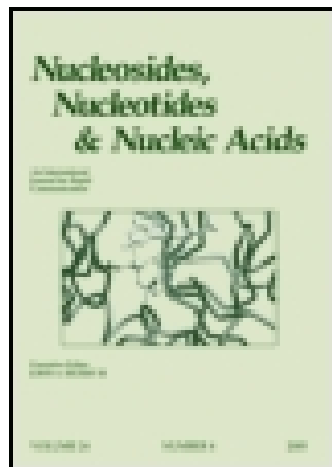


This article was downloaded by: [Michigan State University]

On: 12 February 2015, At: 11:20

Publisher: Taylor & Francis

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Nucleosides and Nucleotides

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/Incn19>

Synthesis of Base-Modified Oligonucleotides Containing 6- and 7-Aryl Lumazines

Yuris Maurinsh^a & Wolfgang Pfeleiderer^a

^a Latvian Institute of Organic Synthesis, 21 Aizkraukles Str., LV-1006 Riga, Latvia; Fakultät für Chemie, Universität Konstanz, Universitätsstrasse 1, D-75434, Konstanz, Germany

Published online: 16 Feb 2007.

To cite this article: Yuris Maurinsh & Wolfgang Pfeleiderer (1995) Synthesis of Base-Modified Oligonucleotides Containing 6- and 7-Aryl Lumazines, *Nucleosides and Nucleotides*, 14:3-5, 795-798

To link to this article: <http://dx.doi.org/10.1080/15257779508012473>

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at <http://www.tandfonline.com/page/terms-and-conditions>

CHEMISTRY

SYNTHESIS OF BASE-MODIFIED OLIGONUCLEOTIDES CONTAINING 6- AND 7-ARYL LUMAZINES

Yuris Maurinsh* and Wolfgang Pfeleiderer

*Latvian Institute of Organic Synthesis, 21 Aizkraukles Str., LV-1006 Riga, Latvia;
Fakultät für Chemie, Universität Konstanz, Universitätsstrasse 1, D-75434 Konstanz, Germany

Abstract. 6-Phenyl, 7-phenyl, 6-(4-biphenyl)-, 7-(4-biphenyl)lumazine N¹-(2'-deoxy-D-ribofuranosides) were synthesized and incorporated in the different positions of self-complementary oligodeoxyribonucleotides, and the influence of modifications on the melting points of duplexes was studied.

Lumazine N¹-(2'-deoxy-D-ribofuranosides), which can be regarded as structural analogs of thymidine, bearing substituents both at 6- and 7-position of the lumazine moiety or unsubstituted, were synthesized and incorporated into oligonucleotides,¹⁻⁴ to study the influence of lumazine moiety on hybridization and fluorescence properties of oligonucleotides. Now we are reporting the synthesis of monosubstituted 6- or 7-phenyl and 6- or 7-(biphenyl)lumazine N¹-(2'-deoxy-D-ribofuranosides).

Synthesis of nucleotides **6-13** was accomplished by the reaction of lumazine derivatives **1-4** with 2-deoxy-3,5-di-O-p-toluoyl-D-erythropentofuranosyl chloride **5** (Scheme). Lumazines **1-4** (1.4 eq.) were silylated with hexamethyldisilazane and trimethylchlorosilane in acetonitrile, ZnCl₂ (0.5 eq.), and a solution of **5** (1.0 eq.) in CH₂Cl₂ during 3 h at -25°C was dropped into the reaction mixture. An anomeric mixture of nucleosides **6-13** was obtained after flash chromatography. Increasing the reaction temperature, amount of ZnCl₂, sugar **5**, decreasing the addition time of **5**, or changing the solvents (chloroform, 1,2-dichloroethane) led to the increasing amounts of α-anomers **10-13** or to the mixtures of N¹, N³-diribosides (up to 30%).

Separation of the anomers by the recrystallization from chloroform-acetone was successful only in the case of 7-substituted lumazines which allowed to obtain β-anomers **7** (39%) and **9** (58%) and α-anomers **11** (16%) and **13** (19%), which were deacylated with NaOMe in MeOH to give the deprotected nucleosides **15**, **17**, **19** and **21** (yield 86-93%). Inseparable anomeric mixtures (both by recrystallization and chromatography) of 6-substituted ribosides **6/10** and **8/12** were deprotected with NaOMe in MeOH, with treatment by DMTrCl to obtain 5'-dimethoxytrityl derivatives **22/26** and **24/28**, which could be easily separated by flash chromatography. Detritylation with 1% p-toluenesulphonic acid in CH₂Cl₂/MeOH (4:1) gave the individual nucleosides **14**, **16**, **18** and **20** (yield 66-89%). Treatment of **15**, **17**, **19** and **21** with DMTrCl in pyridine gave 5'-dimethoxytrityl derivatives **23**, **25**, **27** and **29**.



TABLE
The list of prepared oligonucleotides and their T_m values^a

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

^aThe transitions were measured at 260 nm in NaHPO₄/NaH₂PO₄ buffer pH 7; 0.03 M [Na⁺].

^bNot determinable.

The phosphoramidites **30-33** were synthesized by the reaction of **22-25** with (2-cyanoethoxy)bis(diisopropylamino)phosphine) in the presence of tetrazole in CH₂Cl₂ with 60-91% yield.

A series of self-complementary oligonucleotides containing 6-phenyllumazine, 7-phenyllumazine, 6-(4-biphenyl)lumazine, and 7-(4-biphenyl)lumazine as modified bases in the different positions were synthesized (Table) using solid-phase phosphoramidite method on Applied Biosystems synthesizer 380B in 0.5 μ mol scale applying NPE/NPEOC strategy.⁵ The coupling yield of modified phosphoramidites was monitored by colorimetric assay of the released dimethoxy trityl kation, ranging between 95.5% and 99.5%. Purity of the synthesized oligonucleotides was controlled by reversed-phase HPLC and polyacryl gel electrophoresis.

As it follows from the Table, the presence of lumazine bases can influence the stability of self-complementary duplexes in different ways. Incorporation of phenyllumazines at the 5'-end of the strand did not change the stability of duplex, whereas presence of one or two 7-phenyllumazine moieties (sequence 4 and 5) in the middle of the strand increased the stability of duplex for 1.1°C and 1.9°C, respectively. 7-(4-Biphenyl)lumazine, similarly positioned (sequences 10 and 11), raised the melting point for 2.9°C and 9.8°C, respectively. Two 6-phenyllumazine nucleotides (sequence 2) increased the T_m of duplex for 5.1°C, in contrary to 6-(4-biphenyl)lumazine which, probably due to the orientation of bulky biphenyl group, caused the decrease of T_m by 3.1°C (sequence 7) in the first case or hindered the formation of duplex at all in the second case (sequence 8).

REFERENCES

1. Ritzmann, G.; Ienaga, K.; Pfeleiderer, W. *Liebigs Ann. Chem.* **1977**, 1217.
2. Bannwarth, W.; Pfeleiderer, W.; Müller, F. *Helv. Chim. Acta* **1991**, *74*, 1991.

3. Bannwarth, W.; Müller, F. *Helv. Chim. Acta* **1991**, *74*, 2000.
4. Rösler, A.; Pfeleiderer, W. *Collect. Czech. Chem. Commun.* **1993**, *58*, special issue, 187.
5. Himmelsbach, F.; Schulz, B.S.; Trichtringer, T.; Charubala, R.; Pfeleiderer, W. *Tetrahedron* **1984**, *40*, 59.