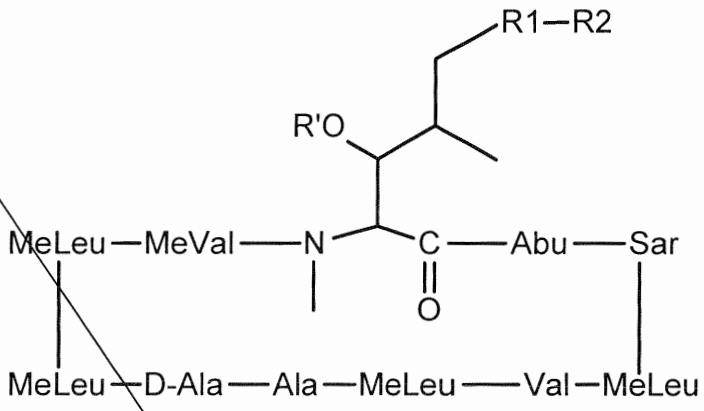
CLAIMS

1. A compound of Formula I:



Formula I

wherein

a. R' is H or acetyl;

b. R1 is a straight chain or branched alkane or alkene group from 2 to 15 carbon atoms in length; and

c. R2 is selected from the group consisting of :

   i. a hydroxyl group;

   ii. an unsubstituted, N–substituted, or N,N-disubstituted amide;

   iii. a N-substituted or unsubstituted acyl protected amine;

   iv. a carboxylic acid;

   v. a N-substituted or unsubstituted amine;

   vi. a nitrile;

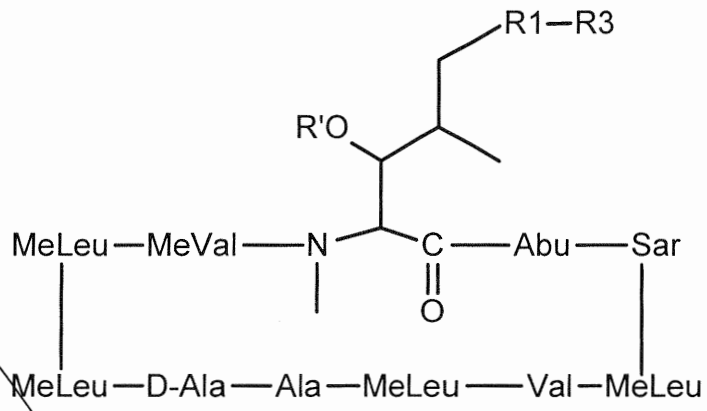
   vii. an ester;

   viii. a ketone;

   ix. a hydroxy, dihydroxy, trihydroxy, or polyhydroxy alkyl; and

   x. a substituted or unsubstituted aryl.

2. A compound of Formula II:



Formula II

wherein

a. R' is H or acetyl;

b. R1 is a straight chain or branched alkane or alkene group from 2 to 15 carbon atoms in length; and

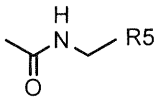
c. R3 is selected from the group consisting of :

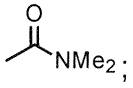
   i. a saturated or unsaturated. straight or branched aliphatic chain containing a substituent selected from the group consisting of ketones, hydroxyls, nitriles, carboxylic acids, esters and 1,3-dioxolanes;

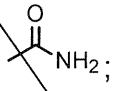
   ii. an aromatic group containing a substituent selected from the group consisting of halides, esters and nitro; and

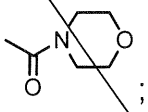
   iii. a combination of the saturated or unsaturated, straight or branched aliphatic chain of (i) and the aromatic group of (ii).

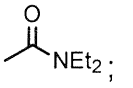
3. The compound of claim 1, wherein R2 is selected from the group consisting of

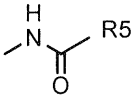
a. ;

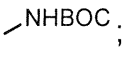
b. ;

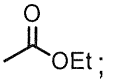
c. ;

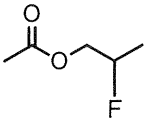
d. ;

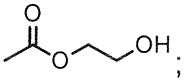
e. ;

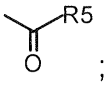
f. ;

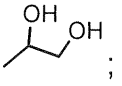
g. ;

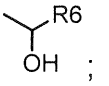
h. ;

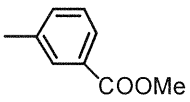
i. ;

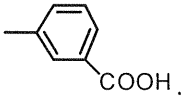
j. ;

k. ;

l. ;

m. ;

n. ; and

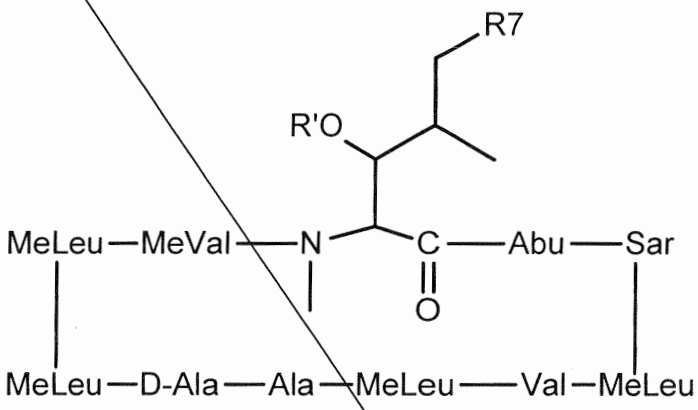
o. .

wherein

i. R5 is a saturated or unsaturated straight chain or branched aliphatic carbon chain between 1 and 10 carbons in length; and

ii. R6 is a monohydroxylated, dihydroxylated, trihydroxylated or polyhydroxylated saturated or unsaturated straight chain or branched aliphatic carbon chain between 1 and 10 carbons in length..

4. A compound of Formula IV:



Formula IV

wherein

I. R' is H or Acetyl; and

II. R7 is selected from the group consisting of :

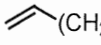
i. COOH;

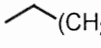
ii. 

;

iii. ;

iv. ;

v. ;

vi. ;

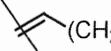
vii. ;

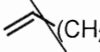
viii. ;

ix. ;

x. ;

xi. ;

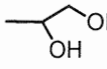
xii. ;

xiii. ;

xiv. ;

xv. ;

xvi. ;

xvii. ;

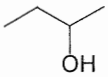
xviii. ;

xix. ;

xx. ;

xxi. ;

xxii. ;

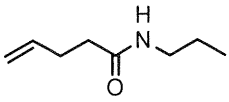
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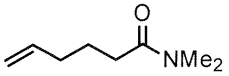
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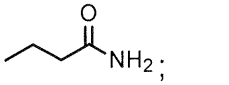
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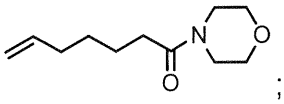
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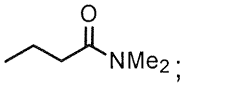
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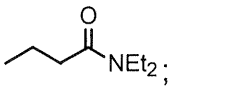
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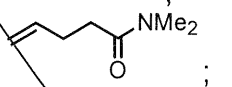
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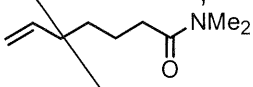
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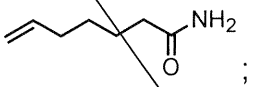
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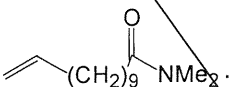
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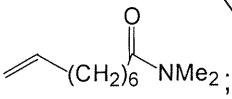
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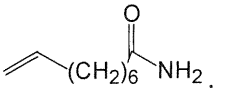
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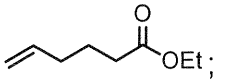
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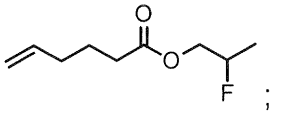
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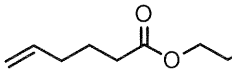
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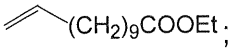
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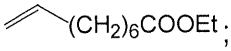
xxxix.  .

