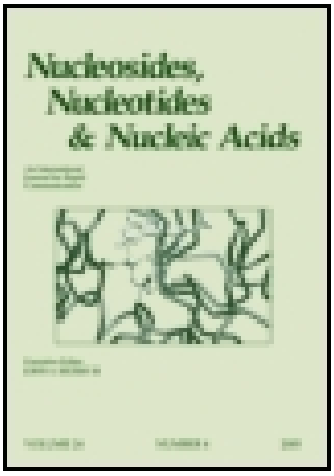


Nucleosides and Nucleotides
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lncn19

Nucleosides, LVIII[1] Synthesis of Base - Modified Oligonucleotides Containing 6- and 7-Aryl Lumazines

Yuris Maurinsh [a] & Wolfgang Pfleiderer [a]
[a] Fakultät für Chemie, Universität Konstanz , Universitätsstrasse 10, D-78464, Konstanz, Germany
Published online: 21 Aug 2006.

To cite this article: Yuris Maurinsh & Wolfgang Pfleiderer (1996) Nucleosides, LVIII[1] Synthesis of Base - Modified Oligonucleotides Containing 6- and 7-Aryl Lumazines, Nucleosides and Nucleotides, 15:1-3, 431-443

To link to this article: http://dx.doi.org/10.1080/07328319608002396

NUCLEOSIDES & NUCLEOTIDES, 15(1-3), 431-443 (1996)

NUCLEOSIDES, LVIII[1]
SYNTHESIS OF BASE - MODIFIED OLIGONUCLEOTIDES CONTAINING 6- AND 7-ARYL LUMAZINES

Yuris Maurinsh and Wolfgang Pfleiderer*

*Fakultät für Chemie, Universität Konstanz, Universitätsstrasse 10
D-78464 Konstanz / Germany

Abstract: 6-Phenyl-, 7-phenyl-, 6-(4-biphenyl)- 7-(4-biphenyl)lumazine N-1-2-deoxy-β-D-ribofuranosides were synthesized, then converted into the corresponding 5'-*O*-dimethoxytrityl-3'-*O*-(β-cyanoethyl, N,N-diisopropyl)phosphoramidites and incorporated into different positions of self-complementary oligonucleotides. The influence of modifications on the melting temperature of the resulting duplexes was studied.

INTRODUCTION

Lumazine-N-1 nucleosides can be regarded as structural analogues of the naturally occurring nucleic acid components thymidine and uridine and have therefore attracted attention in the last two decades from synthetic and chemical points of view [2-11]. The fluorescence properties of the pteridine derivatives can furthermore been utilized to study intra- and intermolecular interactions regarding energy-transfer phenomena[12,13], hybridizations and stacking effects in oligonucleotide and nucleic acid chemistry.

Our efforts have recently been focussed on the synthesis of monosubstituted 6- and 7-phenyl as well as 6- and 7-biphenyl-lumazines as potential strong fluorophors and in form of their N-1 2'-deoxy-β-D-ribofuranosides as new components for the formation of modified oligodeoxyribonucleotide chains. The 6- and 7-aryl substituents look flexible enough to favour also intercalations into double helix structures which should be reflected in increased stabilities and higher melting points.

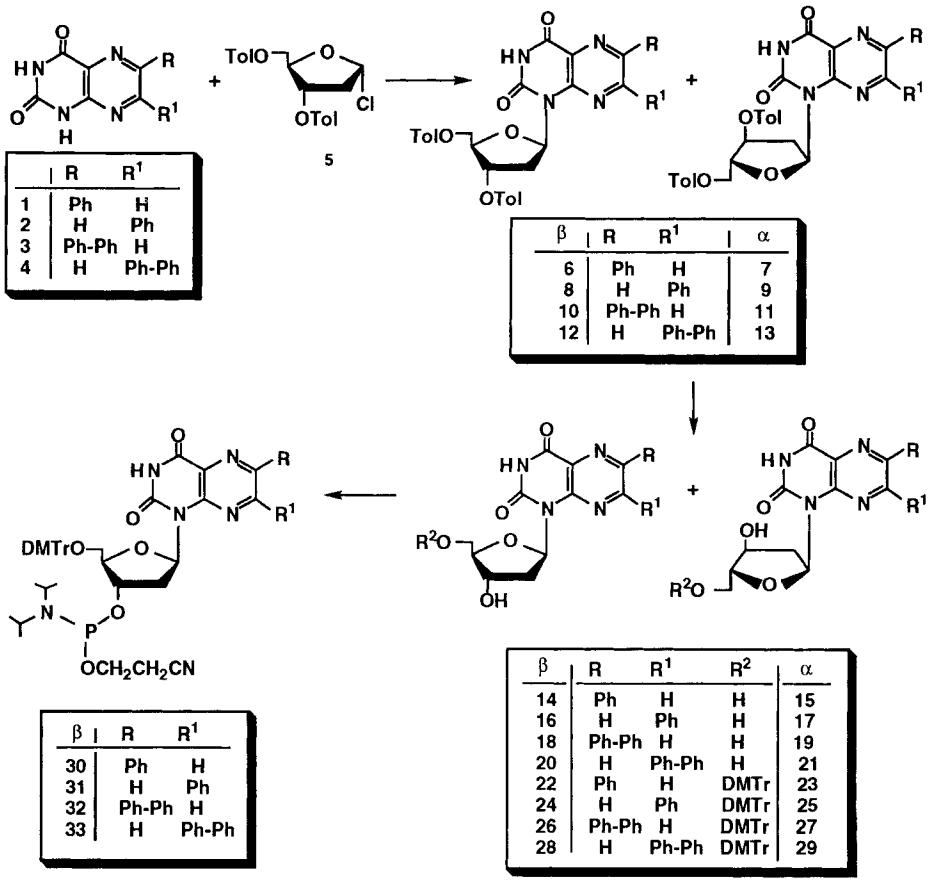
This paper is dedicated to Prof. Yoshihisa Mizuno with best wishes to his 75th birthday

RESULTS AND DISCUSSION

6- (**1**) and 7-Phenyllumazines (**2**) are described in the literature and can be synthesized either by hydrolysis from 6-phenylpterin or by condensation of 5,6-diaminouracil with phenylglyoxal[14], respectively. The corresponding 6- (**3**) and 7-biphenyllumazines (**4**) resulted from a pH-dependent condensation of 5,6-diaminouracil and biphenylglyoxal leading in a basic medium regioselectively to the 7- and in strong H_2SO_4 to the 6-substituted derivative. The glycosylations of **1-4** were achieved in form of their trimethylsilyl derivatives with 2-deoxy-3,5-di-*O*-p-toluoyl-α-D-ribofuranosyl chloride (**5**)[15] in the Hilbert-Johnson-Birkofer reaction[16-18] leading preferentially to N-1 substitution but also to the formation of α,β-anomeric mixtures.

