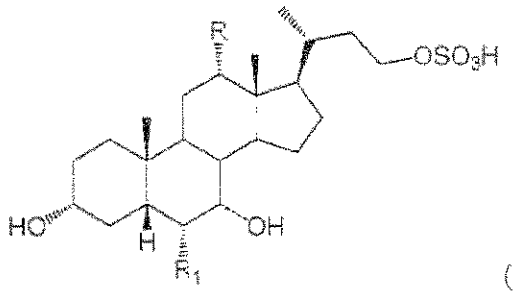
PROCESS FOR PREPARING BILE ACID DERIVATIVES

CROSS-REFERENCE TO RELATED APPLICATION

This application claims priority to, and the benefit of, U.S. Application No. 61/718,966, filed on October 26, 2012, the entire contents of which are incorporated herein by reference.

SUMMARY ~~OF THE INVENTION~~

The present ~~invention~~ disclosure relates to processes for preparing a compound of formula I:



(I),

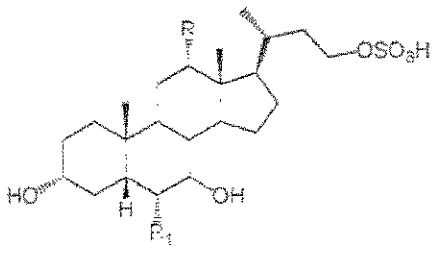
or a pharmaceutically acceptable salt or solvate thereof, wherein

the dashed bond (----) at position 7 indicates that the substituent is in an α or ß stereochemistry;

R is hydrogen or hydroxy; and

R_1 is hydrogen or C_1-C_6 alkyl.

In a first aspect of the present disclosure, there is provided a process for preparing a compound of formula I:



(I),

or a pharmaceutically acceptable salt or solvate thereof, wherein

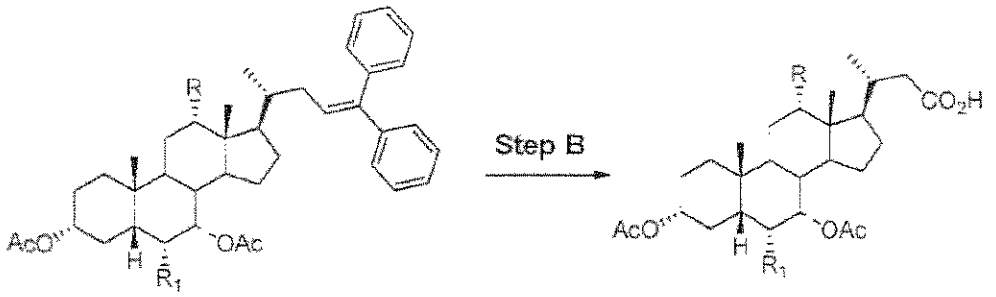
the dashed bond (----) at position 7 indicates that the substituent is in an α or ß stereochemistry;

R is hydrogen or hydroxy; and

R_1 is hydrogen or C_1-C_6 alkyl;

comprising the step of

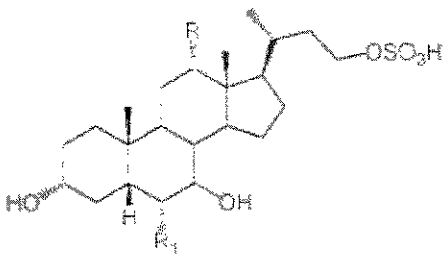
Step B: converting a compound of formula 3A to a compound of formula 4A:



3A 4A

wherein Step B comprises reacting a compound of formula 3A with $RuCl_3$, $NaIO_4$, and an acid to form a compound of formula 4A.