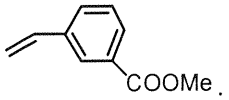
xl.  ;

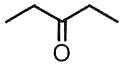
xli.  ;

xlii.  ;

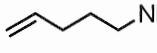
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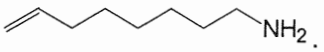
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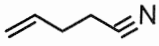
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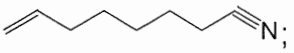
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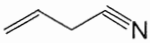
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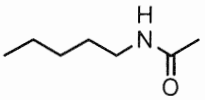
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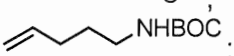
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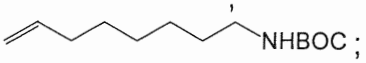
l. ;

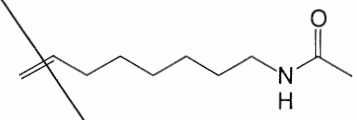
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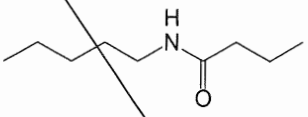
lii. ;

liii. ;

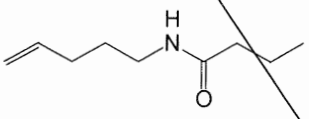
liv. ;

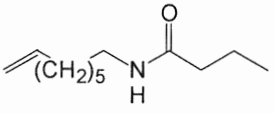
lv. ;

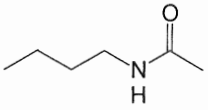
lvi. ;

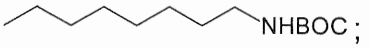
lvii. ;

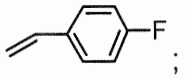
lviii. ;

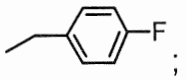
lix. ;

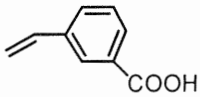
lx. ;

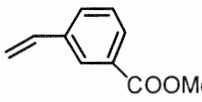
lxi. ;

lxii. ;

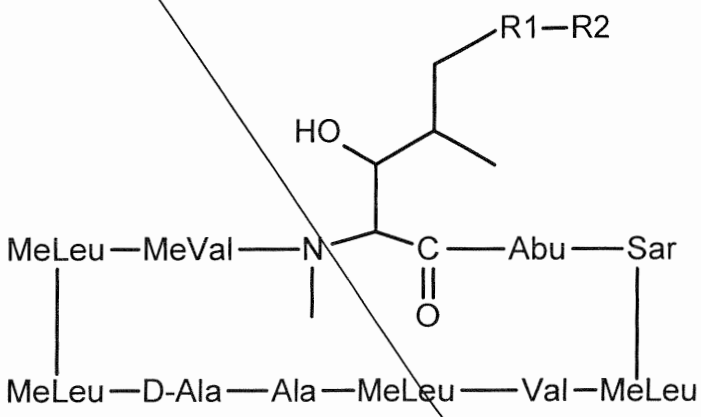
lxiii.  ;

lxiv.  ;

lxv.  ; and

lxvi.  .

5. A process to produce a compound of Formula VII:

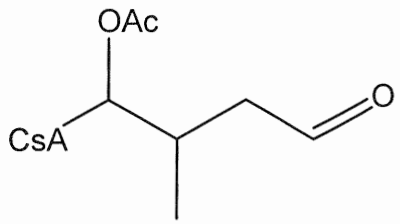


Formula VII

wherein R1 and R2 are as defined in claim 1,

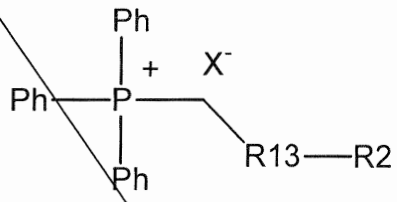
comprising the steps of

a. reacting acetyl CsA aldehyde modified at amino acid 1 of Formula IX:



Formula IX

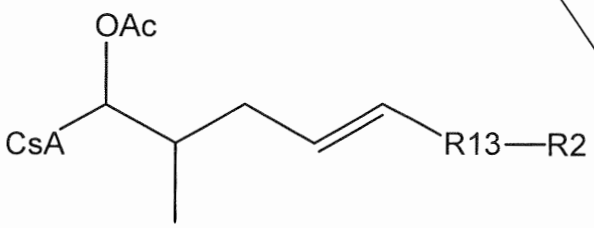
with a phosphonium salt of Formula XXXVIII:



Formula XXXVIII

wherein R13 is a straight chain or branched alkane or alkene from 1 to 13 carbon atoms in length;

in the presence of a base to produce an acetylated compound of Formula XXXIX:

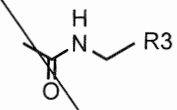


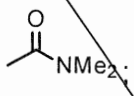
Formula XXXIX

b. deacetylating the compound of Formula XXXIX using a base; and

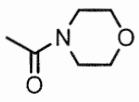
c. where R1 is saturated, hydrogenating the double bond of the compound of Formula XXXIX by reacting the compound with a hydrogenating agent to produce a saturated analogue of Formula I.

6. The process of claim 5, wherein R2 is selected from the group consisting of

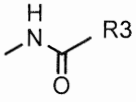
a. 

b. ;

c. ;

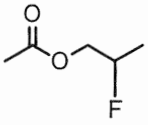
d. ;

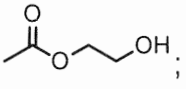
e. ;

f. 

g. ;

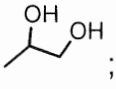
h. ;

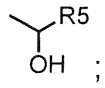
i. ;

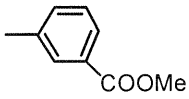
j. ;

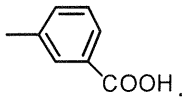
k. ;

l. ;

m. ;

n. ;

o. ; and

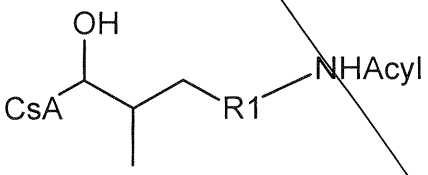
p. .

wherein

i. R5 is a saturated or unsaturated straight chain or branched aliphatic carbon chain between 1 and 10 carbons in length; and

ii. R6 is a monohydroxylated, dihydroxylated, trihydroxylated or polyhydroxylated saturated or unsaturated straight chain or branched aliphatic carbon chain between 1 and 10 carbons in length.

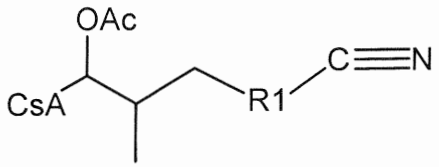
7. A process of producing a compound of the Formula XIV:



Formula XIV

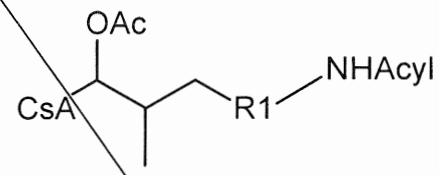
comprising the steps of

a. reacting the compound of Formula XV:



Formula XV

in the presence of a reducing agent and an acylating agent to produce acetylated compounds of Formula XVI:



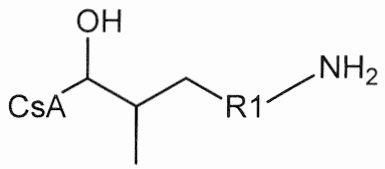
Formula XVI

and

b. deacetylating the compound of Formula XVI using a base;

wherein R1 of Formulae XIV, XV and XVI is a straight chain or branched alkane or alkene group between 2 and 15 carbons in length.