In order to form predominantly the anticipated 1-(2-deoxy-β-D-ribofuranosyl)-lumazines the reaction conditions have been altered regarding temperature, solvent and catalyst. Best results were obtained with $ZnCl_2$ as a Lewis acid catalyst, acetonitrile as a solvent and slow addition of **5** in CH_2Cl_2 within 3 hours at a reaction temperature of -25 °C. Faster addition of the halo-sugar or use of $CHCl_3$ or 1,2-dichloroethane as the solvent led to increasing amounts of the α-anomer and the N^1,N^3-disubstitution product. Work-up was performed by chromatographical means leading to the isolation of α,β-anomeric mixtures which are difficult to be separated into the pure components. In the 7-phenyl- and 7-biphenyl-lumazine series fractional recrystallization from $CHCl_3$/acetone was quite successful and gave the β-anomers **8** and **12** in yields of 39% and 58%, respectively, besides the α-anomers **9** (16%) and **13** (19%). Deacylation of these products by sodium methoxide in MeOH according to Zemplen[19] worked well and the free 7-substituted lumazine N^1-2'-deoxyribonucleosides **16**, **17**, **20** and **21** were isolated in high yields. The structural assignment to the α- and β-nucleoside series was derived from the ^{1}H-NMR spectra showing in analogy to former findings with pteridine nucleosides[11] a characteristic large chemical shift difference between the H-C(2') and the H-C(2") of 0.6 - 0.9 ppm for the β-nucleosides whereas the same signals are much less separated in the corresponding α-anomers.

The inseparable anomeric mixtures **6/7** and **10/11** of the 6-substituted lumazine deoxynucleoside series were first deprotected by MeONa in MeOH and the resulting mixtures of **14/15** and **18/19**, respectively, subsequently treated with dimethoxytrityl chloride to give the corresponding 5'-*O*-dimethoxytrityl derivatives **22/ 23** and **26/27**. On this stage the anomeric mixtures could easily be separated by flash chromatography into the pure components **22**, **23**, **26** and **27**. The corresponding free 6-phenyl- and 6-biphenyl-1-(2-deoxy-α– and -β-ribofuranosyl)-lumazines **14** and **15** as well as **18** and **19** resulted from detritylation with 1% p-toluenesulfonic acid in CH_2Cl_2/MeOH 4:1. On the other hand, tritylation of the 7-phenyl (**16**, **17**) and 7-biphenyl analogues (**20**, **21**) afforded 5'-*O*-dimethoxytrityl derivatives **24**, **25**, **28** and **29**. Finally, the 6- and 7-substituted lumazine-N^1-2'deoxy-β-ribonucleosides **22**, **24**, **26** and **28** have been converted into the corresponding 3'-*O*-(β–cyanoethyl, N,N-diisopropyl)-phosphoramidites **30** - **33** by the treatment with (β-cyanoethoxy)-bis-(diisopropylamino)phosphane in the presence of tetrazole in CH_2Cl_2 yielding 60-91% of isolated material.



	R	R¹
1	Ph	H
2	H	Ph
3	Ph-Ph	H
4	H	Ph-Ph

β	R	R¹	α
6	Ph	H	7
8	H	Ph	9
10	Ph-Ph	H	11
12	H	Ph-Ph	13

β	R	R¹
30	Ph	H
31	H	Ph
32	Ph-Ph	H
33	H	Ph-Ph

β	R	R¹	R²	α
14	Ph	H	H	15
16	H	Ph	H	17
18	Ph-Ph	H	H	19
20	H	Ph-Ph	H	21
22	Ph	H	DMTr	23
24	H	Ph	DMTr	25
26	Ph-Ph	H	DMTr	27
28	H	Ph-Ph	DMTr	29

The newly synthesized monomeric building blocks **30** - **33** have then been used in a DNA-synthesizer forming a series of self-complementary mixed oligonucleotides containing as modified bases in different positions instead of the thymidine residue the 6- and 7-phenyl- as well as 6- and 7-biphenyllumazine moieties (Tab.1). The assembly of the oligodeoxyribonucleotides was performed by the solid-phase phosphoramidite method on an Applied Biosystems synthesizer 380B on 0.5 μmol scale using standard synthesis and deprotection cycles, except for the 6-(4-biphenyl)lumazine phosphoramidite **32**, which showed insufficient solubility in CH_3CN. For this reason the automated synthesis cycle was interrupted at this point and a manual step inserted using solutions of **32** and tetrazole, respectively, in a mixture of CH_3CN/CH_2Cl_2 2:1. Thereafter, the synthesis was continued in the usual manner. The coupling yields of the modified phosphoramidites were monitored by the common colorimetric assay of the released dimethoxytrityl cation, ranging between 96 and 99.5%. The purity of the synthesized oligonucleotides was controlled by reverse-phase HPLC and polyacrylamide gel electrophoresis showing only minor failure sequences.

Tab. 1. Self-complementary oligonucleotides and their T_m values*

No.	Oligonucleotide sequence	Lu	T_m (°C)
1	5'-d(GG-TT-CC-AT-GC-AT-GG-AA-CC)-3'	-	60.4
2	5'-d(GG-TT-CC-AT-GC-A**Lu**-GG-AA-CC)-3'	6-Ph	60.0
3	5'-d(GG-TT-CC-A**Lu**-GC-A**Lu**-GG-AA-CC)-3'	6-Ph	65.5
4	5'-**Lu**-d(GG-TT-CC-AT-GC-AT-GG-AA-CC)-3'	6-Ph	60.8
5	5'-d(GG-TT-CC-AT-GC-A**Lu**-GG-AA-CC)-3'	7-Ph	61.5
6	5'-d(GG-TT-CC-A**Lu**-GC-A**Lu**-GG-AA-CC)-3'	7-Ph	63.4
7	5'-**Lu**-d(GG-TT-CC-AT-GC-AT-GG-AA-CC)-3'	7-Ph	60.9
8	5'-d(GG-TT-CC-AT-GC-A**Lu**-GG-AA-CC)-3'	6-Ph-Ph	57.3
9	5'-d(GG-TT-CC-A**Lu**-GC-A**Lu**-GG-AA-CC)-3'	6-Ph-Ph	**
10	5'-**Lu**-d(GG-TT-CC-AT-GC-AT-GG-AA-CC)-3'	6-Ph-Ph	59.4
11	5'-d(GG-TT-CC-AT-GC-A**Lu**-GG-AA-CC)-3'	7-Ph-Ph	64.3
12	5'-d(GG-TT-CC-A**Lu**-GC-A**Lu**-GG-AA-CC)-3'	7-Ph-Ph	70.2
13	5'-**Lu**-d(GG-TT-CC-AT-GC-AT-GG-AA-CC)-3'	7-Ph-Ph	60.4

* The transitions were measured at 260 nm in NaH_2PO_4 / Na_2HPO_4 buffer pH 7 ; Na^+ conc. 0.03 M.

