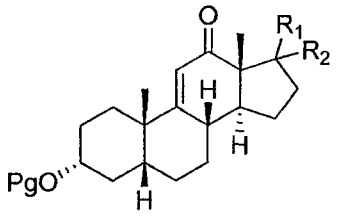
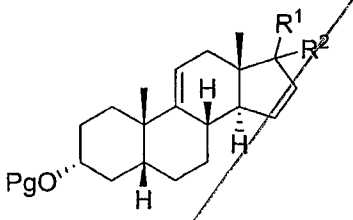
Claims:

1. A process for preparing a 12-keto compound **3**:



3

from the corresponding Δ-9,11-ene compound **4**:

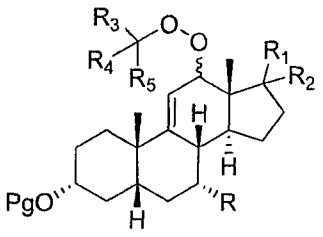


4

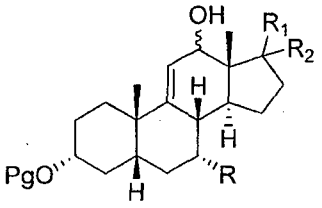
where Pg is a hydroxyl protecting group, R is hydrogen, hydroxyl, or –OPg, R^1 is the 17-side chain of a bile acid, which bile acid is selected from the group consisting of cholic acid, deoxycholic acid, taurocholic acid, and glycocholic acid, wherein the carboxyl functionality of said side chain is optionally esterified with a C_1-C_6 alkyl group, and R^2 is hydrogen, or R^1 and R^2 together with the carbon atom attached thereto form a keto group or a keto protecting group;

said process comprises;

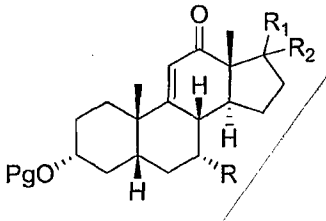
effecting allylic oxidation at the 12-position of compound **4** by reaction with an alkylhydroperoxide of the formula $(R^3)(R^4)(R^5)C\text{-}O\text{-}OH$ in the presence of a co-oxidant, wherein each of R^3, R^4, and R^5 is independently C_1-C_3 alkyl, to first provide a mixture of compounds **1**, **2** and **3**:



1



2



3

and optionally wherein compound **2** is then further oxidized to provide the Δ-9,11-ene-12-one compound **3**.

2. A process for converting an 11-β-hydroxysteroid to the corresponding 12-ketosteroid wherein said process comprises:

a) selecting an appropriately protected 11-β-hydroxysteroid;

b) dehydrating the 11-β-hydroxysteroid to provide the Δ-9,11-ene functionality in said steroid;

c) effecting allylic oxidation at the 12-position by reacting the steroid product of b) above with alkylhydroperoxide in the presence of a co-oxidant; and

d)hydrogenating the Δ-9,11-ene functionality to yield the 9-α-hydro-11-dihydro-12-ketosteroid; and

e) optionally reducing the 12-keto functionality of the 9-α-hydro-11-dihydro-12-ketosteroid produced in d) above with an effective amount of a reducing agent to provide the 9-α-hydro-11-dihydro-12-α-hydroxysteroid.

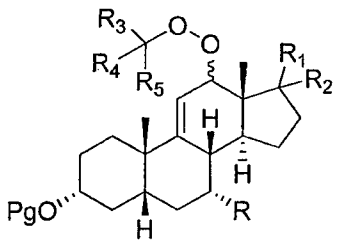
3. The process of claim 2, wherein the 11-β-hydroxysteroid is prepared by reducing a corresponding 11-ketosteroid with at least a stoichiometric amount of a reducing agent to provide the 11-β-hydroxysteroid.

4. The process of claim 2, wherein the 11-β-hydroxysteroid is hydrocortisone or a hydrocortisone derivative.

5. The process of any one of claims 1 and 2, wherein the allylic oxidation is effected by a more than one equivalent of *tert*-butyl hydroperoxide and in the presence of CuI.

6. The process of any one of claims 1 and 2, wherein the co-oxidant is selected from the group consisting of aqueous sodium hypochlorite, palladium on carbon, $Pd(OCOCF_3)_2$, $Pd(OAc)_2$ and CuI.

