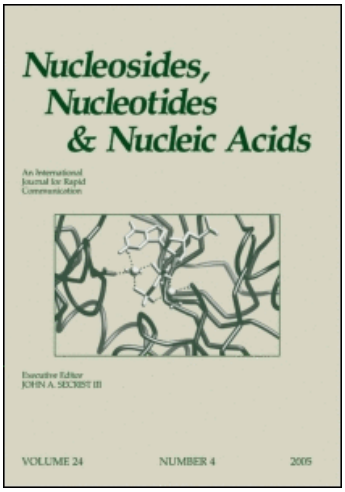

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Nucleosides. LIV[1] Synthesis and Properties of 3'-Azido- and 2',3'-Dideoxy-6,7-diphenyllumazine Nucleosides

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NUCLEOSIDES. LIV[1]
SYNTHESIS AND PROPERTIES OF 3'-AZIDO- AND 2',3'-DIDEOXY-6,7-DIPHENYLLUMAZINE NUCLEOSIDES

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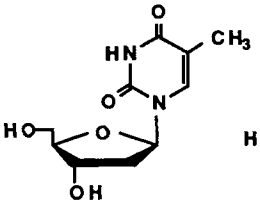
Abstract. The best approach for the synthesis of1-(3-azido-2,3-dideoxy-β-D-erythro-pentofuranosyl)lumazine (**5**) and its 6,7-dimethyl- (**4**) and 6,7-diphenyl derivatives (**3**) has been found in the interconversion of the corresponding 1-(2-deoxy-β-D-threo-pentofuranosyl)-lumazines. Monomethoxytritylation at the 5'-position (**1 7, 3 4, 4 9**) followed by mesylation at the 3'-OH group and subsequent nucleophilic displacement by lithium azide afforded **1 9, 2 9** and **4 7** which were deprotected by acid treatment to give **3**-**5** in good yields. The syntheses of 1-(2,3-dideoxy-β-D-glycero-pentofuranosyl)- 6,7-diphenyllumazine (**6**) and its 6,7-dimethyl derivative (**7**) were achieved from 1-(2-deoxy- β-D-erythro-pentofuranosyl)- 6,7-diphenyllumazine and the corresponding 6,7-dimethyllumazine (**2 6**) via their 5'-O-p-toluoyl- (**2 0, 3 0**), and 3'-deoxy-3'-iodo derivatives (**2 4, 3 1**) to form, after radical dehalogenation and final deprotection, **6** and **7**. The newly synthesized lumazine nucleosides have been characterized by elemental analyses, UV- and NMR spectra.

The rapid spread of AIDS has led to massive efforts to cure this disease. A number of nucleoside analogues has been found to show potent antiretroviral activity in vitro and some of these compounds, such as 3'-azido-3'-deoxythymidine (AZT) (**1**) and 2',3'-dideoxycytidine (**2**) have shown clinical benefit in AIDS patients[2,3].

In memory of Roland K. Robins and in admiration of his most valuable contributions to nucleoside, nucleotide and nucleic acid chemistry.



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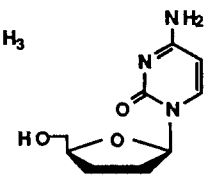

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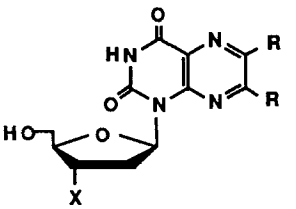
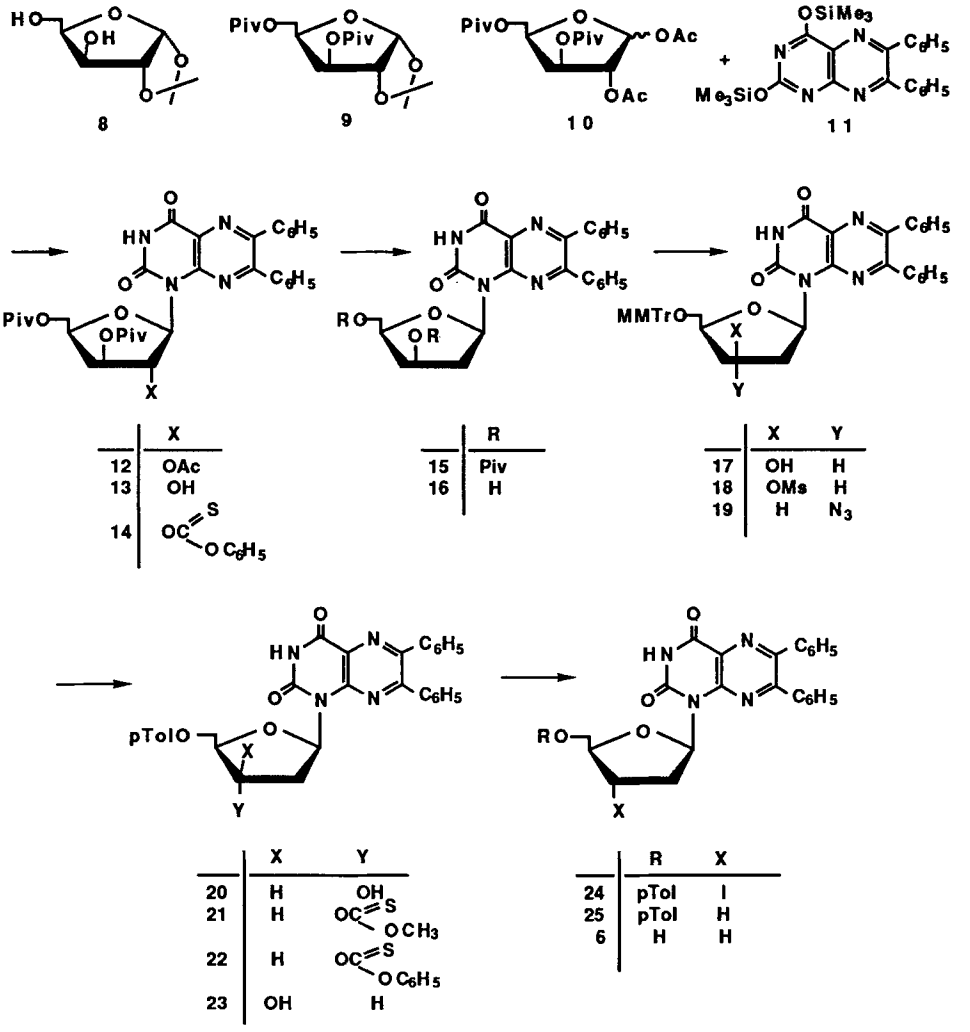


	R	X
3	C_6H_5	N_3
4	CH_3	N_3
5	H	N_3
6	C_6H_5	H
7	CH_3	H

Since lumazine nucleosides possess similar structural features as the thymidine derivative potential antiviral activity was also assumed for the 3'-azido (**3 - 5**) as well as the 2',3'-dideoxynucleoside derivatives (**6**,**7**) of this series. In order to investigate such biological activities firstly 3'-azido- (**3**) as well as 1-(2,3-dideoxy-ß-D-ribofuranosyl)-6,7-diphenyllumazine (**6**) have been synthesized.

The sugar component for the glycosylation reactions 1,2-di-O-acetyl-3,5-di-O-pivaloyl-D-xylofuranose (**1 0**) was prepared by an alternative and effective approach to the method of Horwitz et al.[4] starting from 1,2-O-isopropylidene-α–D-xylofuranose (**8**) via its 3,5-di-O-pivaloyl derivative **9** to give **1 0** in good yield[5]. Silylated 6,7-diphenyllumazine (**11**)[6] was then glycosylated with **1 0** using $BF_3.OEt_2$ in ethyl acetate[7] to yield, after silica gel chromatography, **1 2** in 72 % yield. The 2'-O-acetyl group was selectively removed by treatment with pyridine /acetic acid (4:1)[8] to give 80 % of 6,7-diphenyl-1-(3,5-di-O-pivaloyl-ß-D-xylofuranosyl)lumazine (**1 3**). Treatment of **1 3** with phenoxythiocarbonyl chloride in CH_3CN in presence of 4-dimethylaminopyridine (DMAP) afforded in 92 % the 3'-O-phenoxythiocarbonyl derivative **1 4**. Its reduction with n-Bu_3SnH[9] yielded 72 % of 1-(2-deoxy-3,5-di-O-pivaloyl-ß-D-threo-pentofuranosyl)- 6,7-diphenyllumazine (**1 5**), from which the pivaloyl groups were cleaved by sodium methoxide to give **1 6**. The monomethoxytrityl group was then introduced into the 5'-OH-position to form **1 7** in 69 % yield followed subsequently by 3'-OH mesylation to **1 8** in 84 % yield and nucleophilic displacement of this function by sodium azide[10] in DMF at 80°C overnight. Work-up and silica gel column chromatography afforded 64 % of **1 9** which on further deblocking by acid treatment using p-toluenesulfonic acid in dichloromethane / MeOH 4:1 gave the desired 1-(3-azido-2,3-dideoxy-ß-D-erythro-pentofuranosyl)-6,7-diphenyllumazine (**3**) in 74 % yield.

