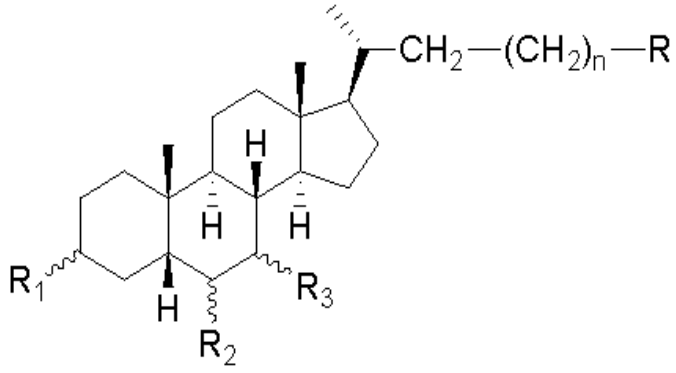
CLAIMS

1. A compound of formula (I)




(I)

wherein

$R_1$ is OH or H;

$R_2$ is Et or =CH-$CH_3$;

$R_3$ is OH or H;

n is 0, 1, or 3;

R is $CH_2OH$, COOH, $CH_2OSO_3H$, or CN;

proviso that

when $R_2$ is Et or =CH-$CH_3$ and $R_3$ is OH:

if n is 0 or 1 then R is $CH_2OH$ or CN when $R_1$ is alpha-OH or R is COOH, $CH_2OH$ or $CH_2OSO_3H$ when $R_1$ is beta-OH or H;

if n is 3 then $R_1$ and R are as defined above;

including inorganic and organic pharmaceutically acceptable salts, solvates or amino acid conjugates thereof;

excluding a compound wherein

| compund ID | N | $R_1$ | $R_2$ | $R_3$ | R |
|---|---|---|---|---|---|
| BAR504 | 1 | alpha-OH | alpha-Et | alpha-OH | CH2OH |
| BAR502 | 0 | alpha-OH | alpha-Et | alpha-OH | CH2OH |

2. The compound according to claim 1 wherein $R_2$ is Et or =CH-$CH_3$, $R_3$ is OH and

if n is 0 or 1, then R is $CH_2OH$ or CN when $R_1$ is alpha-OH or R is $CH_2OH$, $CH_2OSO_3H$ or COOH when $R_1$ is beta-OH or H;

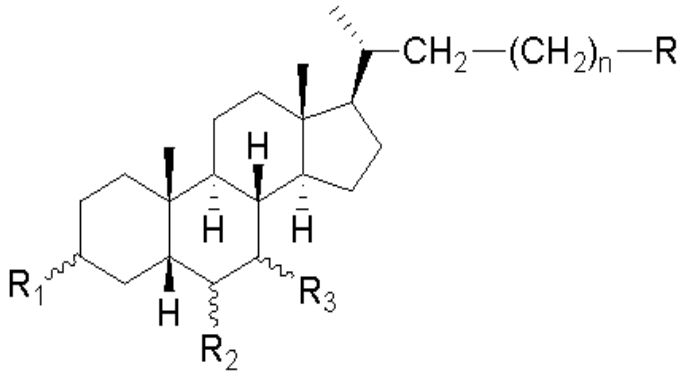
if n is 3 then $R_1$, $R_3$ and R are as defined above.

3. The compound according to claim 2 wherein

n is 0 or 1, R is $CH_2OH$ or CN and $R_1$ is alpha-OH or n is 0 or 1, R is COOH, $CH_2OH$ or $CH_2OSO_3H$ and $R_1$ is beta-OH or H.

4. The compound according to claim 2 wherein $R_2$ is Et, n is 3, $R_1$ is alpha-OH and $R_3$ is alpha-OH.

5. Use of a compound of formula (I)




(I)

wherein

$R_1$ is OH or H;

$R_2$ is Et or =CH-$CH_3$;

$R_3$ is OH or H;

n is 0, 1, or 3;

R is $CH_2OH$, COOH, $CH_2OSO_3H$, or CN;

proviso that

when $R_2$ is Et or =CH-$CH_3$ and $R_3$ is OH:

