

Anal. Calc. for $C_{25}H_{20}N_4O_6$ (472.5): C, 63.55; H, 4.27; N, 11.86. Found: C, 63.60; H, 4.25; N, 12.03.

The faster-moving band gave colorless material (0.16 g, 15%) that was identified as **35** by comparison with an authentic sample.

*2,2'-Anhydro-3-(3,5-di-*O*-mesyl-β-*D*-arabinofuranosyl)-6,7-diphenyllumazine* (**37**). — (*a*) *From* **21**. A mixture of **21** (0.682 g, 1 mmol) and $NaHCO_3$ (5 mg) was heated under reflux in absol. *N,N*-dimethylformamide (5 mL) for 10 min. The solution was evaporated to dryness *in vacuo* and the residue dissolved in chloroform for chromatography on three preparative silica gel plates (40 × 20 × 0.2 cm) in 8:1 chloroform–methanol. The main band was eluted and yielded, on crystallization from methanol–water, colorless crystals (0.432 g, 73%), m.p. 152–154°.

Anal. Calc. for $C_{25}H_{22}N_4O_9S_2$ (586.6): C, 51.19; H, 3.78; N, 9.55; S, 10.93. Found: C, 51.19; H, 3.91; N, 9.32; S, 10.69.

From the slower moving band were isolated colorless crystals (72 mg, 14%), which were identified by u.v. and ^{1}H-n.m.r. spectroscopy as 2,2'-anhydro-3-(5-*O*-mesyl-β-D-arabinofuranosyl)-6,7-diphenyllumazine (**38**).

(*b*) *From* **33**. Compound **33** (70 mg, 0.163 mmol) was treated with methanesulfonylchloride (0.1 mL) in abs. pyridine (15 mL) for 1.5 h at room temp. The solution was evaporated, the residue dissolved in chloroform (100 mL), and the solution washed twice with water (20 mL). The organic layer was dried ($MgSO_4$), and evaporated to a small volume for separation on a preparative silica gel plate (40 × 20 × 0.2 cm) in 8:1 chloroform–methanol. From the main band was obtained **37** (68 mg, 71%).

*3-β-*D*-Arabinofuranosyl-6,7-diphenyllumazine* (**39**). — (*a*). *From* **34**. To a solution of **34** (0.43 g, 1 mmol) in hot ethanol (100 mL) was added 40mM NaOH (40 mL). After being stirred for 30 min, the solution was made neutral with acetic acid and evaporated to dryness. The residue was purified by chromatography on a silica gel column (15 × 3 cm) in 19:1 chloroform–methanol. The main fraction yielded pure material (0.341 g, 79%). Crystallization from ethanol–water gave colorless crystals, m.p. 199–200°.

(*b*) *From* **40**. A solution of **40** (0.2 g, 0.29 mmol) in 4:1 acetic acid–water was heated under reflux (50 mL) for 20 min, and then evaporated to dryness. The residue was purified by chromatography on a preparative silica gel plate (40 × 20 × 0.2 cm) in 9:1 chloroform–methanol. On crystallization from ethanol–water the main band yielded colorless crystals (97 mg, 75%), m.p. 199–200°.

Anal. Calc. for $C_{23}H_{20}N_4O_6 \cdot 0.5\ H_2O$ (457.4): C, 60.39; H, 4.62; N, 12.22. Found: C, 60.38; H, 4.56; N, 12.29.

*6,7-Diphenyl-3-(5-*O*-trityl-β-*D*-arabinofuranosyl)lumazine* (**40**). — Compound **31** (1.345 g, 2 mmol) was dissolved in ethanol (60 mL), 25mM sodium hydroxide (60 mL) added, and the solution boiled under reflux for 2 h. After neutralization with acetic acid, the solution was evaporated to dryness, and the residue dissolved again in little 19:1 chloroform–methanol and purified by chromatography on a silica gel column (10 × 3 cm) with the same solvent mixture (1.3 L). The main

fraction was collected and evaporated, and the residue again chromatographed on a silica gel column (15 × 3 cm) with 49:1 chloroform–methanol to afford a chromatographically pure, main fraction. Crystallization from 3:1 ethanol–water (80 mL) yielded colorless crystals (0.21 g, 15%), m.p. 179–183°.

Anal. Calc. for $C_{42}H_{34}N_4O_6$ (690.8): C, 73.03; H, 4.96; N, 8.11. Found: C, 73.23; H, 4.92; N, 8.01.

2-Methoxy-4-oxo-6,7-diphenyldihydropteridine (**42**). — 4-Amino-2-methoxy-5-nitroso-uracil (1.0 g, 5.8 mmol) was reduced catalytically in 100 mL of water with Raney–nickel (0.2 g) in a shaking apparatus at room temperature. The reaction solution was then acidified with glacial acetic acid (5 mL), filtered from the catalyst and concentrated to a smaller volume (30 mL). Ethanol (50 mL) and benzil (1.5 g) were added and the mixture refluxed for 45 min. The solution was reduced to half its volume, and, after cooling, the precipitate collected. The material was treated several times with acetone, to remove excess benzil. The residue was crystallized from ethanol (150 mL) to give colorless crystals (0.6 g, 31%), m.p. 220°.

Anal. Calc for $C_{19}H_{14}N_4O_2$ (330.3): C, 69.08; H, 4.27; N, 16.96. Found: C, 69.12; H, 4.28; N, 17.10.

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