

This article was downloaded by:

On: 27 January 2011

Access details: *Access Details: Free Access*

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.informaworld.com/smpp/title~content=t713597286>

Molecular and Crystal Structure of d(CGCGmo⁴CG): N⁴-Methoxy-cytosineguanine Base Pairs in Z-DNA

L. Van Meervelt^{ab}; M. H. Moore^a; P. Kong Thoo Lin^c; D. M. Brown^c; O. Kennard^a

^a University Chemical Laboratory, Cambridge, U. K. ^b Lab. voor Kristallografie, Leuven, Belgium ^c M. R. C. Laboratory of Molecular Biology, Cambridge, U. K.

To cite this Article Van Meervelt, L. , Moore, M. H. , Lin, P. Kong Thoo , Brown, D. M. and Kennard, O.(1990) 'Molecular and Crystal Structure of d(CGCGmo⁴CG): N⁴-Methoxy-cytosineguanine Base Pairs in Z-DNA', *Nucleosides, Nucleotides and Nucleic Acids*, 9: 3, 467 – 469

To link to this Article: DOI: 10.1080/07328319008045177

URL: <http://dx.doi.org/10.1080/07328319008045177>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

**MOLECULAR AND CRYSTAL STRUCTURE
OF d(CGCGmo⁴CG) : N⁴-METHOXYCYTOSINE-
GUANINE BASE PAIRS IN Z-DNA.**

L. Van Meervelt^{1,3}, M. H. Moore¹, P. Kong Thoo Lin², D. M. Brown², O. Kennard¹.

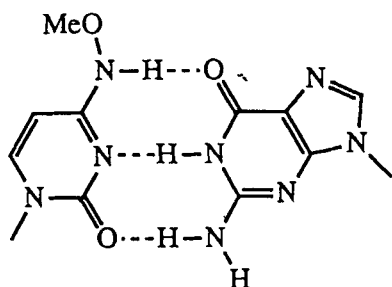
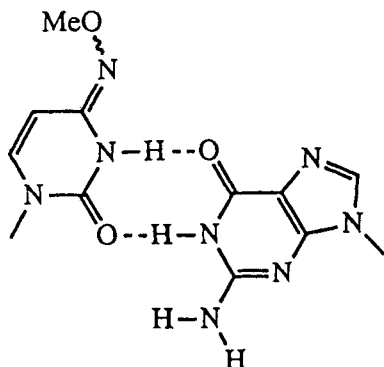
¹University Chemical Laboratory, Lensfield Road, Cambridge, U. K.

²M. R. C. Laboratory of Molecular Biology, Hills Road, Cambridge, U. K.

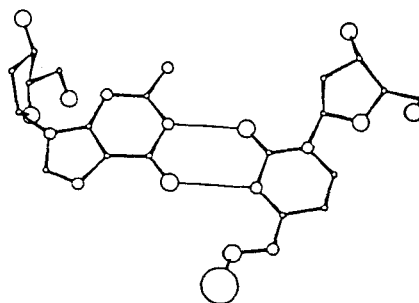
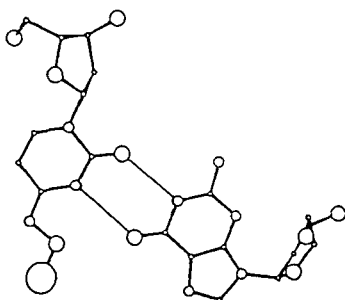
³Lab. voor Kristallografie, Celestijnenlaan 200C, Leuven, Belgium

ABSTRACT. The base analogue N⁴-methoxycytosine (mo⁴C) is ambivalent in its hydrogen-bonding potential. In d(CGCGmo⁴CG) it is in the imino form and so mimics thymine when wobble base pairing with guanine.

The design of oligonucleotide probes based on protein amino acid sequences is complicated by the genetic code redundancy. Mixed probes in which all codon assignments are taken into account are commonly used¹. An alternative approach utilises base analogues which are degenerate in their hydrogen bonding potential. For example N⁴-methoxycytosine has a K_T value^{2,3} close to unity. Therefore it may Watson-Crick base pair with adenine or guanine, but a wobble structure may also exist. Melting studies and dot blot hybridisation experiments have shown that duplexes containing N⁴-methoxycytosine base paired with adenine and guanine have comparable stability to those containing natural base pairs⁴.

mo⁴C-G Watson-Crick pairmo⁴C-G wobble pair

The hexamer d(CGCGmo⁴CG) was synthesised by automated phosphoramidite methodology, purified by chromatography and crystallised in space group P2₁2₁2₁ with $a=18.17$, $b=30.36$, $c=43.93\text{\AA}$. Intensities were collected on a Syntex P2₁ diffractometer at 4°C to 1.7Å resolution using an ω -scan mode with CuK α radiation. A semi-empirical absorption correction was applied. The structure was solved by molecular replacement (MERLOT) using the Z-DNA hexamer as a model, and refined by restrained least-squares (NUCLSQ). No hydrogen bond restraints were used to avoid any bias towards a particular mo⁴C-G pairing. Because of the unknown stereochemistry of the methoxy group a cytosine moiety was used for the mo⁴C base. Electron density maps, displayed on an E&S PS390 clearly indicated a wobble base pair geometry. During the refinement peaks in agreement with a syn stereochemistry were located in F_o-F_c maps. Refinement using 2559 reflections in the range 10-1.7Å converged with a final $R=0.17$ ($R_w=0.13$) including 79 solvent molecules. The mo⁴C base mimics thymine when wobble base pairing with guanine, causing only a small distortion of the backbone in comparison with the parent sequence d(CGCGCG)⁵.



REFERENCES

1. R. Lathe, J. Mol. Biol., 183, 1-12 (1985).
2. D.M. Brown, M.J.E. Hewlins and P. Schell, J. Chem. Soc. C, 1925-1929 (1968).
3. Y.V. Morozov, F.A. Savin, V.O. Chechov, E.I. Budowsky and D.Y. Yakovlev, J. Photochem., 20, 229 (1982).
4. N.N. Anand, D.M. Brown and S.A. Salisbury, Nucleic Acids Res., 15, 8167-8176 (1987).
5. R.V. Gessner, C.A. Frederick, G.J. Quigley, A. Rich and A.H.-J. Wang, J.Biol.Chem., 264, 7921-7935 (1989).