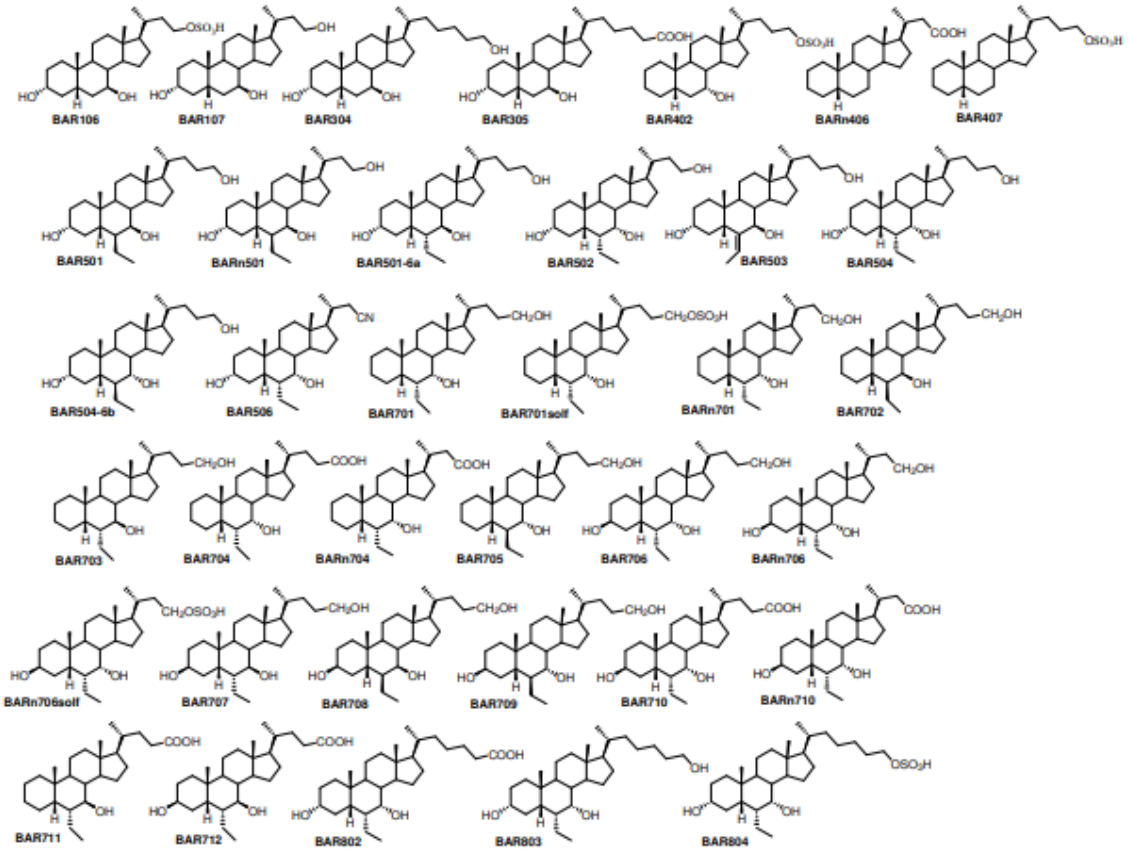
if n is 0 or 1 then R is $CH_2OH$ or CN when $R_1$ is alpha-OH or R is $CH_2OH$, $CH_2OSO_3H$ or COOH when $R_1$ is beta-OH or H;

if n is 3 then $R_1$ and R are as defined above;

including inorganic and organic pharmaceutically acceptable salts, solvates or amino acid conjugates thereof in the preparation of a medicament for the

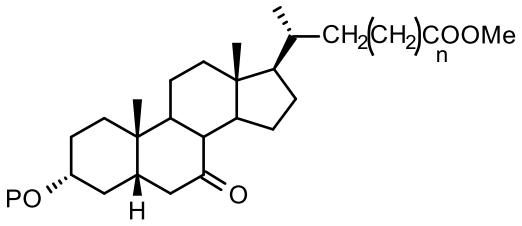
prophylactic and/or treatment of diseases responsive to FXR and/or TGR5/GPBAR1 modulation selected from the group of gastrointestinal disorders, liver diseases, cardiovascular diseases, atherosclerosis, metabolic diseases, infectious diseases, cancer, renal disorders, inflammatory disorders, and neurological disorders.

