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## Nucleosides, Nucleotides and Nucleic Acids

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

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

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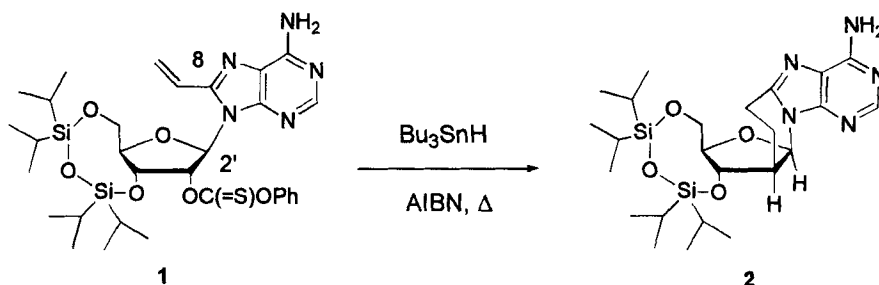
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**Abstract.** O-2' phenoxythionocarbonate of 8-vinyladenosine gives under Barton-McCombie conditions a C-2' radical that reacts intramolecularly with the vinyl group to afford a 6-endocycloproduct.

In order to gain further insight with regard to the proposed C-2' radical intermediate mediated by ribonucleotide reductases,<sup>1</sup> 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.<sup>2</sup> The base of the substrate bound to the enzyme active site<sup>3</sup> is in a synperiplanar conformation ( $\chi = -21.6^\circ$ ) 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<sup>4</sup> was envisioned as a model reaction of the reductase reaction. The precursor 1 was prepared by conventional means<sup>4</sup> from the corresponding 8-vinyladenosine.<sup>5</sup> Slow addition of a toluene solution of Bu<sub>3</sub>SnH (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-endopropduct **2** in 65% yield, besides a complex mixture of by-products. The 5-exopropduct was not detected even if the reaction was conducted under more concentrated conditions of stannyl hydride.<sup>6</sup>



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

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.<sup>8</sup>

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## 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 endopropduct 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.