** Could not be measured

The influence of the modified bases on the stability of the duplex formation was measured by performing the melting profiles and determining the melting temperatures as an informative parameter. Introduction of an additional lumazine nucleotide into the choosen self-complementary sequence 5'-d(GG-TT-CC-AT-GC-AT-GG-AA-CC)-3' at the 5'-end (sequence *4, 7, 10, 13*) influences hybridization of the unmodified sequence *1* very little. There is also no change in T_m in the case of introduction of the 6-phenullumazine unit in position 7 (*2*) but two 6-phenyllumazine nucleotide moieties in position 7 and 11 (*3*) raise the T_m by about 5 °C. Analogous modifications with 7-phenyllumazine nucleotides show minor effects increasing the T_m by 1.1 °C (*5*) and 3 °C (*6*), respectively. A more dramatic effect on the duplex stability is observed by the 7-(4-biphenyl)lumazine modifications which cause in position 7 (*11*) an increase of 2.9 °C and on double substitution in position 7 and 11 an enhancement of almost 10 °C (*12*). Interestingly, the presence of one 6-(4-biphenyl)lumazine nucleotide in sequence *8* was associated with a decline of T_m by 3.1 °C and two modifications of this type (*9*) caused an even more severe structural change that the melting temperature could not been measured at all.

CONCLUSIONS

We have synthesized new types of 6- and 7-substituted lumazine nucleoside phosphoramidites which can effectively be incorporated in oligonucleotide sequences in

different positions of the chain. The presence of such modified bases can influence in different ways the stability of oligonucleotide duplexes. The 7-(4-biphenyl)lumazine moiety revealed sofar the most striking stabilisation effects which may be considered in the antisense approach as an alternative combination to improve helical interactions.

EXPERIMENTAL

General. Products were dried under high vacuum. TLC: Precoated silica gel thin-layer sheets F1500 LS 254 from *Schleicher & Schüll.* Flash chromatography (FC): silica gel (Baker, 30-60 mm); 0.2-0.3 bar. M.p.: *Gallenkamp* melting-point apparatus; no corrections. UV: *Perkin-Elmer, Lambda 15*; λ_{max} in nm (log ε).

Melting curves: *Perkin-Elmer Lambda 2;* temperature control by Peltier element; programmer PTP-6. ^{1}H-NMR: *Bruker AC 250*; δ in ppm rel. to TMS as internal standard. ^{31}P-NMR: *Joel 400 MHz*; δ in ppm rel. to H_3PO_4. Oligonucleotides were prepared on controlled pore glass (CPG 500 A) as solid support using an *Applied Biosystems* synthesizer 380B in 0.5 μmol scale.

6-(4-Biphenyl)lumazine (3). In 85% sulfuric acid (100 ml) was dissolved 5,6-diaminouracil (3.55 g; 0.025 mol) and then 4-biphenylglyoxal monohydrate[20] (5.7 g; 0.025 mol) added with stirring. The mixture was stirred for 2 h at 65 °C and then poured onto ice and neutralized by aqueous ammonia to pH 5. After standing over night the precipitate was collected and purified by reprecipitation from dilute KOH (300 ml) and dropwise addition into boiling 1N AcOH (300 ml). The precipitate was filltered off after cooling and dried at 100 °C in the oven. Yield: 4.35 g (55%). Yellowish crystal powder. M.p > 320 °C. UV (MeOH): 205 (4.60), 293 (4.54), 361 (4.12). ^{1}H-NMR (DMSO-d_6): 11.01 (br 2 NH); 9.33 (s, H-C(7)); 8.24 (d, 2 arom.H); 7.85 (d, 2 arom.H); 7.75(d, 2 arom.H); 7.50 (m, 3 arom.H). Anal. calc. for $C_{18}H_{12}N_4O_2 \cdot H_2O$ (334.3): C, 64.67; H, 4.22; N, 16.76. Found: C, 64.58; H, 4.17; N, 16.48.

7-(4-Biphenyl)lumazine (4). In a mixture of H_2O (100 ml) and conc. aqueous ammonia (100 ml) were dissolved 5,6-diaminouracil (3.55 g; 0.025 mol) and then a solution of 4-biphenylglyoxal monohydrate (5.7 g; 0.025 mol) in EtOH (250 ml) added. A yellow precipitate was obtained after heating under reflux for 2 h and cooling. Purification was achieved by reprecipitation from dilute KOH/ dilute AcOH on heating. Yield: 5.16 g (65%). Yellowish crystal powder. M.p. > 320 °C. UV (MeOH): 206 (4.56), 236 (4.35); 273sh (4.03), 363 (4.53). ^{1}H-NMR (DMSO-d_6): 11.96 (s, HN); 11.65 (s, HN); 9.20 (s, H-C(6)); 8.32 (d, 2 arom.H); 7.90 (d, 2 arom.H); 7.89 (d, 2 arom.H); 7.47 (m, 3 arom.H). Anal. calc. for $C_{18}H_{12}N_4O_2 \cdot H_2O$ (334.3): C, 64.67; H, 4.22; N, 16.76. Found: C, 64.62; H, 4.44; N, 16.42.

6-Phenyl-1-(2-deoxy-3,5-di-*O*-p-toluoyl-β-D-ribofuranosyl)lumazine (6) and 6-Phenyl-1-(2-deoxy-3,5-di-*O*-p-toluoyl-α-D-ribofuranosyl)lumazine (7). 6-Phenyl-lumazine (**1**)[14] (2.88 g; 12.0 mmol) was suspended with stirring in acetonitrile (200 ml),

hexamethyldisilazane (HMDS) (5 ml) and chlorotrimethylsilylmethane (5 ml) were added. After 10 min $ZnCl_2$ (0.82 g; 6.0 mmol) was given into the reaction mixture and cooled to -25 °C. Then 3,5-di-*O*-p-toluoyl-2-deoxy-α-D-erythropentosyl chloride (**5**)[15] (3.33 g; 8.57 mmol) was dissolved in dichloromethane (175 ml) and added dropwise during 3 h into the reaction mixture maintaining the temperature at -25 °C. Stirring was continued overnight. The conventional workup consisted of evaporation, dissolving in CH_2Cl_2, washing with $NaHCO_3$ solution, drying over Na_2SO_4 and chromatographical purification by FC (silica gel, 25 x 4 cm, CH_2Cl_2 (500 ml), CH_2Cl_2/acetone 40:1 (400 ml), 30:1 (500 ml)) to give an anomeric mixture of compounds **6** and **7**. Yield: 3.9 g (77%).

7-Phenyl-1-(2-deoxy-3,5-di-*O*-p-toluoyl-β-D-ribofuranosyl)lumazine (8) and 7-Phenyl-1-(2-deoxy-3,5-di-*O*-p-toluoyl-α-D-ribofuranosyl)lumazine (9). As described in the preceding procedure 7-phenyllumazine (**2**)[14] (2.88 g; 12.0 mmol) was treated with 0.82 g (6.0 mmol) of $ZnCl_2$ and 3.33 g (8.57 mmol) of **5** analogously. Purification was achieved by FC (silica gel 25 x 4 cm, CH_2Cl_2 (500 ml), CH_2Cl_2/acetone 40:1 (400 ml), 30:1 (500 ml)) to give a mixture of **8** and **9**. The product containing fractions were evaporated, the residue was dissolved with stir-ing in 500 ml of boiling acetone and 250 ml of CH_2Cl_2 and then cooled overnight in the ice-box at +5 °C. The precipitate of the α-anomer **9** was filtered off to yield 0.85 g (16 %) of colorless crystals. The filtrate was evaporated to dryness and the residue was recrystallized from CH_2Cl_2-petroleum ether. Yield: 2.02 g (39%) of **8**.