2',3'-Dideoxynucleosides are typically synthesized from 2'-deoxynucleosides via Barton-type deoxygenation reactions, or from intact nucleosides by

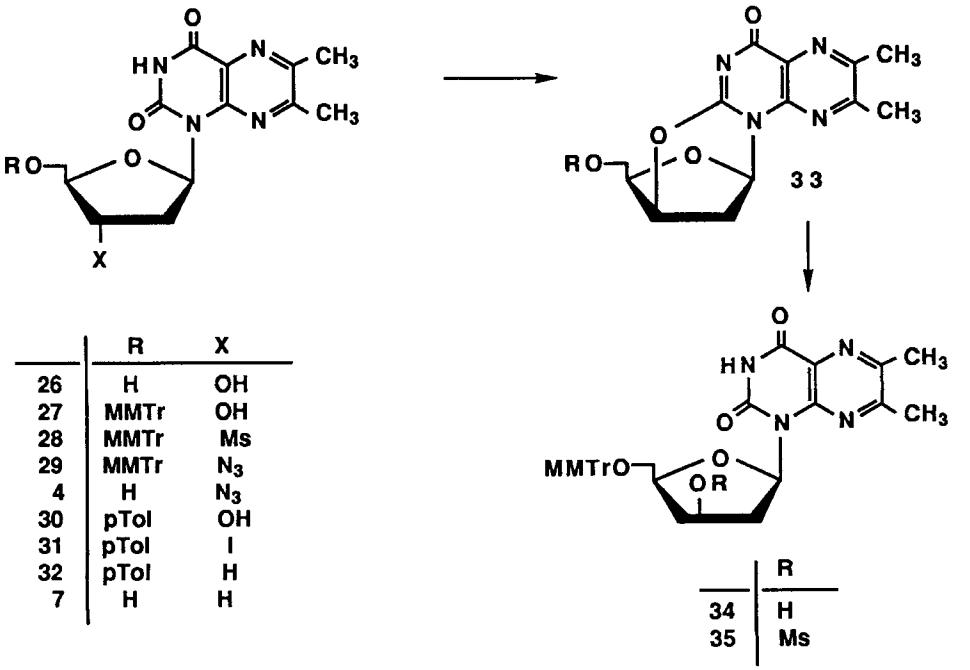


multistep routes involving deoxygenation reactions to 2',3'-unsaturated dideoxynucleosides[11], which are then hydrogenated. The synthesis of 1-(2,3-dideoxy-ß-D-glycero-pentofuranosyl)-6,7-diphenyllumazine (**6**) was tried first from 1-(2-deoxy-ß-D-erythro-pentofuranosyl)-6,7-diphenyllumazine[6,12], which could selectively be toluoylated at the 5'-OH group to give in the first step1-(2-deoxy-5'-O-p-toluoyl-ß-D-erythro-pentofuranosyl)-6,7-diphenyllumazine (**20**). All attempts to convert the 3'- thiocarbonates **21** and **22**, respectively, by n-Bn_3SnH reduction into **25** were not successful. Finally **23**, prepared from **16** by selective toluoylation, gave the 3'-iodide **24** when reacted with methyltriphenoxyphosphonium iodide in DMF[13]. Its reductive dehalogenation with n-Bu_3SnH in

toluene using azodiisobutyronitrile (AIBN) as a catalyst afforded the protected 2',3'-dideoxy nucleoside **25** in 77 % yield and the final deacylation by 0.01 N NaOMe at room temperature for 15 h resulted in 88 % yield of 1-(2,3-dideoxy-β-D-glycero-pentofuranosyl)-6,7-diphenyllumazine (**6**).

The syntheses of 3'-azido- (**4**) and1-(2,3-dideoxy-β-D-glyceropento-furanosyl)-6.7-dimethyllumazine (**7**) were performed starting from 1-(2-deoxy-β-D-erythro-pentofuranosyl)-6,7-dimethyllumazine (**26**)[6,12]. The 5'-O-monomethoxytrityl derivative **27**[14] was first converted into 1-(2-deoxy- 5-O-monomethoxytrityl-3-O-mesyl-β-D-erythro-pentofuranosyl)-6,7-dimethyl-lumazine (**28**) which on treatment with DBU gave 2,3'-anhydro-1-(2-deoxy-5-O-monomethoxytrityl-β-D-threo-pentofuranosyl)-6,7-dimethyllumazine (**33**). Base hydrolysis opened the anhydro ring to afford **34**, subsequent mesylation gave **35** which reacted with lithium azide in DMF to give **29** in 77% yield. Acid deprotection of **29** finally furnished 1-(3-azido-2,3-dideoxy-β-D-erythro-pentofuranosyl)- 6,7-dimethyllumazine (**5**).

In another series of reactions compound **26** was firstly selectively acylated at the 5'-position to 1-(2-deoxy-5-O-toluoyl-1-β-D-erythro-pentofuranosyl)-

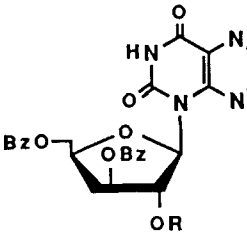


	R	X
26	H	OH
27	MMTr	OH
28	MMTr	Ms
29	MMTr	N_3
4	H	N_3
30	pTol	OH
31	pTol	I
32	pTol	H
7	H	H

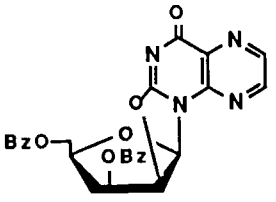
	R
34	H
35	Ms

6,7-dimethyllumazine (**30**), followed by displacement of the 3'-OH group by iodine using methyltriphenoxyphosphonium iodide[13] to **31**, dehalo-genation by n-Bu_3SnH in a radical chain reaction to **32** which provided 1-(2,3-dideoxy-β-D-glycero-pentofuranosyl)-6,7-dimethyllumazine (**7**) in good overall yield after deprotection.

The first attempt to synthesize1-(3-azido-2-deoxy-β-D-erythro-pentofuranosyl)-lumazine (**5**) was undertaken from 1-(2-O-acetyl-3,5-di-O-benzoyl-β-D-threo-pentofuranosyl)-lumazine (**36**) which resulted from a glycosylation reaction of lumazine with 1,2-O-diacetyl-3,5-di-O-benzoylxylofuranose[15] via the



	R
36	Ac
37	H
38	Ms



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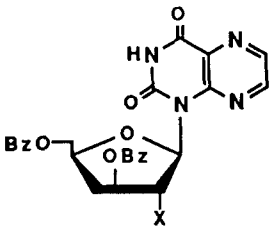
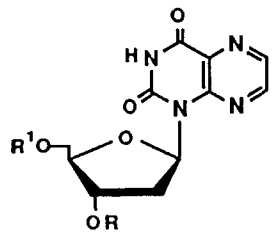
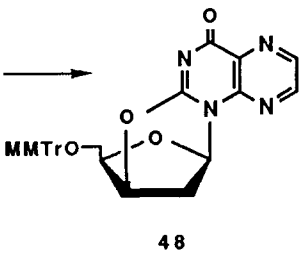


	X
40	Br
41	OC(=S)OCH$_3$
42	OC(=S)OC$_6$H$_5$
43	H





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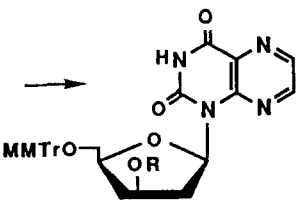

	R	R^1
44	pTol	pTol
45	MMTr	OH
46	MMTr	Ms
47	MMTr	N_3
5	H	N_3

	R
49	H
50	Ms

"silyl"-method in presence of trimethylsilyl triflate as catalyst. Selective deacetylation of **36** and led to **37** which was mesylated to **38** and finally cyclized by 1.8-diaza-bicyclo(5.4.0)-undec-7-ene (DBU) to 2.2'-anhydro-1-(3.5-di-O-benzoyl-ß-D-lyxofuranosyl)-lumazine (**39**). Treatment of **39** with 8% HBr in DMF afforded 1-(2-bromo-3,5-di-O-benzoyl-ß-D-xylofuranosyl)-lumazine (**40**) which turned out to be relatively unstable in cyclizing back to the 2,2'-anhydronucleoside **39**. This instability seems to be also responsible for the fact that all attempts to reduce **40** to **43** failed by forming more easily **39** under the applied reaction conditions. Finally we converted **37** into the corresponding 2'-O-methoxythiocarbonyl- (**41**) and 2'-O-phenoxy-thiocarbonyl derivative (**42**), respectively, in order to perform the Barton reduction with azodiisobutyronitrile / n-Bu_3SnH to **43**. Only **42** could be transformed into **43** in 48% yield whereas the analogous reaction with **41** failed completely.

The low overall yield in the interconversion of **36** into **43** forced us to try the synthesis of **5** from 1-(2-deoxy-β-D-erythro-pentofuranosyl)-lumazine[6,12] for which, however, the glycosylation of lumazine to **44** had to be improved over the reported syntheses. Based upon the results of Freskos[16] we found that treatment of 2,4-bis-trimethylsiloxypteridine[6] by subsequent addition of 1 equivalent CuI and 3,5-di-O-p-toluoyl-2-deoxy-erythro-pentofuranosyl chloride led to a 79% yield of a 1-(2-deoxy-3,5-di-O-p-toluoyl-α,β-D-erythro-pentofuranosyl)-lumazine mixture in a 1 / 10 ratio from which **44** was obtained in 72%. Deacylation[6] and monomethoxytritylation[14] to **45** was achieved by known methods. In a sequence of reactions **45** was first mesylated to **46**, this compound then cyclized by DBU treatment to the 2,3'-anhydro nucleoside **48** which gave **49** after base hydrolysis, and subsequent mesylation afforded **50**. Nucleophilic displacement of the 3'-mesyl group by lithium azide in DMF resulted in a 75% yield of **47** which led on detritylation by p-toluenesulfonic acid in CH_2Cl_2 / MeOH to 1-(3-azido-2-deoxy-β-D-erythro-pentofuranosyl)-lumazine (**5**).

Physical Properties

The newly synthesized compounds were characterized by elemental analyses, UV and ^{1}H-NMR spectra. The azido group was detected by IR spec-

troscopy. The UV data and the R_f-values in various chromatographical systems taken from precoated silica-gel thin layer sheets are listed in table 1.
It can be seen from the UV data that structurally related compounds show in general very similar spectra what the UV maxima and the extinction coefficients are concerned. Formation of an anhydro-nucleoside structure (**3 3,3 9**) is reflected in a small hypsochromic shift of the longest transition.

The ^{1}H-NMR data are reported in the experimental part and do not show any peculiarities in comparison to the common types of nucleosides. It should be mentioned that the N-1-(2-deoxy-β-D-erythro-pentofuranosyl)-lumazines show in $CDCl_3$ a large chemical shift difference between the H-2'α and the H-2'β signals characteristic for the β-anomer whereas the same protons resonate in the α-anomer more closely or even coincide with each other.

