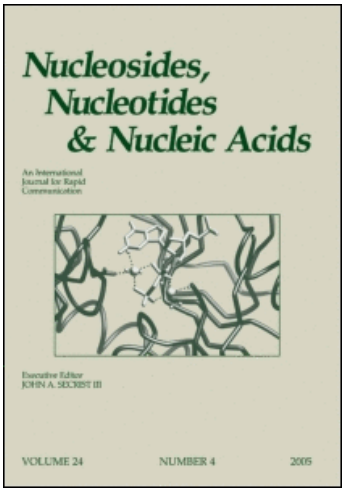


Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Synthesis of a C-8 Modified Adenosine Analogue as a Potential Mechanistic Probe for Ribonucleotide Reductases

G. C. Magnin[a]; J. Dauvergne[a]; A. Burger[a]; J-F. Biellmann[a]
[a] Laboratoire de Chimie Organique Biologique Associé au CNRS, Faculté de Chimie, Universitë Louis Pasteur, Strasbourg, France

To cite this Article Magnin, G. C. , Dauvergne, J. , Burger, A. and Biellmann, J-F.(1999) 'Synthesis of a C-8 Modified Adenosine Analogue as a Potential Mechanistic Probe for Ribonucleotide Reductases', Nucleosides, Nucleotides and Nucleic Acids, 18: 4, 611 — 612
To link to this Article: DOI: 10.1080/15257779908041513
URL: http://dx.doi.org/10.1080/15257779908041513

NUCLEOSIDES & NUCLEOTIDES, 18(4&5), 611–612 (1999)

SYNTHESIS OF A C-8 MODIFIED ADENOSINE ANALOGUE AS A POTENTIAL MECHANISTIC PROBE FOR RIBONUCLEOTIDE REDUCTASES.

G. C. Magnin, J. Dauvergne, A. Burger *, and J.-F. Biellmann

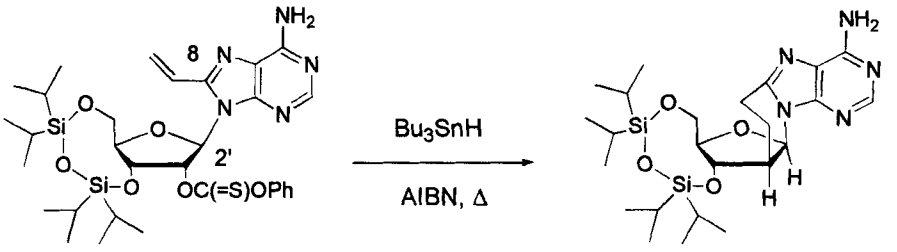
Laboratoire de Chimie Organique Biologique Associé au CNRS, Faculté de Chimie, Université Louis Pasteur, 1 rue Blaise Pascal, 67008 Strasbourg, France

Abstract. O-2' phenoxythionocarbonate of 8-vinyladenosine gives under Barton-McCombie conditions a C-2' radical that reacts intramolecularly with the vinyl group to afford a 6-endocycloproduct.

In order to gain further insight with regard to the proposed C-2' radical intermediate mediated by ribonucleotide reductases,[1] we have designed and prepared nucleoside analogues as radical traps. Our choice to introduce a functionality at C-8 as the trapping group was based on the following observations. 8-Azidoadenosine diphosphate is substrate of *Escherichia coli* reductase.[2] The base of the substrate bound to the enzyme active site [3] is in a synperiplanar conformation (χ = -21.6°) where the C-8 is close to C-2'. Thus intramolecular radical trapping of a C-2' radical and a vinyl functionality at C-8 should be possible. We present here the preparation of an adenosine derivative 1 and its reactivity study when a radical is chemically produced at C-2'.

To generate the radical at C-2', the Barton-McCombie radical mediated deoxygenation [4] was envisioned as a model reaction of the reductase reaction. The precursor **1** was prepared by conventional means [4] from the corresponding 8-vinyladenosine.[5] Slow addition of a toluene solution of Bu_3SnH (1.5 eq.) and a catalytic

amount of AIBN (20% mol.) over a period of 4 h. to a solution of derivative **1** in toluene (0.05 M) at 80° C gave to the 6-endoproduct **2** in 65% yield, besides a complex mixture of by-products. The 5-exoproduct was not detected even if the reaction was conducted under more concentrated conditions of stannyl hydride.[6]



1 **2**

The cyclonucleoside **2** has been prepared by a different synthetic pathway.[7] Comparison of the NMR and MS data with the literature data confirmed the assigned structure.[7]

In summary, we have shown that a vinyl functionality at the 8-position of adenosine reacts intramolecularly with a C-2' radical to give a 6 endocycloproduct.[8]

Acknowledgements. We thank ANRS and CNRS for their financial support.

REFERENCES

1. For a review, see for example : Stubbe, J.; van der Donk, W. A *Chem. Biol.*, **1995**, *2*, 793-801.
2. Roy, B.; Lepoivre, M.; Decout, J. L.; Lhomme, J.; Fontecave, M. *Biochem. Biophys. Res. Commun.*, **1992**, *187*, 432-437.
3 Eriksson, M.; Uhlin, U.; Ramaswamy, S.; Ekberg, M., Regnström, K.; Sjöberg, B.-M.; Eklund, H. *Structure*, **1997**, *5*, 1077-1092.
4. Robins, M. J.; Wilson, J. S.; Hansske, F. *J. Am. Chem. Soc.*, **1983**, *105*, 4059-4065.
5. Moriarty, R. M.; Epa, W. R.; Awasthi, A. K. *Tetrahedron Lett.*, **1990**, *31*, 5877-5880.
6. For other examples of endoproduct formation, see : Curran, D. P. in *Comprehensive Organic Synthesis*, Trost, B. M.; Flemming, I.; Ed. : Pergamon Press, Oxford, **1991**, *vol. 4*, pp. 779-831.
7. Usui, H.; Ueda, T. *Chem. Pharm. Bull.*, **1986**, *34*, 15-23.
8. Addition of the glycosylic radical on the vinyl group may account for the biological activity observed for 8-vinyladenosine, see : Manfredini, S.; Baraldi, P. G.; Bazzanini, R.; Marangoni, M.; Simoni, D.; Balzarini, J.; De Clercq, E. *J. Med. Chem.*, **1995**, *38*, 199-203.