7. A compound of formula **1**:



1

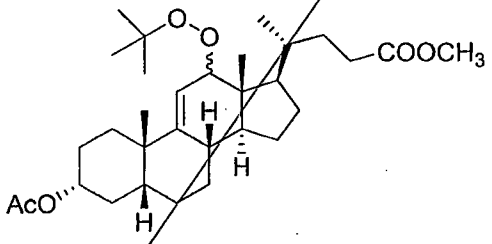
wherein

Pg is a hydroxyl protecting group,

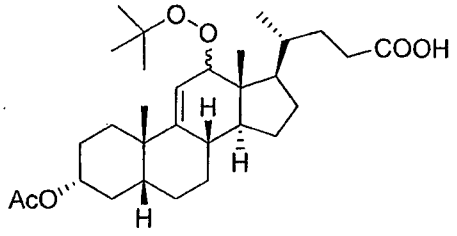
R is hydrogen, hydroxyl, or –OPg, R^1 is the 17-side chain of a bile acid selected from the group consisting of cholic acid, deoxycholic acid, taurocholic acid, and glycocholic acid, wherein the carboxyl functionality of said side chain is optionally esterified with a C_1-C_6 alkyl group, and R^2 is hydrogen, or R^1 and R^2 together with the carbon atom attached thereto form a keto or a keto protecting group, and

each of R^3, R^4 and R^5 is independently C_1-C_3 alkyl.

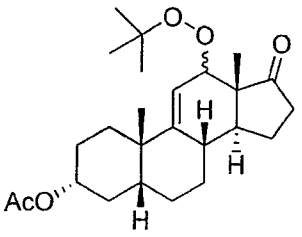
8. The compound of claim 7, wherein the compound of formula **2** is selected from the group consisting of compounds **42**, **43**, **44**, **45** and **46**:



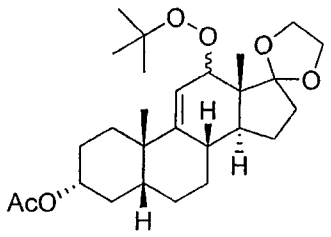
42



43

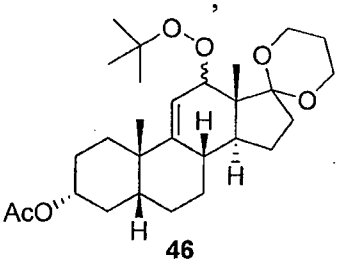


44



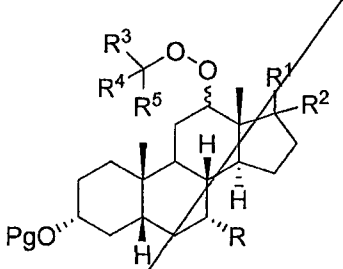
45

, and



46

9. A compound of formula **5**



5

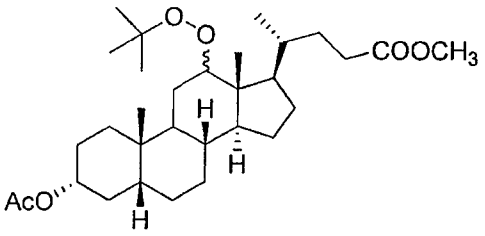
wherein

Pg is a hydroxyl protecting group;

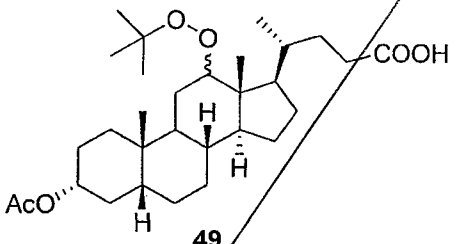
R is hydrogen, hydroxyl, or –OPg, R^1 is the 17-side chain of a bile acid selected from the group consisting of cholic acid, deoxycholic acid, taurocholic acid, and glycocholic acid, wherein the carboxyl functionality of said side chain is optionally esterified with a C_1-C_6 alkyl group, and R^2 is hydrogen, or R^1 and R^2 together with the carbon atom attached thereto form a keto or a keto protecting group; and

each of R^3, R^4 and R^5 is independently C_1-C_3 alkyl.