8: M.p. 204-206 °C. UV (MeOH): 235 (4.63), 275 (3.97), 347 (4.24). ^{1}H-NMR ($CDCl_3$): 9.47 (br, NH), 9.02 (s, H-C(6)); 7.25-8.10 (13 arom. H, H-C(1')); 5.93 (m, H-C(3')); 4.60-4.73 (m, H-C(4'), H-C(5'), H-C(5")); 3.50 (m, H-C(2')); 2.60 (m, H-C(2")); 2.42 (s, Me); 2.32 (s, Me). Anal. calc. for $C_{33}H_{28}N_4O_7$ (592.6): C, 66.89; H 4.76; N, 9.45. Found: C, 66.41; H, 4.86; N, 9.41.

9: M.p. 223-224 °C. UV (MeOH): 235 (4.63), 275 (3.96), 346 (4.26). ^{1}H-NMR ($CDCl_3$): 9.05 (s, H-C(6)), 8.63 (br, NH); 7.16-8.09 (13 arom. H, H-C(1')); 5.59 (m, H-C(3')); 5.16 (m, H-C(4')); 4.66 (m, H-C(5')); 4.48 (m, H-C(5")); 3.06-3.28 (m, H-C(2'), H-C(2")); 2.43 (s, Me); 2.38 (s, Me). Anal. calc. for $C_{33}H_{28}N_4O_7$ (592.6): C, 66.89; H, 4.76; N, 9.45. Found: C, 67.22; H, 4.90; N, 9.16.

6-(4-Biphenyl)-1-(2-deoxy-3,5-di-*O*-p-toluoyl-β-D-ribofuranosyl)lumazine (10) and 6-(4-Biphenyl)-1-(2-deoxy-3,5-di-*O*-p-toluoyl-α-D-ribofuranosyl)lumazine (11). Analogous to synthesis of **6/7** from 2.7 g; (8.54 mmol) of 6-(4-biphenyl)lumazine (**3**), 2.37 g (6.1 mmol) of **5** and 0.42 g (3.05 mmol) of $ZnCl_2$. Purification was achieved by FC (silica gel 25 x 4 cm, CH_2Cl_2 (500 ml), CH_2Cl_2-acetone 40:1 (400 ml), 30:1 (500 ml)) to give an anomeric mixture of **10** and **11**. Yield: 2.78 g (68%).

7-(4-Biphenyl)-1-(2-deoxy-3,5-di-*O*-p-toluoyl-β-D-ribofuranosyl)lumazine (12) and 7-(4-Biphenyl)-1-(2-deoxy-3,5-di-*O*-p-toluoyl-α-D-ribofuranosyl)lumazine (13). Analogous to procedure of **6/7** from 7-(4-biphenyl)lumazine (**4**) (2.05 g; 6.48 mmol), 1.80 g (4.62 mmol) of **5** and 0.31 g (2.31 mmol) of $ZnCl_2$. Purification was achieved by FC (silica gel 20 x 4 cm, CH_2Cl_2 (200 ml), CH_2Cl_2-acetone 20:1 (200 ml), 9:1 (500 ml)) to give a

mixture of **12** and**13**. The product fraction was evaporated to a syrup which was dissolved with stirring in 500 ml of boiling acetone and 250 ml of CH_2Cl_2. After standing overnight at +5 °C the precipitated α-anomer **13** was filtered off to yield 0.6 g (19%) of colorless crystals. The filtrate was again evaporated to dryness and the residue recrystallized from CH_2Cl_2-petroleum ether to give 1.8 g (58%) of **12**.

12: M.p. 249-250 °C. UV (MeOH): 237 (4.72), 269sh (4.17), 361 (4.46). ^{1}H-NMR ($CDCl_3$): 9.69 (br, NH), 9.08 (s, H-C(6)); 7.12-8.18 (17 arom. H, H-C(1')); 5.94 (m, H-C(3')); 4.59-4.77 (m, H-C(4'), H-C(5'), H-C(5")); 3.50 (m, H-C(2')); 2.60 (m, H-C(2")); 2.42 (s, Me); 2.34 (s, Me). Anal. calc. for $C_{39}H_{32}N_4O_7$ (668.7): C, 70.05; H, 4.82; N, 8.38. Found: C, 69.62; H, 4.80; N, 8.33.

13: M.p. >270 °C dec. UV (MeOH): 237 (4.70), 269sh (4.14), 361 (4.45). ^{1}H-NMR ($CDCl_3$): 12.00 (br, NH), 9.26 (s, H-C(6)); 7.19-8.35 (17 arom. H, H-C(1')); 5.63 (m, H-C(3')); 5.02 (m, H-C(4')); 4.53 (m, H-C(5'), H-C(5")); 3.00-3.17 (m, H-C(2'), H-C(2")); 2.35 (s, Me); 2.31 (s, Me). Anal. calc. for $C_{39}H_{32}N_4O_7 \cdot 0.5\ H_2O$ (677.7): C, 69.11; H, 4.91; N, 8.27. Found: C, 68.80; H, 4.91; N, 8.05.

6-Phenyl-1-(2-deoxy-β-D-ribofuranosyl)lumazine (14). Compound **22** (0.25 g; 0.38 mmol) was dissolved in CH_2Cl_2 (4 ml), 1% solution of p-toluenesulfonic acid in CH_2Cl_2-MeOH (4:1) (0.2 ml) added and the reaction mixture stirred for 15 min. After addition of MeOH (10 ml) the solution concentrated to 5 ml of its volume. The precipitated crystalls were filtered off, carefully washed with ether and dried, to give compound **14**. Yield: 0.12 g (89%). M.p. >220 °C dec.. UV (H_2O): 278 (4.22), 351 (3.87). ^{1}H-NMR (DMSO-d_6): 12.02 (br, NH), 9.35 (s, H-C(7)); 8.17 (2 arom. H); 7.56 (3 arom. H); 7.02 (pt, H-C-(1')); 5.20 (d, OH-C(3')); 4.64 (t, OH-C(5')); 4.42 (m, H-C(3')); 3.74 (m, H-C(4')); 3.66 (m, H-C(5')); 3.55 (m, H-C(5")); 2.91 (m, H-C(2')); 2.08 (m, H-C(2")). Anal. calc. for $C_{17}H_{16}N_4O_5 \cdot 0.5\ H_2O$ (365.3): C, 55.89; H, 4.69; N, 15.34. Found: C, 55.45; H, 4.83; N, 15.03.