In a second aspect of the present disclosure, there is provided a process for preparing a compound of formula I:



(I),

or a pharmaceutically acceptable salt or solvate thereof, wherein

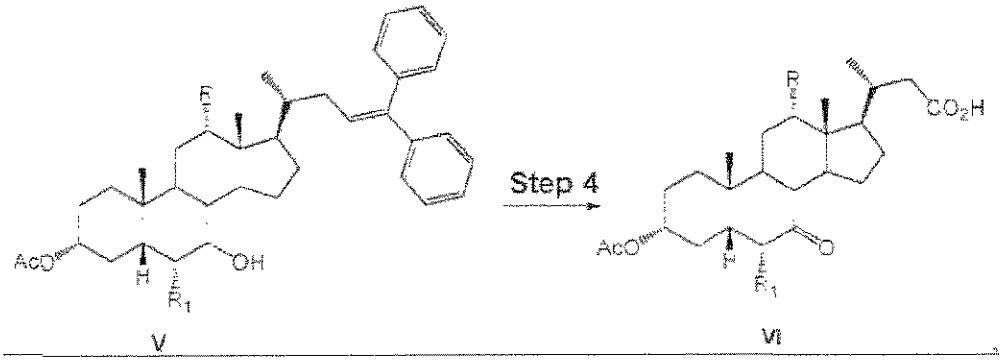
the dashed bond (----) at position 7 indicates that the substituent is in an α or ß stereochemistry;

R is hydrogen or hydroxy; and

R_1 is hydrogen or C_1-C_6 alkyl.

comprising the step of

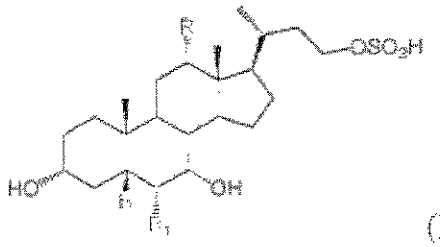
Step 4: converting a compound of formula V to a compound of formula VI:



V VI

wherein Step 4 comprises reacting a compound of formula V with $RuCl_3$, $NaIO_4$, and an acid to form a compound of formula VI.

In a third aspect of the present disclosure, there is provided a process for preparing a compound of formula I:



(I),

or a pharmaceutically acceptable salt or solvate thereof, wherein

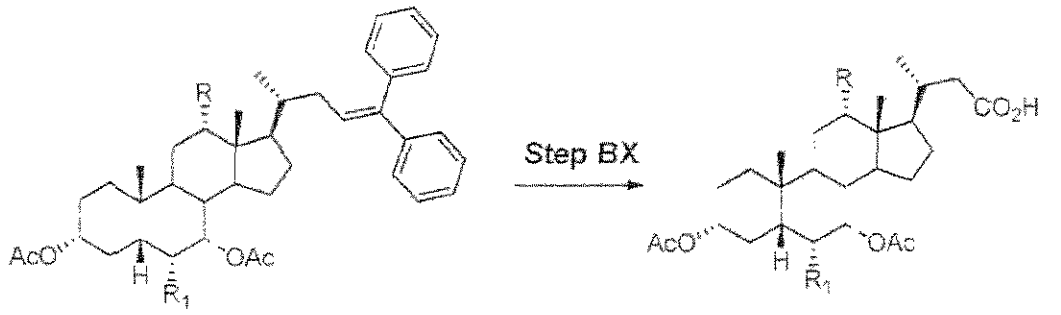
the dashed bond (----) at position 7 indicates that the substituent is in an α or ß stereochemistry;

R is hydrogen or hydroxy; and

R_1 is hydrogen or C_1-C_6 alkyl,

comprising the step of

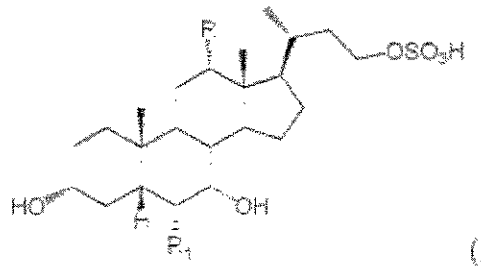
Step BX: converting a compound of formula 3A to a compound of formula 4A:



3A 4A

wherein Step BX comprises reacting a compound of formula 3A with O_3 gas to form a compound of formula 4A.