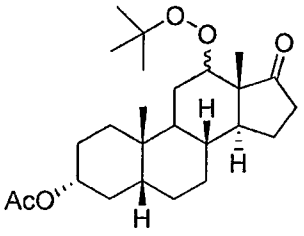
10. The compound of claim 9, wherein the compound of formula **5** is selected from the group consisting of compounds **48**, **49**, **50**, **51** and **52**:



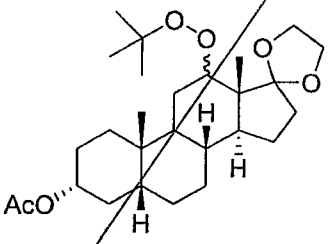
48



49

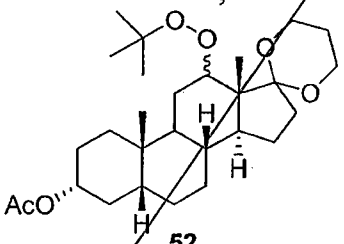


50



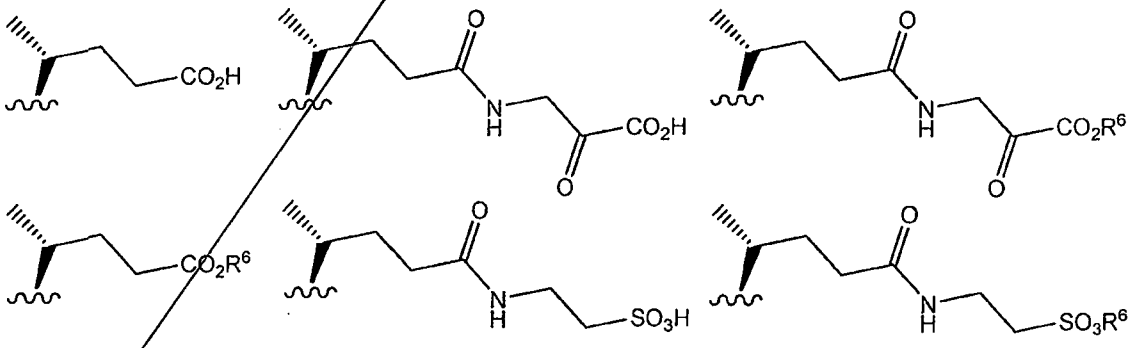
51

, and



52

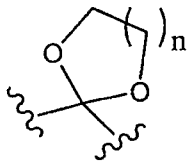
11. The compound of any of claims 7 or 9, wherein R^1 is selected from the group consisting of



wherein R^6 is lower alkyl and the wavy line ~~~ represents the point of connection to the 17-position of steroidal scaffold.

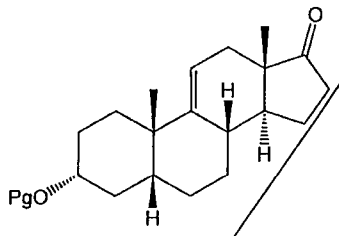
12. The compound of any of claims 7 or 9, wherein R^1 and R^2 together with the carbon atom attached thereto form a keto group.

13. The compound of any of claims 7 or 9, wherein R^1 and R^2 together with the carbon atom attached thereto form:



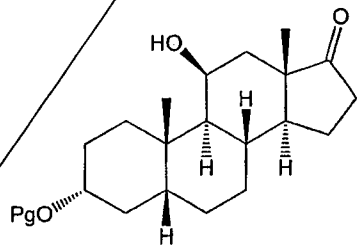
wherein n is 1, 2, or 3 and the wavy line ∿∿ represents the point of connection to the rest of the molecule.

14. A method for preparing compound 12



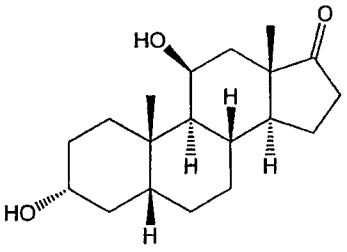
12

comprising contacting compound **13** wherein Pg is a hydroxyl protecting group:



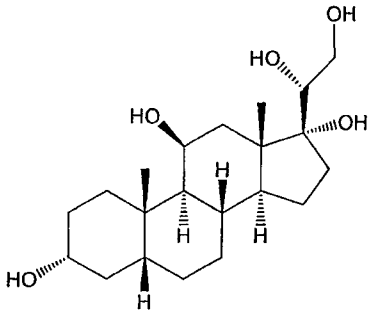
13

under dehydrating conditions to provide compound **12,** wherein compound **13** is prepared by a method comprising selectively protecting the 3-hydroxyl group of compound **17**



17

wherein compound **17** is prepared by a method comprising contacting compound **16**

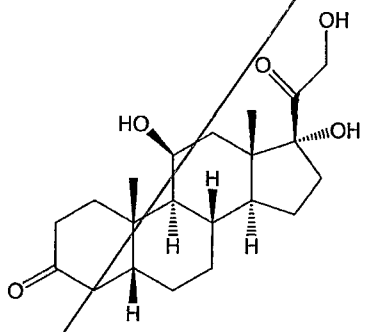


16

with a vicinal alcohol oxidizing agent under oxidizing conditions.