6-Pheyl-1-(2-deoxy-α-D-ribofuranosyl)lumazine (15). Compound **15** was obtained analogously to the preceding procedure from 0.3 g (0.46 mmol) of **23**. Yield: 0.14 g (84 %) of **15** as a colorless solid. M.p.>220 °C (decomp.). UV (H_2O): 273 (4.24), 350 (3.89). ^{1}H-NMR (DMSO-d_6): 12.03 (br, NH), 9.37 (s, H-C(7)); 8.17 (2 arom. H); 7.52 (3 arom. H); 6.93 (pt, H-C-(1')); 5.26 (d, OH-C(3')); 4.68 (t, OH-C(5')); 4.26 (m, H-C(3')); 4.14 (m, H-C(4')); 3.65 (m, H-C(5')); 3.41 (m, H-C(5")); 2.78 (m, H-C(2')); 2.42 (m, H-C(2")). Anal. calc. for $C_{17}H_{16}N_4O_5 \cdot 0.25\ H_2O$ (360.8): C, 56.59; H, 4.47; N, 15.53. Found: C, 56.52; H, 4.78; N, 15.51.

7-Phenyl-1-(2-deoxy-β-D-ribofuranosyl)lumazine (16). Compound **8** (4.0 g; 6.75 mmol) was treated in 8 ml of 2N NaOMe and 100 ml MeOH by stirring at r.t. for 2 h. Water (1 ml) was added and the mixture neutralized by 10% acetic acid to pH 7. After concentration to half of the volume and standing overnight in the ice-box the precipitate was collected, washed with little H_2O, EtOH and ether and dried in a vacuum at 50 °C. Yield: 2.2 g (91 %). M.p. >220 °C dec. UV (H_2O): 223 (4.26), 276 (3.79), 347 (4.24). ^{1}H-NMR (DMSO-d_6): 11.95 (br, NH), 9.23 (s, H-C(6)); 8.24 (2 arom. H); 7.62 (3 arom. H); 7.24 (pt, H-C-(1')); 5.20 (d,

OH-C(3')); 4.63 (t, OH-C(5')); 4.43 (m, H-C(3')); 3.75 (m, H-C(4')); 3.64 (m, H-C(5')); 3.52 (m, H-C(5"); 2.95 (m, H-C(2')); 2.12 (m, H-C(2")). Anal. calc. for $C_{17}H_{16}N_4O_5$ (356.3): C, 57.30; H, 4.53; N, 15.72. Found: C, 57.10; H, 4.68; N, 15.46.

7-Phenyl-1-(2-deoxy-α-D-ribofuranosyl)lumazine (**17**). Compound **17** was obtained analogously to the preceding procedure from 1.0 g (1.9 mmol) of **11**, 2 ml of 2N NaOMe and 50 ml MeOH. Yield: 0.61 g (90 %). M.p. >220 °C dec. UV (H_2O): 223 (4.32), 275 (3.91), 347 (4.26). ^{1}H-NMR (DMSO-d_6): 11.97 (br, NH), 9.23 (s, H-C(6)); 8.35 (2 arom. H); 7.58 (3 arom. H); 7.05 (pt, H-C-(1')); 5.35 (d, OH-C(3')); 4.68 (t, OH-C(5')); 4.25 (m, H-C(3')); H-C(4')); 3.62 (m, H-C(5')); 3.40 (m, H-C(5"); 2.96 (m, H-C(2')); 2.51 (m, H-C(2")). Anal. calc. for $C_{17}H_{16}N_4O_5$ (356.3): C, 57.30; H, 4.53; N, 15.72. Found: C, 57.14; H, 4.66; N, 15.82.

6-(4-Biphenyl)-1-(2-deoxy-β-D-ribofuranosyl)lumazine (**18**). Analogous to procedure of **14** with 0.18 g (0.27 mmol) of **26** dissolved in 4 ml of CH_2Cl_2 and treated with 0.2 ml of 1% solution of p-toluenesulphonic acid in CH_2Cl_2-MeOH (4:1) for 15 min. Yield: 0.08 g (69%). M.p. >208 °Cdec. UV (MeOH): 296 (4.35), 359 (3.88). ^{1}H-NMR (DMSO-d_6): 12.01 (br, NH), 9.41 (s, H-C(7)); 8.29 (2 arom. H); 7.76-7.90 (4 arom. H); 7.38-7.54 (3 arom. H); 7.02 (pt, H-C-(1')); 5.17 (d, OH-C(3')); 4.62 (t, OH-C(5')); 4.43 (m, H-C(3')); 3.74 (m, H-C(4')); 3.66 (m, H-C(5')); 3.53 (m, H-C(5")); 2.88 (m, H-C(2')); 2.07 (m, H-C(2")). Anal. calc. for $C_{23}H_{20}N_4O_5 \cdot 0.25\ H_2O$ (436.9): C, 63.22; H, 4.67; N, 12.82. Found: C, 63.32; H, 4.81; N, 12.34.

6-(4-Biphenyl)-1-(2-deoxy-α-D-ribofuranosyl)lumazine (**19**). Analogous to procedure of **14** from 0.2 g (0.27 mmol) of **27**. Yield: 0.08 g (69 %). M.p. >195 °C dec. UV (MeOH): 296 (4.39), 359 (3.91). ^{1}H-NMR (DMSO-d_6): 12.04 (br, NH), 9.41 (s, H-C(7)); 8.29 (2 arom. H); 7.88 (2 arom. H); 7.77 (2 arom. H); 7.41 7.54 (3 arom. H); 6.93 (pt, H-C-(1')); 5.26 (d, OH-C(3')); 4.68 (t, OH-C(5')); 4.16 4.26 (m, H-C(3'), H-C(4)); 3.63 (m, H-C(5')); 3.45 (m, H-C(5")); 2.79 (m, H-C(2')); 2.45 (m, H-C(2")). Anal. calc. for $C_{23}H_{20}N_4O_5 \cdot 0.25\ H_2O$ (436.9): C, 63.22; H 4.67; N 12.82. Found: C, 63.42; H, 4.68; N 12.58.

7-(4-Biphenyl)-1-(2-deoxy-β–D-ribofuranosyl)lumazine (**20**). Analogous to procedure of **16** with 1.0 g (1.50 mmol) of **12**, 4 ml of 2N NaOMe and 50 ml MeOH. Yield: 0.60 g (93 %). M.p. >230° dec. UV (MeOH): 236 (4.25), 268sh (3.98), 361 (4.45). ^{1}H-NMR ((D$_6$)DMSO): 11.93 (br, NH), 9.27 (s, H-C(6)); 8.34 (2 arom. H); 7.92 (2 arom. H); 7.78 (2 arom. H); 7.46 (3 arom. H); 7.26 (pt, C-(1')); 5.20 (br., OH-C(3')); 4.63 (br., OH-C(5')); 4.43 (m, H-C(3')); 3.78 (m, H-C(4')); 3.65 (m, H-C(5')); 3.52 (m, H-C(5")); 2.97 (m, H-C(2')); 2.14 (m, H-C(2")). Anal. calc. for $C_{23}H_{20}N_4O_5 \cdot 0.25\ H_2O$ (436.9): C, 63.22; H, 4.67; N 12.82. Found: C, 63.37; H, 4.73; N, 12.45.

