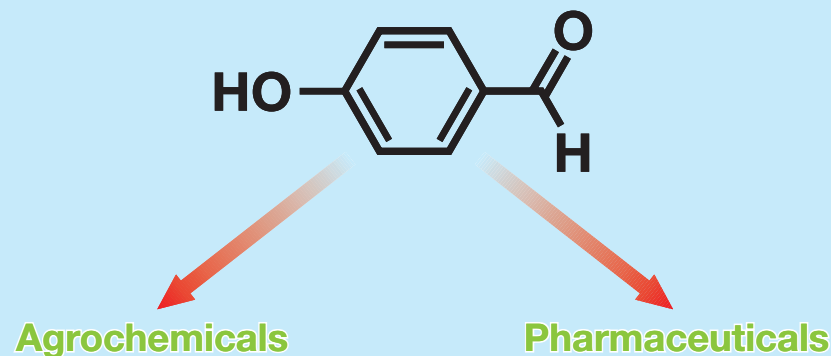


# Retro-Strecker Reaction used for the Production of 4-Hydroxybenzaldehyde

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## Abstract

Aromatic aldehydes like 4-hydroxybenzaldehyde are important intermediates in the agro and pharmaceutical industry. Besides the industrial process of selective ozonolysis we are famous for, we have developed a new technology to prepare aldehydes from amino acids. The reaction is carried out in aqueous medium using an organic catalyst as well as oxygen or air for regeneration.



## Application of 4-hydroxybenzaldehyde

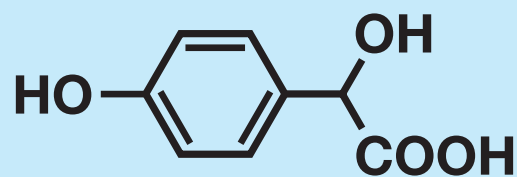
4-Hydroxybenzaldehyde is a versatile intermediate for agrochemicals like Bromoxynil, Ioxynil or Bromofenoxim and pharmaceuticals like Trimethobenzamid.

## Production of 4-hydroxybenzaldehyde

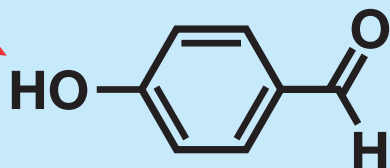
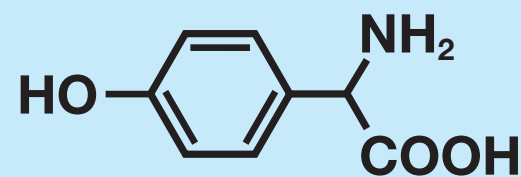
Decarboxylation of  $\alpha$ -hydroxy acids is a simple method to produce aldehydes. Especially aromatic compounds can be easily transformed to the corresponding aldehydes when metal salts (e.g. Fe and Cu) are used as catalyst and oxygen or air as oxidant<sup>1</sup>. 4-Hydroxybenzaldehyde made from 4-hydroxy mandelic acid is one of the important examples for such process.

Although the transformation of  $\alpha$ -amino acids using this method is described in the patent literature<sup>2</sup>, it failed permanently when the conditions described were used in chemical experiments. Typically, a black coloured, sticky precipitate appeared in the reaction solution preventing efficient isolation of the product.

<sup>1</sup> DE 2115551 Haarmann und Reimer    <sup>2</sup> JP 57108034 Ube Ind



Oxidative Decarboxylation  
using oxygen or air and  
metal catalyst (Fe, Cu)



