

This article was downloaded by:

On: 26 January 2011

Access details: *Access Details: Free Access*

Publisher *Taylor & Francis*

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Nucleosides, Nucleotides and Nucleic Acids

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713597286>

Synthesis of Novel Carbocyclic Nucleosides with a Modified Cyclopentane Ring and Evaluation of Their Antiviral Activity

Isabel Nieto^a; M. José Figueira^a; J. Manuel Blanco^a; Olga Caamaño^a; Franco Fernández^a; Erik De Clercq^b; Jan Balzarini^b

^a Departamento de Química Orgánica, Facultad de Farmacia, Universidade de Santiago, Santiago de Compostela, Spain ^b Rega Institute for Medical Research, Katholieke Universiteit Leuven, Leuven, Belgium

To cite this Article Nieto, Isabel , Figueira, M. José , Blanco, J. Manuel , Caamaño, Olga , Fernández, Franco , De Clercq, Erik and Balzarini, Jan(1999) 'Synthesis of Novel Carbocyclic Nucleosides with a Modified Cyclopentane Ring and Evaluation of Their Antiviral Activity', *Nucleosides, Nucleotides and Nucleic Acids*, 18: 4, 641 — 642

To link to this Article: DOI: 10.1080/15257779908041525

URL: <http://dx.doi.org/10.1080/15257779908041525>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

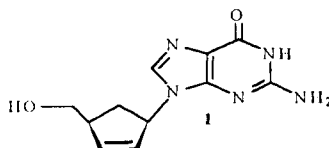
SYNTHESIS OF NOVEL CARBOCYCLIC NUCLEOSIDES WITH A MODIFIED CYCLOPENTANE RING AND EVALUATION OF THEIR ANTIVIRAL ACTIVITY

Isabel Nieto,¹ M. José Figueira,¹ J. Manuel Blanco,¹ Olga Caamaño,*¹ Franco Fernández,¹ Erik De Clercq,² Jan Balzarini.²

^a *Departamento de Química Orgánica, Facultad de Farmacia, Universidade de Santiago, E-15706 Santiago de Compostela, Spain.* ^b *Rega Institute for Medical Research, Katholieke Universiteit Leuven, B-3000 Leuven, Belgium.*

Abstract: New carbocyclic nucleosides with purine (compounds **2a–2c**), 8-azapurine (compounds **2d** and **2e**) or pyrimidine (compound **3**) as base were prepared and assayed for *in vitro* activity.

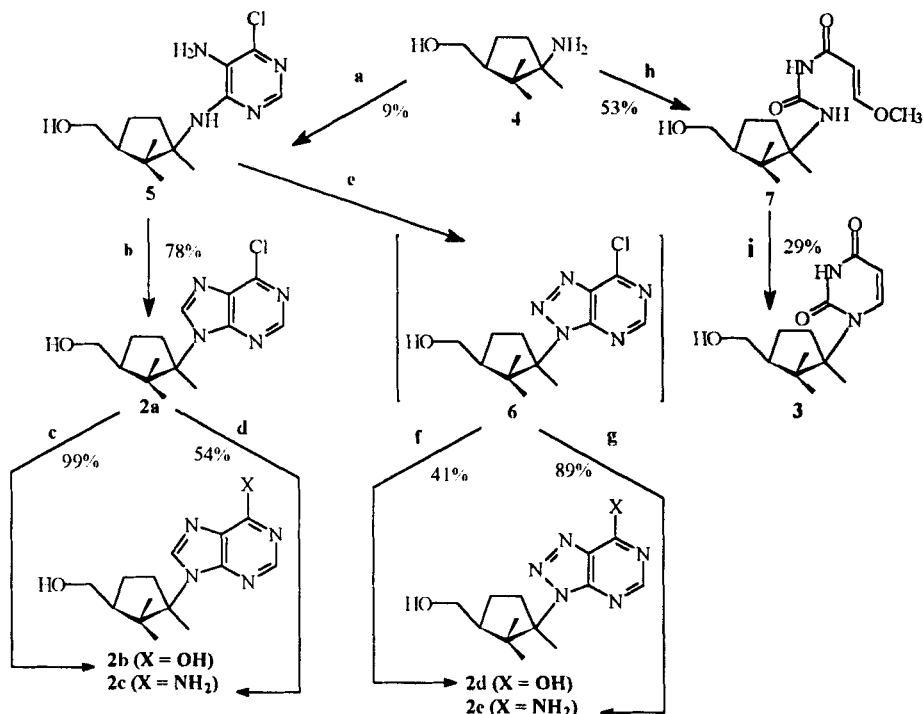
The discovery of carbocyclic nucleosides with antiviral activity, such as carbovir (**1**),¹ prompted us to search for congeners with a modified cyclopentane moiety. Here work we describe the synthesis of carbocyclic nucleosides **2** and **3**, and report their antiviral activity.



(1*S*,3*R*)-3-Amino-2,2,3-trimethylcyclopentylmethanol (**4**) identified as a convenient starting compound for the synthesis of **2** and **3**, was prepared from (+)-camphoric acid.² Standard methods^{3,4} were then used to construct purine or pyrimidine about the amino group.

Compounds **2b–2e** and **3** were tested in E₆SM cell cultures for their broad spectrum antiviral activity⁵ against herpes simplex virus-1 (KOS), herpes simplex virus-2 (G), vaccinia virus, vesicular stomatitis virus, thymidine kinase-deficient herpes simplex

virus-1 TK⁻ (B2006) and herpes simplex virus-1 TK⁻ (VMW1837); in HeLa cell cultures against vesicular stomatitis virus, Coxsackie virus B4 and respiratory syncytial virus; in



a) 5-Amino-4,6-dichloropyrimidine, Et₃N, n-butanol, reflux, 72 h; b) CH(OEt)₃, 12N HCl, r.t., 72 h; c) 0.33 N NaOH, reflux, 6 h; d) 14M NH₄OH, reflux 18 h; e) NaNO₂, AcOH, or 1N HCl; f) H₂O, r.t., 18 h; g) 14M NH₄OH, reflux, 5 min; h) methyl 3-methoxiacriloyl isocyanate, C₆H₆, DMF, r.t., overnight; i) 2N H₂SO₄, reflux, 3.5 h.

Vero cell cultures against *parainfluenza*-3 virus, *reovirus*-1, *Sindbis* virus, *Coxsackie* virus B4 and *Punta Toro* virus; and in HEL cell cultures against varicella-zoster virus (strains OKA,YS, 07/1 and YS/R) and cytomegalovirus. No specific antiviral activity was obtained with any of the compounds at subtoxic concentrations.

REFERENCES

1. Vince, R., Hua, M. *J. Med. Chem.* **1990**, *33*, 17-21.
2. Nieto, M.I.; Blanco J.M.; Caamaño, O.; Fernández, F.; Gómez, G.; *Tetrahedron*, **1998**, *54*, 7819-7830.
3. Patil, S.D.; Schneller, M.; Hosoya, M.; Snoeck, R.; Andrei, G.; Balzarini, J.; De Clercq, E. *J. Med. Chem.*, **1992**, *35*, 3372-3377.
4. Shealy, Y.F.; O'Dell, C.A. *J. Heterocyclic Chem.*, **1976**, *13*, 1015-1020.
5. De Clercq, E., in "In vitro and ex vivo test systems to rationalize drug design and delivery", D. Crommelin, P. Couvreur, D. Duchêne (Eds.), Editions de Santé, Paris, France, 1994, pp 108-125.