7-(4-Biphenyl-1-(2-deoxy-α-D-ribofuranosyl)lumazine (**21**). Analogous to procedure of **16** with 0.84 g (1.26 mmol) of **13**, 4 ml of 2N NaOMe and 50 ml MeOH. Yield: 0.47 g (86 %). M.p. >230 °C dec. UV (MeOH): 237 (4.26), 268sh (3.96), 362 (4.47). ^{1}H-NMR

(DMSO-d_6): 11.96 (br, NH), 9.28 (s, H-C(6)); 8.44 (2 arom. H); 7.88 (2 arom. H); 7.78 (2 arom. H); 7.48 (3 arom. H); 7.07 (pt, C-(1')); 5.35 (d, OH-C(3')); 4.68 (t, OH-C(5')); 4.27 (m, H-C(3'), H-C(4')); 3.63 (m, H-C(5')); 3.43 (m, H-C(5"); 2.95 (m, H-C(2')); 2.50 (m, H-C(2")). Anal. calc. for $C_{23}H_{20}N_4O_5 \cdot H_2O$ (450.5): C, 61.33; H, 4.92; N 12.44. Found: C, 66.10; H, 5.09; N, 12.90.

6-Phenyl-1-(2-deoxy-5-*O*-dimethoxytrityl-β-D-ribofuranosyl)lumazine (22) and 6-Phenyl-1-(2-deoxy-5-*O*-dimethoxytrityl-α-D-ribofuranosyl)lumazine (23). The mixture of **6** and **7** (2.25 g; 3.80 mmol) was suspended in MeOH (30 ml) and then 2N NaOMe (10 ml) added. The solution was stirred for 2 h at r.t.. Water (1 ml) was added and the mixture was neutralized with 10% acetic acid to pH 7. The resulting precipitate was filtered off after standing for 12 h at +5 °C, washed with H_2O, EtOH and ether, to give the mixture of **14** and **15** (1.28 g; 95%). This mixture (1.05 g; 2.95 mmol) was then twice coevaporated with absolute pyridine (10 ml), dissolved in absolute pyridine (20 ml), and 4,4'-dimethoxytrityl chloride (1.92 g; 5.80 mmol) added. After stirring overnight at r.t., the reaction solution was neutralized with a cold saturated $NaHCO_3$ (100 ml), extracted with CH_2Cl_2 (2x100 ml) and the pooled organic extracts were dried over Na_2SO_4. After filtration the solution was again evaporated and the residue chromatographed by FC (silica gel, 25 x 4 cm, CH_2Cl_2 (300 ml), CH_2Cl_2-MeOH 199:1 (200 ml), 198.5:1.5 (200 ml), 198:2 (200 ml), 197.5:2.5 (200 ml), 197:3 (200 ml), 196.5:3.5 (200 ml), 196:4 (200 ml), to give after the evaporation of the appropriate fractions 1.22 g (63%) of **22** and 0.41 g (21%) of **23** as colorless amorphous solids.

22: UV (MeOH): 231 (4.46), 274 (4.38), 352 (3.90). ^{1}H-NMR ($CDCl_3$): 12.02 (br, NH); 9.11 (s, H-C(7)); 7.14-8.12 (14 arom. H); 7.07 (m, C-(1')); 6.73-6.83 (4 arom. H); 5.21 (d, OH-C(3')); 4.43 (m, H-C(3')); 3.96 (m, H-C(4')); 3.96 (s, MeO); 3.93 (s, MeO); 3.31 (m, H-C(5')); 3.17 (m, H-C(5")); 2.84 (m, H-C(2')); 2.18 (m, H-C(2")). Anal. calc. for $C_{38}H_{34}N_4O_7$ (658.7): C, 69.29; H, 5.20; N, 8.51. Found: C, 69.00; H, 5.36; N, 8.17.

23: UV (MeOH): 232 (4.48), 274 (4.36), 352 (3.91). ^{1}H-NMR ($CDCl_3$): 12.05 (br, NH); 9.37 (s, H-C(7)); 8.19 (2 arom. H); 7.18-7.61 (12 arom. H); 7.00 (m, C-(1')); 6.88 (4 arom. H); 5.31 (d, OH-C(3')); 4.50 (m, H-C(3')); 4.15 (m, H-C(4')); 3.73 (s, 2 MeO); 3.22 (m, H-C(5')); 3.02 (m, H-C(5")); 2.77 (m, H-C(2')); 2.47 (m, H-C(2")). Anal. calc. for $C_{38}H_{34}N_4O_7 \cdot 0.5\ H_2O$ (667.7): C, 68.35; H, 5.13; N, 8.39. Found: C, 68.59; H, 5.20; N, 8.29.

7-Phenyl-1-(2-deoxy-5-*O*-dimethoxytrityl-β-D-ribofuranosyl)lumazine (24). Compound **16** (1.0 g; 2.81 mmol) was coevaporated in anhydrous pyridine (10 ml), then dissolved in anhydrous pyridine (20 ml) and dimethoxytrityl chloride (1.1 g; 3.25 mmol) added. After stirring over night at r.t., the reaction mixture was diluted with a cold saturated solution of $NaHCO_3$ (100 ml), extracted with CH_2Cl_2 (2x100 ml) and the pooled extracts dried over Na_2SO_4. After filtration the solution was again evaporated, the residue dissolved in little CH_2Cl_2 and applied for chroma-tographical purification by FC (silica gel, 25x4 cm, CH_2Cl_2, then gradient CH_2Cl_2-MeOH 199:1 - 194:4). Yield: 1.5 g (81%) as a foam. UV (MeOH): 225 (4.57), 272sh (3.96), 346 (4.23). ^{1}H-NMR ($CDCl_3$): 9.08 (br, NH), 8.92 (s,

H-C(6)); 7.93 (2 arom. H); 7.50 (3 arom. H); 7.04- 7.35 (9 arom. H, C-(1')); 6.65 (4 arom. H); 4.70 (m, H-C(3')); 3.94 (m, H-C(4')); 3.66 (s, 2 MeO); 3.42 (m, H-C(5')); 3.25 (m, H-C(5")); 3.00 (m, H-C(2')); 2.32 (m, H-C(2")); 2.21 (d, OH-C(3')). Anal. calc. for $C_{38}H_{34}N_4O_7$ (658.7): C, 69.29; H, 5.20; N, 8.51. Found: C, 68.79; H, 5.25; N, 8.36.

7-Phenyl-1-(2-deoxy-5-*O*-dimethoxytrityl-α-D-ribofuranosyl)lumazine (25).

