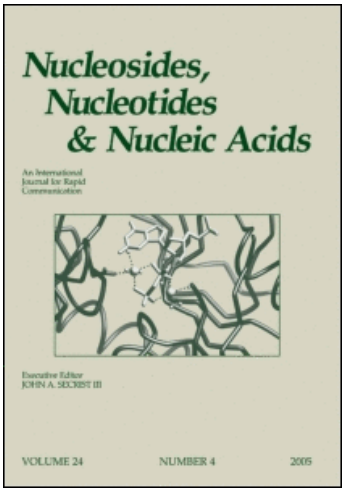


Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Synthesis and ^{15}N NMR of d[CGT($^{15}N^6$)ACG] and d[CGT(CGT)(15N1)ACG]

Xiolian Gao[a]; Roger A. Jones[a]
[a] Department of Chemistry Rutgers, The State University of New Jersey, Piscataway, NJ

To cite this Article Gao, Xiolian and Jones, Roger A.(1987) 'Synthesis and ^{15}N NMR of d[CGT($^{15}N^6$)ACG] and d[CGT(CGT)(15N1)ACG]', Nucleosides, Nucleotides and Nucleic Acids, 6: 1, 433 — 435
To link to this Article: DOI: 10.1080/07328318708056248
URL: http://dx.doi.org/10.1080/07328318708056248

NUCLEOSIDES & NUCLEOTIDES, 6(1&2), 433-435 (1987)

SYNTHESIS AND ^{15}N NMR OF d[CGT($^{15}N^6$)ACG] AND d[CGT($^{15}N^1$)ACG]

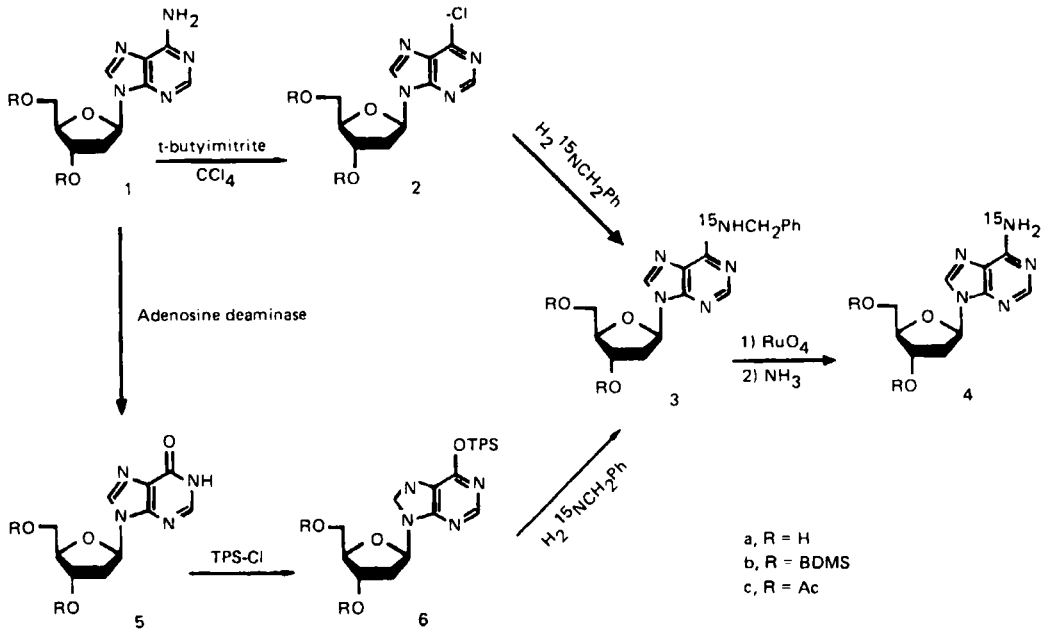
Xiolian Gao and Roger A. Jones*
Department of Chemistry
Rutgers, The State University of New Jersey
Piscataway, NJ 08854

Abstract. Deoxyadenosine has been converted to 6-^{15}N deoxyadenosine, which in turn has been transformed to 1-^{15}N deoxyadenosine. Each of these ^{15}N derivatives was then incorporated into the hexanucleoside pentaphosphate d(CGTACG) via a phosphoramidite procedure. The monomers and the hexamers were characterized by ^{1}H and ^{15}N nmr.

The introduction of ^{15}N to the 6 position was carried out by the two routes shown in Scheme I. In one route a 6-chloropurine derivative (2) was reacted with ^{15}N benzylamine while in the alternative route an O^6-sulfonyl inosine derivative (6c) was used. In each case the displacement reaction was effected in high yield. Debenzylation of 3 under reductive conditions was not successful, but was achieved in high yield using ruthenium tetraoxide oxidation to the corresponding 6-benzoyl compound.[1,2] The $^{15}N^1$ derivative was then obtained by alkylation of 4b with benzyl bromide followed by Dimroth rearrangement and subsequent oxidative debenzylation.

