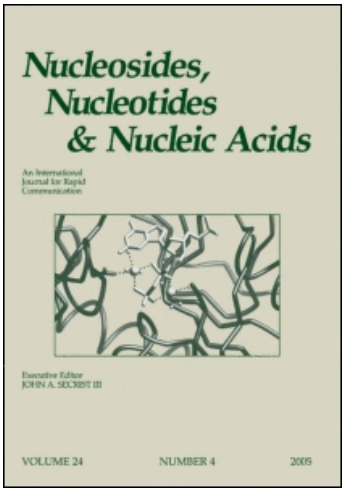

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

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Online publication date: 09 August 2003

To cite this Article Børsting, Philip and Nielsen, Poul(2003) 'Conformationally Restricted Dinucleotides: Tandem Ring-Closing Metathesis and Hydrogenation Approach', Nucleosides, Nucleotides and Nucleic Acids, 22: 5, 1139 — 1141
To link to this Article: DOI: 10.1081/NCN-120022820
URL: http://dx.doi.org/10.1081/NCN-120022820

NUCLEOSIDES, NUCLEOTIDES & NUCLEIC ACIDS
Vol. 22, Nos. 5–8, pp. 1139–1141, 2003

Conformationally Restricted Dinucleotides: Tandem Ring-Closing Metathesis and Hydrogenation Approach

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ABSTRACT

Cyclic dinucleotides with saturated connections between a nucleobase and the phosphate are synthesised using a tandem ring-closing metathesis (RCM) and hydrogenation protocol and found to be significantly stabilised towards ammonia.

Key Words: Conformational restriction; Dinucleotides; Ring-closing metathesis.

Conformationally restricted nucleic acid fragments such as dinucleotides have been introduced as mimics of tertiary nucleic acid structures.[1] The introduction of the functional group tolerant ruthenium catalysts for metathesis reactions[2] has opened new ways for introducing large rings into biomolecules such as peptide structures.[3] We have applied RCM-reactions in the synthesis of conformationally restricted di- and trinucleotide structures containing unsaturated rings involving phosphortriester internucleoside linkages.[4–6] Hereby, we present the application

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DOI: 10.1081/NCN-120022820
1525-7770 (Print); 1532-2335 (Online)

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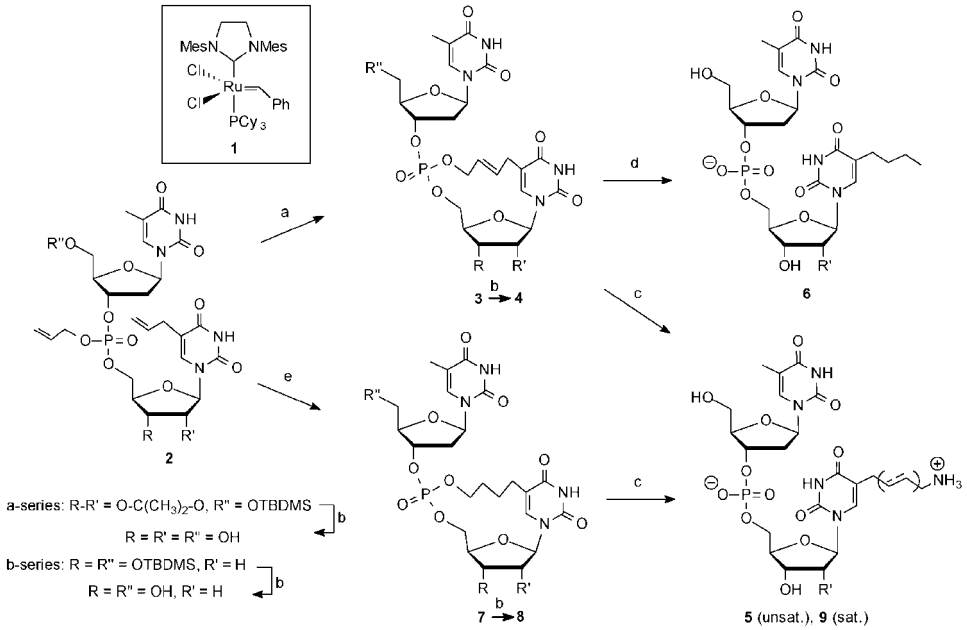

Scheme 1. a) **1**, CH_2Cl_2; b) 90% TFA; c) conc. NH_3; d) H_2, Pd/C, MeOH; e) **1**, CH_2Cl_2 then 1000 psi H_2.

of **1** as an efficient metathesis and hydrogenation catalyst[7] towards cyclic dinucleotides.[5,6]

Two different dinucleotides **2a**/**b** each containing two allyl-groups were prepared from standard phosphoramidite chemistry (Sch. 1). RCM-reactions using **1** afforded the two cyclic dinucleotides **3a**/**b** in medium yields.[5,6] These were conveniently treated with TFA to give deproteced compounds **4a**/**b**. However, instability towards basic conditions was exemplified by the fast and quantitative reactions with ammonia affording **5a**/**b**. This base lability could at least in part be deduced to the allylic nature of the phosphortriester moiety. Therefore, **4a** was treated with standard palladium catalysed hydrogenation conditions giving, surprisingly, the doubly reduced compound **6a**. This problem was solved by using **1** as both RCM and hydrogenation catalyst.[7] Thus, the dinucleotides **2a**/**b** were treated with **1**, and after completion of the RCM reaction as monitored by TLC, the reaction mixture was subjected to 1000 psi H_2 and the saturated cyclic dinucleotides **7a**/**b** were obtained in good yields.[6] Deprotection afforded **8a**/**b**. Subsequently, these compounds were subjected to ammonia and found to be significantly more stable than the unsaturated counterparts **4a**/**b** affording only very slowly the ring-opened dinucleotides **9a**/**b**.

ACKNOWLEDGMENTS

The Nucleic Acid Center is funded by the Danish National Research Foundation for the studies on nucleic acid chemical biology.

REFERENCES

1. Sekine, M.; Kurasawa, O.; Shohda, K.; Seio, K.; Wada, T. Eur. J. Org. Chem. **2001**, 1989–1999.
2. Trnka, T.M.; Grubbs, R.H. Acc. Chem. Res. **2001**, *34*, 18–29.
3. Reichwein, J.F.; Versluis, C.; Liskamp, R.M.J. J. Org. Chem. **2000**, *65*, 6187–6195.
4. Sørensen, A.M.; Nielsen, P. Org. Lett. **2000**, *2*, 4217–4219.
5. Børsting, P.; Sørensen, A.M.; Nielsen, P. Synthesis **2002**, 797–801.
6. Børsting, P.; Nielsen, P. Chem. Commun. **2002**, 2140–2141.
7. Louie, J.; Bielawski, C.W.; Grubbs, R.H. J. Am. Chem. Soc. **2001**, *123*, 11,312–11,313.

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