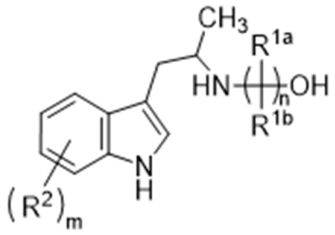
disclosure advantageously provide improvements in, for example, process conditions, reagent selection, complexity of required unit operations, scalability, and the like.

SUMMARY

[0006] Provided herein are solutions to these problems and more.

[0007] In one example provided herein is a process for the preparation of a compound of formula (II) as described herein, the process comprising (a) contacting a compound of formula (III) as described herein with a sulfonic acid to form a compound of formula (IIIa) as described herein; (b) contacting the compound of formula (IIIa) with a base to form compound of formula (IV) as described herein; hydrogenating the compound of formula (IV) to form a compound of formula (V) as described herein; and contacting the compound of formula (V) with a compound of formula (VI) described herein, thereby synthesizing the compound of formula (II).

[0007a] In one aspect, the disclosure provides a process for the preparation of a compound of formula (II):



(II)

or a stereoisomer or salt thereof

each of R^{1a} and R^{1b} is independently hydrogen, halogen, unsubstituted C_{1-3} alkyl, unsubstituted C_{1-3} haloalkyl, unsubstituted C_{1-3} alkoxy, -CN, unsubstituted C_{3-6} cycloalkyl, or unsubstituted C_{3-6} spirocycloalkyl;

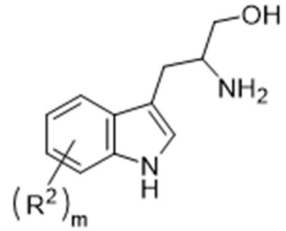
each R^2 is independently halogen, hydroxyl, -CN, unsubstituted C_{1-3} alkyl, unsubstituted C_{1-3} haloalkyl, or unsubstituted C_{1-3} alkoxy;

m is 0, 1 or 2; and

n is 1, 2, or 3;

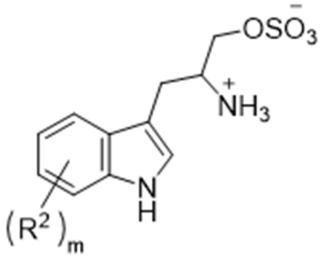
the process comprising:

(a) contacting a compound of formula (III),



(III)

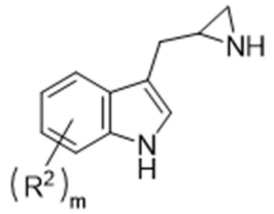
or a stereoisomer or salt thereof with a sulfonic acid to form a compound of formula (IIIa);



(IIIa)

or a stereoisomer or salt thereof

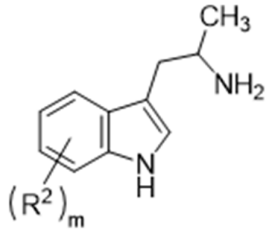
(b) contacting the compound of formula (IIIa) or a stereoisomer or salt thereof with a base to form compound of formula (IV);



(IV)

or a stereoisomer or salt thereof

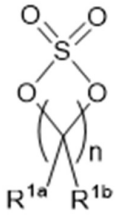
(c) hydrogenating the compound of formula (IV) or a stereoisomer or salt thereof to form a compound of formula (V); and



(V)

or a stereoisomer or salt thereof

(d) contacting the compound of formula (V) or a stereoisomer or salt thereof with a compound of formula (VI);



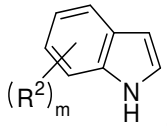
(VI)

thereby forming a compound of formula (II) or a stereoisomer or salt thereof.

[0008] In another example provided herein is a process for the preparation of a compound of formula (II) as described herein, the process comprising (a) contacting a compound of formula (VII) as described herein with a compound of formula (VI) as described herein to make a compound of formula (VIIa) as described herein; (b) contacting the compound of formula (VIIa) with an acid thereby synthesizing a compound of formula (VIIb) as described herein; contacting the compound of formula (VIIb) with 1,1'-carbonyldiimidazole thereby synthesizing a compound of formula (VIIc) as described herein; contacting the compound of formula (VIIc) with a compound of formula (VIII) as described herein to make a compound of formula (Va) as described herein; and contacting the compound of formula (Va) with a base followed by an acid thereby making the compound of formula (II).