15. The method of claim 14, wherein the vicinal alcohol oxidizing agent is $NaIO_4$.

16. The method of claim 15, wherein compound **16** is prepared by a method comprising contacting compound **15**

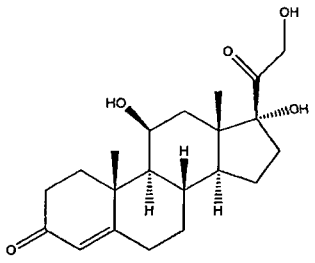


15

with at least 2 equivalents of a reducing agent under conditions wherein the carbonyl groups are reduced to alcohol groups.

17. The method of claim 16, wherein the reducing agent comprises $NaBH_4$.

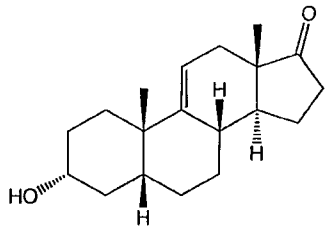
18. The method of claim 17, wherein compound **15** is prepared by a method comprising contacting hydrocortisone :



with at least a molar equivalent of hydrogen under hydrogenation conditions.

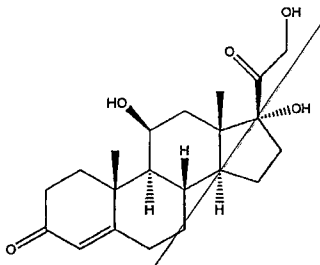
19. The method of claim 18, wherein the hydrogenation conditions comprise Pd/C as a catalyst and DMF as a solvent.

20. A method for preparing a compound of formula **14**

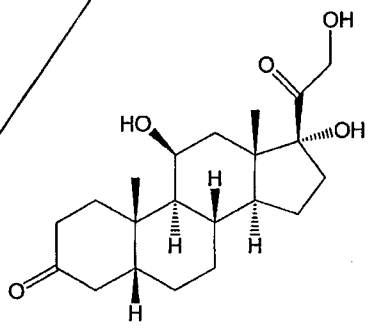


14

a) contacting hydrocortisone:

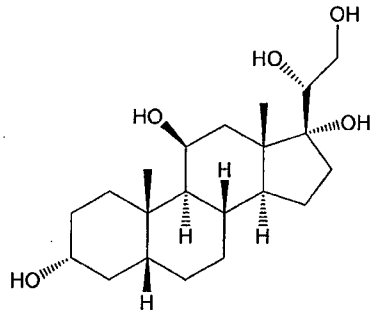


with at least a molar equivalent of hydrogen under hydrogenation conditions to provide 4,5-dihydro-hydrocortisone – compound **15**:



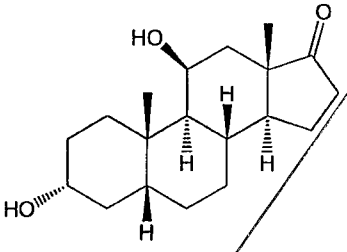
15

contacting compound **15** with at least 2 equivalents of a reducing agent under conditions wherein the carbonyl groups are reduced to alcohol groups to provide compound **16**:



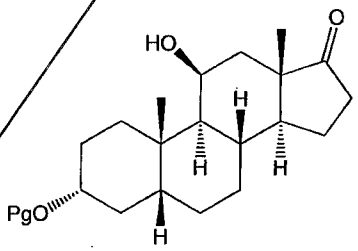
16

c) contacting compound **16** with a vicinal alcohol oxidizing agent under oxidizing conditions to provide compound **17**:



17

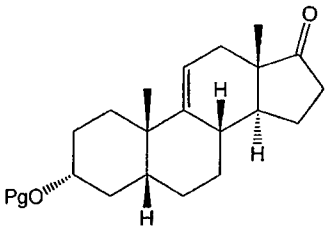
d) selectively protecting the 3-hydroxyl group of compound **17** to provide a compound of formula **13**:



13

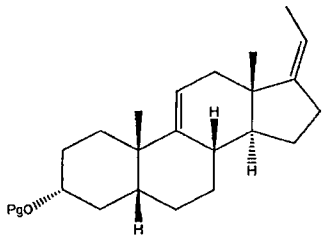
where Pg is a hydroxyl protecting group;

e) contacting the compound of formula **13** under dehydrating conditions to provide a compound of formula **12**; and



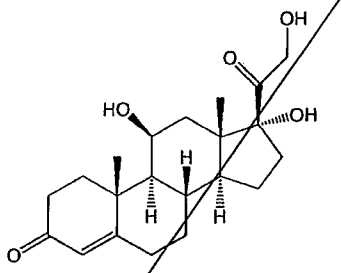
f) removing the hydroxyl protecting group to provide compound **14**.

21. A method of preparing a compound of formula **18**, said method comprising:

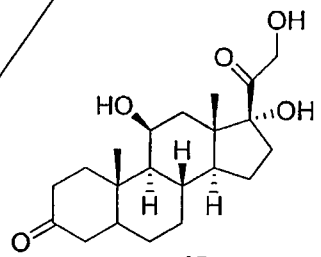


18,

a) contacting hydrocortisone :

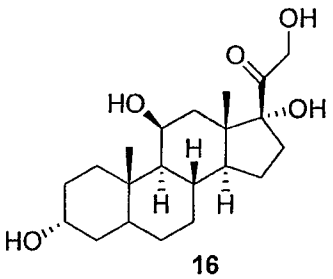


with at least a molar equivalent of hydrogen under hydrogenation conditions to provide 4,5-dihydro-hydrocortisone – compound **15**:



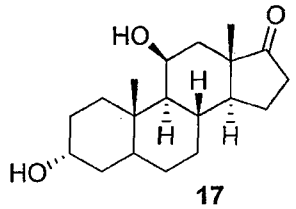
15

contacting compound **15** with at least 2 equivalents of a reducing agent under conditions wherein the carbonyl groups are reduced to alcohol groups to provide compound **16**:



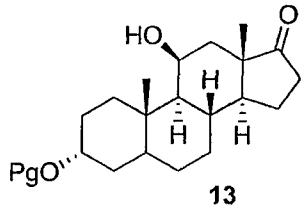
16

c) contacting compound **16** with a vicinal alcohol oxidizing agent under oxidizing conditions to provide compound **17**:



17

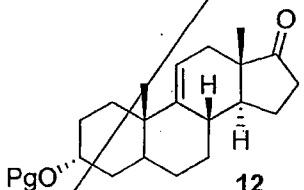
d) selectively protecting the 3-hydroxyl group of compound **17** to provide compound **13**:



13

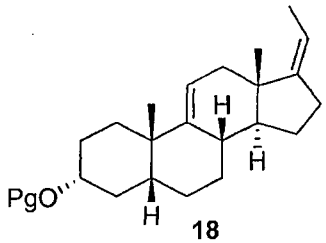
where Pg is a hydroxyl protecting group;

e) contacting the compound of formula **13** under dehydrating conditions to provide compound **12**; and



12 ; and

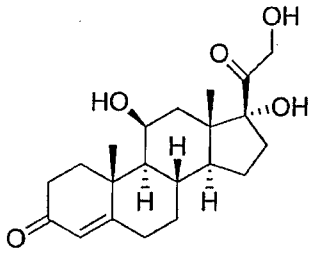
f) converting compound **12** under olefin forming conditions to form compound **18**;



18

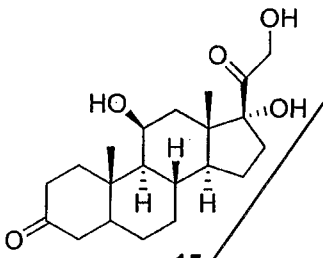
22. A method of preparing deoxycholic acid or a salt thereof, said method comprising:

a) contacting hydrocortisone :



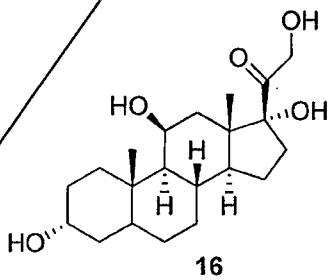
hydrocotisone

with at least a molar equivalent of hydrogen under hydrogenation conditions to provide 4,5β-dihydro-hydrocortisone – compound **15**:



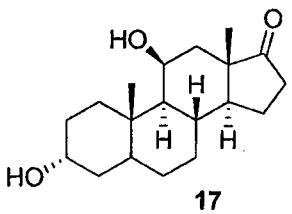
15 ;

contacting compound **15** with at least 2 equivalents of a reducing agent under conditions wherein the carbonyl groups are reduced to alcohol groups to provide compound **16**:



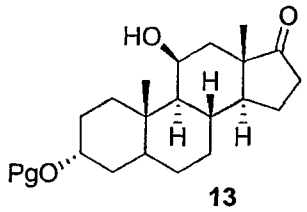
16 ;

c) contacting compound **16** with a vicinal alcohol oxidizing agent under oxidizing conditions to provide compound **17**:



17 ;

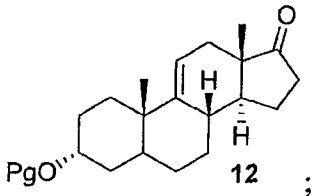
d) selectively protecting the 3-hydroxyl group of compound **17** to provide compound **13**:



13 ;

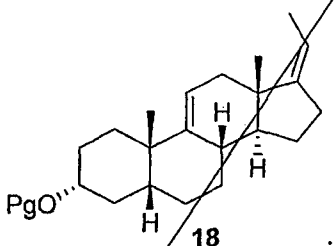
where Pg is a hydroxyl protecting group;

e) contacting compound **13** under dehydrating conditions to provide compound **12**:



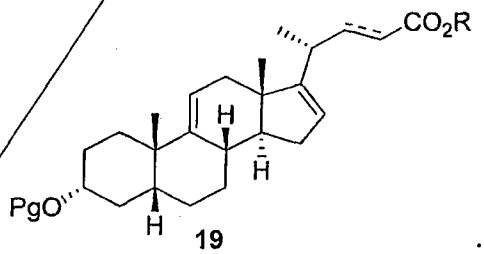
12 ;

f) converting compound **12** under olefin forming conditions to form compound **18:**



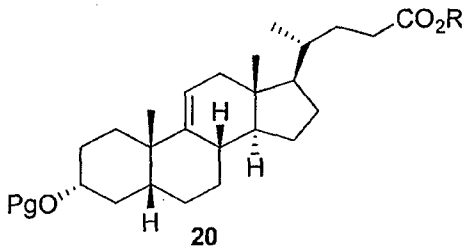
18 ;

g) reacting compound **18** with an alkylpropiolate CH≡CC(O)OR or an alkyl acrylate CH_2=CHC(O)OR wherein R is alkyl in the presence of a Lewis acid to form compound **19** wherein the dashed line ---- is a single or double bond;



19 ;

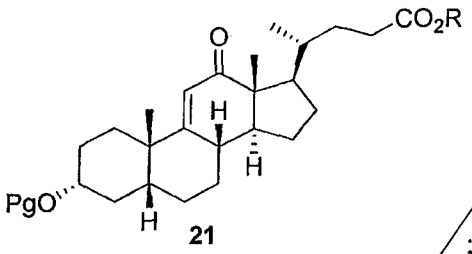
h) reacting the compound of formula **19** with H_2 under hydrogenation conditions to form compound **20**:



20

;

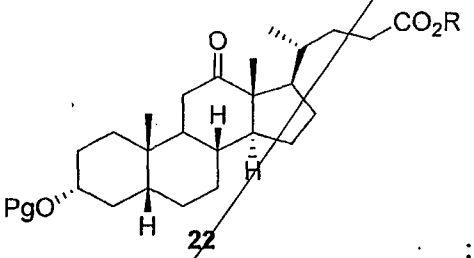
i) reacting compound **20** with an oxidizing agent to form compound **21**:



21

;

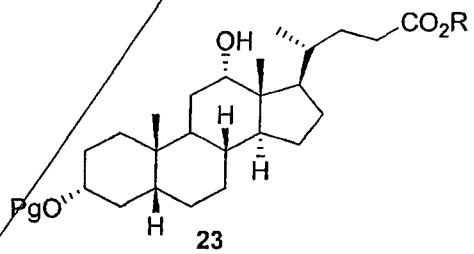
j) reacting compound **21** with H_2 under hydrogenation conditions to form compound **22**:



22

;

k) reacting compound **22** with a reducing agent to form compound **23**:



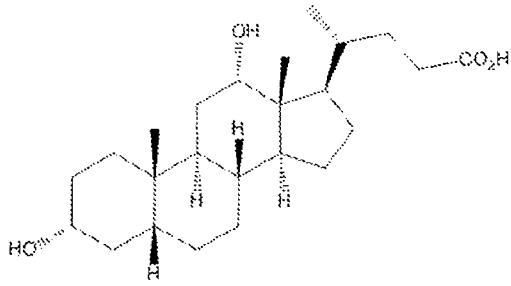
23

; and

l) exposing compound **23** to deprotection and hydrolysis conditions to form deoxycholic acid or the salt thereof.

What is claimed is:

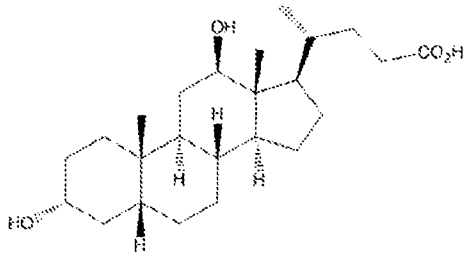
1. A pharmaceutical composition comprising:



DCA

or a pharmaceutically acceptable salt thereof, and a steroidal DCA precursor or byproduct containing an 12-β hydroxy group.

2. The pharmaceutical composition of claim 1 comprising DCA or a pharmaceutically acceptable salt thereof and



12-β DCA

or a pharmaceutically acceptable salt thereof as the steroidal DCA precursor or byproduct containing an 12-β hydroxy group.

3. The pharmaceutical composition of Claim 1, wherein the 12-β DCA is present in an amount less than that of the DCA.

4. The pharmaceutical composition Claim 1, wherein the 12-β DCA is less than 6% of the total amount of the DCA and the 12-β DCA.

5. The pharmaceutical composition Claim 1, wherein the 12-β DCA is less than 3% of the total amount of the DCA and the 12-β DCA.

6. The pharmaceutical composition as claimed in any one of clams 1 to 5 wherein said salt is a sodium salt.

7. The pharmaceutical composition as claimed in any one of claims 1 to 6, wherein the concentration of DCA or pharmaceutically acceptable salt is between 0.001 and 10% w/w, w/v or v/v, such as between 0.01 and 5 % w/w, w/v or v/v.

8. The pharmaceutical composition as claimed in any one of claims 1 to 7, which additionally comprises a lipid, a phospholipid, or a phosphatidylcholine, such as up to 5% w/w, w/v or v/v of a lipid, a phospholipid or a phosphatidylcholine.

9. The pharmaceutical composition as claimed in any one of claims 1 to 7, which additionally comprises at least one additional active ingredient selected from the group consisting of: anti-microbial agents, vasoconstrictors, anti-thrombotic agents, anti-coagulation agents, suds-depressants, anti-inflammatory agents, analgesics, dispersion agents, anti-dispersion agents, penetration enhancers, steroids, tranquilizers, muscle relaxants, and anti-diarrhea agents.

10. The composition as claimed in claim 9, which additionally comprises one or more detergents.

11. A method for removal of fat deposits from selected locations in a mammal comprising administering to the mammal in need thereof a therapeutically effective amount of the composition of any one of claims 1 to 10.

12. The method of claim 11 further comprising administering to the mammal at least one additional active ingredient.

13. The method of claim 11 or 12, which is for treating a pathological localized fat deposit.

14. The method of claim 11 or 12, wherein the fat deposit is associated with a condition selected from the group consisting of: obesity, fat redistribution syndrome, eyelid fat herniation, lipomas, Dercum's disease, lipodystrophy, buffalo hump lipodystrophy, dorsocervical fat, visceral adiposity, breast enlargement, hyperadiposity, diffused body fat around trunk and arms, and cellulite.

16. Use of a composition of claim 1 in the manufacture of a medicament for a non-surgical cosmetic reduction of localized fat deposit in a skin region of a human subject, wherein the medicament comprises a therapeutically effective amount of the composition.

17. The use as claimed in claim 16, wherein said medicament for a non-surgical cosmetic reduction of localized fat deposit in a skin region is for local or subcutaneous administration.