In a fourth aspect of the present disclosure, there is provided a process for preparing a compound of formula I:



(I),

or a pharmaceutically acceptable salt or solvate thereof, wherein

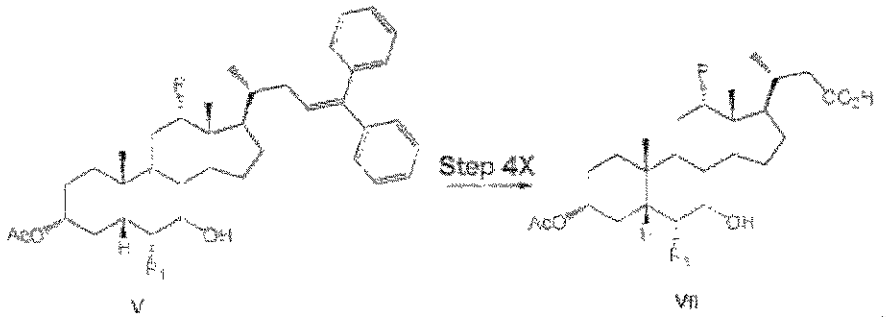
the dashed bond (----) at position 7 indicates that the substituent is in an α or ß stereochemistry;

R is hydrogen or hydroxy; and

R_1 is hydrogen or C_1-C_6 alkyl,

comprising the step of

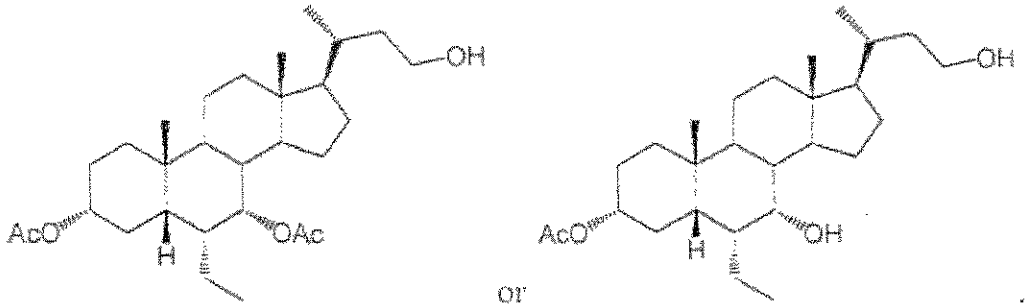
Step 4X: converting a compound of formula V to a compound of formula VII:



V VII

wherein Step 4X comprises reacting a compound of formula V with O_2 gas to form a compound of formula VII.

In a fifth aspect of the present disclosure, there is provided a compound of the following structure:



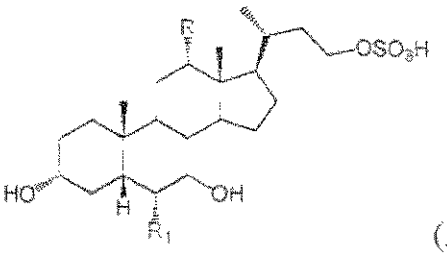
Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which the present disclosure ~~this invention~~ belongs. In the case of conflict, the present specification, including definitions, will control. In the specification, the singular forms also include the plural unless the context clearly dictates otherwise. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present ~~invention~~disclosure, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference. The references cited herein are not admitted to be prior art to the present disclosure~~claimed invention~~. In addition, the materials, methods, and examples are illustrative only and are not intended to be limiting.

Other features and advantages of the ~~invention~~ present disclosure will be apparent from the following detailed description and claims.

BRIEF DESCRIPTION OF THE DRAWINGS

CLAIM

1. A provided a process for preparing a compound of formula I:



(I),

or a pharmaceutically acceptable salt or solvate thereof, wherein

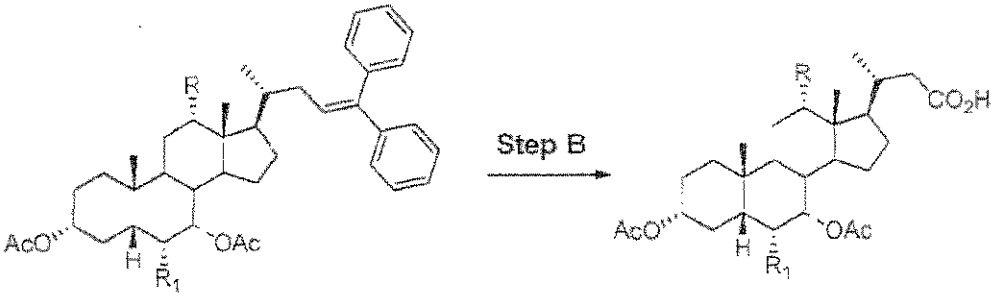
the dashed bond (----) at position 7 indicates that the substituent is in an α or ß stereochemistry;

