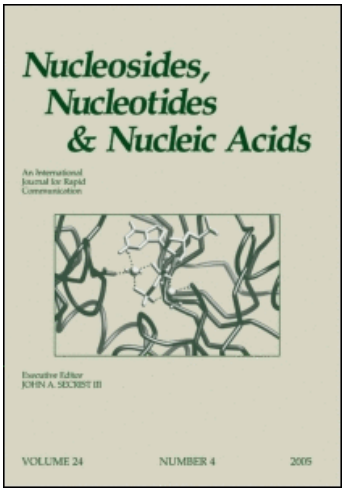

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

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Online publication date: 09 August 2003

To cite this Article Besada, P. , González-Moa, M. J. , Terán, C. , Teijeira, M. and Santana, L.(2003) 'Synthesis of Carbocyclic Analogues of MECA and NECA 1,2-Disubstituted as Potential Adenosine Receptor Agonists', Nucleosides, Nucleotides and Nucleic Acids, 22: 5, 759 — 761
To link to this Article: DOI: 10.1081/NCN-120022628
URL: http://dx.doi.org/10.1081/NCN-120022628

NUCLEOSIDES, NUCLEOTIDES & NUCLEIC ACIDS
Vol. 22, Nos. 5–8, pp. 759–761, 2003

Synthesis of Carbocyclic Analogues of MECA and NECA 1,2-Disubstituted as Potential Adenosine Receptor Agonists

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ABSTRACT

A new class of 1,2-disubstituted carbocyclic nucleosides of MECA and NECA analogues was synthesized in gool yield starting from (±) 6-azabicyclo[3.2.0]heptan-7-one.

Key Words: Carbocyclic nucleosides; Purine derivatives; Adenosine receptors.

The variability of physiological functions of adenosine together with the existence of at least four distinct receptor subtypes (A_1, A_{2A}, A_{2B} and A_3) has spurred numerous structure-activity relationship studies in search of more potent and selective analogues and with an increased metabolic stability.[1] The presence of an alkyl or arylalkyl group in N^6 position of adenine, as in cyclopentyladenosine, and substitution of the hydroxyl group in 5′ of ribose by N-alkylcarboxamide, as in MECA

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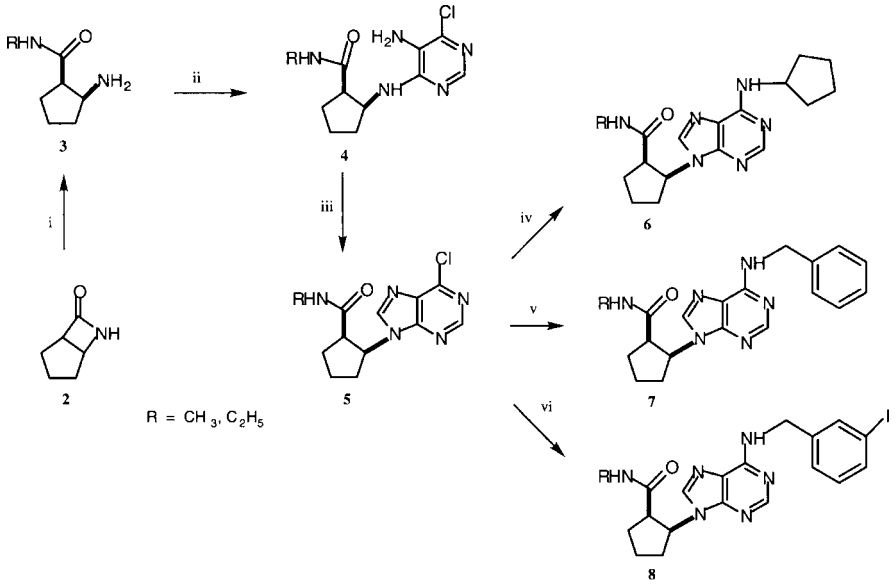
DOI: 10.1081/NCN-120022628
1525-7770 (Print); 1532-2335 (Online)



Scheme. Reagents and conditions: (i) 2M solution of methylamine or ethylamine in methyl alcohol, reflux; (ii) 5-amino-4,6-dichloropyrimidine, *n*-BuOH, Et_3N, reflux; (iii) $CH(OEt)_3$; 12M HCl, r.t.; (iv) cyclopentylamine, ethanol, reflux; (v) benzylamine, ethanol, reflux; (vi) 3-iodobenzylamine hydrochloride, ethanol, Et_3N, reflux.

and NECA, leads to potent and selective agonists. On the other hand, it is well known that many adenosine derivatives having carbocyclic modifications of the ribose ring bind to adenosine receptors.

Taking into account these three types of structural modifications we design the synthesis of a new series of MECA and NECA analogues, which would allow the study of the influence of the alkylaminocarbonyl and the heterocyclic bases in contiguous positions of the cyclopentane (compounds **6–8**). We already applied this type of structural modification to design carbocyclic analogues of nucleosides.[2]

Racemic mixtures of compounds **6–8** with *cis* stereochemistry were prepared with good yields from (±) 6-azabicyclo[3.2.0]heptan-7-one **(2)** as shown in Scheme. The heating of **2** with a 2M solution of methylamine or ethylamine in methyl alcohol afford the corresponding aminecarboxamide **3**, and the primary amino group of these intermediates served as building block for construction of 6-chloropurine nucleus.[2] Finally the 6-chlorine atom of compound **5** was displaced by cyclopentylamine (compound **6**), benzylamine (compound **7**) and 3-iodobenzylamine (compound **8**).

REFERENCES

1. Muller, C.E. Adenosine receptor ligands-recent developments part I agonists. Curr. Med. Chem. **2000**, *7*, 1269–1288.

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2. a) Santana, L.; Teijeira, M.; Terán, C.; Uriarte, E.; Viña, D. Synthesis of 1,2-disubstituted carbocyclic analogs of pyrimidine and purine nucleosides. Synthesis **2001**, *10*, 1532–1538; b) Besada, P.; González-Moa, M.J.; Terán, C.; Santana, L.; Uriarte, E. Novel 1,2-disubstituted carbocyclic nucleoside analogs of purine with a cyclopentene ring. Synthesis **2002**, *16*, 2445–2449.

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