Analogous to the procedure of **24** from **17** (0.5 g; 1.40 mmol) and dimethoxytrityl chloride (1.41 g; 4.20 mmol) of in anhydrous pyridine (20 ml). Yield: 0.86 g (93%) as a foam. UV (MeOH): 229 (4.50), 272sh (4.02), 347 (4.15). ^{1}H-NMR ($CDCl_3$): 9.04 (br, NH), 8.91 (s, H-C(6)); 7.89 (2 arom. H); 7.83 (m, H-C-(1')); 7.04-7.43 (12 arom. H); 6.69 (4 arom. H); 4.87 (d, OH-C(3')); 4.35 (m, H-C(3'), H-C(4')); 3.63 (s, MeO); 3.60 (s, MeO); 3.40 (m, H-C(5')); 3.16 (m, H-C(2')); 3.05 (m, H-C(5")); 2.53 (m, H-C(2")). Anal. calc. for $C_{38}H_{34}N_4O_7 \cdot H_2O$ (676.7): C, 67.45; H, 5.36; N, 8.28. Found: C, 67.65; H, 5.19; N, 7.91.

6-(4-Biphenyl)-1-(2-deoxy-5-*O*-dimethoxytrityl-β-D-ribofuranosyl)lumazine (26) and 6-(4-Biphenyl)-1-(5-*O*-dimethoxytrityl-2-deoxy-α-D-ribofuranosyl)lumazine (27).

The mixture of **10** and **11** (3.5 g; 5.23 mmol) was suspended in MeOH (100 ml), then 2N NaOMe (20 ml) was added and the solution was stirred vigorously at r.t. for 2 h. Water (1 ml) was added and the mixture was neutralized with 10% acetic acid to pH 7. The resulting precipitate was filtered off after standing for 12 h at +5 °C, washed with H_2O, EtOH and ether, to give the mixture of **18** and **19**. Yield: 1.86 g (82%). This anomeric mixture (1.86 g; 4.30 mmol) was twice coevaporated with anhydrous pyridine (10 ml), dissolved in anhydrous pyridine (20 ml), and then 4,4'-dimethoxytrityl chloride (1.89 g; 5.59 mmol) added. After stirring overnight at r.t., the mixture was diluted with CH_2Cl_2 and neutralized with a cold saturated $NaHCO_3$ (100 ml), extracted with CH_2Cl_2 (2x100 ml) and the pooled extracts were dried over Na_2SO_4. The solution was evaporated after filtration and the residue chromatographically separated by FC (silica gel, 25 x 4 cm, CH_2Cl_2 (300 ml), CH_2Cl_2-MeOH 199:1 (200 ml), 198.5:1.5 (200 ml), 198:2 (200 ml), 197.5:2.5 (200 ml), 197:3 (200 ml), 196.5:3.5 (200 ml), 196:4 (200 ml), to give after the evaporation of the product containing fractions compound **26** (1.6 g; 51%) and **27** (0.69 g; 22%) as a solid foam.

26: UV (MeOH): 230sh (4.52), 296 (4.46), 358 (4.06). ^{1}H-NMR ($CDCl_3$): 9.49 (br, NH), 8.81 (s, H-C(7)); 7.14-8.10 (18 arom. H, H-C(1')); 6.74-6.79 (4 arom. H); 4.84 (m, H-C(3')); 4.06 (m, H-C(4')); 3.70 (s, 2 MeO); 3.56 (m, H-C(5')); 3.40 (m, H-C(5")); 3.00 (m, H-C(2')); 2.50 (br., OH-C(3')); 2.39 (m, H-C(2")). Anal. calc. for $C_{44}H_{38}N_4O_7 \cdot H_2O$ (752.8): C, 70.20; H, 5.36; N, 7.44. Found: C; 70.12; H, 5.22; N, 7.26.

27. UV (MeOH): 229sh (4.57), 296 (4.56), 359 (4.09). ^{1}H-NMR ($CDCl_3$): 9.46 (br, NH), 9.10 (s, H-C(7)); 8.16 (2 arom. H); 7.15-7.74 (17 arom. H, H-C(1')); 6.85 (4 arom. H); 5.00 (d, OH-C(3')); 4.37-4.48 (m, H-C(3'), H-C(4')); 3.77 (s, 2 MeO); 3.36 (m, H-C(5')); 3.15 (m, H-C(5")); 3.05 (m, H-C(2')); 2.54 (m, H-C(2")). Anal. calc. for $C_{44}H_{38}N_4O_7$ (734.8): C, 71.92; H 5.21; N 7.62. Found: C, 71.66; H, 5.36; N 7.58.

7-(4-Biphenyl)-1-(2-deoxy-5-*O*-dimethoxytrityl-β-D-ribofuranosyl)lumazine (28).

Analogous to the procedure of **24** from **20** (0.53 g; 1.22 mmol) and dimethoxytrityl chloride

(1.04 g; 3.26 mmol) of in anhydrous pyridine.(20 ml). Yield: 0.7 g (78%) as a foam. UV (MeOH): 234 (4.63), 269sh (4.05), 359 (4.49). ^{1}H-NMR ($CDCl_3$): 8.99 (s, H-C(6)); 8.05 (2 arom. H); 7.74 (2 arom. H); 7.67 (2 arom. H); 7.35- 7.52 (6 arom. H, C-(1')); 7.24 (4 arom. H); 7.12 (3 arom. H); 6.70 (4 arom. H); 4.80 (m, H-C(3')); 4.07 (m, H-C(4')); 3.67 (s, 2 MeO); 3.52 (m, H-C(5')); 3.36 (m, H-C(5")); 3.09 (m, H-C(2')); 2.43 (m, H-C(2")). Anal. calc. for $C_{44}H_{38}N_4O_7 \cdot H_2O$ (752.9): C, 70.20; H, 5.36; N, 7.44. Found: C, 70.33; H, 5.40; N, 7.30.

7-(4-Biphenyl)-1-(2-deoxy-5-*O*-dimethoxytrityl-α-D-ribofuranosyl)lumazine (29). Analogous to the procedure of **24** from **21** (0.27 g; 0.62 mmol) and dimethoxytrityl chloride (0.45 g; 1.33 mmol) of in anhydrous pyridine (20 ml). Yield 0.31 g (68%) as a foam. UV (MeOH): 234 (4.70), 269sh (4.22), 362 (4.50). ^{1}H-NMR ($CDCl_3$): 9.52 (br, NH), 9.12 (s, H-C(6)); 8.02 (2 arom. H); 7.93 (m, C-(1'));7.12-7.52 (16 arom. H) 6.76 (4 arom. H); 5.06 (d, OH-C(3')); 4.46 (m, H-C(3'), H-C(4')); 3.68 (s, MeO); 3.66 (s, MeO); 3.50 (m, H-C(5')); 3.25 (m, H-C(5")); 3.12 (m, H-C(2')); 2.62 (m, H-C(2")). Anal. calc. for $C_{44}H_{38}N_4O_7 \cdot H_2O$ (752.9): C, 70.20; H, 5.36; N, 7.44. Found: C, 70.56; H,5.56; N, 7.10.