Experimental Section

General. - TLC: Precoated silica-gel thin layer sheets F 1500 LS 254 from Schleicher & Schüll. - Prep. TLC: Silica-gel 60 PF_{254} (Merck). - Prep. column chromatography: Silica-gel (Merck 60, 0.063-0.2 mesh). - M.p.: Büchi apparatus, model Dr. Tottoli; no corrections. - UV/VIS: Uvikon 820, Kontron and Perkin Elmer, Lambda 5; λ_{max} in nm (log ε). - ^{1}H-NMR: Bruker WM-250; in δ (ppm) relative to TMS. - IR: Polaris™, Mattson FTIR in cm $^{-1}$.

1-(3-Azido-2,3-dideoxy-ß-D-erythro-pentofuranosyl)-6,7-diphenyllumazine (3). A solution of **1 9** (0.54 g, 0.74 mmole) in 25 ml of 2 % p-toluenesulfonic acid in CH_2Cl_2/MeOH- (4:1) was stirred at 0°C for 20 min and neutralized with saturated sodium bicarbonate. The aqueous solution was dried over sodium sulfate.Yield: 0.26 g (77 %) , m.p.: 152-155°C. IR (KBr): 2103 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 9.31 (s, 1H, NH); 7.29-7.52 (m, 11H, H-C(1') and Ar-H); 4.89 (t, 1H, 5'-OH); 4.70 (q, 1H, H-C(3')); 3.76-4.03 (m, 3H, H-C(4') and H-C(5')); 2.36-3.19 (m, 2H, H-C(2')).

Anal. calc. for $C_{23}H_{19}N_7O_4$. 1/2 H_2O (466.5): C, 59.71; H, 4.32; N, 21.00. Found: C, 59.85, H, 4.44; N, 21.12.

TABLE 1 - Physical Data of 6,7-Diphenyllumazine Nucleosides

Compound	UV-Absorption Spectra in MeOH λ_{max} (nm)			log ε			R_f
3	223	274	359	4.45	4.26	4.16	0.15[a]
6	231	273	359	4.35	4.17	4.11	0.17[a]
12	222	272	358	4.46	4.44	4.36	0.51[a]
13	225	272	359	4.67	4.59	4.36	0.38[a]
14	225	275	359	4.45	4.18	4.13	0.53[d]
15	225	275	359	4.46	4.25	4.14	0.38[d]
16	225	274	358	4.25	4.05	4.00	0.15[b]
17	227	274	358	4.58	4.23	4.12	0.48[b]
18	227	274	358	4.57	4.20	4.13	0.34[a]
19	223	273	358	4.70	4.42	4.24	0.67[a]
23	231	273	358	4.47	4.08	4.04	0.21[c]
24	231	273	359	4.49	4.16	4.08	0.51[c]
25	231	273	359	4.50	4.17	4.09	0.44[a]
4	229		323	4.10		3.98	0.32[b]
7	236		324	4.30		3.81	0.34[b]
28	230		323	4.25		3.79	0.53[b]

1-(3-Azido-2,3-dideoxy-ß-D-erythro-pentofuranosyl)-6,7-dimethyllumazine (4). Detritylation of **29** (0.83 g, 1.37 mmole) was achieved at 0°C with a 1% solution of p-toluenesulfonic acid in CH_2Cl_2/MeOH (4:1) (25 ml) and stirring for 20 min. The solution was diluted with H_2O (2 ml) and then neutralized with sodium bicarbonate. It was extracted several times with $CHCl_3$, the organic layer dried over sodium sulfate and after concentration to a smaller volume purified by column chromatography (3,5 x 7 cm) on silica gel with $CHCl_3$/MeOH (98:2). The main fraction gave an amorphous solid on evapora-tion. Yield: 0.36 g (75 %), m.p. 97-99°C. IR(KBr): 2103 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 9.30 (bs, 1H, NH); 7.24 (dd, 1H, H-C(1')); 4.72 (m, 1H, H-C(3')); 3.82-

TABLE 1 - Continued

Compound	UV-Absorption Spectra in MeOH λ_{max} (nm)			log ε			R_f
29	231		324	4.33		3.80	0.54[b]
30	236		323	4.48		3.89	0.31[b]
31	236		323	4.48		3.89	0.42[b]
32	236		324	4.28		3.82	0.35[a]
33	231	313	[327]	4.34	3.95	[3.76]	0.27[b]
34	[227]	278	328	[4.40]	3.53	3.93	0.36[b]
35	230		322	4.32		3.88	0.41[b]
5	231		314	4.18		3.84	0.32[b]
36	230		315	4.51		3.78	0.33[e]
37	230		316	4.54		3.81	0.10[e]
38	230		312	4.61		3.87	0.51[b]
39	229		311	4.85		4.18	0.22[b]
40	229		312	4.66		3.86	0.50[b]
41	230		316	4.63		3.81	0.51[e]
42	229		314	4.61		3.75	0.43[a]
43	230		315	4.62		3.86	0.28[a]
44	238		315	4.61		3.79	0.68[b]
46	231		314	4.59		3.98	0.46[b]
47	231		316	4.37		3.77	0.59[b]
48	231	[260[	314	4.34	[3.63]	3.80	0.36[b]
49	231	279	315	4.40	3.46	3.78	0.43[b]
50	230		314	4.57		3.97	0.48[b]

a: $CHCl_3$/Acetone (9:1); b: $CHCl_3$/MeOH (95:5); c: $CHCl_3$/THF (14:1);
d: n-Hexane/Et_2O (1:2); e: Toluene/AcOEt (1:2).

3.99 (m, 3H, H-C(4'), H-C(5')); 3.80 (bs, 1H, H-O(5')); 3.07 (m, 1H, H-C(2'ß)); 2.68 (s, 6H, 6,7 CH_3); 2.38 (m, 1H, H-C(2'α)).

Anal. calc. for $C_{13}H_{15}N_7O_4$ (342.5): C, 45.59; H, 4.71; N, 28.62. Found: C, 45.83; H, 4.66; N, 28.21.

1-(3-Azido-2,3-dideoxy-ß-D-erythro-pentofuranosyl)-lumazine (5). Detritylation of **47** (0.91 g, 1.58 mmole) was achieved in a 1% solution of p-TsOH in CH_2Cl_2/MeOH (4:1) at 0°C with stirring. After 2 h H_2O (2 ml) was added dropwise and then neutralized by a saturated solution of sodium bicarbonate. The reaction solution was extracted several times with $CHCl_3$, the organic phase dried over sodium sulfate, concentrated to a small volume and then purified by column chromatography (3 x 7 cm) on silica gel with $CHCl_3$/MeOH (98:2). An amorphous solid was obtained on evaporation. Yield: 0.37 g (76 %), m.p. 88-91°C. IR(KBr): 2103 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 9.76 (bs, 1H, NH); 8.68 (s, 2H, 6,7-H); 7.21 (dd, 1H, H-C(1')); 4.71 (m, 1H, H-C(3')); 3.83-4.05 (m, 3H, H-C(4'), H-C(5')); 3.37 (bs, 1H, 5'-OH); 3.08 (m, 1H, H-C(2'ß)); 2.38 (m, 1H, H-C(2'α)).

Anal. calc. for $C_{11}H_{11}N_7O_4$. 1/2 H_2O (314.3): C, 42.04; H, 3.85; N, 31.19. Found: C, 42.43; H, 3.78; N, 30.96.

1-(2,3-Dideoxy-ß-D-glycero-pentofuranosyl)-6,7-diphenyl-lumazine (6). In 0.01 N sodium methoxide (20 ml) was suspended **27** (0.30 g (0.56 mmole) which dissolved gradually at room temperature. After 15 h H_2O (10 ml) was added and the mixture was neutralized with saturated sodium bicarbonate. On evaporation the product **6** crystallized and was washed after filtration with cold water and n-pentane and dried. Yield: 0.19 g (82 %), m.p.: 165-166°C. ^{1}H-NMR ($CDCl_3$): 9.76 (s, 1H, NH); 7.19-7.50 (m, 11H, Ar-H and H-C(1')); 4.25-4.29 (q, 1H, H-C(4')); 3.66-3.94 (ddd, 2H, H-C(5')); 3.38 (t, 1H, 5'-OH); 2.02-2.78 (m, 4H, H-C(2') and H-C(3')).

Anal. calc. for $C_{23}H_{20}N_4O_4$ (416.4): C, 66.34; H, 4.84; N, 13.45. Found: C, 66.07; H, 4.85; N, 13.21.

1-(2,3-Dideoxy-ß-D-glycero-pentofuranosyl)-6,7-dimethyl-lumazine (7). A suspension of **3 2** (0.33 g, 0.75 mmole) in 0.01 N sodium methoxide in MeOH (20 ml) was stirred at room temperature for 2 h to give a

clear solution. After addition of H_2O (10 ml) and neutralization by dilute acetic acid to pH 7 was evaporated to dryness. The residue was purified by column chromatography (3 x 7 cm) on silica gel with $CHCl_3$/MeOH (98:2). The main fraction was evaporated to give a colourless solid. Yield: 0.20 g (90 %), m.p. 107-109°C. ^{1}H-NMR (DMSO-d_6): 11.78 (s, 1H, NH); 6.80 (dd, 1H, H-C(1')); 3.96 (dd, 1H, H-C(4')); 3.51 (d, 2H, H-C(5')); 2.56 (s, 6H, 6,7-CH_3); 2.17-2.26 (m, 4H, H-C(2'α), H-C(2'ß), H-C(3'α), H-C(3'ß)).

Anal. calc. for $C_{13}H_{16}N_4O_4 \cdot 1/2\ H_2O$ (301.3): C, 51.82; H, 5.69; N, 18.59. Found: C, 51.39; H, 5.38; N, 18.22.