The oligonucleotide synthesis was carried out by a phosphoramidate method in which the cyanoethyl group was used for phosphate protection[3,4] Purification by hplc[5] gave 720 OD_{260} (13.2 μmole) of d[CGT($^{15}N^1$)ACG] and 500 OD_{260} (8.7 μmole) of d[CGT($^{15}N^6$)ACG]. The ^{15}N chemical shifts were recorded over the temperature range of 5° to 80°C. The ^{15}N resonances of the monomers show a linear temperature dependence, while the hexamers display the sinusoidal curve of a helix-to-coil transition (Figure 1). Using the monomer temperature dependence as a baseline, duplex formation is accompanied by an upfield shift of ca. 2.4 ppm for the $^{15}N^1$ resonance (hydrogen bond acceptor) and a downfield shift of ca. 1.9 ppm for the $^{15}N^6$ resonance (hydrogen bond donor). These shifts are consistent in both magnitude and direction with ^{15}N shifts reported from monomer studies[6,7] and from ^{15}N enriched *E. coli* DNA.[8]

Separate experiments were carried out to measure the ^{15}N relaxation times and NOEs, which allowed determination of the correlation time, τ_c (data not shown). These results are consistent with the correlation time determined for the same molecule by proton nmr.[9] Thus, ^{15}N nmr is a sensitive monitor of the helix-to-coil transition. Moreover, by using specifically ^{15}N labeled molecules, ^{15}N nmr may provide unique access to local structural phenomena in large molecules.



Scheme I

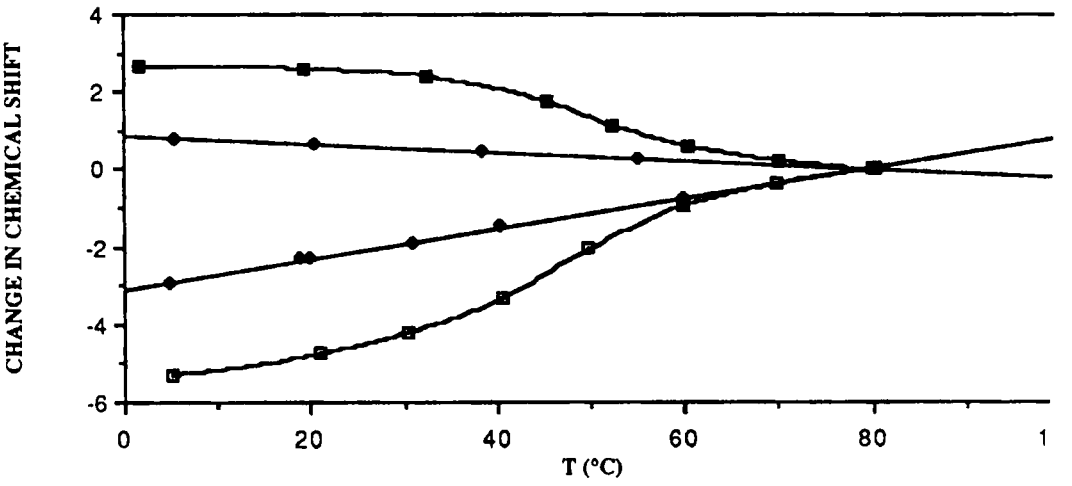


FIGURE 1

Acknowledgments

This work was supported by grants from the National Institutes of Health (GM31483) and the American Cancer Society (CH248B). The XL-400 nmr was purchasd in part with a grant from the National Science Foundation (CHEM-8300444).

REFERENCES

1. Schuda, P.F.; Cichowicz, M.B.; Heimann, M.R. Tetrahedron Lett., 1983, 24, 3829-3830.
2. Carlsen, P.H.J.; Katsuki, T.; Martin, V.S.; Sharpless, K.B. J. Org. Chem., 1981, 46, 3936-3938.
3. McBride, L.J.; Caruthers, M.H. Tetrahedron Lett., 1983, 24, 245-248.
4. Sinha, N.D.; Biernat, J.; Kuster, H. Tetrahedron Lett., 1983, 24, 5843-5846.
5. Gaffney, B.L.; Marky, L.A.; Jones, R.A. Biochemistry, 1984, 23, 5686-5691.
6. Poulter, C.D.; Livingston, C.L. Tetrahredron Lett., 1979, 755-758.
7. Dyllick-Brenzinger, C.; Sullivan, G.R.; Lang, P.P.; Roberts, J.D. Proc. Natl. Acad. Sci. USA, 1980, 77, 5580-5582.
8. James, T.L.; James, J.L.; Lapidot, A. J. Amer. Chem. Soc., 1981, 103, 6748-6750.
9. Clore, G.M.; Gronenborn, A.M. FEBS, 1984, 172, 219-225.