6. The use according to claim 5, wherein said compound of formula (I) is selected from the group consisting of



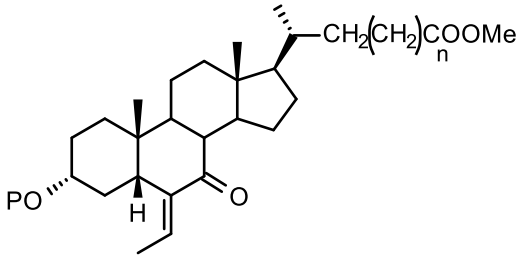

7. The use according to claim 5 or 6 wherein the medicament additionally comprises at least one other pharmaceutical ingredient.

8. A process for preparing a compound of formula (I), according to any one of claims 1-6, wherein $R_2$ is $=CH-CH_3$ or Et and $R_3$ is not H, said process comprising subjecting a compound of formula (VIII) to an aldol condensation thus contacting a compound of formula (VIII)




(VIII)

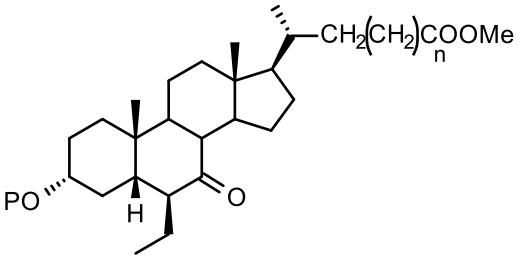
wherein n is 0 or 1, P is an hydroxyl protecting group, with alkyl lithium, such as nBuLi, and subsequently with acetaldehyde, preferably in presence also of $BF_3(OEt)_2$, for obtaining a compound of formula (IX)




(IX)

wherein n and P are as above described and

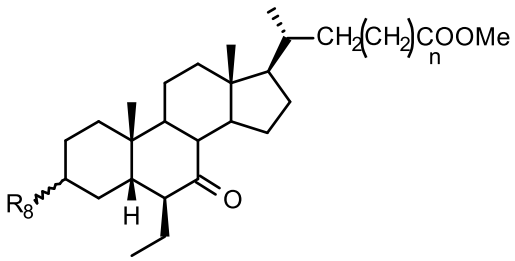
wherein the compound of formula (IX) is subjected to a catalytic hydrogenation, for obtaining a compound of formula (X)




(X).

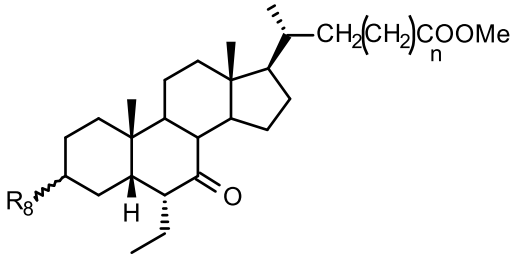
9. The process according to claim 8 wherein the compound of formula (X) is subjected to reduction of carbonyl at C7 by contacting the compound of formula (X) with $NaBH_4$ or $Ca(BH_4)_2$ for obtaining a mixture of alpha-OH and beta-OH at C7; and subsequently subjected to a treatment with $LiBH_4$ which completely reduces the methyl ester function on side chain to $–CH_2OH$.

10. A process for preparing a compound of formula (I), according to any one of claims 1-6, wherein $R_2$ is alpha-Et, said process comprising contacting with MeONa/MeOH a compound of formula (XIV)




(XIV)

wherein n is 0 or 1, $R_8$ is beta-OH, OAc or H for obtaining epimerization of the C6 stereocenter thus obtaining a compound of formula (XI)

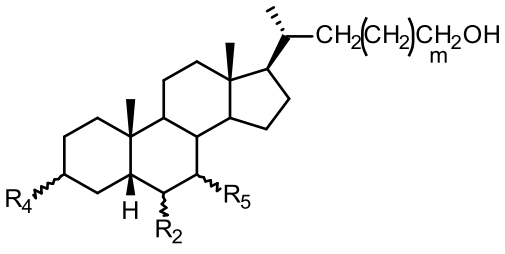



(XI)

wherein, in case $R_8$ is OAc the treatment with MeONa/MeOH affords simultaneously the C3 acetoxy group hydrolysis.

