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Contract Development & Manufacturing Organization (CDMO)

From hazard to asset: the role of hydrogen cyanide in industrial fine chemical synthesis

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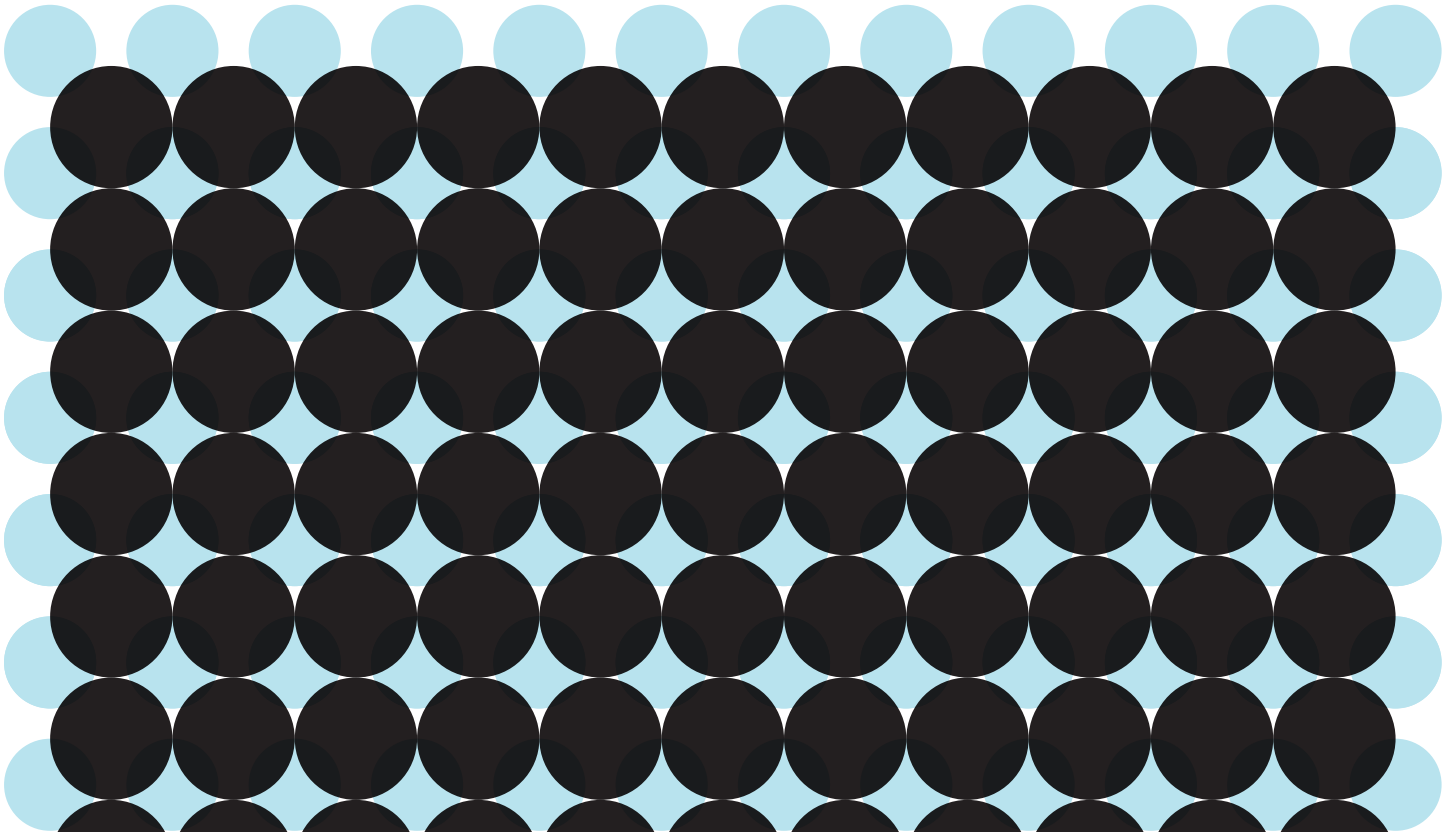
Often perceived as a hazardous compound, hydrogen cyanide (HCN) is in fact an important industrial building block used in chemical synthesis across multiple industries. At Arxada, on-site HCN production is seamlessly integrated into a robust and flexible manufacturing network, ensuring controlled quality and supply continuity. Combined with deep expertise in HCN-based chemistry, it opens access to high-value intermediates. Furthermore, the agile CDMO (Contract Development and Manufacturing Organization) approach delivers tailor-made, end-to-end solutions that accelerate innovation and de-risk complex synthesis challenges.



