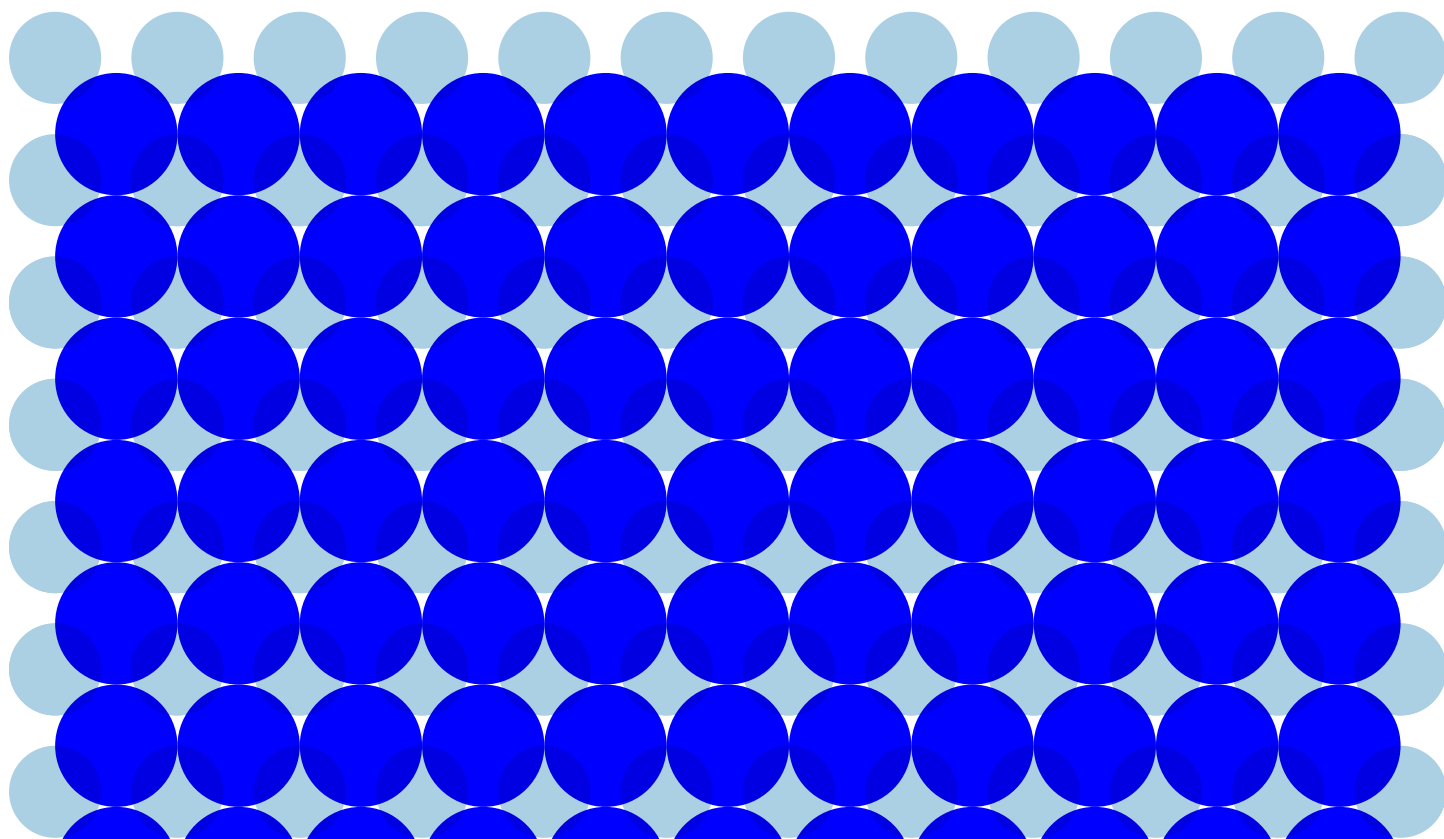


# How can one of the Smallest Aldehydes become a Strong Asset when Selecting a CDMO Partner?

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Choosing a CDMO partner is often a complex exercise where many parameters need to be accounted for. In that context, leveraging existing experience is usually a powerful criteria, and looking into partners who have access to the relevant technologies is key to success. Whilst acetaldehyde could be restricted to “just a small aldehyde”, the depth or the opportunities associated with its production and uses, might be unlocking opportunities – just a thought!



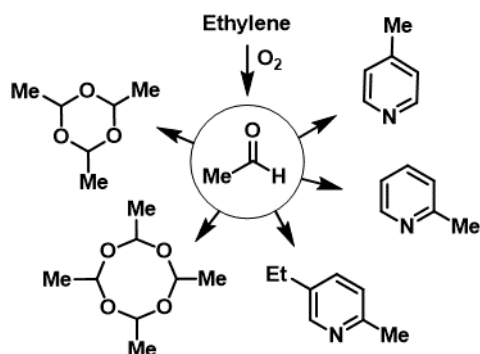
## How can one of the Smallest Aldehydes become a Strong Asset when Selecting a CDMO Partner?

**Acetaldehyde is the second smallest aldehyde (after formaldehyde), bearing a highly reactive function (the aldehyde function), hence a good candidate for chemical syntheses. Due to a somehow challenging profile (safety, physical form and toxicity), its production and handling require know-how and expertise, which Arxada is proud to offer to its customers.**

Acetaldehyde (CAS 75-07-0) is a highly reactive colorless liquid or gas, boiling near room temperature, that was first observed by the Swedish pharmacist/chemist Carl Wilhelm Scheele in 1774. It is one of the most important aldehydes, occurring widely in nature and being produced on a large scale in industry.