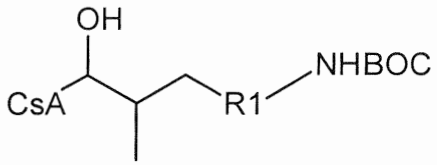
8. A process of producing a compound of the Formula XXX:



Formula XXX

comprising the steps of

a. by dissolving the compound of Formula XLVIII:



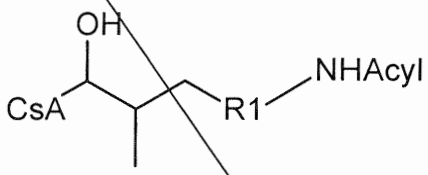
Formula XLVIII

in an anhydrous solvent; and

b. reacting the solution with trifluoroacetic acid (TFA);

wherein R1 of Formulae XXX and XLVIII is a straight chain or branched alkane or alkene group between 2 and 15 carbons in length.

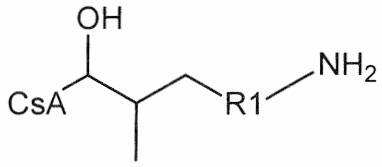
9. A process of producing a compound of the Formula XIV:



Formula XIV

comprising the steps of

a. dissolving the compound of Formula XXX:



Formula XXX

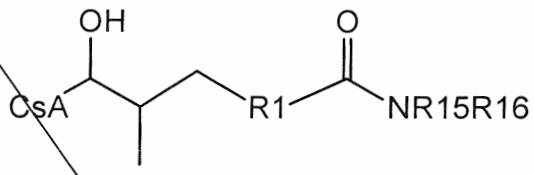
in anhydrous pyridine;

b. reacting the solution with acylating agent; and

c. removing the solvent to yield the compound of Formula XIV;

wherein R1 of Formulae XIV and XXX is a straight chain or branched alkane or alkene group between 2 and 15 carbons in length.

10. A process of producing a compound of the Formula XXXVII:



Formula XXXVII

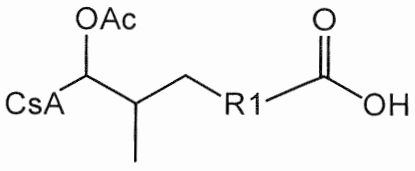
wherein

I. R1 is a straight or branched alkane or alkene group between 2 and 15 carbons in length; and

II. R15 and R16 are independently hydrogen or a saturated or unsaturated straight chain or branched aliphatic group; or where NR15R16 together forms a morpholinyl moiety;

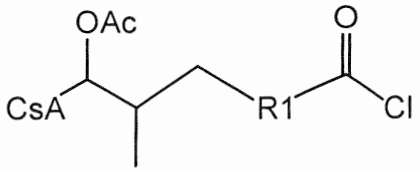
comprising the steps of

a. by combining the compound of Formula XXV:



Formula XXV

with thionylchloride to yield a residue of the Formula XXVI;



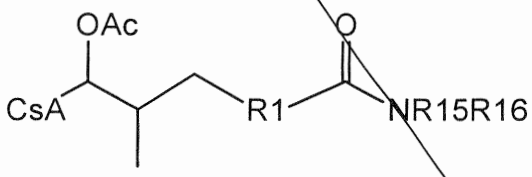
Formula XXVI

b. dissolving the residue in anhydrous solvent and reacting with a compound of the Formula XXVII:

R15R16NH

Formula XXVII

to yield the compound of Formula XXVIII

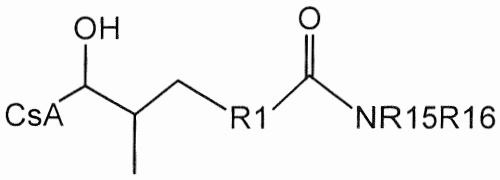


Formula XXVIII

and

c. deacetylating the compound of Formula XXVIII with a base.

11. A process of producing a compound of the Formula XXXVIII:



Formula XXXVIII

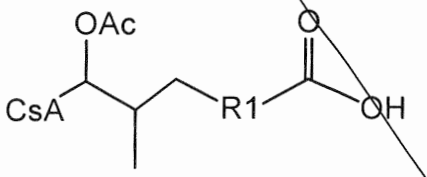
wherein

I. R1 is a straight chain or branched alkane or alkene group between 2 and 15 carbons in length;

II. R15 and R16 are independently hydrogen or a saturated or unsaturated straight chain or branched aliphatic group; or where NR15R16 together forms a morpholinyl moiety;

comprising the steps of

a. dissolving the compound of Formula XXV:



Formula XXV

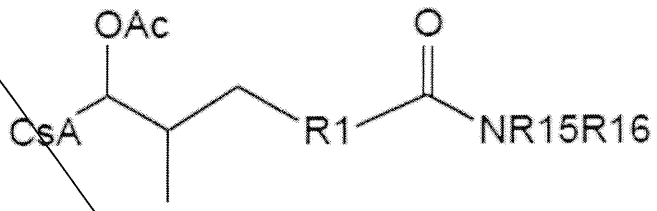
in anhydrous solvent under nitrogen;

b. reacting with dicyclohexylcarbodiimide, 1-hydroxybenzotriazole hydrate and the compound of the Formula XXVII;

R15R16NH

Formula XXVII

to form a compound of Formula XXVIII

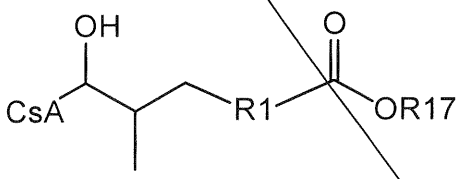


Formula XXVIII

; and

c. deacetylating the compound of Formula XXVIII with a base.

12. A process of producing a compound of the Formula XXXII:



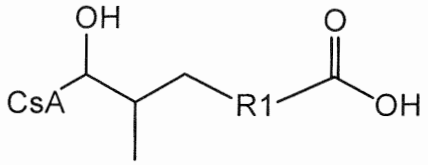
Formula XXXII

wherein

I. R1 is a straight chain or branched alkane or alkene group between 2 and 15 carbons in length; and

II. R17 is a saturated or unsaturated straight chain or branched aliphatic group, optionally containing a halogen or hydroxyl substituent;

by reacting the compound of Formula XXIX:



Formula XXIX

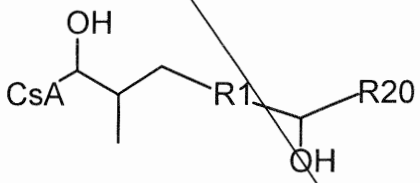
with a compound of Formula XXXI:

R17OH

Formula XXXI

in the presence of an acid.

13. A process of producing a compound of the Formula XL:



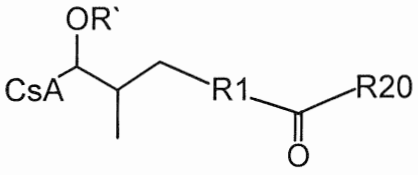
Formula XL

wherein

I. R1 is a straight chain or branched alkane or alkene group between 2 and 15 carbons in length; and

II. R20 is a saturated or unsaturated straight chain or branched aliphatic group;

by reacting the compound of Formula XXXV:



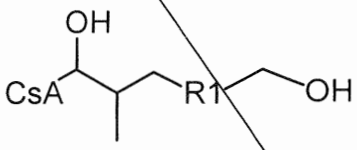
Formula XXXV

wherein R' is H or acetyl

with sodium borohydride; and

where R' is acetyl, deacetylating the compound of Formula XXXV with a base.

