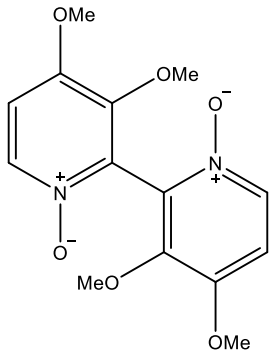
The present inventors have sought to provide an improved synthetic route to Orellanine. In particular, the present inventors have sought to provide a synthetic route that is safe, that provides high yields, and that avoids the need for complex purification steps.

SUMMARY

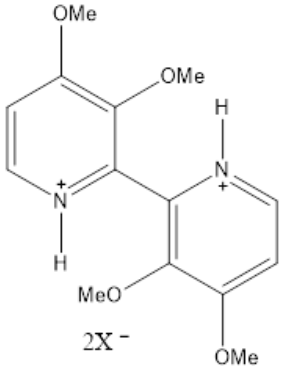
In an aspect, there is provided a method for preparing Orellanine, comprising a step of: reacting a compound of formula (II) in the presence of pyridinium hydrochloride to provide Orellanine.



(II)

The inventors have found that reaction of the compound of formula (II) in the presence of pyridinium hydrochloride provides Orellanine in high yield and purity. This reaction also avoids the gas evolution that is experienced in prior art processes when hydrobromic acid is used as the deprotection agent.

The present disclosure further provides a compound of formula (III):



(III)

wherein X^- is a negatively-charged counterion.

The compound of formula (III) is an intermediate that is prepared during a purification step in an example of the synthetic route to Orellanine.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 shows a synthetic route from 2-bromo-3,4-dimethoxy pyridine to Orellanine.

DETAILED DESCRIPTION OF THE INVENTION

Figure 1 shows a synthetic route to Orellanine. There are four reaction steps:

(i) coupling of 2-bromo-3,4-dimethoxy pyridine (compound of formula V) to provide tetramethyl Orelline (compound of formula IV)

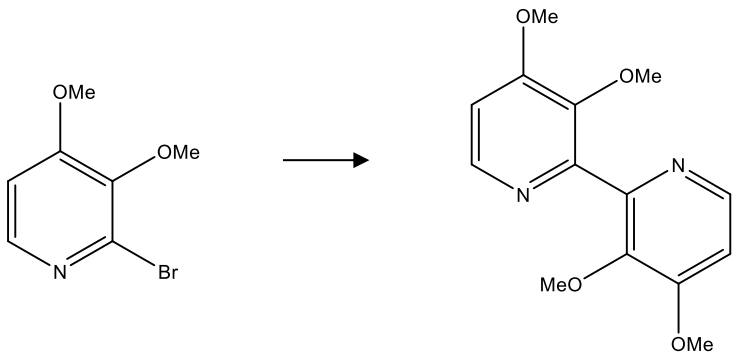
(ii) purification of tetramethyl Orelline (compound of formula IV) by reversible conversion to a salt of tetramethyl Orelline (compound of formula III)

(iii) oxidation of tetramethyl Orelline (compound of formula IV) to provide tetramethyl Orellanine (compound of formula II)

(iv) demethylation of tetramethyl Orellanine (compound of formula II) to provide Orellanine (compound of formula I)

These reaction steps are described in further detail below:

Coupling of 2-bromo-3,4-dimethoxy pyridine (compound of formula V) to provide tetramethyl Orelline (compound of formula IV)

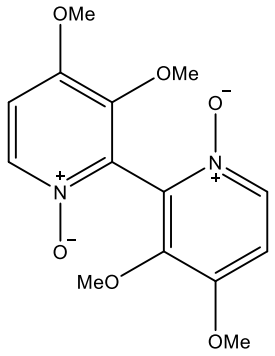


(V) (IV)

CLAIMS

1. A method for preparing Orellanine, comprising a step of:

reacting a compound of formula (II) in the presence of pyridinium hydrochloride to provide Orellanine.



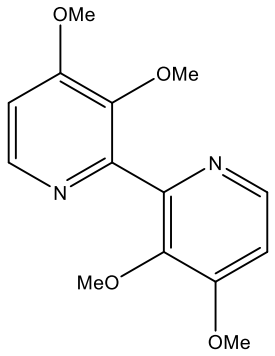
(II)

2. A method according to claim 1, wherein reacting the compound of formula (II) takes place at a temperature in the range of 80 to 125ºC.

3. A method according to claim 2, wherein reacting the compound of formula (II) takes place a temperature of about 105ºC.

4. A method according to any preceding claim, further comprising a step of:

reacting a compound of formula (IV) to provide the compound of formula (II).

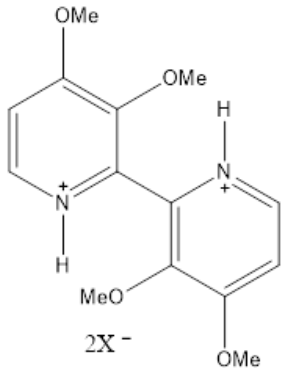


(IV)

5. A method according to claim 4, wherein the compound of formula (IV) is reacted with *m*-chloro perbenzoic acid.

6. A method according to claim 4 or claim 5, wherein the compound of formula (II) is purified by crystallizing the compound of formula (II) from a solution comprising methyl tert-butyl ether.

7. A method according to any one of claims 4-6, further comprising a step of purifying the compound of formula IV by reversible conversion to a compound of formula III



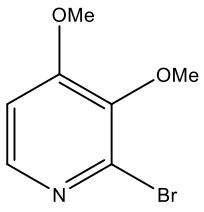
(III)

wherein X^- is a negatively-charged counterion.

8. A method according to claim 7, wherein the compound of formula (IV) is reacted with hydrochloric acid.

9. A method according to claim 7, wherein the compound of formula (IV) is reacted with oxalic acid.

10. A method according to any one of claims 4-9, further comprising a step of:
reacting a compound of formula (V) to provide the compound of formula (IV).



(V)

11. A method according to claim 10, wherein the compound of formula (IV) is reacted in the presence of nickel (II) chloride, zinc and triphenylphosphine.