R is hydrogen or hydroxy; and

R_1 is hydrogen or C_1-C_6 alkyl;

comprising the step of

Step B: converting a compound of formula 3A to a compound of formula 4A:

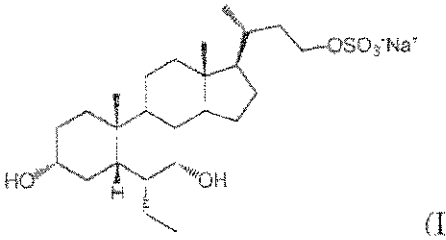


3A 4A

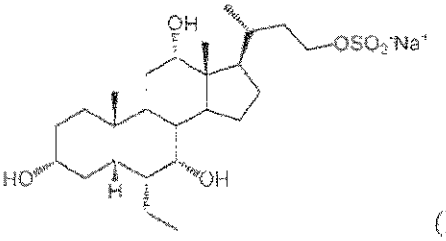
wherein Step B comprises reacting a compound of formula 3A with $RuCl_3$, $NaIO_4$, and an acid to form a compound of formula 4A.

2. The process of claim 1, wherein R_1 is ethyl.

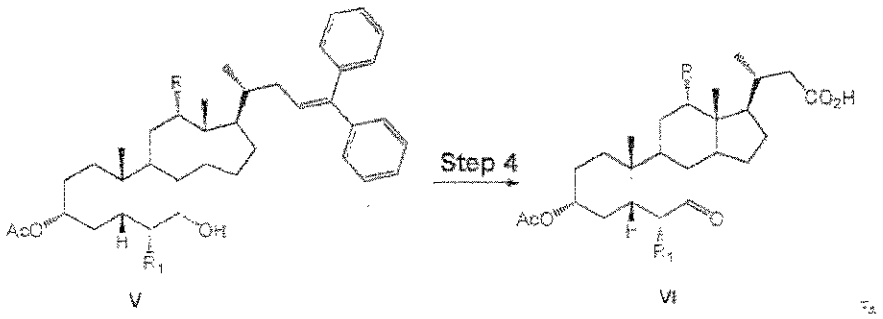
3. The process of claim 1, wherein the compound is selected from