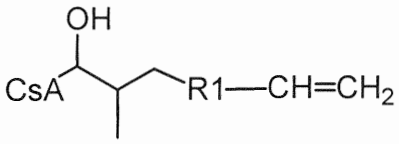
14. A process of producing a compound of the Formula XXIX:



Formula XXIX

wherein R1 is a straight chain or branched alkane or alkene group between 2 and 15 carbons in length;

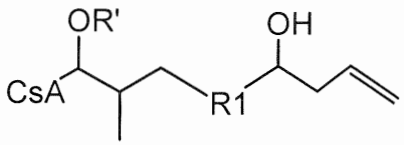
by reacting the compound of Formula XXXIII:



Formula XXXIII

with borane-tetrahydrofuran and sodium peroxide.

15. A process of producing a compound of the Formula XLIII:



Formula XLIII

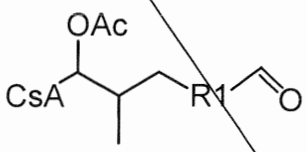
wherein

I. R' is H or Acetyl; and

II. R1 is a straight or branched alkane or alkene group between 2 and 15 carbons in length;

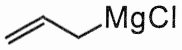
comprising the steps of:

reacting the compound of Formula XLI:



Formula XLI

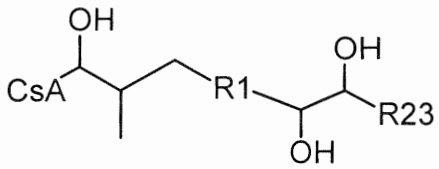
with the compound of Formula XLII;



Formula XLII

in an anhydrous solvent.

16. A process of producing a compound of the Formula XLVI:



Formula XLVI

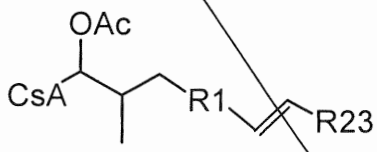
wherein

I. R1 is a straight chain or branched alkane or alkene group from 2 to 15 carbon atoms in length; and

II. R23 is a saturated or unsaturated straight chain or branched aliphatic group;

comprising the steps of:

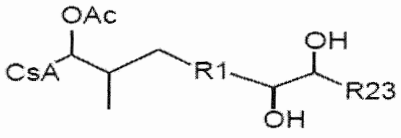
a. reacting the compound of Formula XLV



Formula XLV

with hydrogen peroxide and formic acid;

b. reacting the product with a base to yield the compound of Formula XLVII:



Formula XLVII

; and

c. deacetylating the compound of Formula XLVII with a base.

17. A pharmaceutical composition comprising a therapeutically effective amount of the compound of any one of claims 1 to 4 and one or more pharmaceutical excipients.

18. Use of the compound of any one of claims 1 to 4 in the preparation of a medicament for the treatment of a cyclophilin mediated disease or injury in a mammal

Th, wherein the cyclophilin mediated disease is selected from the group consisting of

a. an infection;
b. inflammation disease;
c. cancer; and
d. cellular, tissue or organ degeneration.

19. The use of claim 18, wherein the infection is selected from the group consisting of a viral infection, a bacterial infection, a fungal infection, and a parasitic infection.

20. The use of claim 19, wherein the viral infection is caused by a virus selected from the group consisting of Hepatitis C virus, Hepatitis B virus, Human Immunodeficiency Virus (HIV), Vaccinia virus, Influenza virus, Flaviviridae viruses, Coronaviridae viruses, Herpesviridae viruses, Papoaviridae viruses, Poxviridae viruses, and Encyphalitis viruses.

21. The use of claim 19, wherein the bacterial infection is caused by a Gram positive bacterium, Enterobacteriaceae bacteria or Pasteurellaceae bacteria.

22. The use of claim 19, wherein the parasitic infection is caused by a protozoan parasite or a helminth parasite,

23. The use of claim 18, wherein the inflammation is selected from the group consisting of asthma, chronic inflammation, coronary artery disease, cardiovascular inflammation, and vasculitis.

24. The use of claim 18, wherein the cancer is selected from the group consisting of small and non-small cell lung, bladder, hepatocellular, pancreatic and breast cancer.

25. The use of claim 18, wherein the cellular, tissue or organ degeneration is selected from the group consisting of cardiovascular disorders, diabetes, gastrointestinal disorders, hepatic disorders, muscular disorders, neurological disorders, renal disorders, and reperfusion injury.

26. The use of claim 25, wherein the muscular disorder is selected from the group consisting of muscular dystrophy, and collagen VI myopathies.

27. The use of claim 25, wherein the neurological disorder is selected from the group consisting of Alzheimer's disease, Parkinson's disease, Huntington's disease, Multiple Systems Atrophy, Multiple Sclerosis, cerebral palsy, stroke, diabetic neuropathy, amyotrophic lateral sclerosis (Lou Gehrig's Disease), vascular aneurysm, spinal cord injury, and cerebral injury.

28. The use of claim 25, wherein the cardiovascular disorder is selected from the group consisting of myocardial reperfusion injury, myocardial infarct, chronic heart failure, post-cardiac arrest syndrome and.stroke,.

29. The use of claim 25, wherein the gastrointestinal disorder is NSAID-induced small intestinal ulceration or asphyxia induced gastrointestinal damage.

30. The use of claim 25, wherein the hepatic disorder is acute hepatotoxicity or cholestasis.

31. The use of claim 25, wherein the renal disorder is hypoxic and ischemic renal injury.

32. The compound of any one of claims 1 to 4 for use in the treatment of a cyclophilin mediated disease or injury in a mammal wherein the cyclophilin mediated disease is selected from the group consisting of

a. an infection;
b. inflammation disease;
c. cancer; and
d. cellular, tissue or organ degeneration.

5

33. The compound of claim 32, wherein is the infection is selected from the group consisting of a viral infection, a bacterial infection, a fungal infection, and a parasitic infection.

34. The compound of claim 32, wherein the viral infection is caused by a virus selected from the group consisting of Hepatitis C virus, Hepatitis B virus, Human Immunodeficiency Virus (HIV), Vaccinia virus, Influenza virus, Flaviviridae viruses, Coronaviridae viruses, Herpesviridae viruses, Papoaviridae viruses, Poxviridae viruses, and Encyphalitis viruses.

35. The compound of claim 32, wherein the bacterial infection is caused by a Gram positive bacterium, Enterobacteriaceae bacteria or Pasteurellaceae bacteria.

36. The compound of claim 32, wherein the parasitic infection is caused by a protozoan parasite or a helminth parasite,

37. The compound of claim 32, wherein the inflammation is selected from the group consisting of asthma, coronary artery disease, cardiovascular inflammation and vasculitis.

38. The compound of claim 32, wherein the cancer is selected from the group consisting of small and non-small cell lung, bladder, hepatocellular, pancreatic and breast cancer.

39. The compound of claim 32, wherein the cellular, tissue or organ degeneration is selected from the group consisting of cardiovascular disorders, diabetes, gastrointestinal disorders, hepatic disorders, muscular disorders, neurological disorders, renal disorders, and reperfusion injury.

40. The compound of claim 39, wherein the muscular disorder is selected from the group consisting of muscular dystrophy, and collagen VI myopathies.

41. The compound of claim 39, wherein the neurological disorder is selected from the group consisting of Alzheimer's disease, Parkinson's disease, Huntington's disease, Multiple Systems Atrophy, Multiple Sclerosis, cerebral palsy, stroke, diabetic neuropathy, amyotrophic lateral sclerosis (Lou Gehrig's Disease), vascular aneurysm,spinal cord injury, and cerebral injury.

42. The compound of claim 39, wherein the cardiovascular disorder is selected from the group consisting of myocardial reperfusion injury, myocardial infarct, chronic heart failure, post-cardiac arrest syndrome and stroke.

