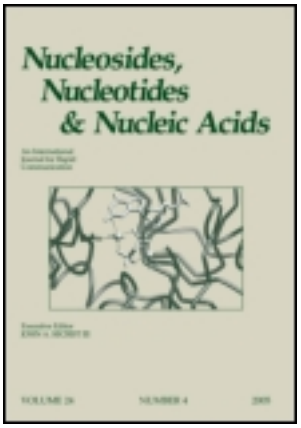

Nucleosides and Nucleotides
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lncn19

Synthesis of (±)-cis-3-Aminomethyl-1-indanylmethanol as a Precursor of Carbocyclic Analogues of Nucleosides

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Version of record first published: 04 Oct 2006

To cite this article: M. Escobar, F. Fernández, X. García-Mera & J. E. Rodriguez-Borges (1999): Synthesis of (±)-cis-3-Aminomethyl-1-indanylmethanol as a Precursor of Carbocyclic Analogues of Nucleosides, Nucleosides and Nucleotides, 18:4-5, 625-626

To link to this article: http://dx.doi.org/10.1080/15257779908041520

NUCLEOSIDES & NUCLEOTIDES, 18(4&5), 625–626 (1999)

SYNTHESIS OF (±)-*cis*-3-AMINOMETHYL-1-INDANYLMETHANOL AS A PRECURSOR OF CARBOCYCLIC ANALOGUES OF NUCLEOSIDES.

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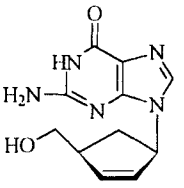
ABSTRACT:: Aminoalcohol precursor of carbocyclic analogues of nucleosides (±)-*cis*-3-aminomethyl-1-indanylmethanol was efficiently synthesized starting from benzonorbornadiene (**5**) previously prepared by addition of cyclopentadiene to 1-bromo-2-fluorobenzene.

In the search for new antitumor and antiviral therapeutic agents, much recent attention has been focused on carbocyclic analogues of nucleosides[1] (CANs). The potent antiviral properties of carbovir[2] (**1**) prompted us to examine the effect of the structural and configurational features of the aminoalcohol moiety on the antiviral activity of CANs.

Synthesis of CANs generally involves construction of the purine or pyrimidine base about the amino group of an appropriate aminoalcohol. This linear strategy allows preparation of large numbers of congeneric CANs that can be screened for biological activity. Recently we reported preparation of aminoalcohol **2**[3], a precursor incorporating an indan instead of a cyclopentene ring, and we now describe the preparation of its higher homologue **3**, in which a methylene spacer increases the distance between the five membered ring and the site of base construction.



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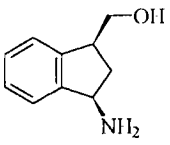

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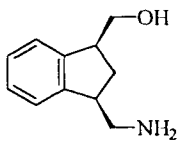
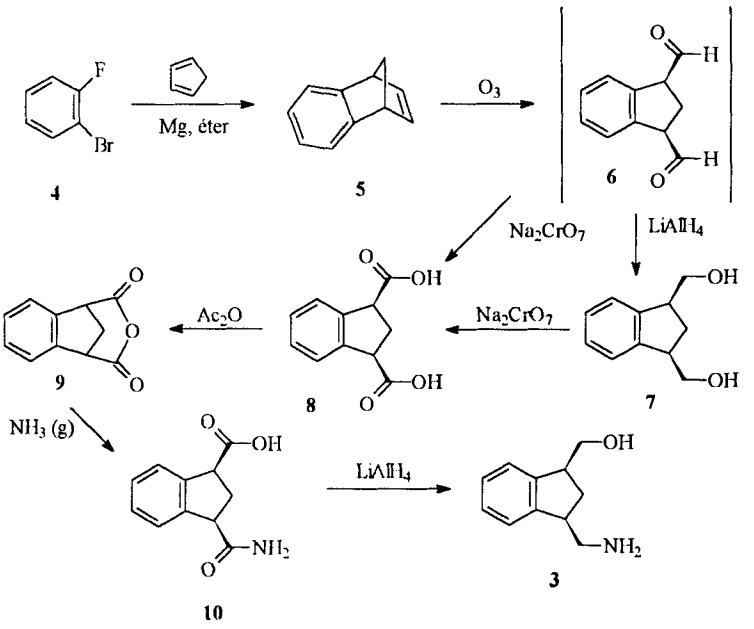


3

Aminoalcohol **3** was prepared from benzonorbornadiene (**5**),which was obtained in 66% yield from 1-bromo-2-fluorobenzene (**4**) by a modification of the original Wittig method[4]: ethyl ether replaced THF as solvent and initiation of the reaction was induced by ultrasound. Ozonolysis[5] of (**5**) provided dialdehyde (**6**), which was reduced with $LiAlH_4$ to obtain diol (**7**) (74%). $Na_2Cr_2O_7$ oxidation of both **6** and **7** afforded diacid (**8**), in 84% and 77% yields respectively, and treatment of **8** with acetic anhydride gave anhydride (**9**), which was opened with ammonia to afford amidoacid (**10**). Reduction of **10** with $LiAlH_4$ finally gave aminoalcohol **3** in 93% yield.



REFERENCES

1. Agrafoglio, L.; Suhas, E.; Farese, A.; Condom, R.; Challand, S.R.; Earl, R.A.; Guedj, R. *Tetrahedron*, **1994**, *50*, 10611-10670.
2. (a) de Clercq, E.; *"Design of anti-AIDS Drugs"*, Ed. Elsevier, Pharmacochemistry Library, Vol.14, **1990**. (b) Vince, R.; Hua, M. *J. Med. Chem.*, **1990**, *33*, 17.
3. Escobar, M.; Fernández, F.; García-Mera, X.; Hergueta, A.R.; Rodríguez-Borges, J.E; *"Synthesis of cis-3-amino-1-indanylmethanol as a Precursor of Carbocyclic Analogues of Nucleosides"*, First International Symposium on New Horizons of Organic Chemistry in Biomedicine, **1996**, Santiago de Compostela, Spain.
4. Wittig, G.; Knauss, E. *Chem. Ver.*, **1958**, *91*, 895.
5. Kluger, R.; Hunt, J.C. *J. Am. Chem. Soc.*, **1989**, *111*, 3325.