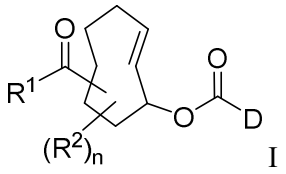
What is Claimed is:

1. A process of preparing a compound of formula I, or a salt thereof:



I

wherein

R^1 is selected from the group consisting of -OR^4 and an amino acid moiety;

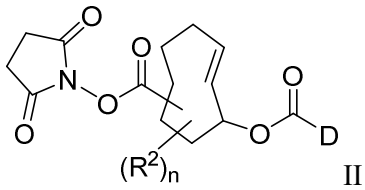
n is 0, 1, 2, 3 or 4;

each R^2 is independently $C_{1\text{-}4}$alkyl, $C_{1\text{-}4}$haloalkyl, and $C_{1\text{-}4}$alkoxy; and

D is a payload moiety;

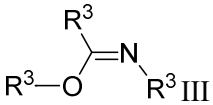
R^4 is hydrogen or $C_{1\text{-}4}$alkyl;

comprising contacting a compound of formula II:



II

with HO-R^4 or an amino acid moiety, or a salt thereof, and a compound of formula III:



III

wherein each R^3 is independently $C_{1\text{-}4}$alkyl, or

wherein a compound of formula III is *N,O*-bis(trimethylsilyl acetamide)

in an organic solvent in the presence of a base.

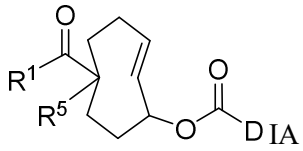
2. The process of claim 1, wherein the payload moiety is an anthracycline moiety, an auristatin moiety, a glycopeptide antibiotic moiety, or a lipopeptide antibiotic moiety.

3. The process of claim 2, wherein the payload moiety is a doxorubicin moiety, daunorubicin moiety, monomethyl auristatin E moiety, vancomycin moiety or daptomycin moiety.

4. The process of any one of claims 1-3, wherein R^1 is an amino acid moiety, an alanine moiety or a glycine moiety.

5. The process of any one of claims 1-4, wherein the compound of formula III is *N*,*O*-bis(trimethylsilyl)acetamide.

6. The process of any one of claims 1-5, wherein the compound of formula I is represented by formula IA:



IA

wherein

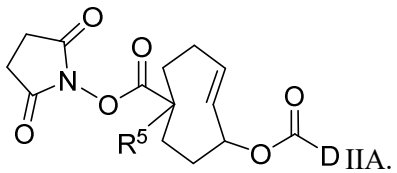
R^1 is selected from the group consisting of -OR^4 and an amino acid moiety;

R^4 is hydrogen or $C_{1\text{-}4}$alkyl;

R^5 is hydrogen or $C_{1\text{-}4}$alkyl; and

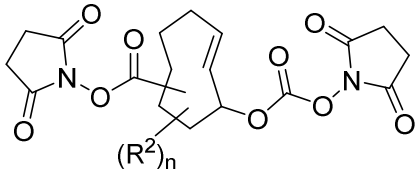
D is a payload moiety;

and the compound of formula II is represented by formula IIA:



IIA.

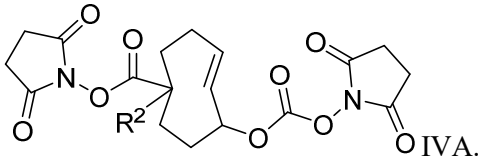
7. The process of any one of claims 1-5, further comprising preparing the compound of formula II by reacting a compound of formula IV:



IV

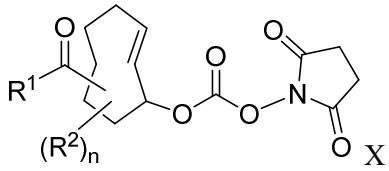
with a payload moiety, or a salt thereof, in an organic solvent in the presence of a base.

8. The process of claim 6, wherein the compound of formula IV is represented by formula IVA:



IVA.