Traditionally, acetaldehyde was mainly used as a precursor to acetic acid but this application declined as acetic acid is now produced more efficiently from methanol by the Monsanto and Cativa processes. It is still an important precursor of various derivatives, for which it serves as raw materials. As such, acetaldehyde is produced by Arxada in Visp via direct catalytic oxidation of cracker-based ethylene, before further transformations on-site (Figure 1).

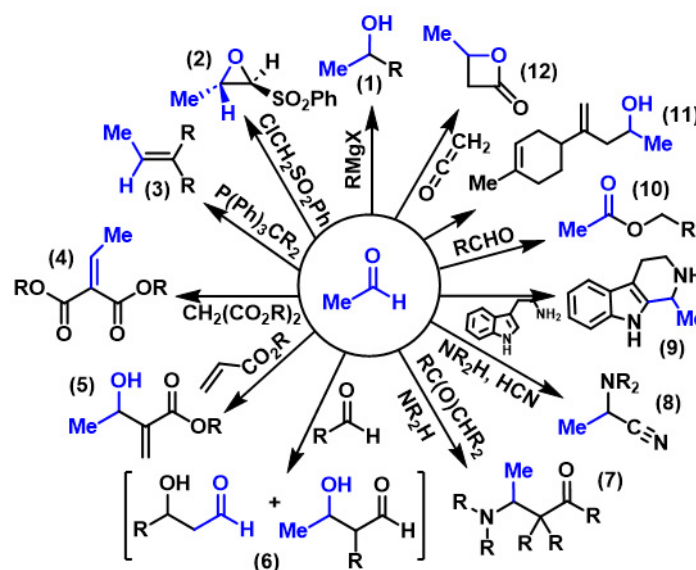
Figure 1. Arxada's portfolio of products based on acetaldehyde.



On the Arxada's Visp premise, acetaldehyde is used for the production of paraldehyde (CAS 123-63-7, cyclic trimer of acetaldehyde) and metaldehyde (CAS 108-62-3, cyclic tetramer of acetaldehyde). Paraldehyde can then be reacted with ammonia, leading to a variety of pyridine derivatives, such as 5-ethyl-2-methylpyridine (CAS 104-90-5), 2-picoline (CAS 109-06-8, 2-methylpyridine) and 4-picoline (CAS 108-89-4, 4-methylpyridine). 5-Ethyl-2-methylpyridine is further transformed on-site to produce vitamin B3 (CAS 59-67-6, niacin), an important product with a market of 600Mil USD in 2022, for which Arxada is a leader via its food and pharma grades.

Most products discussed in the above section belong to the Arxada portfolio as part of the Nutrition & Infrastructure department within the Nutrition, Care and Environmental (NCE) division.<sup>1</sup> However and as always for the products out the Verbund,<sup>2</sup> the produced acetaldehyde can be redirected towards the multi-purpose assets for bespoke projects / CDMO requests, broadening the scope of the achievable for this reactant. Thanks to its highly reactive nature, acetaldehyde can therefore be used in several reactions (Figure 2).

Figure 2. Non-exhaustive potential acetaldehyde transformations.



Various transformations are depicted in the above figure:

- Engaged with an organomagnesium nucleophile, acetaldehyde can deliver secondary alcohols **(1)** via a Grignard reaction;
- Trans epoxides **(2)** can be produced via Darzens reaction between acetaldehyde and halomethyl sulfones;
- Using Wittig reagents with acetaldehyde, alkenes **(3)** can be obtained;
- Knoevenagel condensation on acetaldehyde can lead to ethylidene substituted compounds **(4)**;
- Baylis-Hillman condensation between acrylates and acetaldehyde can offer allylic alcohols **(5)**;
- Aldols **(6)** can be formed in crossed and directed aldol reactions with other aldehydes;
- In a Mannich reaction,  $\beta$ -amino carbonyl compounds **(7)** can be formed in presence of amines and carbonyl derivatives;

<sup>1</sup> For more information, please contact the N&I team at [performance.intermediates@arxada.com](mailto:performance.intermediates@arxada.com), and/or consult the corresponding portfolio online (<https://www.arxada.com/en/products?sortType=Ascending>).

<sup>2</sup> Generally speaking, a Verbund system creates efficient value chains that extend from basic chemicals, with more energy efficient processes and high yields. In this case, Arxada is referring to its background integrated network, the acetylene generator unit, driving the production of acetaldehyde (amongst others chemicals).

- Engaged with hydrogen cyanide and primary or secondary amines, acetaldehyde can deliver  $\alpha$ -aminonitriles **(8)** via a Stecker synthesis;
- In a Pictet-Spengler reaction,  $\beta$ -arylethylamines undergoes condensations with acetaldehyde followed by ring closure towards the corresponding aromatic **(9)**;
- In a Tishchenko reaction, acetaldehyde and ketones can offer esters **(10)**;
- Engaged with the relevant alkenes, a ene reaction can take place to offer  $\alpha$ -hydroxy alkenes **(11)**;
- Acetaldehyde can react with an alkenes in 2+2 reactions, delivering  $\beta$ -butyrolactone **(12)** when this alkene is ketene.

Thanks to these numerous options, one skilled in the art could rapidly visualize the infinite opportunities unlocked by having access to its own source of acetaldehyde at its CDMO partner.

In conclusion, thanks to its experience in producing and handling fresh acetaldehyde, which aside from being “one the smallest aldehyde” could be seen as an open door to many different species (due to the numerous derivatization opportunities), Arxada can support its key partners with acetaldehyde based on backward integration, hence derisking supply chains.

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## Our offer

- Extensive experience in production and safe handling of acetaldehyde
- Up-to-date multi-purpose assets with flexible distillation and filtration set-ups
- Ability to derivatize on-demand
- Focus on *what matters to you*

To discuss how Arxada could support your project for which acetaldehyde can be relevant, get in touch with:  
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