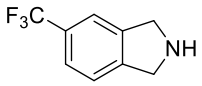
Summary

It has now been found that the compound of formula (1A) or a pharmaceutically acceptable salt thereof can be prepared using a process and a synthesis route, which is more practical, economical and suitable for use in a large scale. Intermediate compounds are prepared with improved methods utilizing commercially available starting materials and resulting in acceptable yields. Moreover, the compound of formula (1A) is obtained as a high purity and low colored product directly by crystallization without the need of purification by chromatography.

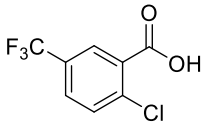
Thus, in one aspect, the present disclosure provides a process for the preparation of a compound of formula (V) or a pharmaceutically acceptable salt thereof



(V)

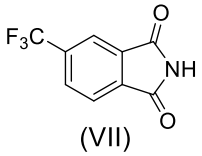
comprising the steps of either

a) treating a compound of formula (VI)



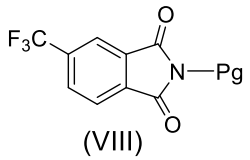
(VI)

with copper cyanide to obtain a compound of formula (VII)



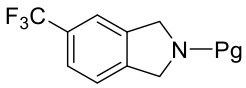
(VII) ;

b) protecting the compound of formula (VII) to obtain a compound of formula (VIII) wherein Pg is a protecting group



(VIII) ;

c) reducing the compound of formula (VIII) to obtain a compound of formula (IX)

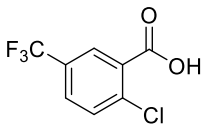


(IX) ; and

d) deprotecting the compound of formula (IX) to obtain a compound of formula (V); and optionally converting it to its pharmaceutically acceptable salt;

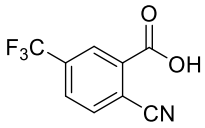
or

a') treating a compound of formula (VI)



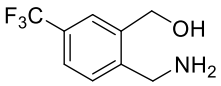
(VI)

with hexacyanoferrate[II] salt in the presence of a catalyst to obtain a compound of formula (X) or a pharmaceutically acceptable salt thereof



(X) ;

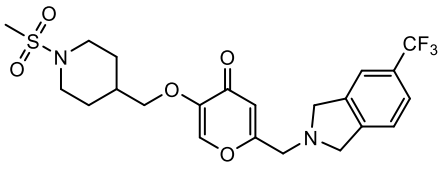
b') reducing the compound of formula (X) or a pharmaceutically acceptable salt thereof to obtain a compound of formula (XI) or a pharmaceutically acceptable salt thereof



(XI) ;

c') treating the compound of formula (XI) or a pharmaceutically acceptable salt thereof with thionyl chloride to obtain a compound of formula (V); and optionally converting it to its pharmaceutically acceptable salt.

In another aspect, the present disclosure provides a process for the preparation of a compound of formula (1A) or a pharmaceutically acceptable salt thereof

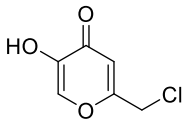


(1A)

comprising the steps of

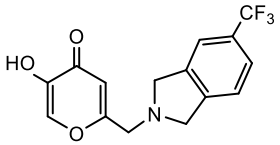
i) preparing hydrochloride salt of 5-(trifluoromethyl)isoindoline (V) according to any of the processes as defined above;

ii) reacting hydrochloride salt of 5-(trifluoromethyl)isoindoline (V) with a compound of formula (XII)



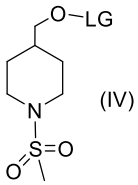
(XII)

to produce a compound of formula (III);



(III)

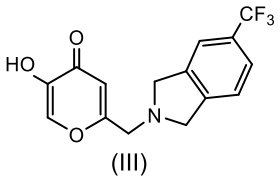
iii) reacting a compound of formula (III) with a compound of formula (IV)



(IV)

wherein LG is a leaving group selected from a mesyl or a tosyl group, to produce compound of formula (1A), and optionally converting it to its pharmaceutically acceptable salt.

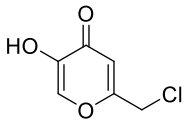
In still another aspect, the present disclosure provides a process for the preparation of a compound of formula (III)



(III)

comprising the steps of

a'') reacting a compound of formula (XII)



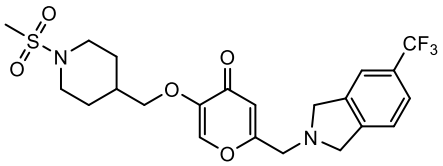
(XII)

with hydrochloride salt of 5-(trifluoromethyl)isoindoline (V) in dimethyl sulfoxide in the presence of N,N-diisopropylethylamine;

b'') adding isopropyl alcohol and water to the mixture; and

c'') isolating the compound of formula (III).

In still another aspect, the present disclosure provides a process for the preparation of a compound of formula (1A) or a pharmaceutically acceptable salt thereof

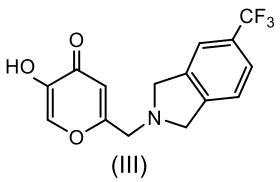


(1A)

comprising the steps of

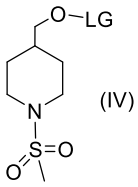
i') preparing a compound of formula (III) according to any of the processes as defined above;

ii') reacting a compound of formula (III)



(III)

with a compound of formula (IV)

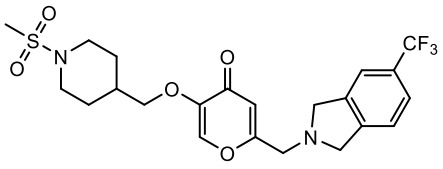


(IV)

wherein LG is a leaving group selected from a mesyl or a tosyl group,

to produce compound of formula (1A), and optionally converting it to its pharmaceutically acceptable salt.

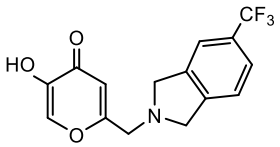
In still another aspect, the present disclosure provides a process for the preparation of a compound of formula (1A) or a pharmaceutically acceptable salt thereof



(1A)

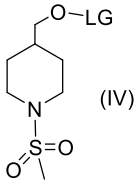
comprising the steps of

i'') reacting a compound of formula (III)



(III)

with a compound of formula (IV);



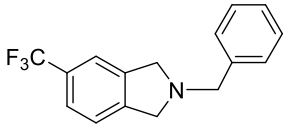
(IV)

wherein LG is a leaving group selected from a mesyl or a tosyl group,
in dimethyl sulfoxide in the presence of cesium carbonate;

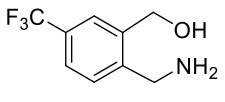
ii'') adding acetonitrile and water to the mixture; and

iii'') isolating the compound of formula (1A); and optionally converting it to its pharmaceutically acceptable salt.

In still another aspect, the present disclosure provides new intermediate compound of formula (IXa), or (XI) or a pharmaceutically acceptable salt thereof



(IXa)



(XI)

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Detailed description of the invention