From hazard to asset: the role of hydrogen cyanide in industrial fine chemical synthesis

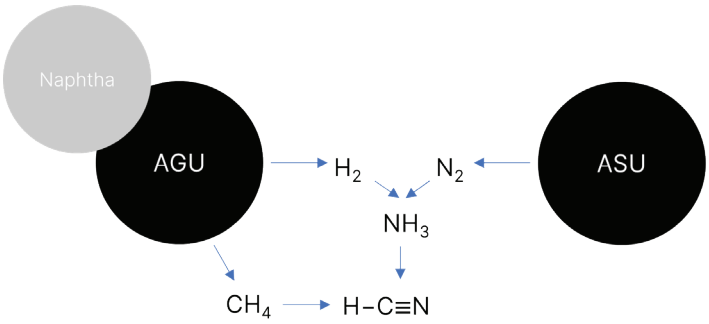
Hydrogen cyanide (HCN) is a reactive and versatile intermediate widely employed in the synthesis of nitriles, ¤-amino acids, and a range of fine and specialty chemicals. Owing to its dual nucleophilic and electrophilic character, HCN participates in several key transformations, including hydrocyanation of unsaturated compounds and the Strecker synthesis of α-aminonitriles. While its handling requires stringent safety controls due to its highly reactive and hazardous nature, HCN remains essential to numerous industrial-scale processes. At Arxada's Visp facility, HCN is manufactured on-site through a fully integrated production network, allowing for stringent quality control, continuous availability, and cost efficiency. This infrastructure supports both large-scale manufacturing and tailored fine chemical synthesis, enabling the strategic and safe deployment of HCN across a broad range of applications.

HCN is a highly reactive and functionally diverse building block in industrial organic chemistry. Structurally simple, consisting of a hydrogen atom bonded to a carbon–nitrogen triple bond, HCN typically acts as a nucleophile via its conjugate base - the cyanide anion (CN^-). This attribute enables its involvement in a broad range of key transformations, such as carbon–carbon bond-forming reactions. Although it requires stringent safety measures due to its hazardous nature, HCN continues to play a crucial role in production of nitriles, cyanohydrins, α-amino acids, and a wide range of fine and specialty chemicals, with global output exceeding one million tons annually. The use of HCN extends across multiple sectors, including polymer manufacturing, agrochemical synthesis, and pharmaceutical development. Large proportion of produced HCN is used in hydrocyanation processes. HCN adds across unsaturated carbon–carbon bonds to form aliphatic nitriles, which can easily undergo further transformations. E.g. adiponitrile serves as a precursor to Nylon-6,61 with application in automotive and textile industry, acetone cyanohydrin[2] is primarily used in synthesis of methyl methacrylate, a key component of acrylic polymers.

In the context of nitrogen-containing building blocks, the Strecker synthesis employs HCN to form α-aminonitriles via addition to imines derived from aldehydes or ketones and ammonia.3 Moreover, HCN can be applied in Sandmeyer-type cyanation reactions, where aryl diazonium salts are converted into aryl nitriles using CuCN.[4]

At Arxada's Visp facility, HCN is produced on-site as part of a fully integrated production infrastructure. The Visp's cracker (Acetylene Generating Unit, AGU) produces (among other streams) methane that is fed into the cyanide unit, where it is subsequently converted into HCN (Figure 1). This level of backward integration provides Arxada with full control over production parameters, including purity, throughput, and supply continuity, critical for both high-volume and precision fine chemical applications. Based on the technologies derived thereof, Arxada can offer a variety of basic chemicals and performance intermediates as portfolio products as well as CDMO tailor-made solutions.

