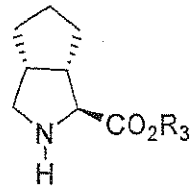
pages 223-22. There remains however, a need for economical processes for the preparation of these compounds.

SUMMARY ~~OF THE INVENTION~~

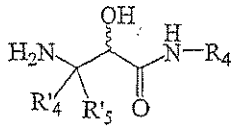
[006] ~~In one aspect,~~ tThe ~~invention~~disclosure provides processes and intermediates for producing a bicyclic pyrrolidine derivative of Formula **1**, which is useful in producing protease inhibitors.



1

In Formula **1**, R_3 is an acid protecting group which can be removed under acidic, basic, or hydrogenation conditions. Under acidic conditions, R_3 is, for example, *t*-butyl; under basic conditions, R_3 is, for example, methyl or ethyl; under hydrogenation conditions, R_3 is, for example, benzyl.

[007] Another ~~aspect~~embodiment of the ~~invention~~disclosure includes processes and intermediates for the preparation of a compound of Formula **2**, which is also useful in producing protease inhibitors.



2

In Formula **2**,

R_4 is H, an optionally substituted aliphatic, an optionally substituted cycloaliphatic, an optionally substituted aryl, an optionally substituted aralkyl, or an optionally substituted heteroaralkyl;

R'_4 is H, an optionally substituted aliphatic, an optionally substituted aryl, an optionally substituted aralkyl or an optionally substituted heteroaralkyl; and

R'_5 is an optionally substituted aliphatic, an optionally substituted cycloaliphatic, an optionally substituted aryl, an optionally substituted aralkyl, or an optionally substituted heteroaralkyl; or

R'_4 and R'_5 together with the atom to which they are attached may form a 3- to 7-membered optionally substituted cycloaliphatic ring.

[008] The processes and intermediates described herein are also useful for a process for preparating a protease-inhibiting compound of Formula **3** shown below.

[0052] In some further embodiments, R_1 is P_2-.

[0053] In some further embodiments, R_1 is P_3–L_2-P_2-.

[0054] In some further embodiments, R_1 is P_4-L_3-P_3–L_2-P_2-.

[0055] In some further embodiments, R_1 is RW-.

[0056] In some embodiments, the process for preparing compounds of Formula **3** further includes the steps of hydrolyzing the ester of a compound of Formula **1a**; to provide a carboxylic acid and reacting the carboxylic acid thus obtained with a compound containing the R_2 group, wherein R_2 is -(NH-$CR_4'R_5'$-CH(OH)C(O))-NHR_4, in the presence of a coupling reagent to produce the compound of Formula **3**.

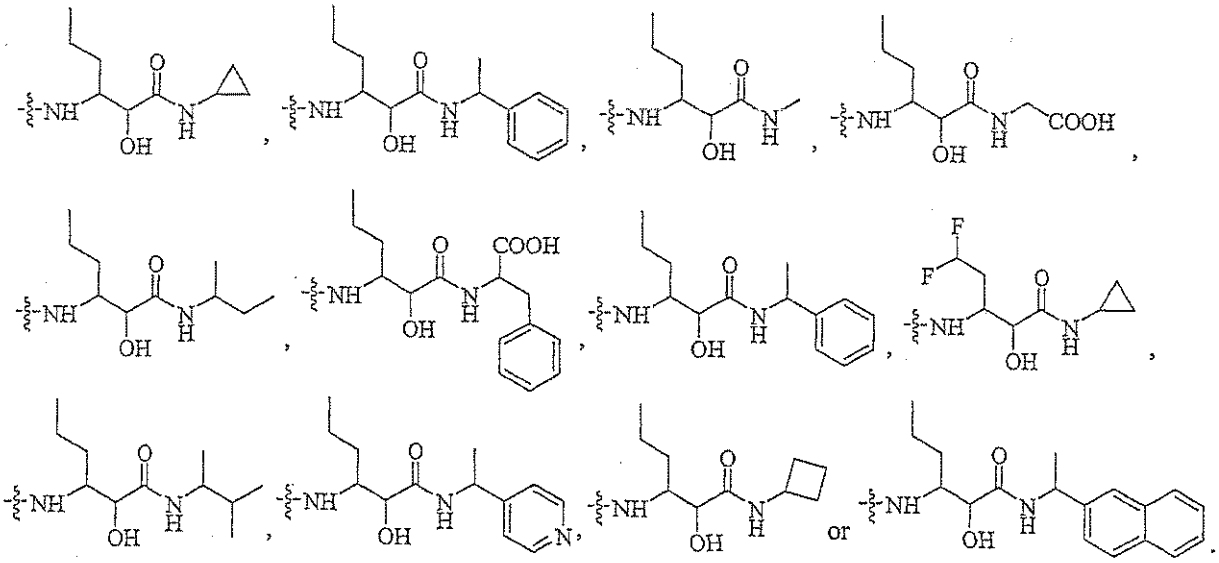
[0057] In some further embodiments, R_4 is H, an optionally substituted aliphatic, optionally substituted cycloaliphatic, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted aralkyl, or an optionally substituted heteroaralkyl;