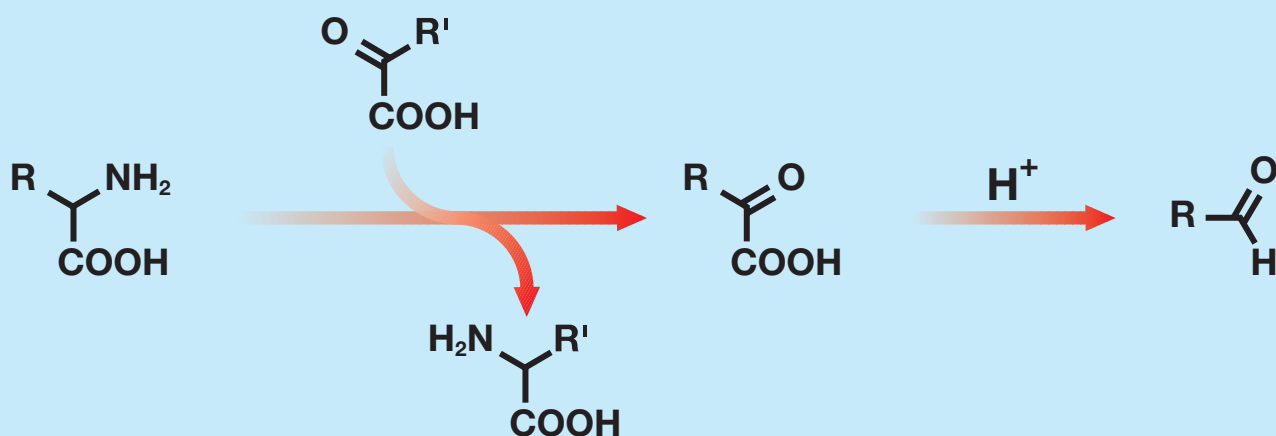
### Amino acids as origin

Anyhow, amino acids are still potential starting materials if one takes into account the variety in structure of natural  $\alpha$ -amino acids and their availability in bulk from fermentation processes for instance or if one of the enantiomers is commercially not used.

DSM is one of the biggest manufacturers of amino acids and aldehydes. Although, the technology of classical

resolution and isomerisation of the racemic mixture is carried out for most of the amino acids, there is still a lack in technology when the "not wanted" enantiomer cannot be transformed by means of a Schiff base. An easy and of course economically friendly process for a Retro-Strecker reaction for such compounds is in our interest.

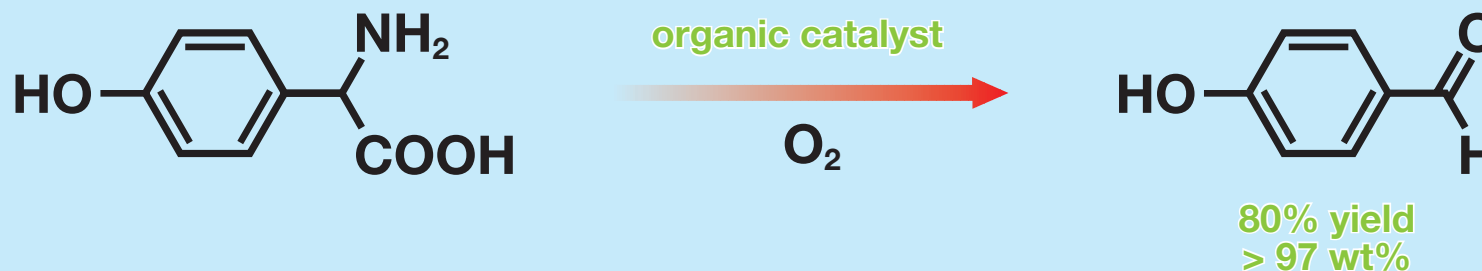
In doing so we developed a process based on the bio-mimetic reaction of amino transformation. For example,  $\alpha$ -keto acid derivatives or diketo compounds react with amino acids to the amino pendent and the free  $\alpha$ -keto acid is decarboxylized to the aldehyde in acid medium. Due to the nature of this reaction it only can be successful in conversion and isolated yield when an excess of the reactant is used.