1,2-O-Isopropylidene-3,5-di-O-pivaloyl-α-D-xylofuranose (9). A solution of 1,2-O-isopropylidene-α-D-xylofuranose (**8**) (18.8 g, 0.1 mole) in dry pyridine (100 ml) was cooled in an ice-bath. Pivaloyl chloride (25.2 ml, 0.2 mole) was then added dropwise with stirring. The mixture was allowed to stand at room temperature protected from moisture for 5 h, then MeOH (5 ml) was added slowly into the solution and after 10 min. the solution was concentrated to dryness. The oil was extracted with $CHCl_3$ (50 ml) and H_2O (30 ml). The organic phase was dried over sodium sulfate and evaporated to dryness to give a colorless solid. Yield: 31.2 g (87 %). ^{1}H-NMR ($CDCl_3$): 5.94 (d, 1H, H-C(1)); 5.26 (d, 1H, H-C(2)); 4.55 (m, 1H, H-C(4)); 4.46 (d, 1H, H-C(3)); 4.22 (m, 2H, H-C(5)); 1.34-1.56 (2s, 6H, isopropyl); 1.18-1.23 (2s, 18H, 2 x pivaloyl).

Anal. calc. for $C_{18}H_{30}O_7$ (358.4): C, 60.32; H, 8.44. Found: C, 60.13; H, 8.39.

1,2-Di-O-acetyl-3,5-di-O-pivaloyl-D-xylofuranose (10). In 75% formic acid (300 ml) 1,2-O-isopropylidene-3,5-di-O-pivaloyl-α-D-xylofuranose (**9**) (17.9 g, 50 mmole) was heated to 50°C for 2 h. It was evaporated to dryness, coevaporated with n-butanol (2 x 50 ml) followed by toluene (2 x 50 ml) and dry pyridine (20 ml). Treatment with acetic anhydride (40 ml) in dry pyridine (100 ml) for 2 h afforded acetylation. The reaction mixture was evaporated to a smaller volume, then poured into ice water and extracted with $CHCl_3$ (3x 50 ml). The organic phase was washed with H_2O, dried over sodium sulfate and evaporated after filtration to give a solid. Yield: 14.5 g (95 %). ^{1}H-NMR ($CDCl_3$): 6.14-6.43 (2d, 1H, Hα-C(1) and Hß-C(1)); 5.36-5.57 (m, 2H, H-C(2) and H-C(3));

4.68 (m, 1H, H-C(4)); 4.02-4.31 (m, 2H, H-C(5)); 2.15 (2s, 6H, 2 x COMe); 1.18-1.24 (2s, 18H, 2 x pivaloyl).

Anal. calc. for $C_{19}H_{30}O_9$ (402.4): C, 56.71; H, 7.51. Found: C, 56.58; H, 7.53.

1-(2-O-Acetyl-3,5-di-O-pivaloyl-ß-D-xylofuranosyl)-6,7-diphenyllumazine (12). A mixture of 6,7-diphenyllumazine (3.16 g ,10 mmole) and hexamethyldisilazane (100 ml) was refluxed overnight in the presence of a few crystals of ammonium sulfate. The clear solution was concentrated in va-cuum, the resulting syrup dissolved in ethyl acetate (150 ml) and then 1,2-di-O-acetyl-3,5-di-O-pivaloyl-D-xylofuranose (**10**) (4.02 g, 10 mmol) and $BF_3 . OEt_2$ (7 ml) added. The mixture was stirred at room temperature for 2 h and then neutralized with saturated sodium bicarbonate. The organic layer was washed with H_2O and dried over sodium sulfate. The crude product was purified by column chromatography (220 g of silica gel, eluted with $CHCl_3$) to give on evaporation of the main fraction a colorless solid. Yield: 4.73 g (72 %), m.p.: 130-132°C. ^{1}H-NMR ($CDCl_3$): 8.45 (s, 1H, NH); 7.30-7.47 (m, 10H, Ar-H); 6.82 (d, 1H, H-C(1')); 6.01 (t, 1H, H-C(2')); 5.47 (t, 1H, H-C(3')); 4.51 (t, 1H, H-C(4')); 4.37 (d, 2H, H-C(5')); 2.05 (s, 3H, -OAc); 1.12-1.27 (2s, 18H, 2 x pivaloyl).

Anal. calc. for $C_{35}H_{38}N_4O_9$ (658.7): C, 63.82; H, 5.81; N, 8.51. Found: C, 63.37; H, 5.71; N, 8.50.

1-(3,5-Di-O-pivaloyl-ß-D-xylofuranosyl)-6,7-diphenyllumazine (13). In a mixture of pyridine/acetic acid (4:1, 75 ml) 1-(2-O-acetyl-3,5-di-O-pivaloyl-ß-D-xylofuranosyl)-6,7-diphenyllumazine (**12**) (4.73 g, 7.4 mmole) was dissolved at room temperature and then hydrazine monohydrate(1.3 ml) added and stirred for 22 h. It was evaporated, extracted with $CHCl_3$ and wash-ed with H_2O. The organic layer was dried over sodium sulfate, then concen-trated to a small volume and put onto a short silica gel column for chromatogra-phy with $CHCl_3$/ MeOH (99:1)to give a solid on evaporation of the main frac-tion. Yield: 3.21 g (72 %), m.p.: 141-143°C. ^{1}H-NMR ($CDCl_3$): 8.84 (brs, 1H, NH); 7.28-7.52 (m, 10H, Ar-H); 6.91 (d, 1H, H-C(1')); 5.25 (d, 1H, H-C(2')); 5.08 (t, 1H, H-C(3'));

4.39-4.58 (m, 3H, H-C(4') and H-C(5')); 3.46 (s, 1H, 2'-OH); 1.18-1.24 (2s, 18H dipivaloyl).

Anal. calc. for $C_{33}H_{36}N_4O_8 \cdot H_2O$ (634.7): C, 62.44; H, 6.03; N, 8.82. Found: C, 62.52; H, 5.88; N, 8.61.

1-(3,5-Di-O-pivaloyl-2-O-phenoxythiocarbonyl-ß-D-xylofuranosyl)-6,7-diphenyllumazine (14). To a solution of **13** (1.86 g, 3 mmole) in dry CH_3CN was added 4-N,N-dimethylaminopyridine (DMAP) (1.08 g, 15.7 mmole) and phenoxythiocarbonyl chloride (PTC-Cl) (0.54 g, 3.6 mmole). The mixture was stirred for 10 min. and then poured into ice-water (30 ml) . It was extracted with ethyl acetate (3 x 20 ml), dried over sodium sulfate and evaporated in vacuo. The residue was dissolved in $CHCl_3$ and chromatographed on silica gel with $CHCl_3$ to give a solid. Yield: 2.07 g (92 %), m.p.: 130-131°C. ^{1}H-NMR ($CDCl_3$): 8.50 (s, 1H, NH); 7.18-7.54 (m, 15H, Ar-H); 7.05 (d, 1H, H-C(1')); 6.56 (d, 1H, H-C(2')); 5.65 (t, 1H, H-3'); 4.61 (t, 1H, H-C(4')); 4.41 (d, 2H, H-C(5')); 1.19-1.31 (2s, 18H, dipivaloyl).

Anal. calc. for $C_{40}H_{40}N_4O_9$ (752.8): C, 63.82; H, 5.30; N, 7.44. Found: C, 63.39; H, 5.30; N, 7.44.

1-(2-Deoxy-3,5-di-O-pivaloyl-ß-D-threo-pentofuranosyl)-6,7-diphenyllumazine (15). To a solution of **14** (1.85 g, 3 mmole) in toluene (60 ml) was added under nitrogen atmosphere azodiisobutyronitrile (AIBN) (2 g, 12 mmole) and n-Bu_3SnH (4.8 ml, 18 mmole). It was heated under reflux for 1.5 h and then evaporated. The residue was purified by silica gel column chromatography (4 x 15 cm) by elution with 1) 500 ml of n-hexane, 2) 700 ml of n-hexane/diethylether (1:2) to give a solid. Yield: 1.31 g (73 %), m.p.: 139 - 142°C. ^{1}H-NMR ($CDCl_3$): 8.58 (s, 1H, NH); 7.30-7.50 (m, 10H, Ar-H); 7.12 (t, 1H, H-C(1')); 5.45 (m, 1H, H-C(3')); 4.26-4.44 (m, 3H, H-C(4') and H-C(5')); 2.71-3.04 (m, 2H, H-C(2')); 1.18-1.25 (2s, 18H, dipivaloyl).

Anal. calc. for $C_{35}H_{36}N_4O_7 \cdot 1/2\ H_2O$ (609.7): C, 65.01; H, 6.11; N, 9.19. Found: C, 64.70; H, 6.09; N, 9.29.

6,7-Diphenyl-1-(2-deoxy-ß-D-threo-pentofuranosyl)lumazine (16). A solution of **15** (1.31 g, 2.2 mmole) in 0.05 N sodium methoxide (100 ml) was stirred over night and then neutralized with 10% acetic acid. A solid

crystallized on evaporation and gave after filtration and washing with cold H_2O and diethylether yellowish crystals. Yield: 0.79 g (84 %), m.p.: 142-143°C. ^{1}H-NMR (DMSO-d_6): 12.21 (s, 1H, NH); 7.34-8.30 (m, 10H, Ar-H); 6.99 (dd, 1H, H-C(1')); 5.02 (d, 1H, 3'-OH); 4.61 (t, 1H, 5'-OH); 4.18 (brs, 1H, H-C(3')); 3.46-3.75 (m, 3H, H-C(4') and H-C(5')); 2.35-2.64 (m, 2H, H-C(2')).

Anal. calc. for $C_{23}H_{20}N_4O_5$ (450.4): C, 61.33; H, 4.92; N, 12.44. Found: C, 61.78; H, 4.89; N, 12.35.

1-(2-Deoxy-5-O-p-monomethoxytrityl-ß-D-threo-pentofuranosyl)-6,7-diphenyllumazine (17). To a solution of **16** (1.4 g, 3.2 mmole) in dry pyridine (15 ml) was added p-monomethoxytrityl chloride (1.2 g, 3.6 mmole) and stirred over night. The reaction mixture was poured into ice-water (25 ml), the solid collected, dissolved in $CHCl_3$, washed with H_2O and dried over sodium sulfate. The crude product was purified by a silica gel column chromatography (2 x 15 cm, $CHCl_3$/MeOH 98:2) to give a colorless solid. Yield: 1.5 g (69 %), m.p.: 161-162°C. ^{1}H-NMR ($CDCl_3$): 9.66 (s, 1H, NH); 6.77-7.57 (m, 25H, H-C(1') and Ar-H); 4.88 (d, 1H, 3'-OH); 4.31 (m, 1H, H-C(3')); 3.37 (s, 3H, -OMe); 3.54 (d, 2H, H-C(5')); 2.38-2.83 (m, 2H, H-C(2')).