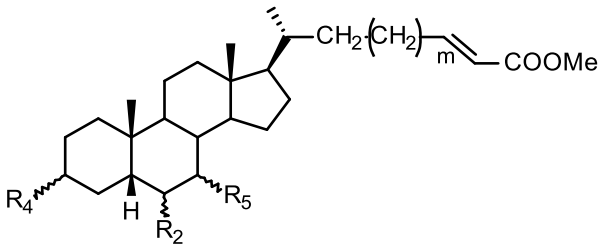
11. The process according to claim 10 wherein a reduction of carbonyl at C7 is obtained contacting a compound of formula (XI) or corresponding compound having COOH at the side chain, with $LiBH_4$ obtaining almost exclusively alpha-OH at C7; wherein the treatment with $LiBH_4$ simultaneously reduces, if present, the methyl ester function on side chain to –CH2OH and de-protects OAc if present at C3.

12. A process for preparing a compound of formula (I), according to any one of claims 1-2 or any one of claims 4-6, wherein n= 3 said process comprising subjecting a corresponding compound of formula (IV)




(IV)

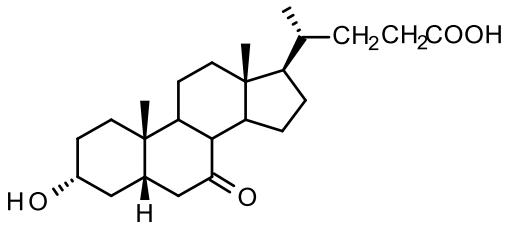
wherein m=n-2=1, $R_4$ and $R_5$, if other than H, are OP, wherein P is an alcoholic protecting function, and $R_2$ is H or Et, to a one pot Swern oxidation/Wittig C2 homologation for obtaining a protected methyl ester of formula (V)




(V)

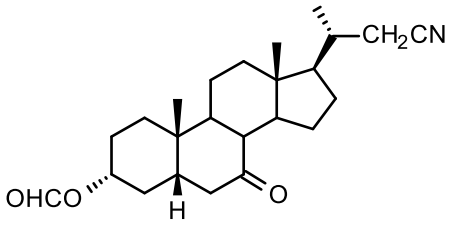
wherein m=1, $R_2$ is as defined in claim 1, $R_4$ and $R_5$, if other than H, are OP, wherein P is an alcoholic protecting function.

13. A process for preparing a compound of formula (I), according to any one of claims 1-3 or any one of claims 5-6, wherein n=0, said process comprising contacting a compound of formula (XII)



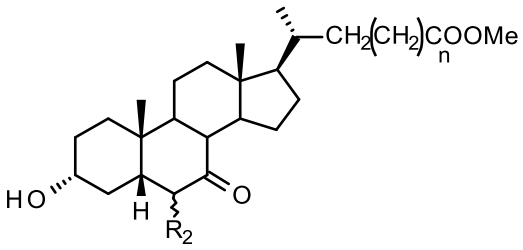

(XII)

with HCOOH and $HClO_4$ and subsequently contacting the resulting compound with TFA, trifluoroacetic anhydride and $NaNO_2$ for obtaining a compound of formula (VII)




(VII)

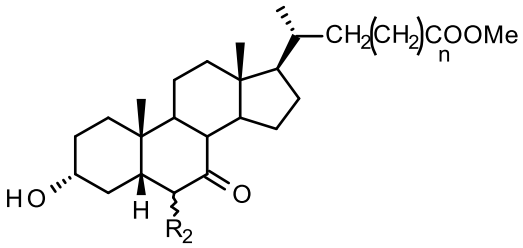
14. A process for preparing a compound of formula (I), according to any one of claims1-6, wherein $R_1$ is beta-OH, said process comprising starting from a compound having formula (XIII)




(XIII)

wherein $R_2$ is Et, n is 0 or 1 and inverting the C3 hydroxyl configuration by treatment with tosyl chloride in presence of a base then followed by a treatment with $CH_3COOK$.

15. A process for preparing a compound of formula (I), according to any one of claims 1-6, wherein $R_1$ is H, said process comprising subjecting a compound of formula (XIII)




(XIII)

wherein n is 0 or 1, $R_2$ Et or H, to tosylation and elimination at C-3 hydroxyl group followed by double bond reduction by way of a catalytic hydrogenation.