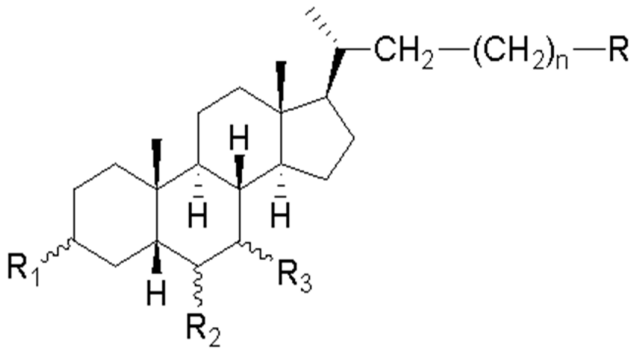
CLAIMS

1. A compound of formula (I)



(I)

wherein

R_1 is OH or H;

R_2 is Et~~,~~ or =CH-CH_3 ~~or H~~;

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;

~~when R_2 is H:~~

~~if R_1 is alpha-OH and R_3 is beta-OH then R is CH_2OH or CH_2OSO_3H when n is 0 or R is CH_2OH or COOH when n is 3;~~

~~if R_1 is H, n is 1 and R_3 is alpha-OH then R is CH_2OSO_3H;~~

~~if R_1 and R_3 are H then R is CH_2OSO_3H or COOH when n is 0 or R is CH_2OSO_3H when n is 1;~~

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
~~BAR107~~	~~0~~	~~alpha-OH~~	~~H~~	~~beta-OH~~	~~CH2OH~~
~~BARn406~~	~~0~~	~~H~~	~~H~~	~~H~~	~~COOH~~
BAR504	1	alpha-OH	alpha-Et	alpha-OH	CH2OH
~~BAR407~~	~~1~~	~~H~~	~~H~~	~~H~~	~~CH2OSO3H~~
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.

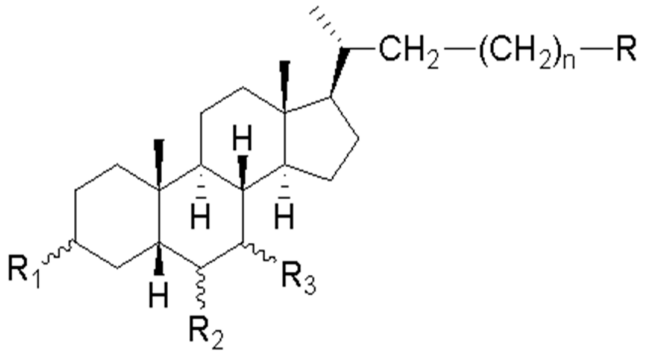
~~5. The compound according to claim 1 wherein R_2 is H and~~

~~if R_1 is alpha-OH and R_3 is beta-OH then R is CH2OH or CH_2OSO_3H when n is 0 or R is CH2OH or COOH when n is 3;~~

~~if R_1 is H, n is 1 and R_3 is alpha-OH then R is CH_2OSO_3H;~~

~~if R_1 and R_3 are H then R is CH_2OSO_3H or COOH when n is 0 or R is CH_2OSO_3H when n is 1.~~

~~6.~~5. A ~~compound for use as a medicament, said~~ method for the prevention 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, comprising administration of a compound of formula (I)



(I)

wherein

R_1 is OH or H;

R_2 is Et, or =CH-CH_3, ~~or H~~;

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;

~~when R_2 is H:~~

~~if R_1 is alpha-OH and R_3 is beta-OH then R is CH_2OH or CH_2OSO_3H when n is 0 or R is CH_2OH or COOH when n is 3;~~