Anal. calc. for $C_{43}H_{36}N_4O_6$. 1/2 H_2O (713.8): C, 72.35; H, 5.22; N, 7.85. Found: C, 72.39; H, 5.29; N, 7.80.

1-(2-Deoxy-3-O-mesyl-5-O-p-monomethoxytrityl-ß-D-threo-pentofuranosyl)-6,7-diphenyllumazine (18). To a cold solution (0°C) of **17** (1.4 g, 2 mmole) in dry pyridine (30 ml) was added slowly methanesulfonyl chloride (0.4 ml, 5.2 mmole) and then the reaction mixture stirred at room temperature for 2 h. The mixture was slowly poured into ice-water (50 ml). The solid was collected, washed well with H_2O and dried in a desiccator. Recrystallization from EtOH (20 ml) afforded colorless crystals. Yield: 1.1 g (84 %), m.p.: 152-156°C. ^{1}H-NMR ($CDCl_3$): 8.75 (s, 1H, NH); 6.77-7.50 (m, 24H, Ar-H); 6.99 (t, 1H, H-C(1')); 5,42 (m, 1H, H-C(3')); 4.26 (8q, 1H, H-C(4')); 3.76 (s, 3H, -OMe); 2.74-3.66 (m, 4H, H-C(2') and H-C(5')); 2.65 (s, 3H, -Me).

Anal. calc. for $C_{44}H_{38}N_4O_8S$. 1/2 H_2O (791.8): C, 66.74; H, 4.96; N, 7.07. Found: C, 66.39; H, 5.00; N, 7.02.

1-(3-Azido-2,3-dideoxy-5-O-p-monomethoxytrityl-ß-D-erthro-pentofuranosyl)-6,7-diphenyllumazine (19). A mixture of **18** (1.0 g, 1.27 mmole) and sodium azide (0.1 g) in DMF (15 ml) was heated to 80°C over night. The DMF was evaporated, the residue dissolved in $CHCl_3$ (30 ml), washed with H_2O and purified after drying over sodium sulfate by column chromatography (3 x 15 cm, $CHCl_3$) to give a colorless solid. Yield: 0.65 g (70 %), m.p.: 129-131°C. IR(KBr): 2103 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 8.82 (s, 1H, NH); 6.73-7.47 (m, 25H, H-C(1') and Ar-H); 4.68-4.71 (q, 1H, H-C(3')); 3.73-4.02 (m, 3H, H-C(4') and H-C(5')); 3.80 (s, 3H, -OMe); 2.36-3.15 (m, 2H, H-C(2')).

Anal. calc. for $C_{43}H_{35}N_7O_5$. 1/2 H_2O (738.8):C, 69.91; H, 4.91; N, 13.27. Found: C, 69.94; H, 4.84; N, 13.06.

1-(2-Deoxy-5-O-p-toluoyl-ß-D-threo-pentofuranosyl)-6,7-diphenyllumazine (23). A solution of p-toluoyl chloride (0.42 ml, 3 mmole) in 1,2-dichloroethane (5 ml) was added dropwise to a stirred solution of **16** (1.29 g, 3 mmole) in dry pyridine (40 ml) at -5°C. Stirring was continued for 30 min at 0°C. The reaction mixture was poured into ice-water (100 ml) and extracted with $CHCl_3$. The combined extracts were washed with saturated sodium bicarbonate and water, dried over sodium sulfate and evaporated to dryness. The crude product was purified through a silica gel column (3 x 15 cm, $CHCl_3$/MeOH (98:2), 400 ml) to give a colorless solid. Yield: 1.27 g (77 %). ^{1}H-NMR (DMSO-d_6): 12.21 (s, 1H, NH); 7.27-7.84 (m, 14H, phenyl); 7.08 (t, 1H, H-C(1')); 5.33 (d, 1H, 3'-OH); 4.16-4.61 (m, 4H, H-C(3'), H-C(4') and H-C(5')); 2.68-2.72 (m, 2H, H-C(2')); 2.34 (s, 3H, CH_3).

Anal. calc. for $C_{31}H_{26}N_4O_6$. 1/2 H_2O (559.6): C, 66.54; H, 4.86; N, 10.01. Found: C, 66.68; H, 4.88; N, 10.21.

1-(2,3-Dideoxy-3-iodo-5-O-p-toluoyl-ß-D-erythro-pentofuranosyl)-6,7-diphenyllumazine (24). A mixture of **23** (1.1 g, 2 mmole) and methyltriphenoxyphosphonium iodide (2 g, 4 mmole) in dry DMF (5 ml) was stirred for 2 h. The mixture was poured into H_2O (50 ml), the solid dissol-ved in $CHCl_3$ and washed well with H_2O. The crude product was purified through a silica gel column (3 x 12 cm, $CHCl_3$ 350 ml) to give a yellowish solid. Yield: 1 g (75 %), m.p.: 124-126°C. ^{1}H-NMR ($CDCl_3$): 8.94 (s, 1H, NH); 7.18-7.95 (m, 14H,

Ar-H and H-C(1')); 4.55 (t, 1H, H-C(3')); 4.43-4.50 (m, 3H, H-C(4') and H-C(5')); 2.85-3.35 (m, 2H, H-C(2') and H-(2")); 2.37 (s, 3H, -Me).

Anal. calc. for $C_{31}H_{25}N_4O_5$. 1/2 H_2O (669.5): C, 55.61; H, 3.91; N, 8.37. Found: C, 55.64; H, 3.97; N, 8.37.

1-(2,3-dideoxy-5-O-p-toluoyl-ß-D-glycero-pentofuranosyl)-6,7-diphenyllumazine (25). A solution of **24** (0.66 g, 1 mmole) in dry toluene (20 ml) was treated under dry nitrogen atmosphere with n-Bu_3SnH (1.2 ml) and azodiisobutyronitrile (AIBN) (0.4 g) . The stirred mixture was then heated to 85°C for 2 h and after cooling dropwise added to n-hexane (150 ml). The resulting precipitate was collected by filtration, washed with n-hexane and dried in a desiccator. Yield: 0.43 g (81 %), m.p.: 128-130°C. ^{1}H-NMR ($CDCl_3$): 9.10 (s, 1H, NH); 7.17-7.94 (m, 15H H-C(1') and Ar-H); 4.51-4.60 (m, 1H, H-C(4')); 4.36-4.47 (m, 2H, H-C(5')); 2.36 (s, 3H, -Me); 2.06-2.73 (m, 4H, H-C(2') and H-C(3')).

Anal. calc. for $C_{31}H_{26}N_4O_5$. 1/2 H_2O (543.6): C, 68.62; H, 5.01; N, 10.33. Found: C, 68.90; H, 5.05; N, 10.69.

1-(2-Deoxy-ß-D-erythro-pentofuranosyl)-6,7-dimethyllumazine (26). A mixture of 6,7-dimethyllumazine[17] (3.84 g) and a few crystals of ammonium sulfate in hexamethyldisilazane (HMDS) (25 ml) was heated under reflux for 4 h. The clear solution was evaporated to dryness, the residue dissolved in dry benzene (100 ml), then 3,5-di-O-p-toluoyl-2-deoxy-D-erythro-pentofuranosyl chloride (8.0 g) added and stirred for 2 days at room temperature. The reaction solution was evaporated to dryness, and the residue recrystallized from MeOH (100 ml) to give colourless crystals of 6.7-dimethyl-1-(2-deoxy-3,5-di-O-p-toluoyl-β-D-erythro-pentofuranosyl)-lumazine. Yield : 4.68 g (46 %), m.p.: 152-155°C. Lit.[6] m.p. 154-155°C.

The reaction product (4.36 g, 4.0 mmole) was stirred in 0.1 N $NaOCH_3$ (100 ml) for 2 h at room temperature. The precipitate was dissolved by addition of H_2O (50 ml), then the solution neutralized by Dowex-50 (H^+-form) to pH 5. After evaporation the residue was recrystrallized from n-propanol (800 ml) by addition of ether (120 ml) to give colourless crystals. Yield: 1.89 g (77 %), m.p. 175°C (decomp.). Lit.[6]: 180°C (decomp.). The material was chromatographically and spectrophotometrically identical with an authentic sample.

1-(2-Deoxy-3-O-mesyl-5-O-p-monomethoxytrityl-ß-D-erythro-pentofuranosyl)-6,7-dimethyllumazine (28). A solution of 1-(2-deoxy-5-O-p-monomethoxytrityl-ß-D-erythro-pentofuranosyl)-6,7-dimethyllumazine (**27**) (2.32 g, 4.0 mmole) in dry pyridine (20 ml) was treated by slow addition of methanesulfonyl chloride (0.5 ml, 6.5 mmole) at room temperature for 2 h with stirring. The reaction mixture was diluted with ice-water (100 ml), the product extracted by CH_2Cl_2 (30 ml) and then the organic layer dried over sodium sulfate. After evaporation crystallization from EtOH (10 ml) gave colourless crystals. Yield: 2.38 g (91 %), m.p. 113-115°C. ^{1}H-NMR (DMSO-d_6): 11.90 (s, 1H, NH); 6.78-7.42 (m, 14H, Ar-H); 7.03 (dd, 1H, H-C(1')); 5.42 (q, 1H, H-C(3')); 4.19 (dd, 1H, H-C(4')); 3.70 (s, 3H, OMe); 3.15 (s, 3H, SO_2CH_3) ; 3.02-3.40 (m, 2H, H-C(5')); 2.33-2.64 (m, 8H, 6,7-CH3, H-C(2'α),H-C(2'ß)).

Anal. calc. for $C_{34}H_{34}N_4O_8S$ (658.7): C, 61.99; H, 5.20; N, 8.50. Found: C, 61.71; H, 5.34; N, 8.32.