R_4' is H, an optionally substituted aliphatic, an optionally substituted aryl, an optionally substituted aralkyl, or an optionally substituted heteroaralkyl; and

R_5' is H, an optionally substituted aliphatic, an optionally substituted cycloaliphatic, an optionally substituted aryl, an optionally substituted aralkyl, or an optionally substituted heteroaralkyl; or

R_4' and R_5', together with the atom to which they are attached, form a 3- to 7-membered optionally substituted cycloaliphatic ring.

[0058] In some further embodiments, R_2 is

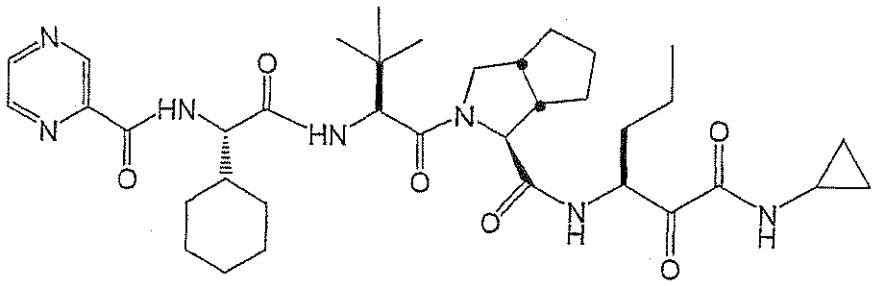


[0059] The ~~invention~~disclosure further relates to a process for preparing a compound of Formula **4**

dissolves, e.g., methylene chloride. The acid can be any acid, inorganic or organic, e.g., acetic acid or propionic acid.

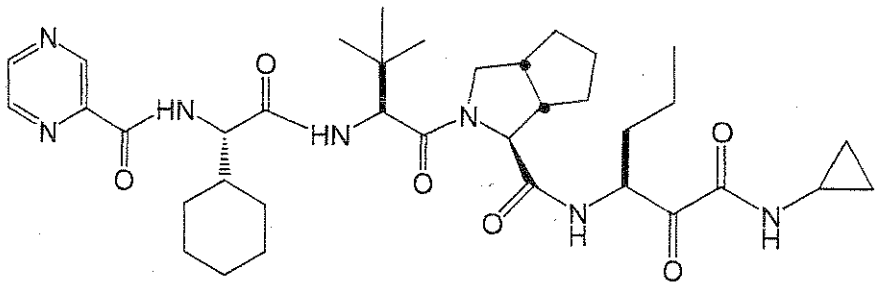
[0064] In still some further embodiments, the process further includes concentrating the solution of the compound of Formula 4 to obtain the compound in a solid form. Such a concentrating process can be, e.g., distillation of the solvent under reduced pressure (e.g., vacuum) by natural evaporation of the solvent. The solid form in which hthe compound of Formula 4 is obtained can be, e.g., crystalline or semicrystalline, and can be of higher purity than that before being dissolved into an organic solvent and then concentrated in acid condition.

[0065] As such, the ~~invention~~disclosure also relates to process of purifying the compound of Formula 4.



4

[0065a] In one aspect, there is provided a process of purifying the compound of Formula 4, comprising:



4

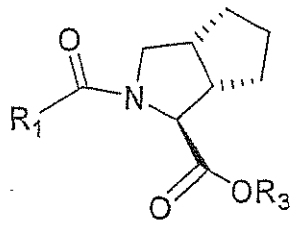
a) dissolving the compound of Formula 4 in an organic solvent to obtain a solution of the compound of Formula 4,

b) adding an acid to the solution of the compound of Formula 4, and

c) concencentrating the solution of the compound of Formula 4 to obtain the compound in a solid form.

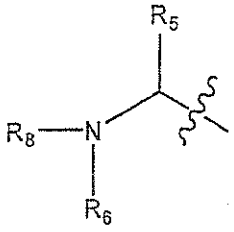
[0066] In some embodiments, the process includes first dissolving the compound of Formula 4 in an organic solvent to obtain its solution, adding an acid to the solution of the compound of Formula 4, and then concencentrating the solution of the compound of Formula 4 to obtain the compound in a solid form. Examples of sutiable organic solvents, acids, and solid forms have been provided above.