## Our process to 4-hydroxybenzaldehyde

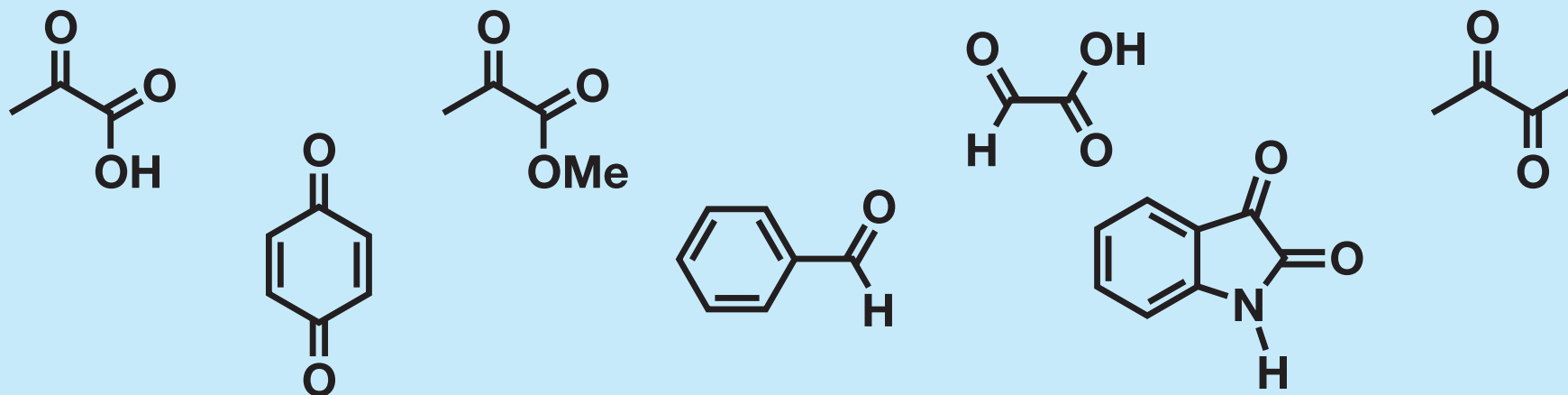
We present a unique process using an organic catalyst and oxygen or air for the production of aromatic aldehydes from amino acids. 4-Hydroxybenzaldehyde as one of the examples is an important intermediate in fine chemistry and agro chemistry. In our case we deal

with 4-hydroxy phenyl glycine as starting material. This compound is produced from phenol and glyoxylic acid/ammonia by DSM. It is transformed to 4-hydroxy benzaldehyde with above keto compounds and oxygen in acid medium in high yields.



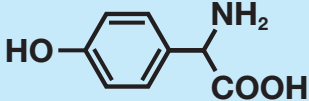
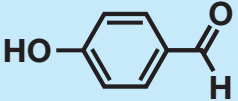
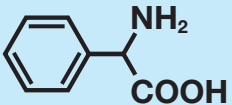
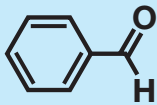
Our invention deals with these keto compounds but in catalytic amounts and uses an oxidant like air or oxygen for regeneration.

## Following keto compounds have been found to be active in oxidative decarboxylation



Pyruvic acid, pyruvic acid methyl ester, glyoxylic acid, diacetyl, 1,4-benzoquinone, benzaldehyde and isatin

### Examples using such keto compounds for oxidative decarboxylation

Educt	Product	Catalyst	Conversion [%]	Isolated Yield [%]	Purity [wt%]
		pyruvic acid	76	62	92,6
		glyoxylic acid	75	60	98,5
		diacetyl	100	37	96,6
		isatin	100	80	97,3
		isatin	100	67	99,0

### Our process combines following advantages

being environmentally friendly

- organic compound is used in catalytic amount instead of toxic metal salt
- oxygen or air as oxidant
- easy and cheap purification
- less by-products and therefore less waste
- aqueous reaction medium

and the remarkable features of our process to 4-hydroxybenzaldehyde

- high selectivities in the range of 90-94 %
- isolated yields at 80-85 %
- a purity of >97 wt.% of the product after an easy purification step (extraction)