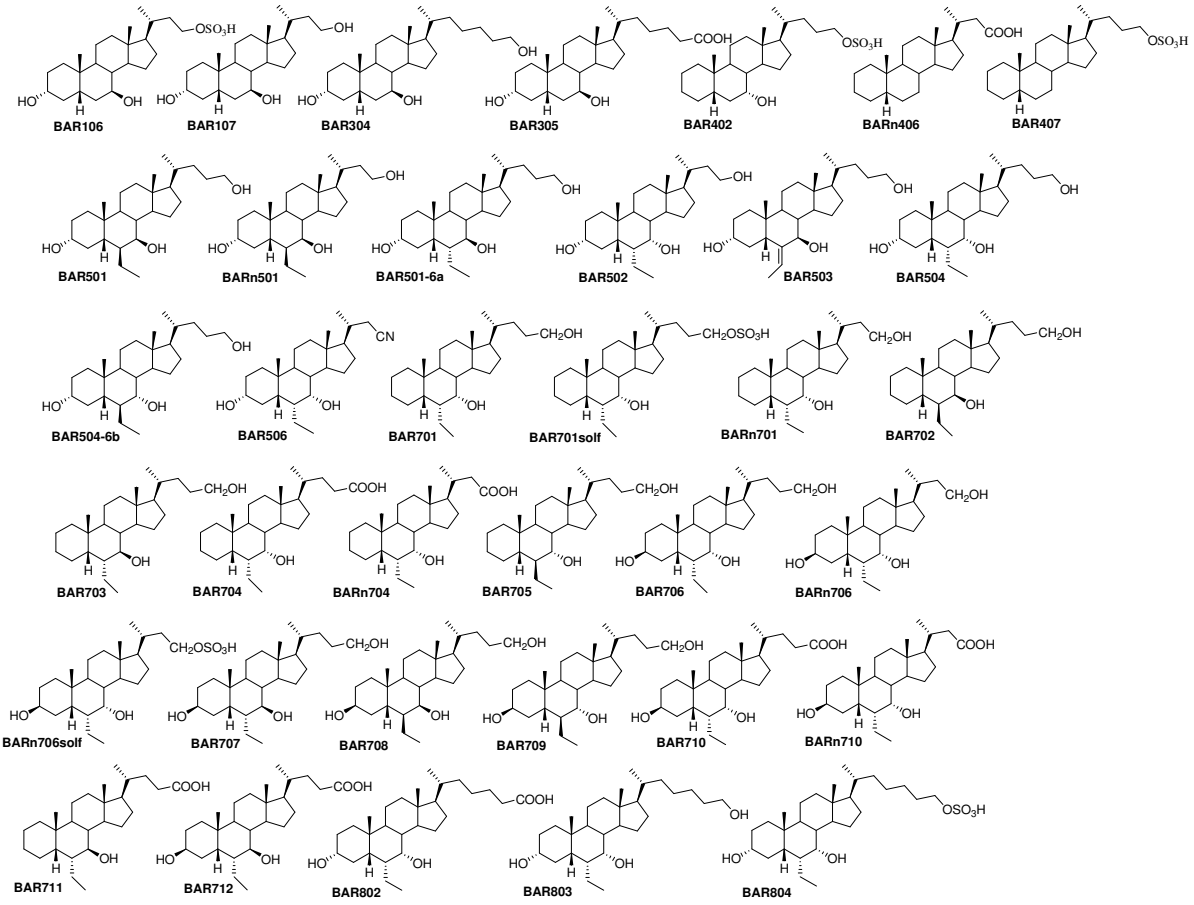
~~if R_1 is H, n is 1 and R_3 is alpha-OH then R is CH_2OSO_3H;~~

~~if R_1 and R_3 are H then R is CH2OSO3H or COOH when n is 0 or R is CH_2OSO_3H when n is 1;~~

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

~~7. A compound for use as a medicament, according to claim 6, said compound of formula (I) as defined in any one of claims 2-5.~~

~~8.~~6. ~~A compound for use as a medicament, according to claim 6,~~ The method according to claim 5 wherein said compound of formula (I) ~~being~~ is selected ~~in~~ from the group consisting of

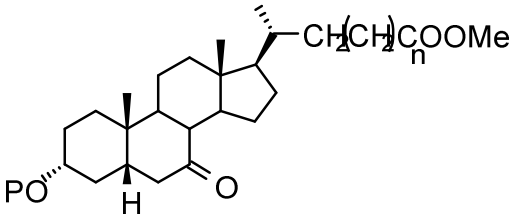


7. The method according to claim 5 or 6 wherein the compound of formula (I) is administered with at least another pharmaceutical ingredient.

~~9.~~8. ~~A~~ Use of a compound of formula (I) according to any one of claims 1-6 in the preparation of a medicament for ~~use, as~~ the prophylactic and/or treatment of diseases responsive to FXR and/or TGR5/GPBAR1 ~~modulator, in the prevention and/or treatment~~ 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~~, said compound of formula (I), as defined in anyone of claims 6-8~~.

