This article was downloaded by: [The Aga Khan University] On: 17 October 2014, At: 04:06 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, Nucleotides and Nucleic Acids

Publication details, including instructions for authors and subscription information: http://www.tandfonline.com/loi/lncn20

DNA Containing Non-Nucleosidic Phenanthrene Building Blocks with Asymmetrical Linkers

Simon M. Langenegger^a, Vladimir L. Malinovskii^a, Daniel Wenger^a, Sarah Werder^a & Robert Häner^a

 $^{\rm a}$ Department of Chemistry and Biochemistry , University of Bern , Bern, Switzerland

Published online: 10 Dec 2007.

To cite this article: Simon M. Langenegger , Vladimir L. Malinovskii , Daniel Wenger , Sarah Werder & Robert Häner (2007) DNA Containing Non-Nucleosidic Phenanthrene Building Blocks with Asymmetrical Linkers, Nucleosides, Nucleotides and Nucleic Acids, 26:8-9, 901-903, DOI: 10.1080/15257770701506319

To link to this article: <u>http://dx.doi.org/10.1080/15257770701506319</u>

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



DNA CONTAINING NON-NUCLEOSIDIC PHENANTHRENE BUILDING BLOCKS WITH ASYMMETRICAL LINKERS

Simon M. Langenegger, Vladimir L. Malinovskii, Daniel Wenger,

Sarah Werder, and Robert Häner Department of Chemistry and Biochemistry, University of Bern, Bern, Switzerland

□ The synthesis and hybridization properties of oligonucleotides containing phenanthrene building blocks with non-nucleosidic linkers of different length are described. It was found that the length of the linkers, as well as the combination of unequal linkers can have a substantial influence on the thermal stability of the modified DNA.

Keywords phenanthrene building blocks; non-nucleosidic linkers; thermal stability

Modified oligonucleotides have found widespread application as diagnostic and research tools. Furthermore, due to the repetitive, well-defined arrangement of their building blocks, nucleic acids, and related types of oligomers are ideal objects for the designed construction of larger assemblies and architectures.^[1–7] In previous work we showed that nonnucleosidic phenanthrene building blocks with identical linkers on both sides can be used as base surrogates leading to stable hybrids.^[8,9] We have now extended our studies to the investigation of hybrids containing nonidentical linkers. These data are described herein.

The synthesis of the phenanthrene-derived phosphoramidite building blocks containing linkers of different lengths is shown in Scheme 1. The preparation of the phenanthrene derivatives started from phenanthrene-3,6-dicarboxylic acid (1), which had been prepared according to the method described previously.^[8,10] Derivatization with the corresponding α,ω -aminoalcohols gave the amides **2a–d**. Subsequent phosphitylation provided the phosphoramidites **3a–d**. The phenanthrene-derived phosphoramidite building blocks **3a–d** were subsequently incorporated into oligonucleotides by standard oligonucleotide synthesis. Coupling yields with the modified phosphoramidites were equal to the ones obtained with automated nucleoside building blocks. After deprotection (conc. ammonia,

Address correspondence to Robert Häner, Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, Bern CH 3012, Switzerland. E-mail: robert.haener@ioc.unibe.ch



SCHEME 1 Synthesis of the phenanthrence-derived phosphoramidite building blocks.

55°C), all oligomers were purified by reversed-phase HPLC and characterized by high-resolution mass spectrometry.

Thermal denaturation experiments revealed that all phenanthrene containing oligonucleotides form a stable duplex. The data indicate that the linker length is an important factor for the overlap of the phenanthrene residues. A remarkable destabilisation results if the linker is too short for