(IA),



(IB),

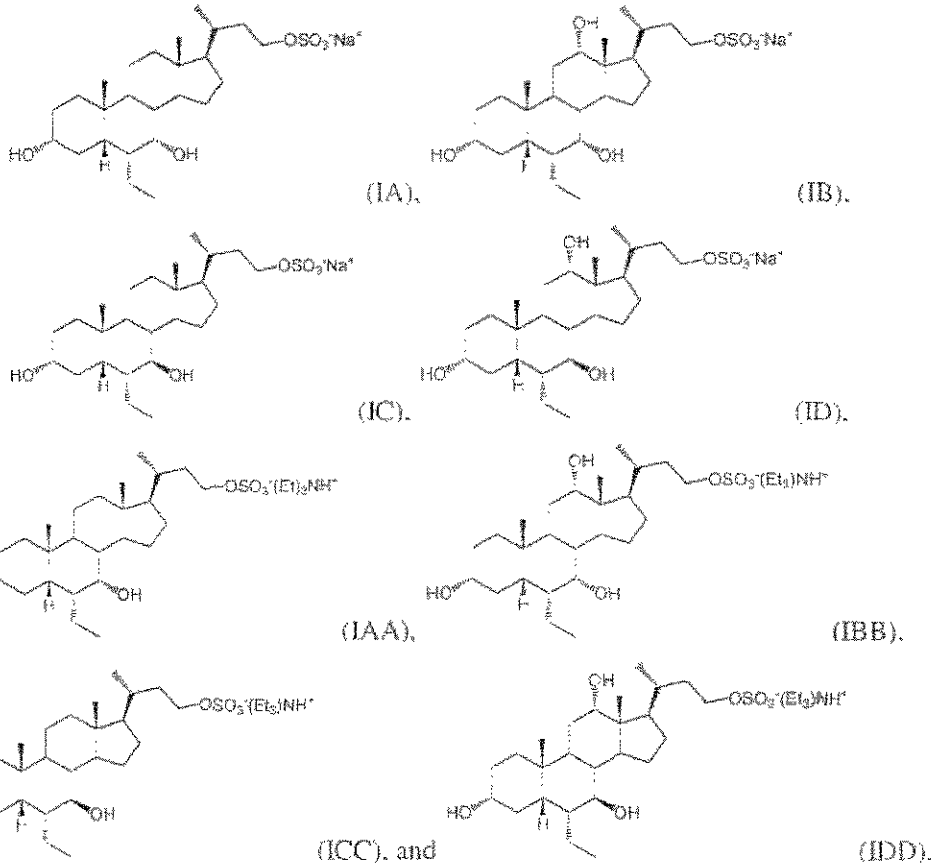


V VI

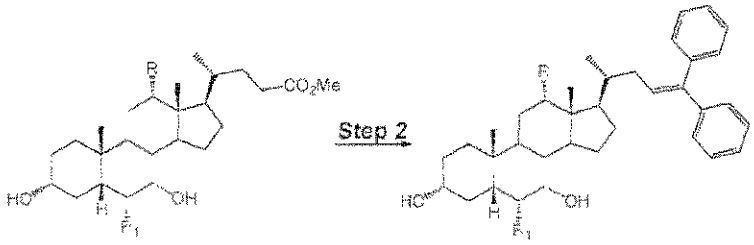
wherein Step 4 comprises reacting a compound of formula V with $RuCl_3$, $NaIO_4$, and an acid to form a compound of formula VI.

11. The process of claim 10, wherein R_1 is ethyl.

12. The process of claim 10, wherein the compound is selected from

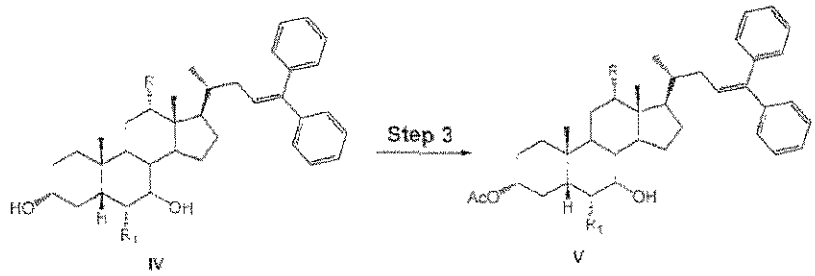


13. The process of claim 10, wherein Step 4 comprises reacting a compound of formula V with $NaIO_4$.



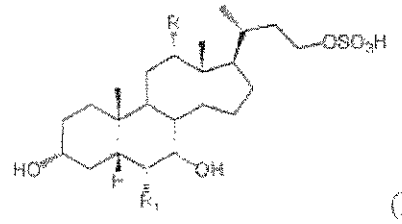
III IV ; and

Step 3: converting a compound of formula IV to a compound of formula V:



IV V

19. A process for preparing a compound of formula I:



(I),

or a pharmaceutically acceptable salt or solvate thereof, wherein

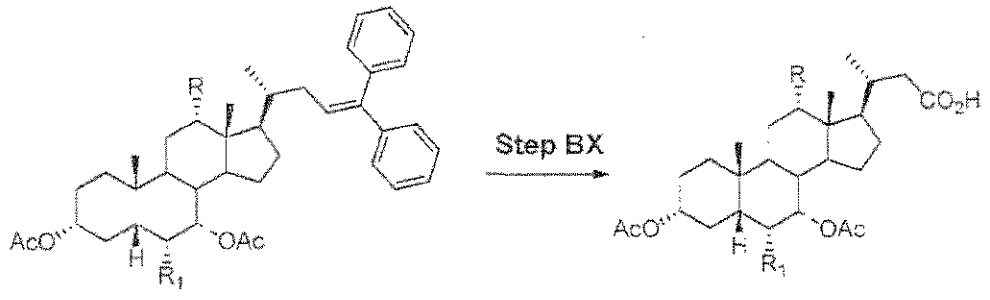
the dashed bond (----) at position 7 indicates that the substituent is in an α or ß stereochemistry;

R is hydrogen or hydroxy; and

R_1 is hydrogen or C_1-C_6 alkyl,

comprising the step of

Step BX: converting a compound of formula 3A to a compound of formula 4A:



3A 4A

wherein Step BX comprises reacting a compound of formula 3A with O_3 gas to form a