9. A process of preparing a compound of formula X, or a salt thereof:



X

wherein

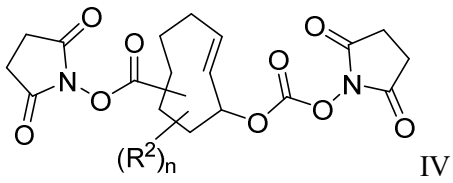
R^1 is selected from the group consisting of -OR^4 and an amino acid moiety;

n is 0, 1, 2, 3 or 4;

each R^2 is independently $C_{1\text{-}4}$alkyl, $C_{1\text{-}4}$haloalkyl, and $C_{1\text{-}4}$alkoxy; and

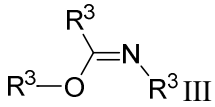
R^4 is hydrogen or $C_{1\text{-}4}$alkyl;

comprising contacting a compound of formula IV:



IV

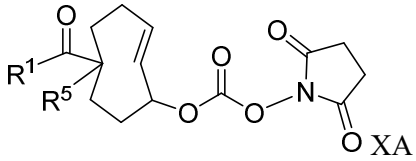
with HO-R^4 or an amino acid, or a salt thereof, and a compound of formula III:



III

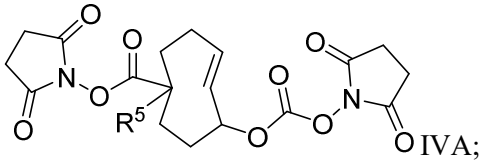
wherein each R^3 is independently $C_{1\text{-}4}$alkyl, in an organic solvent in the presence of a base.

10. The process of claim 9, wherein the compound of formula X is represented by formula XA:



XA

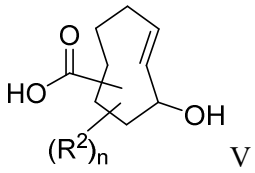
and the compound of formula IV is represented by formula IVA:



IVA;

wherein R^5 is hydrogen or $C_{1\text{-}4}$alkyl.

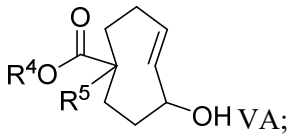
11. The process of claim 9, further comprising preparing the compound of formula IV, or a salt thereof, comprising contacting a compound of formula V, or a salt thereof:



V

with N,N'-disuccinimidylcarbonate in an organic solvent in the presence of a base.

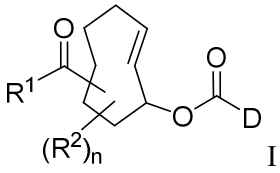
12. The process of claim 11, wherein the compound of formula V is represented by formula VA:



VA;

wherein R^5 is hydrogen or C_{1-4}alkyl.

13. A process of preparing a compound of formula I, or a salt thereof:



I

wherein

R^1 is selected from the group consisting of -OR^4 and an amino acid moiety;

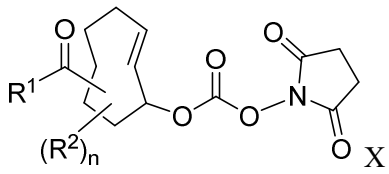
n is 0, 1, 2, 3 or 4;

each R^2 is independently C_{1-4}alkyl, C_{1-4}haloalkyl, and C_{1-4}alkoxy;

D is a payload moiety; and

R^4 is hydrogen or C_{1-4}alkyl;

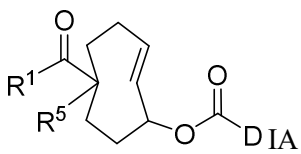
comprising contacting a compound of formula X, or a salt thereof:



X

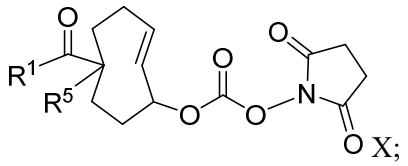
with a payload moiety, or a salt thereof, in an organic solvent in the presence of a base.

14. The process of claim 13, wherein the compound of formula I is represented by formula IA:



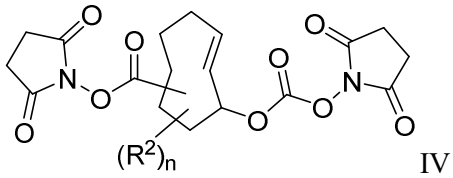
IA

and the compound of formula X is represented by formula XA:



wherein R^5 is hydrogen or $C_{1\text{-}4}$alkyl.

15. A process of preparing a composition comprising a compound of formula IV, or a salt thereof:

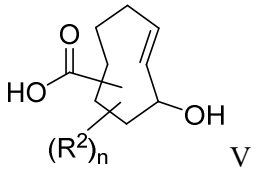


wherein

n is 0, 1, 2, 3, or 4; and

each R^2 independently hydrogen or $C_{1\text{-}4}$alkyl;

comprising contacting one equivalent of a compound of formula V, or a salt thereof:



with 3-5 equivalents of N,N'-disuccinimidylcarbonate in 15-25 volumes of an anhydrous organic solvent in the presence of a base at a temperature from 15-30 °C for 5-10 hours.