[0067] The ~~invention~~disclosure further feathers compounds of Formula **1a,**



1a

Wherein R_1 is P_2-;



P_2- is ;

R_5 is H, an aliphatic, a cycloaliphatic, a heterocycloaliphatic, an aryl, or a heteroaryl; each of which, except for H, is optionally substituted with one or more substituents each independently selected from Group J consisting of halo, cycloaliphatic, aryl, heteroaryl, alkoxy, aroyl, heteroaroyl, acyl, nitro, cyano, amido, amino, sulfonyl, sulfinyl, sulfanyl, sulfoxy, urea, thiourea, sulfamoyl, sulfamide, oxo, carboxy, carbamoyl, cycloaliphaticoxy, heterocycloaliphaticoxy, aryloxy, heteroaryloxy, aralkyloxy, heteroarylalkoxy, alkoxycarbonyl, alkylcarbonyloxy, and hydroxy;

R_6 is an optionally substituted aliphatic, an optionally substituted heteroalkyl, an optionally substituted heteroaryl, an optionally substituted phenyl; or R_5 and R_6, together with the atoms to which they are attached, may form a 5- to 7-membered, optionally substituted monocyclic heterocycle, or a 6- to 12-membered, optionally substituted bicyclic heterocycle, in which each heterocycle ring optionally contains an additional heteroatom selected from -O-, -S-, or -NR^X-;

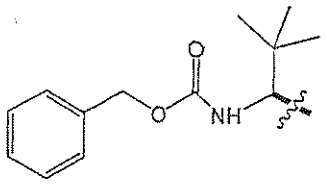
R^X is H, aliphatic, cycloaliphatic, (cycloaliphatic)aliphatic, aryl, araliphatic, heterocycloaliphatic, (heterocycloaliphatic)aliphatic, heteroaryl, carboxy, sulfanyl, sulfinyl, sulfonyl, (aliphatic)carbonyl, (cycloaliphatic)carbonyl, ((cycloaliphatic)aliphatic)carbonyl, arylcarbonyl, (araliphatic)carbonyl, (heterocycloaliphatic)carbonyl, ((heterocycloaliphatic)aliphatic)carbonyl, (heteroaryl)carbonyl, or (heteroaraliphatic)carbonyl;

R_8 is H or a protecting group; and

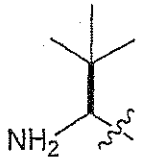
R_3 is an optionally substituted alkyl.

[0068] In some embodiments, R_3 is *t*-butyl.

[0069] In some other embodiments, P_2- is



[0070] In some further embodiments, P_2- is



[0071] The ~~invention~~disclosure further relates to compounds of Formula **1a** show above, in which

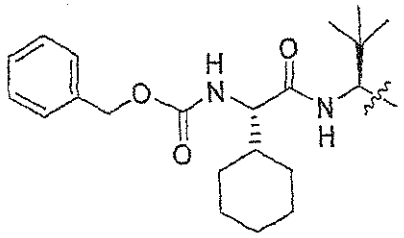
R_1 is P_3-L_2-P_2-;

R_8 is H or a protecting group; and

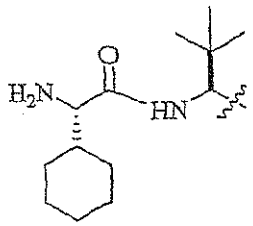
R_3 is an optionally substituted alkyl.

[0072] In some embodiments, R_3 is *t*-butyl.

[0073] In some embodiments, P_3-L_2-P_2- is



[0074] In some embodiments, P_3-L_2-P_2- is



[0075] Also within the scope of the present ~~invention~~disclosure are the compounds of 3,7-dipropyl-3,7-diazabicyclo[3.3.1]nonane, and 3,7-dipropyl-3,7-diazabicyclo[3.3.1]nonan-9-one.

DESCRIPTION OF THE INVENTION

I. *Definitions*

[0076] For purposes of this invention, the chemical elements are identified in accordance with the Periodic Table of the Elements, CAS version, Handbook of Chemistry and Physics, 75th Ed. Additionally, general principles of organic chemistry are described by Thomas Sorrell in Organic Chemistry, University Science Books, Sausalito (1999), and by M.B. Smith and J. March in Advanced Organic Chemistry, 5th Ed., John Wiley & Sons, New York (2001), the entire contents of which are hereby incorporated by reference.

[0077] As described herein, compounds of the invention may optionally be substituted with one or more substituents, such as are illustrated generally above, or as exemplified by particular classes, subclasses, and species of the invention.

[0078] As used herein the term "aliphatic" encompasses the terms alkyl, alkenyl, and alkynyl, each of which is optionally substituted as set forth below.

[0079] As used herein, an "alkyl" group refers to a saturated aliphatic hydrocarbon group containing 1-8 (e.g., 1-6 or 1-4) carbon atoms. An alkyl group can be straight or branched. Examples of alkyl groups include, but are not limited to, methyl, ethyl, propyl, isopropyl,