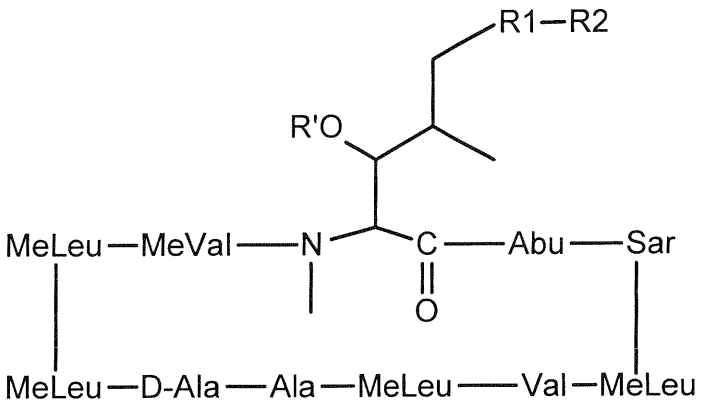
43. The compound of claim 39, wherein the gastrointestinal disorder is NSAID-induced small intestinal ulceration or asphyxia induced gastrointestinal damage.

44. The compound of claim 39, wherein the hepatic disorder is acute hepatotoxicity or cholestasis.

45. The compound of claim 39, wherein the renal disorder is hypoxic and ischemic renal injury.

Claims

1. A compound of Formula I:



Formula I

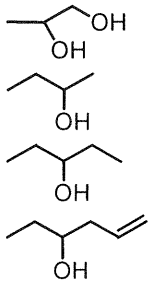
wherein

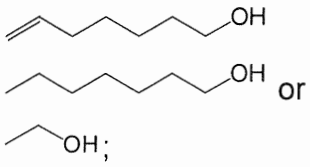
a. R' is H or acetyl;

b. R1 is a saturated or unsaturated straight chain or branched alkane or alkene group from 2 to 15 carbon atoms in length; and

c. R2 is selected from the group consisting of :

   i. a hydroxyl group, wherein when R1 andR2 are taken together, R1-R2 is one of:



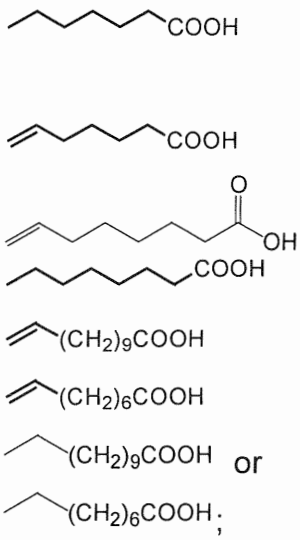


or

ii. an unsubstituted, N–substituted, or N,N-disubstituted amide;

iii. a N-substituted or unsubstituted acyl protected amine;

iv. a carboxylic acid, wherein when R1 andR2 are taken together, R1-R2 is one of:

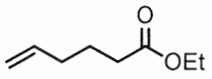


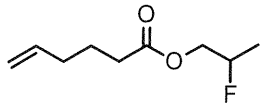
or

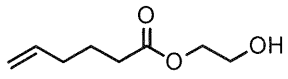
v. a N-substituted or unsubstituted amine;

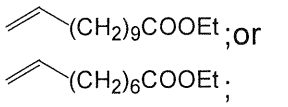
vi. a nitrile;

vii. an ester, wherein when R1 andR2 are taken together, R1-R2 is one of:





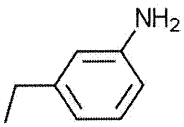


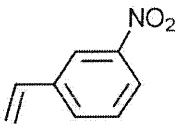


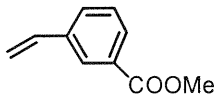
viii. a ketone;

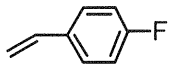
ix. a hydroxy, dihydroxy, trihydroxy, or polyhydroxy alkyl; and

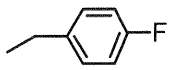
x. a substituted or unsubstituted aryl, wherein when R1 and R2 are taken together, R1-R2 is one of::

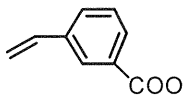


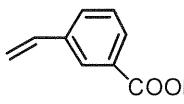






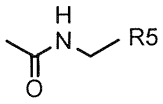


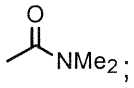


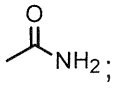


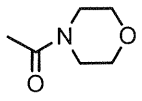
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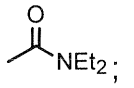
2. The compound of claim 1, wherein R2 is one of:

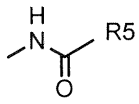
a. 

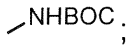
b. ;

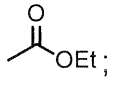
c. ;

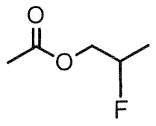
d. ;

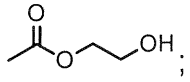
e. ;

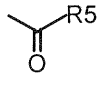
f. 

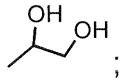
g. ;

h. ;

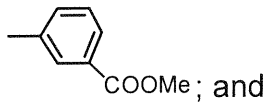
i. ;

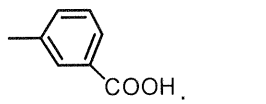
j. ;

k. ;

l. ;

m. ;

n. ; and

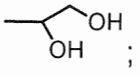
o. .

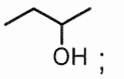
wherein

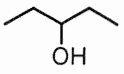
i. R5 is a saturated or unsaturated straight chain or branched aliphatic carbon chain between 1 and 10 carbons in length; and

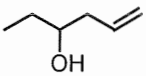
ii. R6 is a monohydroxylated, dihydroxylated, trihydroxylated or polyhydroxylated saturated or unsaturated straight chain or branched aliphatic carbon chain between 1 and 10 carbons in length.

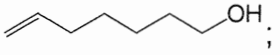
3. The compound of claim 1 wherein R1-R2 is selected from the group consisting of :

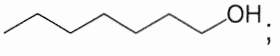
i. ;

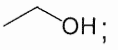
ii. ;

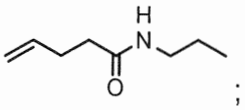
iii. ;

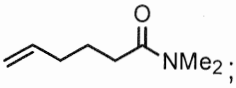
iv. ;

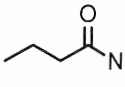
v. ;

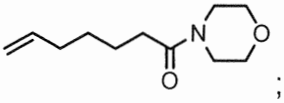
vi. ;

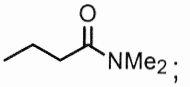
vii. ;

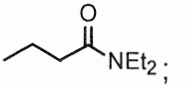
viii. ;

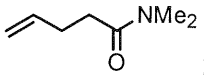
ix. ;

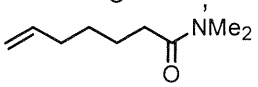
x. ;

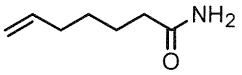
xi. ;

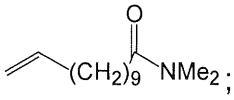
xii. ;

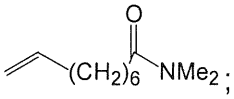
xiii. ;

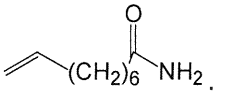
xiv. ;

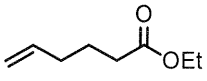
xv. ;

