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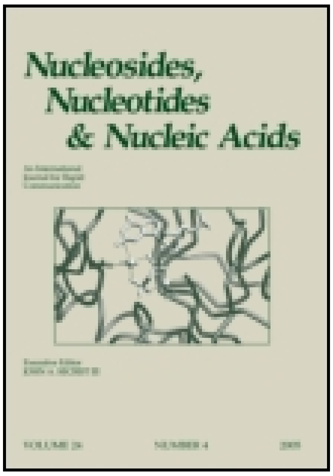

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lncn20

NEW CARBOCYCLIC NUCLEOSIDES DERIVED FROM INDAN

F. Abad [a] , F. Álvarez [a] , F. Fernández [a] , X. García-Mera [b] & J. E. Rodríguez-Borges [a]

[a] Universidad de Santiago , Dpto. Química Orgánica, Facultad de Farmacia, Santiago de Compostela, E-15706, Spain

[b] Universidad de Santiago , Dpto. Química Orgánica, Facultad de Farmacia, Santiago de Compostela, E-15706, Spain

Published online: 07 Feb 2007.

To cite this article: F. Abad , F. Álvarez , F. Fernández , X. García-Mera & J. E. Rodríguez-Borges (2001) NEW CARBOCYCLIC NUCLEOSIDES DERIVED FROM INDAN, Nucleosides, Nucleotides and Nucleic Acids, 20:4-7, 1127-1128, DOI: 10.1081/NCN-100002503

To link to this article: http://dx.doi.org/10.1081/NCN-100002503

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NEW CARBOCYCLIC NUCLEOSIDES DERIVED FROM INDAN

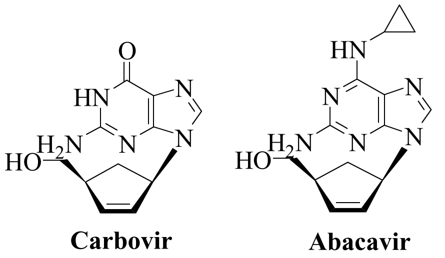
F. Abad, F. Álvarez, F. Fernández, X. García-Mera,*
and J. E. Rodríguez-Borges

Dpto. Química Orgánica, Facultad de Farmacia, Universidad
de Santiago, E-15706 Santiago de Compostela, Spain

ABSTRACT

Seven new carbocyclic nucleosides derived from indan (**1a–g**) were efficiently prepared from 1,2-indanedimethanol *vía* Mitsunobu reaction with 6-chloroadenine and subsequent introduction of the appropriate substituent.

Carbovir (1) and Abacavir (2) are carbocyclic analogues of nucleosides (CANs), in both of which the core of the pseudo-sugar moiety is a cyclopentene ring. Recently, others CANs with interesting antiviral properties have been prepared in which a cyclopentane ring is fused to another saturated ring; this structure appears to facilitate interaction with viral enzymes (3).



Scheme 1.

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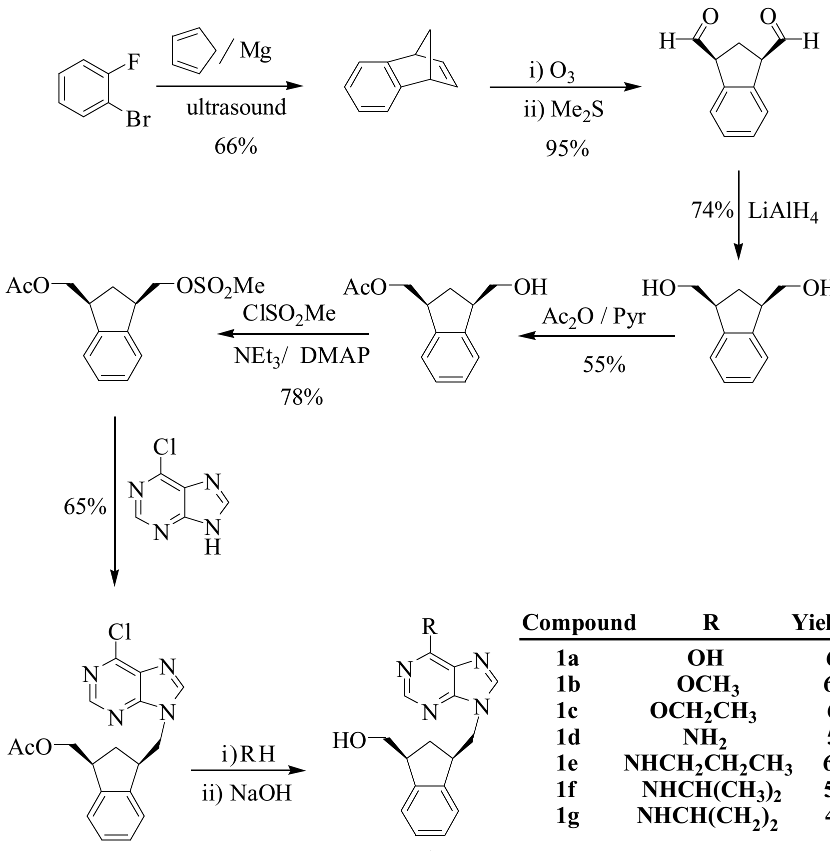

1

Compound	R	Yield (%)
1a	**OH**	**63**
1b	**OCH_3**	**65**
1c	**OCH_2CH_3**	**60**
1d	**NH_2**	**54**
1e	**$NHCH_2CH_2CH_3$**	**60**
1f	**$NHCH(CH_3)_2$**	**52**
1g	**$NHCH(CH_2)_2$**	**44**

Scheme 2.

We hypothesize that CANs with a cyclopentene ring fused to an aromatic ring would possess these conformational advantages and also be more liposoluble, which would favour their access to the CNS, an important reservoir for the replication of viruses such as HIV.

We report now a suitable synthetic route to CANs of type 1, (X=OR or NHR; R=H, alkyl or cycloalkyl). Our approach proceeds via generation of benzonorbornadiene, preparation of the corresponding difunctionalized diol, Mitsunobu reaction with 6-chloroadenine, introduction of the appropriate substituent at position 6 of the adenine, and final deacetylation.

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