1-(3-Azido-2,3-dideoxy-5-O-p-monomethoxytrityl-ß-D-erythro-pentofuranosyl)-6,7-dimethyllumazine (29). A solution of **28** (0.5 g, 0.76 mmole) in dry DMF (3 ml) was treated with lithium azide (0.1 g, 1.6 mmole) with stirring at 80°C over night under anhydrous conditions. The DMF was removed in high vacuum, the residue dissolved in CH_2Cl_2 (10 ml), then washed with H_2O and the organic layer dried over sodium sulfate. The product was purified by silica gel column chromatography (3 x 5 cm) with $CHCl_3$/MeOH (99:1). The main fraction was evaporated to a colourless solid foam. Yield: 0.3 g (77 %), m.p. 121-124°C. IR (KBr): 2103 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 8.58 (bs, 1H, NH); 6.76-7.44 (m, 15H, H-C(1'), Ar-H); 4.50 (q, 1H, H-C(3')); 3.98 (q, 1H, H-C(4'); 3.77 (s, 3H, OCH_3); 3.42 (dq, 2H, H-C(5')); 3.02 (m, 1H, H-C(2'ß); 2.49-2.63 (2s, 6H, 6.7 CH_3); 2.40 (m, 1H, H-C(2'α)).

Anal. calc. for $C_{33}H_{37}N_7O_5$ (605.7): C, 65.44; H, 5.16; N, 16.19. Found: C, 65.01; H, 5.33; N, 16.01.

1-(2-Deoxy-5-O-p-toluoyl-ß-D-erythro-pentofuranosyl)-6,7-dimethyllumazine (30). A solution of p-toluoyl chloride (1.1 ml, 8.33 mmole) in 1,2-dichloroethane (15 ml) was added slowly to **26** (2.5 g, 8.1 mmole) in dry pyridine (30 ml). The solution was stirred over night, then diluted with ice-water (50 ml) to get a precipitate. After filtration the solid was dissolved

in $CHCl_3$ (30 ml), washed with H_2O and then the organic layer dried over sodium sulfate. After evaporation the residue was dissolved in CH_2Cl_2 (5 ml) and added dropwise with vigorous stirring into n-hexane (100 ml) forming a colourless solid. Yield: 3.1 g (73 %), m.p. 152-154°C. ^{1}H-NMR(DMSO-d_6): 11.82 (s, 1H, NH); 7.28-7.84 (2d, 4H, Ar-H); 7.02 (dd, 1H, H-C(1')); 5.36 (d, 1H, H-O(3')); 4.29-4.66 (m, 3H, H-C(4'), H-C(5')); 3.99 (m, 1H, H-C(3')); 2.89 (m, 1H, H-C(2'ß)); 2.51-2.57 (2s, 6H, 6,7 CH_3); 2.36 (s, 3H, C-CH_3); 2.15 (m, 1H, H-C(2'α)).

Anal. calc. for $C_{21}H_{22}N_4O_6$ (426.4): C, 59.15; H, 5.20; N, 13.14. Found: C, 59.58; H, 5.37; N, 13.15.

1-(2,3-Dideoxy-3-iodo-5-O-p-toluoyl-ß-D-erythro-pentofuranosyl)-6,7-dimethyllumazine (31). In dry DMF (5 ml) was dissolved **30** (0.86 g, 2.0 mmole) and methyltriphenoxyphosphonium iodide (1.9 g, 4.0 mmole) and then the mixture stirred at room temperature for 2 h. It was evaporated in high vacuum, the residue in $CHCl_3$ (15 ml) and washed subsequently with a solution of sodium thiosulfate and H_2O. The organic layer was dried over sodium sulfate and purified after evaporation to a smaller volume by column chromatography (3 x 12 cm) on silica gel with CH_2Cl_2/MeOH (99:1). The main fraction gave on evaporation a colourless amorphous solid. Yield: 0.77 g (72 %), m.p. 116°C (decomp.). ^{1}H-NMR ($CDCl_3$): 8.80 (s, 1H, NH); 7.22-7.95 (m, 5H, H-C(1'), Ar-H); 4.85 (q, 1H, H-C(3')); 4.50-4.76 (m, 3H, H-C(4'), H-C(5')); 3.24 (dq, 1H, H-C(2')); 2.88 (m, 1H, H-C(2'α)); 2.61, 2.64 (2s, 6H, 6,7 CH_3); 2.39 (s, 3H, C-CH_3).

Anal. calc. for $C_{21}H_{21}IN_4O_4$ (536.3): C, 47.03; H, 3.95; N, 10.45. Found: C, 47.06; H, 3.87; N, 10.45.

1-(2,3-Dideoxy-5-O-p-toluoyl-ß-D-glycero-pentofuranosyl)-6,7-dimethyllumazine (32). In dry toluene (20 ml) was dissolved **31** (0.64 g, 1.2 mmole) under N_2-atmosphere. It was heated to 85°C in an oil-bath and then azodiisobutyronitrile (0.4 g) and n-Bu_3SnH (1.2 ml) added with stirring. After heating for 2 h was evaporated to dryness. The residue was put onto a silica gel column for chromatography with n-hexane (300 ml) followed by $CHCl_3$/MeOH (99:1, 400 ml). The main fraction was evaporated to an amorphous solid. Yield: 0.40 g (82 %), m.p. 99-101°C. 1H-NMR ($CDCl_3$): 8.71

(bs, 1H, NH); 7.18-7.93 (m, 4H, Ar-H); 7.11 (dd, 1H, H-C(1')); 4.40-4.62 (m, 3H, H-C(4'), H-C(5')); 2.60 (s, 6H, 6,7 CH_3); 2.44-2.60 (m, 3H, H-C(2'α), H-C(2'ß), H-C(3'ß)); 2.39 (s, 3H, C-CH_3); 2.14 (m, 1H, H-C(3'α).

Anal. calc. for $C_{21}H_{22}N_4O_5$. 1/2 H_2O (419.4): C, 60.14; H, 5.52; N, 13.35. Found: C, 59.70; H, 5.37; N, 13.29.

2,3'-Anhydro-1-(2-deoxy-5-O-p-monomethoxytrityl-ß-D-threo-pentofuranosyl)-6,7-dimethyllumazine (33). To a solution of **28** (2.3 g, 3.5 mmole) in dry CH_2Cl_2 (35 ml) was added 1.8-diazabicyclo[5.4.0]-undec-7-ene (DBU) (0.76 ml, 5.0 mmole) and then heated 1 h under reflux. After cooling it was washed with H_2O (2 x 10 ml), the organic layer dried over sodium sulfate and then evaporated to dryness to give a chromatographically pure material. Yield: 1.75 g (89 %), m.p. 142-145°C. ^{1}H-NMR (DMSO-d_6): 6.68-7.34 (m, 14H, Ar-H); 6.99 (d, 1H, H-C(1')); 5.48 (s, 1H, H-C(3')); 4.50 m, 1H, H-C(4')); 3.66 (s, 3H, O-CH_3); 3.14 (m, 2H, H-C(5')); 2.34-2.70 (m, 8H, 6,7 CH_3, H-C(2'α), H-C(2'ß)).

Anal. calc. for $C_{33}H_{30}N_4O_5$. 1/2 H_2O (571.7): C, 69.33; H, 5.46; N, 9.80. Found: C, 69.76; H, 5.54; N, 9.88.

1-(2-Deoxy-5-O-p-monomethoxytrityl-ß-D-threo-pentofuranosyl)-6,7-dimethyllumazine (34). A solution of **33** (1.68 g, 3.0 mmole) in EtOH (30 ml) was treated with 1N sodium hydroxide (3 ml) for 1 h under reflux. After cooling it was neutralized with dilute acetic acid, then evaporated to dryness and the residue dissolved in CH_2Cl_2 (30 ml). After washing with H_2O, drying of the organic layer over sodium sulfate was evaporated to a colourless solid, which was used without further purification. Yield: 1.56 g (90 %), m.p. 175 °C ^{1}H-NMR (DMSO-d_6): 12.0 (s, 1H, NH); 6.81-7.39 (m, 1H, Ar-H); 6.89 (dd, 1H, H-C(1')); 5.24 (d, 1H, H-O(3')); 4.23 (s, 1H, H-C(3')); 4.04 (s, 1H, H-C(4')); 3.72 (s, 3H, O-CH_3); 3.22 (m, 2H, H-C(5')); 2.59 (m, 1H, H-C(2'ß)); 2.53 (2s, 6H, 6,7-CH_3); 2.30 (dd, 1H, H-C(2'α)).

Anal. calc. for $C_{32}H_{32}N_4O_6$ (580.7): C, 68.28; H, 5.56; N, 9.65. Found: C, 68.39; H, 5.75, N, 9.49.

1-(2-Deoxy-3-O-mesyl-5-O-p-monomethoxytrityl-ß-D-threo-pentofuranosyl)-6,7-dimethyllumazine (35). A solution of **34** (0.58 g, 1.0 mmole) in dry pyridine (5 ml) was treated with methanesulfonyl chloride (0.5

ml, 6.5 mmole) by dropwise addition and subsequent stirring for 2 h at room temperature. It was diluted with ice-water (100 ml), then extracted with CH_2Cl_2 (2 x 20 ml), the organic layer washed with H_2O (3 x 10 ml) and then dried over sodium sulfate. Purification was achieved by column chromatography (3 x 10 cm) on silica gel with $CHCl_3$/MeOH (99:1) to give a colourless solid on evaporation of the main fraction. Yield: 0.6 g (91 %), m.p. 132-134°C. ^{1}H-NMR ($CDCl_3$): 9.00 (s, 1H, NH); 6.75-7.42 (m, 14H, Ar-H); 6.87 (dd, 1H, H-C(1')); 5.36-5.41 (m, 1H, H-C(3')); 4.30 (q, 1H, H-C(4')); 3.77 (s, 3H, OCH_3); 3.50 (m, 2H, H-C(5')); 3.21 (m, 1H, H-C(2'ß)); 2.85 (s, 3H, SO_2CH_3); 2.79 (m, 1H, H-C(2'α)); 2.46, 2.60 (2s, 6H, 6,7 CH_3).