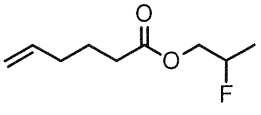
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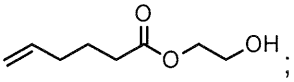
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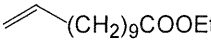
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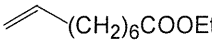
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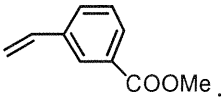
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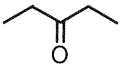
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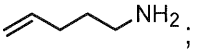
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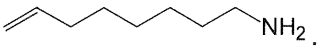
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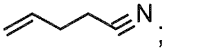
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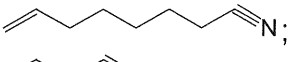
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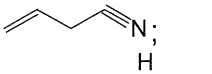
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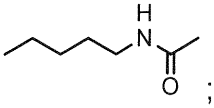
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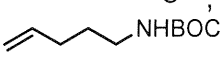
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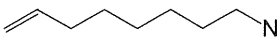
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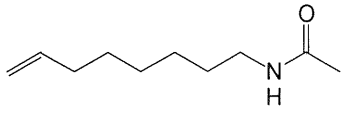
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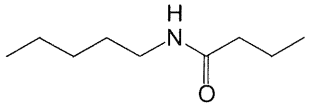
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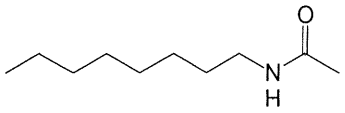
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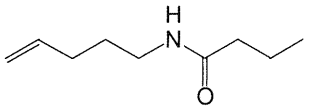
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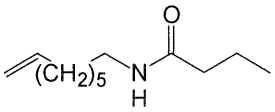
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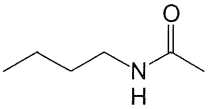
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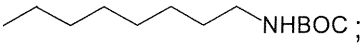
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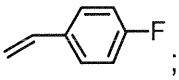
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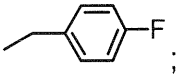
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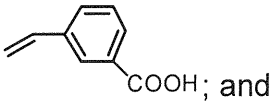
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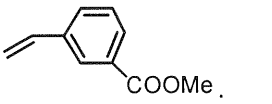
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xlii.  ;

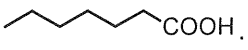
xliii.  ;

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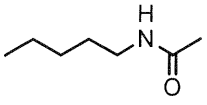
xlv.  ; and

xlvi.  .

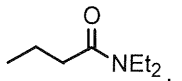
4. The compound of claim 1 wherein R' is H and R1-R2 is

 .

5. The compound of claim 3 wherein R' is H and R1-R2 is

 .

6. The compound of claim 1 wherein R1 is a straight chain of 6-12 carbons and R2 is a carboxylic acid, an ester or an N-substituted amine as defined in claim 1.

7. The compound of claim 1 wherein R1-R2 is .

8. The compound of claim 1 wherein when R2 is
   a) N–substituted or N,N-disubstituted amide; or
   b) N-substituted or N,N-disubstituted amine; the N–substituted or N,N-disubstituted amide and the N-substituted or N,N-disubstituted amine are substituted with:
      i. a substituted or unsubstituted alkyl, alkenyl, or alkynyl;
      ii. a formyl;
      iii. a substituted or unsubstituted acyl;
      iv. an alkylsulfonyl; or
      v. a substituted or unsubstituted aryl.

9. The compound of claim 8 wherein
   a) the substituted or unsubstituted alkyl, alkenyl, or alkynyl is 2 to 15 carbons in length;
   b) the substituted or unsubstituted acyl is a saturated or unsaturated straight or branched chain aliphatic between1 to 10 carbons in length;
   c) the alkylsulfonyl is 1 to 4 carbons in length; and
   d) the substituted or unsubstituted aryl is a monocyclic or fused polycyclic.

10. The compound of claim 9 wherein the substituted or unsubstituted acyl is a saturated or unsaturated straight or branched chain aliphatic between 1 to 7 carbons in length.

11. The compound of claim 9 wherein the substituted or unsubstituted acyl is a saturated or unsaturated straight or branched chain aliphatic between 2 to 4 carbons in length.

12. The compound of claim 9 wherein the substituted or unsubstituted alkyl N–substituted or N,N-disubstituted amide is between 1 and 7 carbons in length.

13. The compound of claim 9 wherein the N,N-disubstituted amide forms a nitrogen heterocylic ring.

14. The compound of claim 13 wherein the nitrogen heterocyclic ring comprises O or S as a heteroatom.

15. The compound of any one of claims 8 to 12 wherein the substituted alkyl, alkenyl, or alkynyl; the substituted acyl; and/or the substituted aryl are substituted with one or more of:

a) halogen;
b) nitro;
c) cyano;
d) hydroxy;
e) thiol;
f) optionally substituted amino;
g) optionally halogenated C1-4 alkoxy;
h) optionally halogenated C1-4 alkoxy-C1-4 alkoxy;
i) formyl;

j) C2-4 alkanoyl; or
k) C1-C4 alkylsulfonyl.

16. The compound of claim 15 wherein the substituted alkyl, alkenyl, or alkynyl; the substituted acyl; and the substituted aryl are substituted with 1 to 3 substituents.

17. The compound claims 15 or 16 wherein

a) the halogen is fluorine, chlorine, bromine, or iodine;
b) the thiol is C1-4 alkylthio;
c) the amino is mono-C1-4 alkylamino, di-C1-4 alkylamino, or a 5- to 6-membered cyclic amino;
d) the C2-4 alkanoyl is acetyl or propionyl;
e) the C1-4 alkoxy is methoxy, ethoxy, propoxy, or butoxy;
f) the C1-4 alkoxy-C1-4 alkoxy is methoxymethoxy, methoxyethoxy, or ethoxyethoxy; and
g) the C1-4 alkylsulfonyl is methanesulfonyl or ethanesulfonyl.

18. The compound of claim 15 or 16 wherein

a) the halogenated C1-4 alkoxy is trifluoromethoxy or trifluoroethoxy; and
b) the halogenated C1-4 alkoxy-C1-4 alkoxy is trifluoromethoxyethoxy or trifluoroethoxyethoxy.

19. The compound of claim 17 wherein the 5- to 6-membered cyclic amino is tetrahydropyrrole, piperazine, piperidine, morpholine, thiomorpholine, pyrrole, or imidazole.

20. The compound of claim 8 wherein

a) the substituted or unsubstituted acyl is acetyl, propionyl, butyryl, or isobutyryl;
b) the alkylsulfonyl is methanesulfonyl or ethanesulfonyl; or
c) the substituted or unsubstituted aryl is phenyl, naphthyl, anthryl, phenanthryl or acenaphthylenyl.

21. The compound of claim 20 wherein the substituted aryl is substituted with

a) lower alkoxy;
b) halogen;
c) lower alkyl, alkenyl, or alkynyl;
d) optionally substituted amino;
e) optionally substituted hydroxyl;
f) cyano;
g) optionally substituted amidino;
h) carboxyl;
i) lower alkoxycarbonyl; or
j) optionally substituted carbamoyl.

22. The compound of claim 21 wherein

a) lower alkoxy is C1-6 alkoxy;
b) halogen is fluorine, chlorine, bromine, or iodine;
c) lower alkyl is C1-6 alkyl;
d) lower alkenyl is C2-6 alkenyl;
e) lower alkynyl is C2-6 alkynyl;
f) lower alkoxycarbonyl is C1-6 alkoxycarbonyl; or
g) substituted carbamoyl is substituted with C1-6 alkyl or acyl.

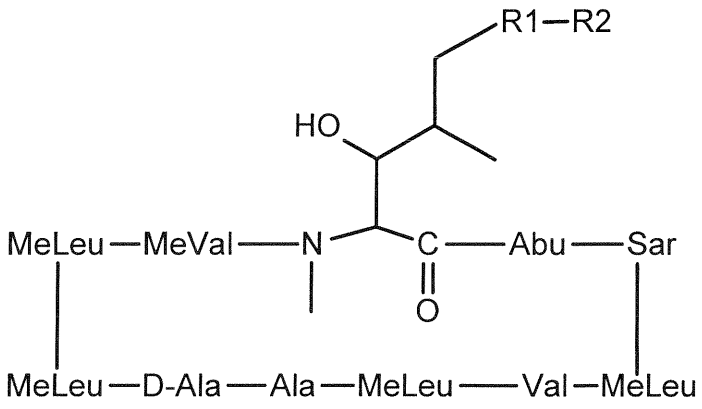
23. The compound of claim 21 wherein

a) C1-6 alkoxy is one of methoxy, ethoxy or propoxy;
b) C1-6 alkyl is one of methyl, ethyl or propyl;
c) C2-6 alkenyl is vinyl or allyl;
d) C2-6 alkynyl is ethynyl or propargyl;
e) C1-6 alkoxycarbonyl is methoxycarbonyl or ethoxycarbonyl.