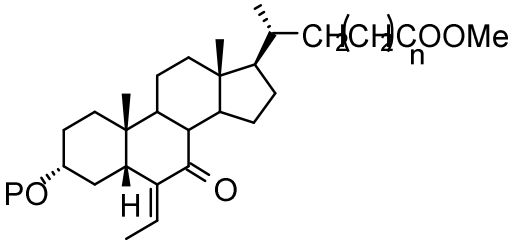
~~10.~~9. ~~A pharmaceutical composition comprising a compound of formula (I) and~~ The use according to claim 8 wherein the medicament additionally comprises at least ~~another~~ one other pharmaceutical ingredient.~~; said compound of formula (I), as defined in anyone of claims 6-8.~~

~~11.~~10. A process for preparing a compound of formula (I), according to ~~anyone~~ any one of claims ~~1-4 or as defined in any one of claims 6-8~~ 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)

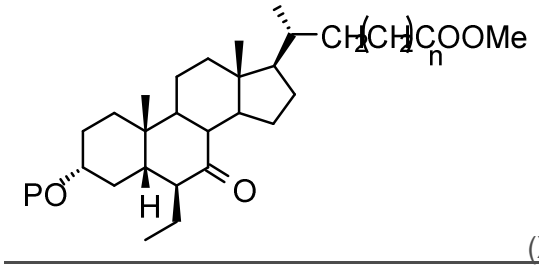
wherein n is 0 or 1, P is an hydroxyl protecting group, with alkyl lithium, such as nBuLi, and subsequently with acetaldehyde, preferably in presence also of $BF_3(OEt)_2$, for obtaining a compound of formula (IX)



(IX)

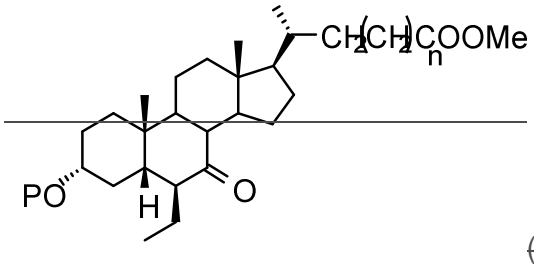
wherein n and P are as above described~~.~~ and

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



(X).

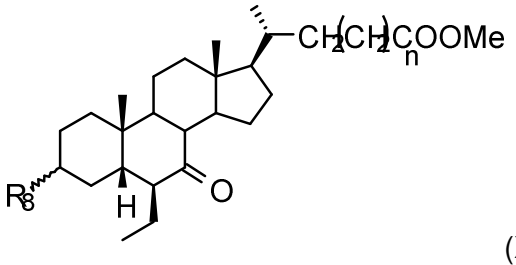
~~12. The process according to claim 11, wherein the compound of formula (IX) is subjected to a catalytic hydrogenation, for obtaining a compound of formula (X)~~



~~(X)~~

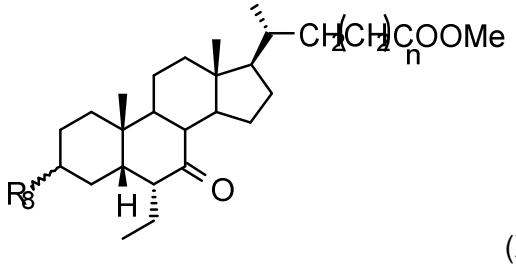
~~13.~~11. The process according to claim ~~12~~ 10 wherein the compound of formula (X) is subjected to reduction of carbonyl at C7 by contacting the compound of formula (X) with $NaBH_4$ or $Ca(BH_4)_2$ for obtaining a mixture of alpha-OH and beta-OH at C7; and subsequently subjected to a treatment with $LiBH_4$ which completely reduces the methyl ester function on side chain to $–CH_2OH$.