Entry	Duplex	Tm(°C)	$\Delta T(^{\circ}C)$
1	5′ AGC TCG GTC ATC GAG AGT GCA	68.0	
	3' TCG AGC CAG TAG CTC TCA CGT		
2	5′ AGC TCG GTC A 2P2 C GAG AGT GCA	62.3	-6.7
	3′ TCG AGC CAG T 2P2 G CTC TCA CGT		
3	5' AGC TCG GTC A 4P4 C GAG AGT GCA	67.3	-0.7
	3' TCG AGC CAG T4P4G CTC TCA CGT		
4	5′ AGC TCG GTC A 2P2 C GAG AGT GCA	66.3	-1.7
	3' TCG AGC CAG T4P4G CTC TCA CGT		
5	5' AGC TCG GTC A 4P4 C GAG AGT GCA	60.0	-8.0
	3′ TCG AGC CAG T 2P2 G CTC TCA CGT		
6	5' AGC TCG GTC A 2P4 C GAG AGT GCA	66.2	-1.8
	3′ TCG AGC CAG T 2P4 G CTC TCA CGT		
7	5' AGC TCG GTC A 4P2 C GAG AGT GCA	68.0	0.0
	3′ TCG AGC CAG T 4P2 G CTC TCA CGT		
8	5′ AGC TCG GTC A 2P4 C GAG AGT GCA	68.0	0.0
	3′ TCG AGC CAG T 4P2 G CTC TCA CGT		
9	5′ AGC TCG GTC A 4P2 C GAG AGT GCA	69.3	1.3
	3′ TCG AGC CAG T 2P4 G CTC TCA CGT		
mPn		-H ()-o n	

TABLE 1 Influence of the replacement of natural base pairs by phenanthrene building blocks containing different types of non-nucleosidic linkers on the thermal stability of duplex DNA (Conditions: 100 mM NaCl, pH 7.4, 10 mM TrisHCl, 1 μ M DNA duplex).

sufficient overlap of the phenanthrenes, (see Table 1, entries 2 and 3). If phenanthrene building blocks with linkers of different length are placed in opposite positions, a difference of 6.3°C in the Tm (melting temperature) is observed between the two different possibilities (see Table 1, entries 4 and 5). Thus, it seems that the interaction of the phenanthrene units with the adjacent base pairs has a significant influence on the thermal stability of the duplex.

Hybrids with asymmetrical phenanthrene building blocks (i.e., when the two linkers on a particular phenanthrene are of different length) are generally well tolerated (Table 1, entries 6–9). The highest Tm value was observed with the hybrid containing the building block **3c** (see Scheme 1) in each oligomer (Table 1, entry 9).

In conclusion, oligodeoxynucleotides containing 3,6-disubstituted phenanthrenes with various combinations of non-nucleosidic linkers were prepared and investigated. The thermal stability of the hybrids was found to be influenced by the length of the linkers, as well as by the relative arrangement of the different linkers. In addition, also the oligonucleotide sequence is important for the stability of the respective hybrids.

REFERENCES

- 1. Seeman, N.C. DNA in a material world. Nature 2003, 421, 427-431.
- 2. Samori, B.; Zuccheri, G. DNA codes for nanoscience. Angew. Chem. Int. Ed. 2005, 44, 1166-1181.
- Shih, W.M.; Quispe, J.D.; Joyce, G.F. A 1.7-kilobase single-stranded DNA that folds into a nanoscale octahedron. *Nature* 2004, 427, 618–621.
- Mirkin, C.A. Programming the assembly of two- and three-dimensional architectures with DNA and nanoscale inorganic building blocks. *Inorg. Chem.* 2000, 39, 2258–2272.
- Chworos, A.; Severcan, I.; Koyfman, A.Y.; Weinkam, P.; Oroudjev, E.; Hansma, H.G.; Jaeger, L. Building programmable jigsaw puzzles with RNA. *Science* 2004, 306, 2068–2072.
- Claridge, S.A.; Goh, S.L.; Frechet, J.M.J.; Williams, S.C.; Micheel, C.M.; Alivisatos, A.P. Directed assembly of discrete gold nanoparticle groupings using branched DNA scaffolds. *Chemistry of Materials* 2005, 17, 1628–1635.
- Wengel, J. Nucleic acid nanotechnology—Towards Angstrom-scale engineering. Org. Biomol. Chem. 2004, 2, 277–280.
- Langenegger, S.M.; Häner, R. DNA containing phenanthroline- and phenanthrene-derived, nonnucleosidic base surrogates. *Tetrahedron Lett.* 2004, 45, 9273–9276.
- Langenegger, S.M.; Häner, R. A DNA mimic made of non-nucleosidic phenanthrene building blocks. *ChemBioChem* 2005, 6, 2149–2152.
- Langenegger, S.M.; Häner, R. The effect of a non-nucleosidic phenanthrene building block on DNA duplex stability. *Helv. Chim. Acta* 2002, 85, 3414–3421.