24. The compound of claim 1 wherein R2 is N–substituted amide substituted with hydroxy substituted C2-15 alkyl.

25. The compound of any one of claims 1-24 wherein R' is H.

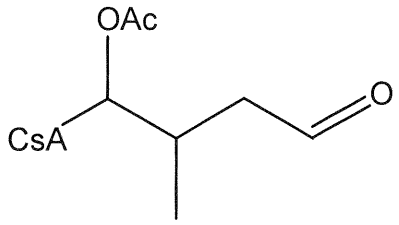
26. A process to produce a compound of Formula I:



Formula I

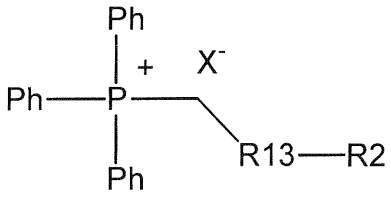
wherein R1 and R2 are as defined in any one of claims 1 - 3,
comprising the steps of

a. reacting acetyl CsA aldehyde modified at amino acid 1 of Formula IX:



Formula IX

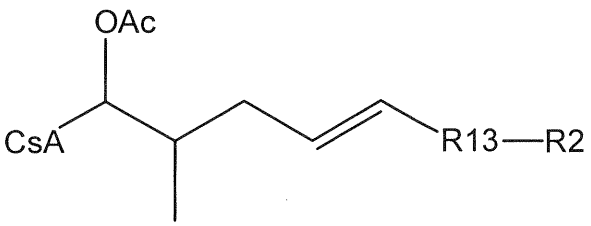
with a phosphonium salt of Formula VIII:



Formula VIII

wherein R13 is a straight chain or branched alkane or alkene from 1 to 13 carbon atoms in length;

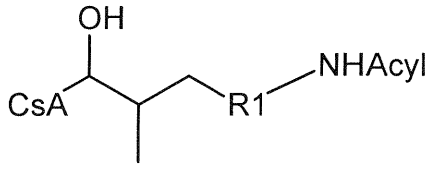
in the presence of a base to produce an acetylated compound of Formula X:



Formula X

b. deacetylating the compound of Formula X using a base; and
c. where R1 is saturated, hydrogenating the double bond of the compound of Formula X by reacting the compound with a hydrogenating agent to produce a saturated analogue of Formula I.

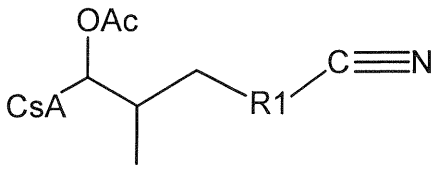
27. A process of producing a compound of the Formula XIV:



Formula XIV

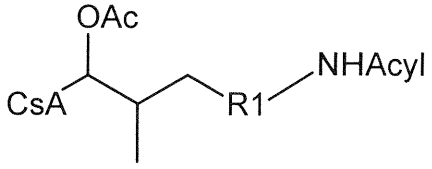
comprising the steps of

a. reacting the compound of Formula XV:



Formula XV

in the presence of a reducing agent and an acylating agent to produce acetylated compounds of Formula XVI:



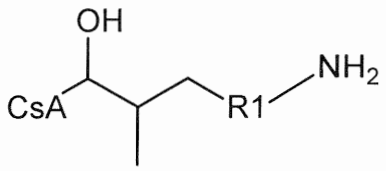
Formula XVI

and

b. deacetylating the compound of Formula XVI using a base;

wherein R1 of Formulae XIV, XV and XVI is a straight chain or branched alkane or alkene group between 2 and 15 carbons in length.

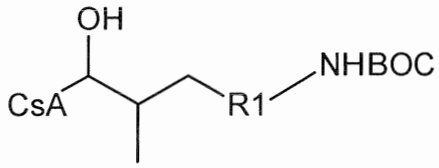
28. A process of producing a compound of the Formula XXI:



Formula XXI

comprising the steps of

a. by dissolving the compound of Formula XX:



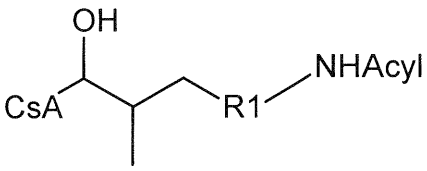
Formula XX

in an anhydrous solvent; and

b. reacting the solution with trifluoroacetic acid (TFA);

wherein R1 of Formulae XX and XXI is a straight chain or branched alkane or alkene group between 2 and 15 carbons in length.

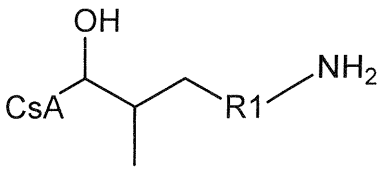
29. A process of producing a compound of the Formula XIV:



Formula XIV

comprising the steps of

a. dissolving the compound of Formula XXI:



Formula XXI

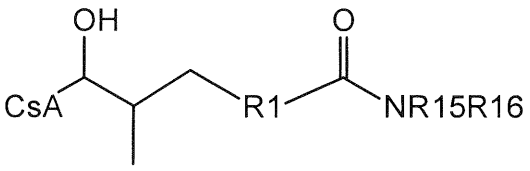
in anhydrous pyridine;

b. reacting the solution with acylating agent; and

c. removing the solvent to yield the compound of Formula XIV;

wherein R1 of Formulae XIV and XXI is a straight chain or branched alkane or alkene group between 2 and 15 carbons in length.

30. A process of producing a compound of the Formula XXIV:



Formula XXIV

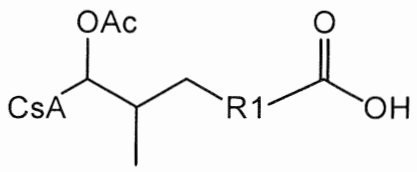
wherein

I. R1 is a straight or branched alkane or alkene group between 2 and 15 carbons in length; and

II. R15 and R16 are independently hydrogen or a saturated or unsaturated straight chain or branched aliphatic group; or where NR15R16 together forms a morpholinyl moiety;

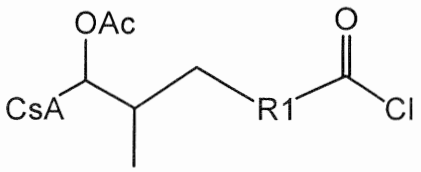
comprising the steps of

a. by combining the compound of Formula XXV:



Formula XXV

with thionylchloride to yield a residue of the Formula XXVI;



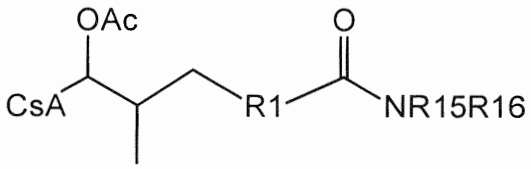
Formula XXVI

b. dissolving the residue in anhydrous solvent and reacting with a compound of the Formula XXVII:

R15R16NH

Formula XXVII

to yield the compound of Formula XXVIII

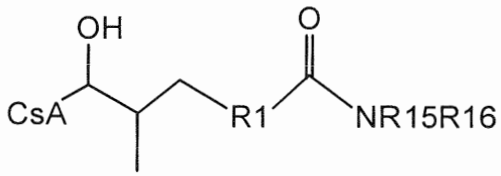


Formula XXVIII

and

c. deacetylating the compound of Formula XXIV with a base.