Anal. calc. for $C_{34}H_{34}N_4O_8$ (658.7): C, 61.99; H, 5.20; N, 8.50. Found: C, 61.96; H, 5.10; N, 8.60.

1-(2-O-Acetyl-3,5-di-O-benzoyl-ß-D-threo-pentofuranosyl)-lumazine (36). Silylation of lumazine (4.1 g, 25 mmole) was achieved by heating in hexamethyldisilazane (HMDS) (100 ml) in presence of a few crystals of ammonium sulfate under reflux for 6 h. The excess of HMDS was removed in high vacuum, the remaining oil dissolved in ethyl acetate (30 ml). A solution of 1,2-di-O-acetyl-3,5-di-O-benzoyl-D-xylofuranose[17] in ethyl acetate (30 ml) was added followed by trimethylsilyl triflate (**6**). Stirring was continued for 2 h at room temperature and then MeOH (5 ml) and H_2O (30 ml) added and neutralized with a saturated solution of sodium bicarbonate. The organic layer was separated, dried over sodium sulfate and evaporated. The residue was purified by column chromatography (7 x 20 cm) on silica gel with toluene/ethyl acetate (9:1). The main fraction gave on evaporation a colourless solid. Yield: 9.43 g (69 %), m.p. 112-114°C. ^{1}H-NMR ($CDCl_3$): 8.78 (bs, 1H, NH); 8.44-8.61 (2d, 2H, 6,7 H); 7.36-8.16 (m, 10H, Ar-H); 6.72 (d, 1H, H-C(1')); 6.25 (dd, 1H, H-C(2')); 5.83 (dd, 1H, H-C(3')); 4.78 (m, 3H, H-C(4'), H-C(5')); 2.13 (s, 3H, OAc).

Anal. calc. for $C_{27}H_{22}N_4O_9$ (546.5): C, 59.34; H, 4.06; N, 10.25. Found: C, 59.31; H, 4.21; N, 10.11.

1-(3,5-Di-O-benzoyl-ß-D-xylofuranosyl)-lumazine (37). To a solution of **36** (1.09 g, 2.0 mmole) in pyridine/acetic acid (4:1, 25 ml) was added hydrazine hydrate (1 ml) and then stirred at room temperature over night. It was evaporated to dryness, the residue treated with H_2O (30 ml) and $CHCl_3$ (30 ml).

The organic layer was dried over sodium sulfate, evaporated to a small volume and put onto a silica gel column (3 x 10 cm) for chromatography with toluene/ethyl acetate (9:1). The main fraction gave on evaporation a colourless solid. Yield: 0.87 g (86 %), m.p. 136-138°C ^{1}H-NMR ($CDCl_3$): 9.85 (s, 1H, NH); 8.42-8.51 (2d, 2H, 6,7H); 7.30-8.05 (m, 10H, Ar-H); 6.79 (d, 1H, H-C(1')); 5.51 (d, 2H, H-C(2'), H-C(3')); 4.70-4.82 (m, 3H, H-C(4'), H-C(5')); 4.31 (bs, 1H, H-O(2')).

Anal. calc. for $C_{25}H_{20}N_4O_8$ (504.5): C, 59.52; H, 4.00; N, 11.11. Found: C, 59.47; H, 4.13; N, 11.17.

1-(3,5-Di-O-benzoyl-2-O-mesyl-ß-D-xylofuranosyl)-lumazine (38). A solution of **37** (4.03 g, 8.0 mmole) in dry pyridine (50 ml) was cooled to -10°C and then methanesulfonyl chloride (1 ml, 13 mmole) added dropwise with stirring. Stirring was continued for 2 h at 0°C, then ice-water (100 ml) added and the precipitate collected. It was dissolved in CH_2Cl_2 (50 ml), washed with H_2O (3 x 20 ml) and then the organic layer dried over sodium sulfate followed by evaporation to dryness. The residue was dissolved in little CH_2Cl_2 and then added dropwise with vigorous stirring into n-pentane (100 ml) to give an amorphous solid. Yield: 3.88 g (84 %), m.p. 128-130°C. ^{1}H-NMR ($CDCl_3$): 9.06 (s, 1H, NH); 8.49-8.62 (2d, 2H, 6,7H); 7.35-8.14 (m, 10H, Ar-H); 7.02 (d, 1H, H-C(1')); 6.23 (dd, 1H, H-C(2')); 5.71 (q, 1H, H-C(3')); 4.73-4.87 (m, 3H, H-C(4'), H-C(5')); 3.20 (s, 3H, SO_2CH_3).

Anal. calc. for $C_{26}H_{22}N_4O_{10}S$ (582.5): C, 53.61; H, 3.81; N, 9.62. Found: C, 53.20; H, 3.94; N, 9.50.

2,2'-Anhydro-1-(3,5-di-O-benzoyl-ß-D-lyxofuranosyl)-lumazine (39). To a solution of **38** (2.91 g, 5 mmole) in dry CH_2Cl_2 (40 ml) was added DBU (1 ml, 6 mmole) and then the mixture heated under reflux for 15 min. After cooling the organic phase was washed with H_2O (3 x 20 ml), then dried over Nsodium sulfate and evaporated to dryness to give a chromatographically pure material. Yield: 2.24 g (93 %), m.p. 125-126°C. ^{1}H-NMR ($CDCl_3$): 8.52-8.76 (2d, 2H, 6,7-H); 7.27-8.05 (m, 10H, Ar-H); 6.87 (d, 1H, H-C(1')); 5.86-5.94 (m, 2H, H-C(2'), H-C(3')); 4.98 (m, 1H, H-C(4')); 4.55 (dq, 2H, H-C(5')).

Anal. calc. for $C_{25}H_{18}N_4O_7$. 1/2 H_2O (495.5): C, 60.60; H, 3.86; N, 11.31. Found: C, 60.83; H, 3.84; N, 11.52.

1-(2-Bromo-2-deoxy-3,5-di-O-benzoyl-ß-D-xylofuranosyl)-lumazine (40). A solution of **39** (1.94 g, 4 mmole) and lithium bromide (0.7 g, 8 mmole) in dry DMF (30 ml) was treated at room temperature with 33% HBr in acetic acid (10 ml) for 1 h. The mixture was poured into ice-water, the precipitate collected, then dissolved in CH_2Cl_2, washed with water and finally dried over sodium sulfate. Purification was achieved by column chromatography (3 x 5 cm) on silica gel with $CHCl_3$/MeOH (99:1). The main fraction gave on evaporation a colourless solid. Yield: 1.51 g (67 %), m.p. 117°C (decomp.). ^{1}H-NMR ($CDCl_3$): 8.90 (bs, 1H, NH); 8.56-8.68 (2d, 2H, 6,7H); 7.32-8.11 (m, 10H, Ar-H); 7.21 (d, 1H, H-C(1')); 5.93 (t, 1H, H-C(2')); 5.68 (q, 1H, H-C(3')); 4.87 (q, 1H, H-C(4')); 4.70 (m, 2H, H-C(5')).

Anal. calc. for $C_{25}H_{19}BrN_4O_7$ (567.4): C, 52.92; H, 3.38; N, 9.88. Found: C, 52.76; H, 3.57; N, 9.73.

1-(3,5-Di-O-benzoyl-2-O-methoxythiocarbonyl-ß-D-xylofuranosyl)-lumazine (41). A mixture of **37** (0.5 g, 1 mmole) and N,N'-thiocarbo-nyl-diimidazole (0.19 g, 1 mmole) in dry $CHCl_3$ (10 ml) was stirred at room tem-perature for 30 min. After evaporation, the residue was dissolved in MeOH (10 ml) and heated to 50°C for 2 h. It was again evaporated, then dissolved in little $CHCl_3$ and purified by column chromatography (1.5 x 10 cm) on silica gel with $CHCl_3$. Yield: 0.34 g (59 %), m.p. 114-115°C. ^{1}H-NMR ($CDCl_3$): 8.92 (bs, 1H, NH); 8.46-8.62 (2d, 2H, 6,7H); 7.35-8.18 (m, 10H, Ar-H); 6.81 (d, 1H, H-C(1')); 6.77 (d, 1H, H-C(2')); 5.91 (d, 1H, H-C(3')); 4.78 (m, 3H, H-C(4'), H-C(5')); 4.02 (s, 3H, SO_2CH_3).

Anal. calc. for $C_{27}H_{22}N_4O_9S$ (578.6): C, 56.05; H, 3.83; N, 9.68. Found: C, 55.77; H, 3.88; N, 9.45.

1-(3,5-Di-O-benzoyl-2-O-phenoxythiocarbonyl-ß-D-xylofuranosyl)-lumazine (42). To a solution of **37** (0.252 g, 0.5 mmole) in dry $CHCl_3$ (5 ml) was added 4-(dimethylamino)-pyridine (DMAP) (0.05 g, 0.5 mmole) and phenoxythiocarbonyl chloride (0.09 ml, 0.6 mmole). After stirring for 10 min. the mixture was quenched with ice-water (10 ml) and extracted with ethyl aceta-te (2 x 20 ml). The organic layer was dried over sodium sulfate, then evapora-ted and the residue purified by column chromatography (1.5 x 7 cm) on silica gel with toluene/ ethyl acetate (2:1). Yield: 0.28 g (88 %), m.p. 116-117°C.

^{1}H-NMR ($CDCl_3$): 8.90 (bs,1H, NH); 8.47-8.62 (2d, 2H, 6,7H); 7.06-8.22 (m, 14H, ar-H); 6.93 (d, 1H, H-C(1')); 6.81 (d, 1H, H-C(2')). 6.00 (d, 1H, H-C(3')); 4.74-4.90 (m, 3H, H-C(4'), H-C(5')).

Anal. calc. for $C_{32}H_{24}N_4O_9S$ (640.6): C, 60.00; H, 3.78; N, 8.74. Found: C, 60.04; H, 3.92; N, 8.36.