16. The process of claim 15, further comprising adding the composition comprising a compound of formula IV to 40-60 volumes of water at room temperature to form an aqueous product mixture.

17. The process of claim 16, further comprising isolating a solid formed in the aqueous product mixture.

18. The process of claim 17, further comprising triturating the solid in acetonitrile at a temperature of from about 30 to about 50 °C to form a triturated solid.

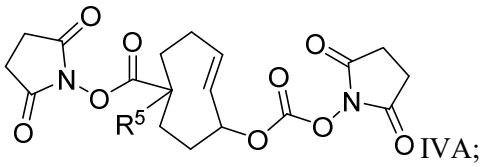
19. The process of claim 18, further comprising isolating the triturated solid.

20. The process of claims 15 wherein the anhydrous organic solvent is anhydrous acetonitrile.

21. The process of any one of claims 15-20, wherein the base is a trialkylamine base.

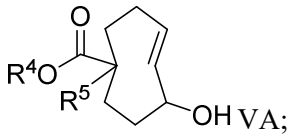
22. The process of claim 21, wherein the base is diisopropylethylamine.

23. The process of any one of claims 15-22, wherein the compound of formula IV is represented by formula IVA:



IVA;

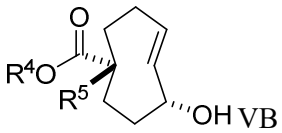
and the compound of formula V is represented by formula VA:



VA;

wherein R^4 is hydrogen or $C_{1\text{-}4}$alkyl; and R^5 is hydrogen or $C_{1\text{-}4}$alkyl.

24. A process for the preparation of an enantiomerically enriched composition comprising a compound of formula VB, or a salt thereof:



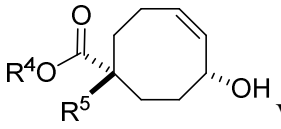
VB

wherein

R^4 is hydrogen or $C_{1\text{-}4}$alkyl; and

R^5 is $C_{1\text{-}4}$alkyl;

comprising isomerizing an enantiomerically enriched composition of a compound of formula VIIB, or a salt thereof:

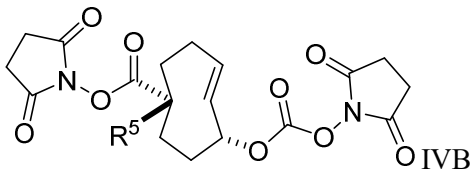


VIIB.

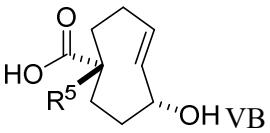
25. The process of claim 24, wherein the isomerizing comprises exposing the compound of formula VA to UV light.

26. The process of claim 24 or 25, wherein when R^4 is $C_{1\text{-}4}$alkyl, the process further comprises a hydrolyzing step to convert R^4 to hydrogen.

27. A process for the preparation of an enantiomerically enriched composition comprising a compound of formula IVB, or a salt thereof:



wherein R^5 is C_{1-4}alkyl, comprising contacting an enantiomerically enriched composition of a compound of formula VB, or a salt thereof:

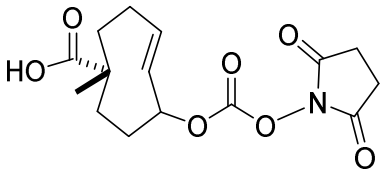
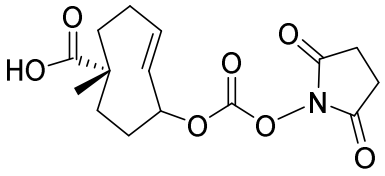


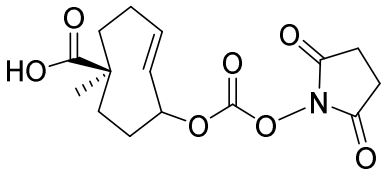
with *N,N'*-disuccinimidyl carbonate (DSC) under conditions to provide the enantiomerically enriched composition comprising a compound of formula IVB.

28. The process of any preceding claim, wherein R^2 or R^5 is methyl.

29. An enantiomerically enriched composition comprising a compound selected from Table 1, or a salt thereof:

Table 1

XC	
XD	

XE	

30. The process of any preceding claim, wherein the enantiomerically enriched composition has a % ee of greater than about 25%, or about 50%, or about 70%, or about 80%, or about 90%, or about 95%, or about 98%, or about 99% or about 100%.