6-Phenyl-1-(2-deoxy-5-*O*-dimethoxytrityl-β-D-ribofuranosyl)lumazine-3′-*O*-(2-cyanoethyl, N,N-diisopropyl)phosphoramidite (30). Compound **22** (0.4 g; 0.62 mmol) was dissolved in CH_2Cl_2 (10 ml). (2-cyanoethoxy)-bis-(diisopropylamino)phosphane (0.368 g; 1.22 mmol) and tetrazole (28 mg; 0.41 mmol) was added to the reaction mixture under N_2. After stirring for 2 h CH_2Cl_2 (50 ml) was added, the mixture was neutralized with saturated aqueous $NaHCO_3$ solution (50 ml) and the organic phase dried over Na_2SO_4. The solvent was removed *in vacuo* and the residue purified by FC (silica gel, 10 x 2 cm) with petroleum ether - ethyl acetate 1:2. Compound **30** was obtained after evaporation of the product fractions and co-evaporation with CH_2Cl_2. Yield: 0.40 g (77%) as a foam. UV (MeOH): 233 (4.41), 275 (4.41), 352 (3.95). ^{31}P-NMR ($CDCl_3$): 149.42, 149.09. Anal. calc. for $C_{46}H_{51}N_6O_8P$ (846.9): C, 65.24; H, 6.07; N, 9.92. Found: C, 64.78; H, 5.97; N, 9.71.

7-Phenyl-1-(2-deoxy-5-*O*-dimethoxytrityl-β-D-ribofuranosyl)lumazine-3′-*O*-(2-cyanoethyl, N,N-diisopropyl)phosphoramidite (31). Analogous to the procedure of **30** from **24** (0.6 g; 0.91 mmol) and (2-cyanoethoxy)-bis-(diisopropylamino)phosphane (0.41g; 1.36 mmol) and tetrazole (32 mg; 0.455 mmol) in CH_2Cl_2 (10 ml). Yield: 0.70 g (91%) as a foam. UV (MeOH): 229 (4.51), 271sh (3.91), 347 (4.21). ^{31}P-NMR ($CDCl_3$): 149.77, 149.42. Anal. calc. for $C_{46}H_{51}N_6O_8P$ (846.9): C, 65.24; H, 6.07; N 9.92. Found: C, 65.05; H, 5.99; N, 9.76.

6-(4-Biphenyl)-1-(2-deoxy-5-*O*-dimethoxytrityl-β-D-ribofuranosyl)lumazine-3′-*O*-(2-cyanoethyl, N,N-diisopropyl)phosphoramidite (32). Analogous to the procedure of **30** from **26** (0.6 g; 0.82 mmol) (2-cyanoethoxy)-bis-(diisopropylamino)phosphane (0.37g; 1.22 mmol) and and tetrazole (28 mg; 0.41 mmol) in CH_2Cl_2 (10 ml). Yield: 0.62 g (81%) as a foam. UV (MeOH): 231 (4.42), 296 (4.54), 360 (4.04). ^{31}P-NMR ($CDCl_3$): 149.22, 149.05.

Anal. calc. for C_{52} $H_{55}N_6O_8P$ (932.0): C, 67.67; H, 6.01; N, 9.10. Found: C, 67.62; H, 5.96; N, 8.95.

7-(4-Biphenyl)-1-(2-deoxy-5-*O*-dimethoxytrityl-β-D-ribofuranosyl)lumazine-3′-O-(2-cyanoethyl, N,N-diisopropyl)phosphoramidite (33). Analogous to the procedure of **30** from **28** (1.1 g; 0.82 mmol), (2-cyanoethoxy)-bis-(diisopropylamino)phosphane (0.68 g; 2.25 mmol) and tetrazole (53 mg; 0.75 mmol) in CH_2Cl_2 (10 ml). Yield: 0.84 g (60%) as a foam. UV (MeOH): 234 (4.55), 271sh (4.03), 359 (4.43). ^{31}P-NMR ($CDCl_3$): 149.81, 149.48. Anal. calc. for C_{52} $H_{55}N_6O_8P$ (932.0): C, 67.67; H, 6.01; N, 9.10. Found: C, 67.32; H, 5.94; N, 8.95.

Melting curves of oligonucleotides were measured at 260 nm in Na_2HPO_4/NaH_2PO_4 buffer at pH 7.0; Na^+ conc. 0.03 M .

ACKNOWLEDGEMENTS

We thank the Alexander von Humboldt Foundation for a fellowship and the Fonds der Chemischen Industrie for financial support of these investigations.

REFERENCES

1. Part LVII: Rhie S-Y.; Pfleiderer W. *Nucleosides & Nucleotides* **1994**, *13*, 1425.
2. Ritzmann G.; Pfleiderer, W. *Chem. Ber.* **1973**, *106*, 1401.
3. Jochims J.C.; Pfleiderer W.; Kobayashi K.; Ritzmann G.; Hutzenlaub W. *Chem. Ber.* **1973**, *106*, 2975.
4. Pfleiderer W.; Ritzmann G.; Harzer K.; Jochims J.C. *Chem. Ber.* **1973**, *106*, 2982.
5. Kobayashi K.; Pfleiderer W. *Chem. Ber.* **1976**, *109*, 3159.
6. Kobayashi K.; Pfleiderer W. *Chem. Ber.* **1976**, *109*, 3194.
7. Ritzmann G.; Ienaga K.; Pfleiderer W. *Liebigs Ann. Chem.* **1977**, 1217.
8. Lutz H.; Pfleiderer W. *Carbohydr. Res.* 1984, *130*, 179.
9. Al-Masoudi N.A.; Pfleiderer W. *Nucleosides & Nuicleotides* **1989**, *8*, 1485.
10. Al-Masoudi N.A.; Pfleiderer W. *Pteridines* **1990**, *2*, 9.
11. Cao X.; Pfleiderer W.; Rosemeyer H.; Seela F.; Bannwarth W.; Schönholzer P. *Helv. Chim. Acta* **1992**, *75*, 1267.
12. Bannwarth W.; Pfleiderer W.; Müller F. *Helv. Chim. Acta* **1991**, *74*, 1991.
13. Bannwarth W.; Müller F. *Helv. Chim. Acta* **1991**, *74*, 2000.
14. Pfleiderer W.; Hutzenlaub W. *Chem. Ber.* **1973**, *106*, 3149.
15. Hoffer M. *Chem. Ber.* **1960**, *93*, 2777.
16. Birkofer L.; Ritter A.; Kühlthau H.P. *Chem. Ber.* **1964**, *97*, 934.
17. Birkofer L.; Ritter A. *Angew.Chem., Int. Ed. Engl.* **1965**, *4*, 417.

18. Niedballa U.; Vorbrüggen H. *J. Org. Chem.* **1974**, *39*, 3654; 3660; 3664; 3668.
19. Zemplen G.; Geres A.; Hadacsy J. *Ber. Deut. Chem. Ges.* **1936**, *69*, 1827.
20. Cavallini G. *J. Med. Chem.* **1964**, *7*, 255.