1-(2-Deoxy-3,5-di-O-benzoyl-ß-D-threo-pentofuranosyl)-lumazine (43). To a solution of **42** (0.64 g, 1 mmole) in dry toluene (10 ml) was added under N^{2-} atmosphere azodiisobutyronitrile (0.06 g) and n-Bu_3SNH (1.6 ml, 6 mmole) with stirring. After 15 min the mixture was heated to 80°C for 8 h. It was evaporated to dryness and the residue purified by column chromatography (1.5 x 10 cm) on silica gel with n-hexane (200 ml) followed by toluene/ethyl acetate (2:1, 600 ml). The main fraction gave on evaporation a colourless solid. Yield: 0.232 g (48 %), m.p. 116-117°C. ^{1}H-NMR (DMSO-d_6): 11.98 (s, 1H, NH); 8.59-8.63 (2d, 2H, 6,7H); 7.14-8.05 (m, 10H, Ar-H); 6.93 (t, 1H, H-C(1')); 5.76 (m, 1H, H-C(3')); 4.51-4.76 (m, 3H, H-C(4'), H-C(5')); 3.16 (m, 1H, H-C(2'ß)); 2.71 (m, 1H, H-C(2'α)).

Anal. calc. for $C_{25}H_{20}N_4O_7$ (488.5): C, 61.47; H, 4.13; N, 11.47. Found: C, 61.09; H, 4.25; N, 11.11.

1-(2-Deoxy-3,5-di-O-p-toluoyl-ß-D-erythro-pentofuranosyl)-lumazine (44)[7]. A mixture of lumazine (8.2 g, 50 mmole) and a few crystals of ammonium sulfate in hexamethyldisilazane (HMDS)(100 ml) was refluxed for 2 days till a clear solution was obtained. The excess of HMDS was distilled off in vacuum, the residue dissolved in dry $CHCl_3$ (200 ml) and then cuprous iodide (9.5 g, 50 mmole) added. After stirring for 5 min at room temperature 2-deoxy-3,5-di-O-p-toluoyl-α-D-erythro-pentofuranosyl chloride (19.4 g, 50 mmole) was added. The mixture was stirred for 15 min, then a saturated solution of sodium bicarbonate added, the organic layer dried over sodium sulfate and then the filtrate evaporated to dryness. The residue was recrystallized from $CHCl_3$ / MeOH (1:2, 225 ml) to give a colourless precipitate. Yield: 18.7 g (72 %), m.p. 154-155°C. Lit[6]: m.p. 156-158°C.

The work-up of the filtrate by silica gel column chromatography (3 x 7 cm) with $CHCl_3$/MeOH (98:2) yielded 1.7 g (6.6 %) of the α-anomer. The products were characterized by comparison with authentic samples.

1-(2-Deoxy-3-O-mesyl-5-O-p-monomethoxytrityl-ß-D-erythro-pentofuranosyl)-lumazine (46). A solution of 1-(2-deoxy-5-O-p-monomethoxytrityl-ß-D-erythro-pentofuranosyl)lumazine[14] in dry pyridine (50 ml) was cooled to -10°C and then dropwise added methanesulfonyl chloride (1 ml) with stirring. The mixture was then stirred for 2 h at 0°C, treated with ice-water (100 ml) and the resulting precipitate collected. The solid was dissolved in CH_2Cl_2 (50 ml), washed with H_2O (3 x 20 ml) and then the organic layer dried over sodium sulfate and filtered. The filtrate was concentrated to a small volume, which was dropwise added with vigorous stirring to n-pentane (100 ml) forming an amorphous solid. Yield: 2.7 g (91 %), m.p. 217-218°C. ^{1}H-NMR (DMSO-d_6): 12.02 (s, 1H, NH); 8.55, 8.59 (2d, 2H, 6,7-H); 6.66-7.38 (m, 14H, Ar-H); 7.05 (dd, 1H, H-C(1')); 5.35 (m, 1H, H-C(3')); 4.18 (q, 1H, H-C(4')); 3.71 (s, 3H, OCH_3); 3.31 (m, 2H, H-C(5')); 3.16 (s, 3H, So_2CH_3); 3.02 (m, 1H, H-C(2'ß)); 2.77-2.53 (m, 1H, H-C(2'α)).

Anal. calc. for $C_{32}H_{30}N_4O_8S$ (630.7): C, 60.94; H, 4.79; N, 8.88. Found: C, 60.57; H, 4.84; N, 8.65.

1-(3-Azido-2,3-dideoxy-5-O-p-monomethoxytrityl-ß-D-erythro-pentofuranosyl)-lumazine (47). A solution of **50** (0.46 g, 0.73 mmole) in dry DMF (3 ml) was treated with lithium azide (0.1 g, 1.6 mmole) at 80°C for 4 h under exclusion of moisture. It was evaporated to dryness in high vacuum, the residue dissolved in CH_2Cl_2 (10 ml), washed with H_2O (2 x 5 ml) and then the organic layer dried over sodium sulfate. After concentration to a small volume purification was achieved by silica gel chromatography (3 x 5 cm) with $CHCl_3$/MeOH (99:1). The main fraction gave on evaporation an amorphous solid. Yield: 0.32 g (75 %), m.p. 119-120°C. ^{1}H-NMR ($CDCl_3$): 8.90-9.10 (bs, 1H, NH); 8.44-8.61 (2d, 2H, 6,7-H); 6.77-7.45 (m, 14H, Ar-H); 7.10 (dd, 1H, H-C(1')); 4.53 (q, 1H, H-C(3')); 3.96 (q, 1H, H-C(4')); 3.77 (s, 3H, OCH_3); 3.41 (m, 2H, H-C(5')); 3.03 (m, 1H, H-C(2'ß)); 2.35 (m, 1H, H-C(2'α)).

Anal. calc. for $C_{31}H_{27}N_7O_3$ (577.6): C, 64.46; H, 4.71; N, 16.97. Found: C, 64.06; H, 4.88; N, 16.76.

2,3'-Anhydro-1-(2-deoxy-5-O-p-monomethoxytrityl-ß-D-threo-pentofuranosyl)-lumazine (48). A solution of **46** (2.52 g, 4 mmole) in dry CH_2Cl_2 (40 ml) was treated with 1.8-diaza-bicyclo[5.4.0]-undec-7-ene (DBU)

(1 ml, 6 mmole) by boiling under reflux for 1 h. After cooling the reaction solution was washed with H_2O (3 x 20 ml), the organic phase dried oner sodium sulfate and then evaporation to a small volume purified by column chromatography (3 x 5 cm) on silica gel with $CHCl_3$/MeOH (98:2).The main fraction was evaporated to give an amorphous solid.Yield: 1.8 g (84 %), m.p. 186-190°C. ^{1}H-NMR (DMSO-d_6): 8.91, 8.87 (2d, 2H, 6,7-H); 6.70-7.33 (m, 14H, Ar-H); 7.02 (d, 1H, H-C(1')); 5.52 (s, 1H, H-C(3')); 4.53 (bs, 1H, H-C(4')); 3.67 (s, 3H, OCH_3); 3.18 (m, 2H, H-C(5')); 2.60 (m, 2H, H-C(2'ß), H-C(2'α)).

Anal. calc. for $C_{31}H_{26}N_4O_5$ (534.7): C, 69.64; H, 4.90; N, 10.49. Found: C, 69.45; H, 4.93; N, 10.40.

1-(2-Deoxy-5-O-p-monomethoxytrityl-ß-D-threo-pentofuranosyl)-lumazine (49). A solution of EtOH (30 ml) and 1 N sodium hydroxide (3 ml) containing **48** (1.6 g, 3 mmole) was heated under reflux for 1 h. After cooling the solution was neutralized with acetic acid to pH 7, evaporated to dryness and then the residue taken up in CH_2Cl_2 (30 ml). It was washed with H_2O, dried over sodium sulfate and then again evaporated to an amorphous solid. The material was chromatographically pure and was not further purified for the next step. Yield: 1.42 g (85 %), m.p. 127-129°C. ^{1}H-NMR ($CDCl_3$): 9.06 (s, 1H, NH); 8.60, 8.68 (2d, 2H, 6,7-H); 6.76-7.17 (m, 14H, Ar-H); 7.01 (dd, 1H, H-C(1')); 5.04 (d, 1H, 3'-OH); 4.35 (m, 1H, H-C(3')); 3.96 (m, 1H, H-C(4')); 3.77 (s, 3H, OCH_3); 3.54 (dq, 2H, H-C(5')); 2.77 (m, 1H, H-C(2'ß); 2.42 (dd, 1H, H-C(2'α)).

Anal. calc. for $C_{31}H_{28}N_4O_6$ (552.6): C, 67.37; H, 5.11; N, 10.14. Found: C, 67.62; H, 5.22, N, 9.90.

1-(2-Deoxy-3-O-mesyl-5-O-p-monomethoxytrityl-ß-D-threo-pentofuranosyl)-lumazine (50). - A solution of **49** (0.55 g, 1 mmole) in dry pyridine (20 ml) was cooled to -10°C and then dropwise added methanesulfonyl chloride (0.5 ml) with stirring. The reaction mixture was stirred for 2 h at 0°C, then diluted with H_2O (50 ml) and the precipitate filtered off. The solid was dissolved in CH_2Cl_2 (20 ml), washed with H_2O (3 x 10 ml) and then the organic layer dried over sodium sulfate. The filtrate was evaporated to a small volume and then added dropwise under vigorous stirring into n-pentane (50 ml) to give an amorphous solid. Yield: 0.54 g (86 %), m.p. 144-147°C. ^{1}H-NMR ($CDCl_3$):

9.12 (s, 1H, NH); 8.56, 8.61 (2d, 2H, 6,7-H); 6.77-7.43 (m, 14H, Ar-H); 5.37 (m, 1H, H-C(3')); 4.23 (q, 1H, H-C(4')); 3.77 (s, 3H, OCH_3); 3.50 (m, 2H, H-C(5')); 3.27 (m, 1H, H-C(2'ß); 2.88 (s, 3H, SO_2CH_3); 2.81 (m, 1H, H-C(2'α)).

Anal. calc. for $C_{32}H_{30}N_4O_8$. 1/2 H_2O (639.7): C, 60.09; H, 4.57; N, 8.76. Found: C, 60.08; H, 4.66; N, 8.78.

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