31. A process of producing a compound of the Formula XXIV:



Formula XXIV

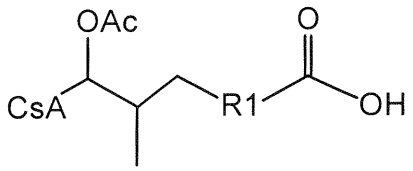
wherein

I. R1 is a straight chain or branched alkane or alkene group between 2 and 15 carbons in length;

II. R15 and R16 are independently hydrogen or a saturated or unsaturated straight chain or branched aliphatic group; or where NR15R16 together forms a morpholinyl moiety;

comprising the steps of

a. dissolving the compound of Formula XXV:



Formula XXV

in anhydrous solvent under nitrogen;

b. reacting with dicyclohexylcarvodiimide, 1-hydroxybenzotriazole hydrate and the compound of the Formula XVIII;

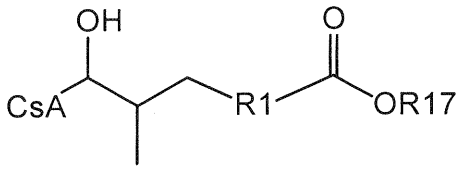
R15R16NH

Formula XXVII

and

c. deacetylating the compound of Formula XVIII with a base.

32. A process of producing a compound of the Formula XXXII:



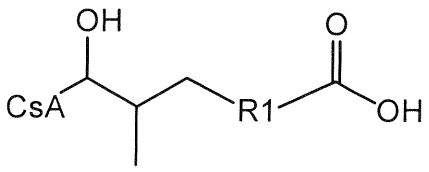
Formula XXXII

wherein

I. R1 is a straight chain or branched alkane or alkene group between 2 and 15 carbons in length; and

II. R17 is a saturated or unsaturated straight chain or branched aliphatic group, optionally containing a halogen or hydroxyl substituent;

by reacting the compound of Formula XXX:



Formula XXX

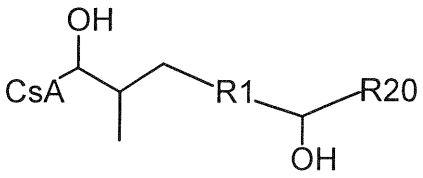
with a compound of Formula XXXI:

R17OH

Formula XXXI

in the presence of an acid.

33. A process of producing a compound of the Formula XXVI:



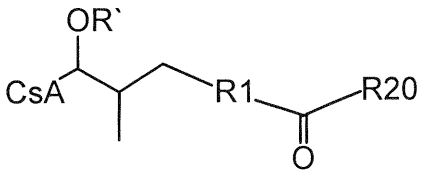
Formula XXVI

wherein

I. R1 is a straight chain or branched alkane or alkene group between 2 and 15 carbons in length; and

II. R20 is a saturated or unsaturated straight chain or branched aliphatic group;

by reacting the compound of Formula XXXV:



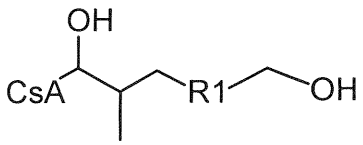
Formula XXXV

wherein R' is optionally H or acetyl

with sodium borohydride; and

where R' is acetyl, deacetylating the compound of Formula XXXV with a base.

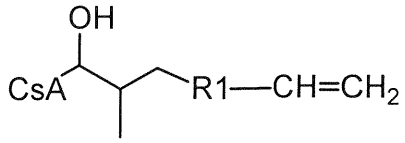
34. A process of producing a compound of the Formula XXIX:



Formula XXIX

wherein R1 is a straight chain or branched alkane or alkene group between 2 and 15 carbons in length;

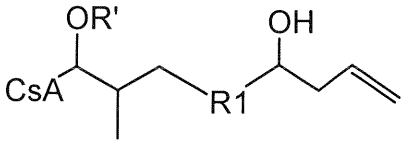
by reacting the compound of Formula XXVIII:



Formula XXVIII

with borane-tetrahydrofuran and sodium peroxide.

35. A process of producing a compound of the Formula XLIII:



Formula XLIII

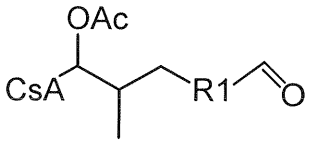
wherein

I. R' is H or Acetyl; and

II. R1 is a straight or branched alkane or alkene group between 2 and 15 carbons in length;

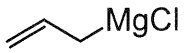
comprising the steps of:

reacting the compound of Formula XLI:



Formula XLI

with the compound of Formula XLII;

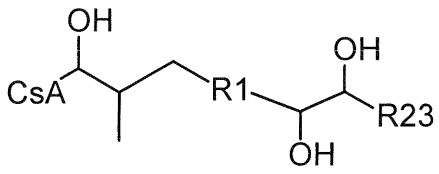


Formula XLII

in an anhydrous solvent; and

deacetylating the compound of Formula XLII with a base.

36. A process of producing a compound of the Formula XLVI:



Formula XLVI

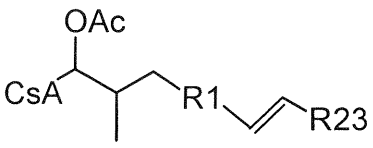
wherein

I. R1 is a straight chain or branched alkane or alkene group from 2 to 15 carbon atoms in length; and

II. R23 is a saturated or unsaturated straight chain or branched aliphatic group;

comprising the steps of:

a. reacting the compound of Formula XLV



Formula XLV

with hydrogen peroxide and formic acid;

b. reacting the product with a base to yield the compound of Formula XLVI; and

c. deacetylating the compound of Formula XLV with a base.

37. A pharmaceutical composition comprising a therapeutically effective amount of the compound of any one of claims 1 to 25 and one or more pharmaceutical excipients.

38. Use of a compound of any one of claims 1 to 25 in the preparation of a medicament to treat a cyclophilin mediated disease in a mammal, wherein the cyclophilin mediated disease is selected from the group consisting of

a. a viral infection;
b. inflammatory disease;
c. cancer;
d. muscular degenerative disease;
e. neurodegenerative disease;
f. injury associated with loss of cellular calcium homeostasis.

39. The use of claim 38, wherein is the viral infection is caused by a virus selected from the group consisting of Human Immunodeficiency virus, Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis D, and Hepatitis E and combinations thereof.

40. The use of claim 38, wherein the inflammatory disease is selected from the group consisting of asthma, autoimmune disease, chronic inflammation, chronic prostatitis,

glomerulonephritis, hypersensitivity disease, inflammatory bowel disease, sepsis, vascular smooth muscle cell disease, aneurysms, pelvic inflammatory disease, reperfusion injury, rheumatoid arthritis, transplant rejection, and vasculitis.

41. The use of claim 38, wherein the cancer is selected from the group consisting of small and non-small cell lung, bladder, hepatocellular, pancreatic and breast cancer.

42. The use of claim 38, wherein the muscular degenerative disorder is selected from the group consisting of myocardial reperfusion injury, muscular dystrophy, and collagen VI myopathies.

43. The use of claim 38, wherein the neurodegenerative disorder is selected from the group consisting of Alzheimer's disease, Parkinson's disease, Huntington's disease, Multiple Systems Atrophy, Multiple Sclerosis, cerebral palsy, stroke, diabetic neuropathy, amyotrophic lateral sclerosis (Lou Gehrig's Disease), spinal cord injury, and cerebral injury.

44. The use of claim 38, wherein the injury associated with loss of cellular calcium homeostasis is selected from the group consisting of myocardial infarct, stroke, acute hepatotoxicity, cholestasis, and storage/reperfusion injury of transplant organs.

45. Use of a therapeutically effective amount of the compound of claims 1 to 25 to treat a cyclophilin mediated disease in a mammal.