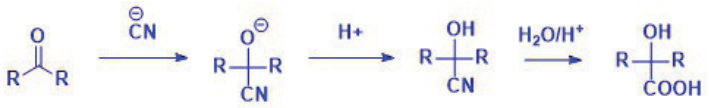
Figure 1: HCN backward integration at Arxada (Visp, Switzerland). AGU – acetylene generation unit, ASU – air separation unit.



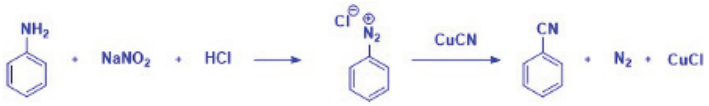
Selected Applications of HCN in Synthetic Chemistry:

1. **Strecker Synthesis – Formation of α-Amino Acids**
   The Strecker synthesis remains a robust route for the formation of α-amino acids or α-amino alcohols via the condensation of an aldehyde or ketone with ammonia, followed by nucleophilic addition of HCN to form an α-aminonitrile. Acidic hydrolysis yields the corresponding α-amino acid. This method, first described by Adolph Strecker in 1850, has been adapted for both batch and continuous flow operations and is still industrially employed particularly in methionine production[5] for animal feed, or production of selected non-proteinogenic amino acids. These can be further be employed in the synthesis of various pharmaceuticals.[6] Additionally, α-aminonitriles are precursors to chiral amines, which are often found in active ingredients of pharmaceuticals and agrochemicals.[7]

2. **Cyanohydrin Formation – Addition to Carbonyl Compounds**
   HCN readily undergoes nucleophilic addition to aldehydes and ketones to afford cyanohydrins, which contain both hydroxyl and nitrile functional groups. Chiral cyanohydrins are valuable intermediates in asymmetric synthesis, and their hydrolysis leads to α-hydroxy acids. Industrial-scale applications include synthesis of key building blocks in the synthesis of cardiovascular drugs, antibiotics, and other APIs (active pharmaceutical ingredients).[8] In agrochemicals, cyanohydrins derived from various aldehydes areused to produce herbicides and insecticides.[9] Additionally, hydrolysis of cyanohydrin intermediatesields lactic acid derivatives, which find applications in biodegradable plastics, cosmetics, and food additives. [10,11]



3. **Sandmeyer-Type Cyanation – Synthesis of Aromatic Nitriles**
   The Sandmeyer reaction enables the transformation of aromatic amines into substituted aromatic compounds via diazonium salt intermediates. In thecyanation variant, copper(I) cyanide is employed to install nitrile groups onto aromatic rings.[12] This transformation is widely used in the production of benzonitrile derivatives, which are essential in the synthesis of some APIs. In the agrochemical industry,nitrile-containing herbicides are synthesized via Sandmeyer cyanation of halogenated phenols.[13] The dye and pigment industry also relies on this reaction to produce azo dyes, where aromatic nitriles act as versatile precursors for further functionalization.[14]



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Summary

This white paper outlines the key chemical transformations and industrial applications enabled by hydrogen cyanide (HCN). Despite its hazardous nature, HCN remains a cornerstone of chemical synthesis across multiple sectors. Arxada is uniquely positioned to harness HCN safely, supporting both large-scale industrial processes and customized client-specific projects. Through its vertically integrated production model and advanced chemical development capabilities, we can effectively address common challenges such as production costs, safety measures, and overcome logistical constraints related to storage and transportation.

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Our offer

- **Backward integrated cyanide operations**
- **Portfolio of HCN-derived intermediates**
- **Experience with various chemistries employing HCN**
- **Fully integrated CDMO services and tailor-made solutions**
- **Focus on what matters to you**

Acknowledgments

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