



# Method for synthesizing 2-acetyl-1-pyrroline and the stable precursor thereof, optionally isotopically marked

**Notre référence :**  
02647-01

## Status des brevets

France priority patent application filed on June the 24th, 2009 and entitled "Methode de synthese de la 2-acetyl-1-pyrroline et de son precurseur stable, marque isotopiquement ou non"



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## Status Commercial

Exclusive or non-exclusive license. Co-development

## Laboratoires

## CONTEXT

The present invention relates to a method for synthesizing 2-acetyl-1-pyrroline (2AP) and of ketal derivatives of 2AP as stable precursors in flavoring compositions.

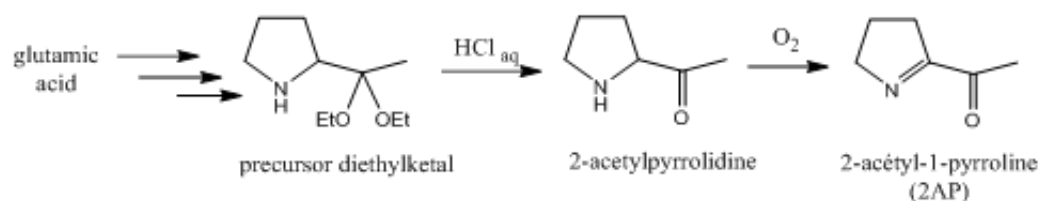
2AP is a volatile molecule which smells of popcorn, basmati rice and toasted bread. It is one of the aromatic compounds of perfume rice, i.e. rice varieties from restricted genetic populations that cannot be cultivated outside their original area.

## TECHNICAL DESCRIPTION

The methods of synthesis of the 2AP of the prior art have several drawbacks: first of all some methods use toxic materials that are difficult to envisage for the use of the final products in the agri-food sector, the final product is often difficult to separate to the other products formed during the last steps (such as its tautomer), and lastly some synthesis do not make it possible to synthesize its isotopically labeled analog in a non-exchangeable position.

The inventors of the present invention have therefore developed a new method of synthesis overcoming these drawbacks and thus easy to implement at low cost, with a minimum number of steps, and providing easy purification of the final molecules, without employing materials that are prohibited by the agri-food industry and using naturally existing compound as starting material (i. e. glutamic acid). This synthesis method offers the additional benefit of readily providing isotopically labeled (deuterium-labeled) compounds in particular for the use as an internal reference in an assay method. Furthermore, it involves ketal intermediates that represent stable precursors for flavoring compounds in order to overcome the stability issue raised by such molecules. In fact, the ketal molecule can be stably kept if they are protected from air and moisture and then can gradually release the flavoring molecules, under the action of the water followed by oxygen.

Thus the present invention relates to a method for synthesizing the 2AP through a ketal intermediate (scheme) starting from the glutamic acid.



## DEVELOPMENT STAGE

The synthetic pathway has allowed the synthesis of the 2-AP and its diethoxyketal precursor. It has also permitted the preparation of the 2-acetyl-1,2,3,4-tetrahydropyridine and its diethoxyketal precursor. The di-deuterated derivatives of 2AP and its diethoxyketal

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precursor were also prepared. Moreover, the di-deuterated 2AP was used as an internal reference in an assay

## BENEFITS

The synthetic method developed for the preparation of the 2AP molecule is unexpensive with a minimum number of steps and avoids the use of materials prohibited by the agri-food sector. Moreover, the stable di-deuterated analog is easily available through the synthetic pathway. Furthermore, the ketal precursor is of high interest to overcome the problem of stability of the 2AP. Additionally, the synthetic pathway can be advantageously applied to the synthesis of a variety of aromatic compounds, i.e. 2-acetyl-1-pyrroline (2AP) or 2-propionyl-1-pyrroline, starting from the glutamic acid and also to 2-acetyl-1,2,3,4-tetrahydropyridine or 2-prioponyl-1,2,3,4-tetrahydropyridine starting from the 2-aminoadipic acid.

## INDUSTRIAL APPLICATIONS

The ketal derivatives (for example the diethoxyketal) of 2AP can be used as stable precursors in flavoring compositions for instance in ready meals based on rice.

It is worth pointing out that the global market for rice production was estimated for 2014-2015 to 500 million tons (milled equivalent). Fragrant rice is estimated to account for 15-18% of the rice trade procuring the highest prices on the world market. Fragrant rice is priced on the trade market at \$1,100 /T or more, whereas coarse rice is \$440 - 580/T (FAO 2012).

For further information, please [contact us](#) (Ref 02647-01)