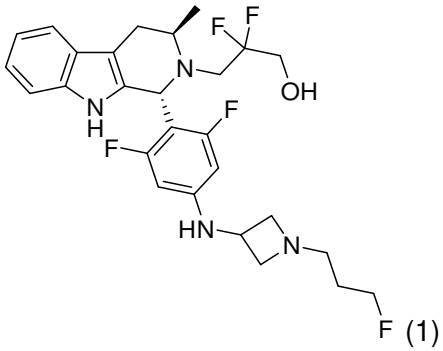
[0009] In another example provided herein is a process for the preparation of a compound of formula (II) as described herein, the process comprising contacting a compound of formula (V) as described herein with a compound of formula (VI) as described herein, wherein the compound of formula (V) is prepared by: (a) contacting a compound of formula (VIIp) as described herein with a compound of formula (VIII) as described herein to make a compound of formula (Vb) as described herein; and (b) contacting the compound of formula (Vb) with an acid thereby making the compound of formula (V).

[0010] In another example provided herein is a process for the preparation of a compound of formula (II), the process comprising (a) contacting alanine with a compound of formula (IX) as described herein to form a compound of formula (XI) as described herein; b) contacting the compound of formula (XI) with a chlorinating agent, a compound of formula


, and an organoaluminum compound to form a compound of formula (Vc) as described herein; and (c) contacting the compound of formula (Vc) with a reducing agent thereby forming a compound of formula (II).

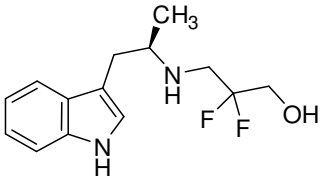
[0011] In another example provided herein is a process for the synthesis of a compound of formula (1), the process comprising contacting a compound of formula (2) (synthesized according to any of the processes described herein) with a compound of formula (10).

[0011a] In one aspect, the disclosure provides a process for the synthesis of a compound having the formula (1), the process comprising:


(1)

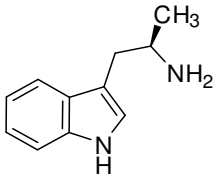
or a pharmaceutically acceptable salt thereof.

(a) contacting a compound of formula (2)

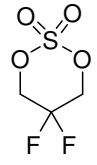

(2)

or a salt thereof

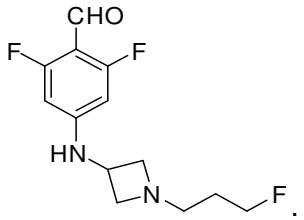
wherein the compound of formula (2) is synthesized according to the process as disclosed herein and wherein the compound of formula (V) has formula (5)


(5)

or a salt thereof and the compound of formula (VI) has formula (6):


(6)

(b) with a compound of formula (10)



or a salt thereof thereby making a compound of formula (1) or a pharmaceutically acceptable salt thereof.

[0012] In one example provided herein is a method of treating cancer by administering an effective amount of a compound of formula (I) or pharmaceutically acceptable salt thereof synthesized according to any of the processes described herein to a patient having cancer.

[0013] In another example provided herein is a method of treating lung cancer, ovarian cancer, endometrial cancer, prostate cancer, uterine cancer, or breast cancer by administering an effective amount of a compound of formula (I) or pharmaceutically acceptable salt thereof synthesized according to any of the processes described herein to a patient having said cancer.

[0014] In another example provided herein are methods of treating breast cancer in a patient having breast cancer by administering an effective amount of a compound of formula (I) or pharmaceutically acceptable salt thereof synthesized according to any of the processes described herein.

DETAILED DESCRIPTION

[0015] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by those of ordinary skill in the art to which the invention belongs. See, *e.g.,* Singleton et al., DICTIONARY OF MICROBIOLOGY AND MOLECULAR BIOLOGY 2nd ed., J. Wiley & Sons (New York, NY 1994); Sambrook et al., MOLECULAR CLONING, A LABORATORY MANUAL, Cold Springs Harbor Press (Cold Springs Harbor, NY 1989). Any methods, devices and materials similar or equivalent to those described herein can be used in the practice of this invention.

[0016] The following definitions are provided to facilitate understanding of certain terms used frequently herein and are not meant to limit the scope of the present disclosure. All references referred to herein are incorporated by reference in their entirety.