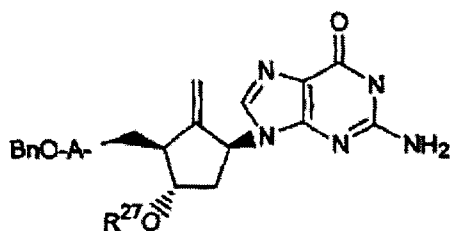


ORIGINAL

*ABSTRACT*

"A COMPOUND - 3"

A compound of formula:



or a salt thereof, wherein:

A is CH<sub>2</sub> or a bond;

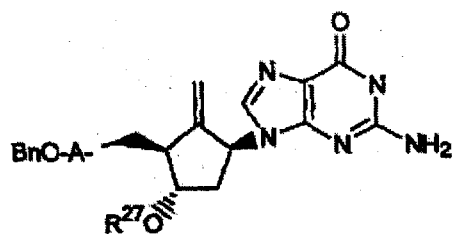
R<sup>27</sup> is hydrogen, benzyl, or SiR<sup>d</sup><sub>2</sub>R<sup>e</sup>;

R<sup>e</sup> is C<sub>1</sub> to C<sub>4</sub> alkyl or phenyl; and

R<sup>d</sup> is C<sub>1</sub> to C<sub>3</sub> alkyl.

**WE CLAIM:**

1. A compound of formula:



or a salt thereof, wherein:

A is CH<sub>2</sub> or a bond;

R<sup>27</sup> is hydrogen, benzyl, or SiR<sup>d</sup><sub>2</sub>R<sup>c</sup>;

R<sup>c</sup> is C<sub>1</sub> to C<sub>4</sub> alkyl or phenyl; and

R<sup>d</sup> is C<sub>1</sub> to C<sub>3</sub> alkyl.

2. A compound as claimed in claim 1, in which A is a bond, and R<sup>27</sup> is hydrogen.

Dated this 20<sup>th</sup> day of January 2012.

*Debashish Banerjee*

[DEBASHISH BANERJEE]  
OF REMFRY & SAGAR  
ATTORNEY FOR THE APPLICANT[S]

The present invention relates to a compound -3.

### RELATED APPLICATIONS

This application claims the priority benefit of U.S. Provisional Application No. 60/432,549 filed December 11, 2002, the disclosure of which is incorporated herein by reference in its entirety.

### BACKGROUND OF THE INVENTION

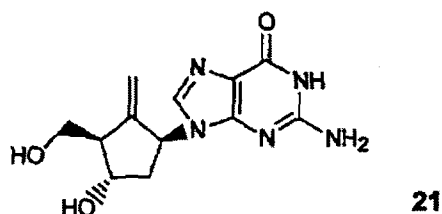
Entecavir, [1S-(1 $\alpha$ , 3 $\alpha$ , 4 $\beta$ )]-2-amino-1,9-dihydro-9-[4-hydroxy-3-(hydroxymethyl)-2-methylenecyclopentyl]-6H-purin-6-one, is currently being evaluated as a drug for use in treating hepatitis B viral infections.

Entecavir and its use as an antiviral agent are described in U.S. Patent 5,206,244 to Zahler *et al.*, assigned to the present assignee. Improved processes of preparing entecavir are described by Bisacchi *et al.*, in WO 98/09964, also to the present assignee.

Colunno, *et al.* in WO 01/64221 describe compositions containing a low dose of entecavir administered on a daily basis to treat hepatitis B virus infection and/or co-infections.

### SUMMARY OF THE INVENTION

This invention is directed to various methods for preparing entecavir as recited in the claims appended hereto. Entecavir (the compound of formula 21) has the structural formula shown below:



This invention is also directed to various intermediates useful in the preparation of entecavir and the methods of preparing such intermediates.

This invention is also directed to a resin adsorption process for isolation and purification of entecavir and intermediates thereof.

## DETAILED DESCRIPTION OF THE INVENTION

### ABBREVIATIONS

For ease of reference, the following abbreviations are used in this application and have the meanings given below:

Ac	=	acyl;
AP	=	HPLC area percent;
Bn	=	benzyl;
BHT	=	2,6-di-tert-butyl-4-methylphenol;
CHP	=	cumene hydroperoxide, or $\alpha,\alpha$ -dimethylbenzylhydroperoxide;
DCM	=	dichloromethane;
de	=	diastereometric excess;
DBU	=	1,8-diazabicyclo[5.4.0]undec-7-ene;
DEAD	=	diethylazodicarboxylate;
DEMA	=	diethoxymethyl acetate;
DIPT	=	(-)-diisopropyl tartrate;
DMAP	=	4- <i>N,N</i> -dimethylaminopyridine;
DMF	=	<i>N,N</i> -dimethylformamide;
DiPMA	=	di-isopropyloxymethyl acetate; [(iPr-O) <sub>2</sub> CHOAc];
DMSO	=	dimethyl sulfoxide;
ee	=	enantiomeric excess;
Et	=	ethyl;
EtOAc	=	ethyl acetate;
Et <sub>3</sub> N	=	triethylamine;
FMSA	=	fluoromethane sulfonic acid;
HCl	=	hydrochloric acid
IPA	=	isopropanol;
K <sub>2</sub> CO <sub>3</sub>	=	potassium carbonate;
KF	=	potassium fluoride;

KHCO <sub>3</sub> =	potassium bicarbonate;
KHMDS =	potassium hexamethyldisilazide or potassium bis(trimethylsilyl)amide;
KOH =	potassium hydroxide;
KOtBu =	potassium <i>tert</i> -butoxide;
LAH =	lithium aluminum hydride;
LiOH =	lithium hydroxide;
<i>m</i> -CPBA =	meta-chloroperbenzoic acid;
MeOH =	methanol
MOP =	2-methoxy-2-propoxy-acetal;
MSA =	methanesulfonic acid;
MTBE =	methyl <i>tert</i> -butyl ether;
NaBH <sub>4</sub> =	sodium borohydride;
Na <sub>2</sub> CO <sub>3</sub> =	sodium carbonate;
NaHCO <sub>3</sub> =	sodium bicarbonate;
NaH =	sodium hydride;
NaOH =	sodium hydroxide;
NaOtBu =	sodium <i>tert</i> -butoxide;
NMP =	N-methyl-2-pyrrolidinone;
TMS =	trimethylsilyl;
PPTS =	pyridinium 4-toluenesulfonate or pyridinium <i>p</i> -toluenesulfonate;
PTSA =	para-toluene sulfonic acid;
Red-Al® or RED-AL® =	sodium bis(2-methoxyethoxy)aluminum hydride;
TBAH =	n-tetrabutyl ammonium hydroxide;
TBHP =	<i>tert</i> -butylhydroperoxide;
TEOF =	tri-ethylorthoformate;
TFA =	trifluoroacetic acid;
THF =	tetrahydrofuran;
Ti(O- <i>i</i> Pr) <sub>4</sub> =	titanium (IV) isopropoxide;
TiPOF =	trisopropylorthoformate;
TMOF =	trimethylorthoformate.