~~14.~~12. A process for preparing a compound of formula (I), according to any one of claims ~~1-4 or as defined in any one of claims 6-8~~ 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)

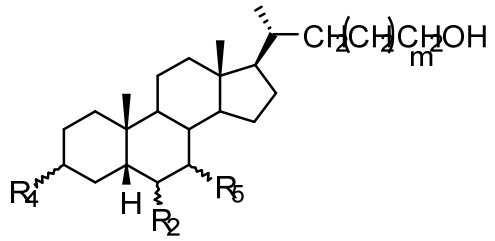


(XI)

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

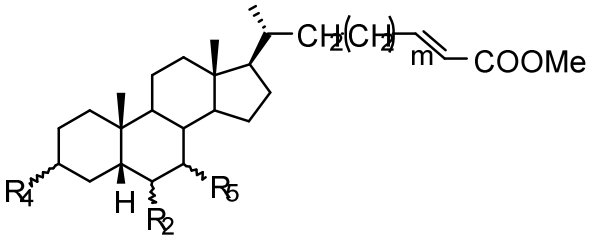
~~15.~~13. The process according to claim ~~14~~ 12 wherein a reduction of carbonyl at C7 is obtained contacting a compound of formula (XI) or corresponding compound having COOH at the side chain, with $LiBH_4$ obtaining almost exclusively alpha-OH at C7; wherein the treatment with $LiBH_4$ simultaneously reduces, if present, the methyl ester function on side chain to –CH2OH and de-protects OAc if present at C3.

~~16.~~14. A process for preparing a compound of formula (I), according to ~~anyone~~ any one of claims 1-2 ~~and 4-5~~ or ~~as defined in~~ any one of claims ~~6-8~~ 4-6, wherein n= 3 said process comprising subjecting a corresponding compound of formula (IV)



(IV)

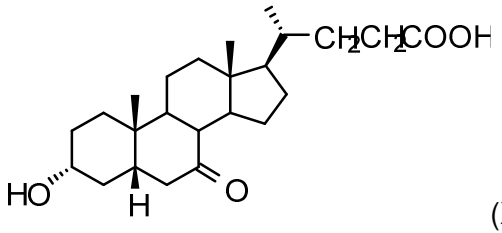
wherein m=n-2=1, R_4 and R_5, if other than H, are OP, wherein P is an alcoholic protecting function, and R_2 is H or Et, to a one pot Swern oxidation/Wittig C2 homologation for obtaining a protected methyl ester of formula (V)



(V)

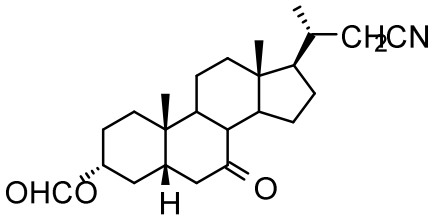
wherein m=1, R_2 is as defined in claim 1, R_4 and R_5, if other than H, are OP, wherein P is an alcoholic protecting function.

~~17.~~15. A process for preparing a compound of formula (I), according to ~~anyone~~ any one of claims 1-3 ~~and 5~~ or ~~as defined in~~ any one of claims ~~6-8~~ 5-6, wherein n=0, said process comprising contacting a compound of formula (XII)



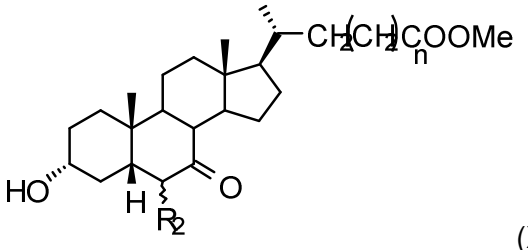
(XII)

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)

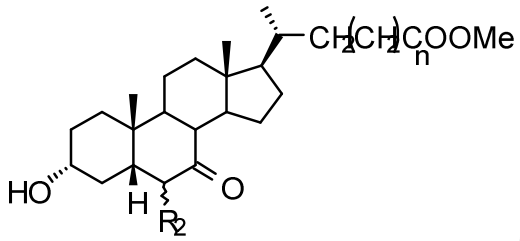
~~18.~~16. A process for preparing a compound of formula (I), according to ~~anyone~~ any one of claims ~~1-5~~ 1-6 ~~or as defined in any one of claims 6-8~~, wherein R_1 is beta-OH, said process comprising starting from a compound having formula (XIII)



(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.

~~19.~~17. A process for preparing a compound of formula (I), according to ~~anyone~~ any one of claims ~~1-5 or as defined in any one of claims 6-8~~ 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.