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## Nucleosides, Nucleotides and Nucleic Acids

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### Ring Opening Reactions: Synthesis of AICAR Analogs as Potential Antimetabolite Agents

S. Costanzi<sup>a</sup>; C. Lambertucci<sup>a</sup>; F. R. Portino<sup>a</sup>; R. Volpini<sup>a</sup>; S. Vittori<sup>a</sup>; G. Cristalli<sup>a</sup>

<sup>a</sup> Dipartimento di Scienze Chimiche, University of Camerino, Camerino, Italy

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## RING OPENING REACTIONS: SYNTHESIS OF AICAR ANALOGS AS POTENTIAL ANTIMETABOLITE AGENTS

S. Costanzi, C. Lambertucci, F. R. Portino, R. Volpini, S. Vittori, and G. Cristalli □ Dipartimento di Scienze Chimiche, University of Camerino, Camerino, Italy

□ In an attempt to improve the  $A_{2A}$  selectivity of the 2-(aryl)alkylthio derivatives of adenosine, we planned the synthesis of the corresponding derivatives of the 5'-N-ethylcarboxamidoadenosine (NECA). For this purpose, we designed the synthesis of 2-mercapto-NECA to be pursued by means of an opening-closure method. We obtained the open AICAR analog; however, ring closure efforts failed to give the desired compound. The newly synthesized AICAR derivative could potentially be endowed with antiviral or antitumoral activity.

### INTRODUCTION

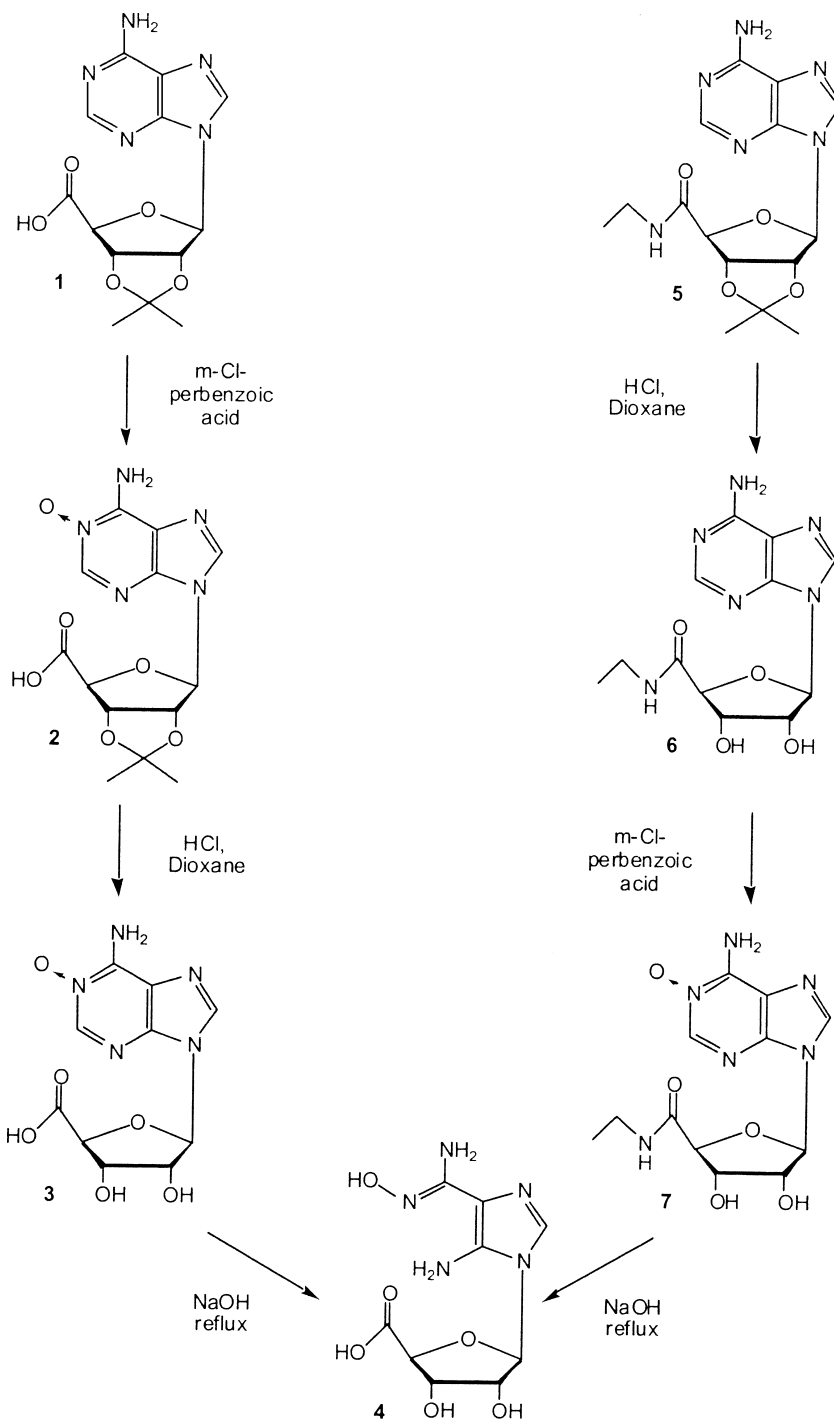
Derivatives of adenosine substituted at the C2 position of the purine ring with (aryl)alkylthio groups have been reported to possess coronary vasodilating activity and platelet aggregation inhibitory activity, probably due to their interaction with the adenosine  $A_{2A}$  receptors.<sup>[1–4]</sup>

In an attempt to improve the  $A_{2A}$  selectivity of the 2-(aryl)alkylthio derivatives of adenosine, since the substitution of the 4'-hydroxymethyl group with an N-ethylcarboxamido substituent usually increased  $A_2$  vs.  $A_1$  binding affinity,<sup>[5–7]</sup> we planned the synthesis of the corresponding derivatives of the 5'-N-ethylcarboxamidoadenosine (NECA).

In 1975, Kikugawa and Suehiro<sup>[8]</sup> reported the synthesis of 2-mercaptopadenosine by the “opening-closure” method and its successive reaction with various 2-(aryl)alkylbromides to obtain the corresponding 2-(aryl)alkylthio derivatives of adenosine. Following a similar scheme, we designed the synthesis of 2-mercapto-NECA, which could have been reacted with (aryl)alkylbromides to obtain the desired compounds.

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Address correspondence to S. Vittori, Dipartimento di Scienze Chimiche, University of Camerino, via S. Agostino 1, Camerino I-62032, Italy; E-mail: sauro.vittori@unicam.it

**SCHEME 1** Preparation of AICAR analog **4**.

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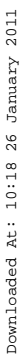
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