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White Paper July 2024

Custom Development & Manufacturing Organization (CDMO)

MALONODINITRILE (MDN): Waste free synthesis and widely usable

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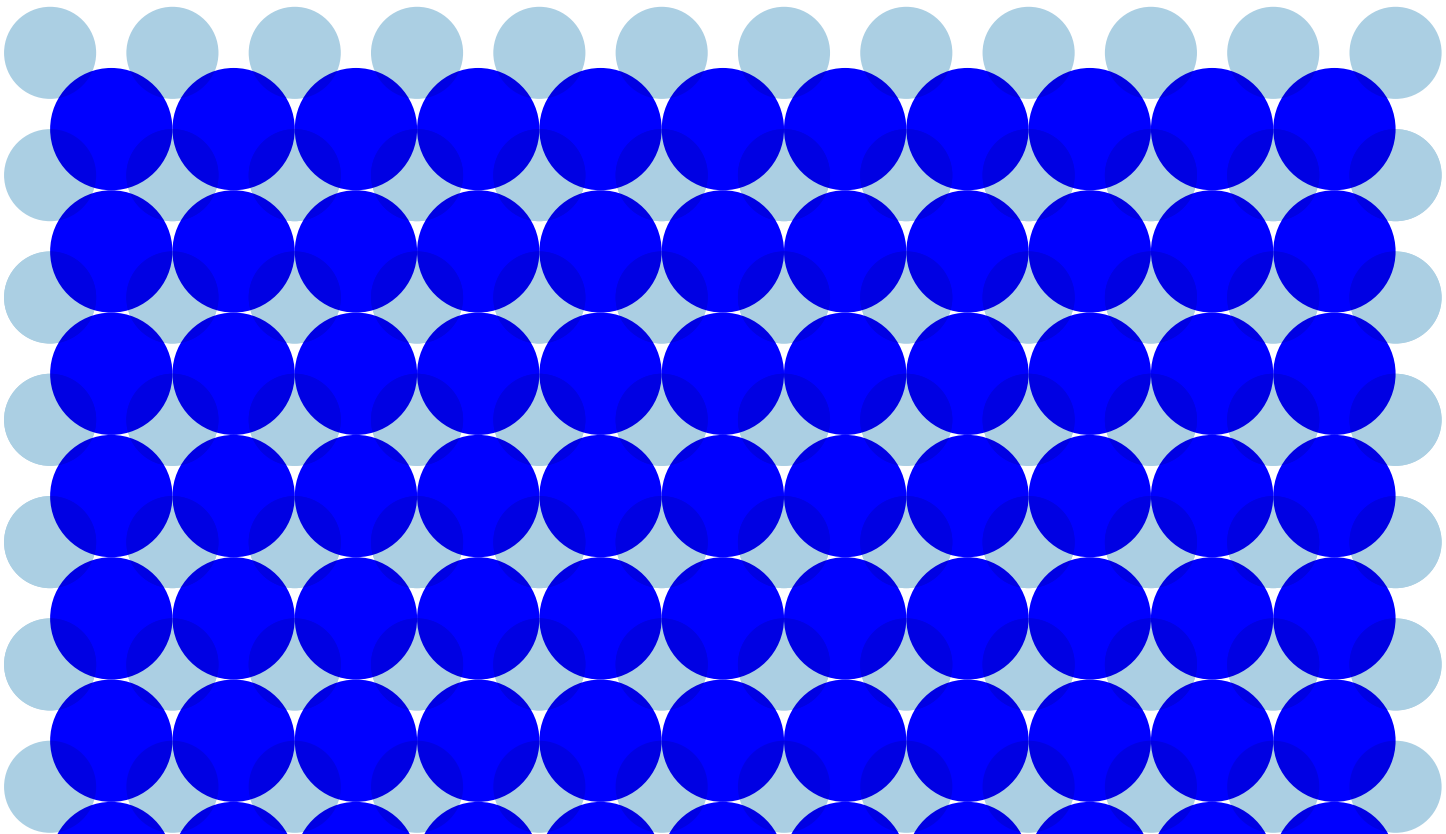
Explore the extraordinary potential of malononitrile (MDN) in the synthesis of a vast array of essential compounds, including fine chemicals, vitamins, pharmaceuticals, pigments, and nonlinear optical materials. With two distinct synthesis pathways—one cost-effective and one environmentally sustainable—MDN is a cornerstone in organic synthesis, renowned for its ability to participate in numerous reactions. Discover how its unique structure, featuring two cyano groups separated by a methylene, makes MDN an indispensable asset in both academic research and industrial applications.



MALONODINITRILE (MDN): Waste free synthesis and widely usable

Malononitrile (MDN) is crucial for synthesizing fine chemicals, vitamins, pharmaceuticals, pigments, nonlinear optical compounds, and various other materials. There are two synthesis pathways for MDN: one cost effective and one sustainable way. MDN is a highly versatile building block in organic synthesis, renowned for its ability to undergo various reactions such as addition, condensation, substitution, cyclization, and polymerization. This reactivity stems from its structure, featuring two cyano groups separated by a methylene.

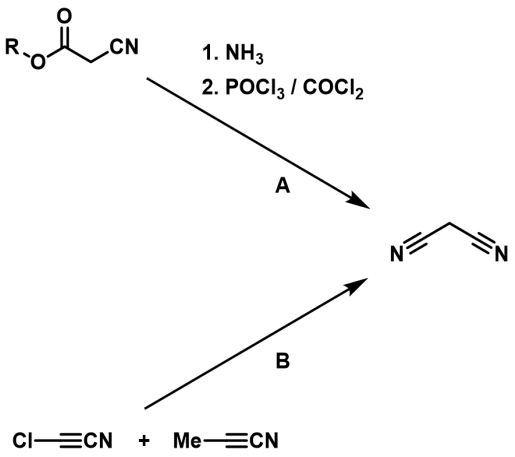
Malononitrile or malonodinitrile (MDN) is a widely used building block in organic synthesis because of its ability to undergo a series of reactions such as addition, condensation, substitution, cyclization, and polymerization to give a wide variety of compounds. This exceptional reactivity is due to the presence of two cyano functional groups separated by a methylene. They are strongly polar and electron-withdrawing, therefore making the hydrogens of the methylene quite acidic.[1-2] This unique reactivity makes MDN an important chemical both in academic research and in medicinal, industrial, and agricultural chemistry. MDN appears as a colorless crystalline powder (albeit with a propensity to adopt yellow or brown hues over time), soluble in many polar and non-polar solvents.

According to the current state of the art, the synthesis process of MDN (Scheme 1) is roughly divided into two categories, namely dehydration methods (**A**) and the gas phase reaction of acetonitrile with cyanogen chloride (**B**).

The first method (**A**, dehydration method) consists in treating cyanoacetates with ammonia to obtain cyanoacetamide. This intermediate is then dehydrated using either phosphoryl chloride or phosgene. The advantages of this method are low cost and commercial availability of the starting materials, low temperatures, and high yields. However, the use of phosphoryl chloride generates a considerable amount of solid waste made of phosphorus-containing byproducts, which are difficult to dispose of and recycle. This could be avoided by replacing phosphoryl chloride with phosgene, a toxic gas that should be carefully handled when used on an industrial scale. The dehydration method is mainly implemented in China.[3-4]

The second method, which Arxada adopts in a dedicated plant in Visp, employs acetonitrile and cyanogen chloride as raw materials (**B**). The only byproduct is HCl, which can be used for other purposes, making this synthetic pathway free of waste. Nevertheless, the required reaction temperature is very high, demanding stringent process control. For this, Arxada relies on a team of experienced experts.[5]

Scheme 1. Different synthetic pathways for MDN; A: Dehydration and B: gas phase reaction of acetonitrile with cyanogen chloride.

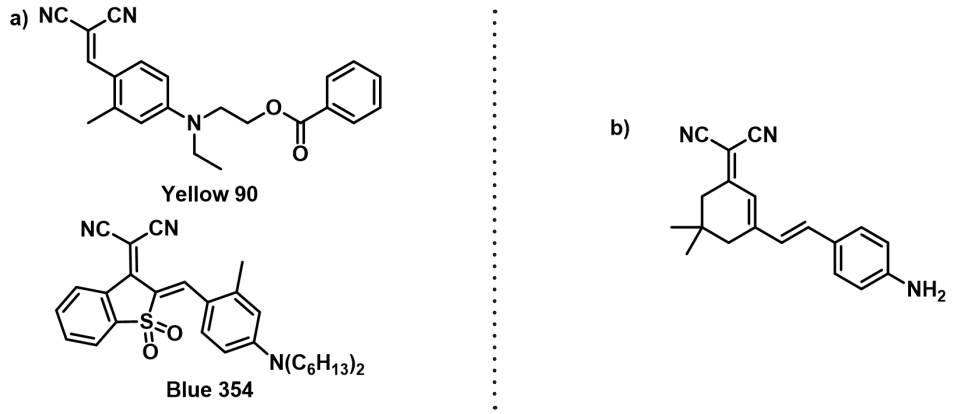


MDN is extensively used as a building block for the synthesis of countless molecules (Scheme 2), namely fine chemicals, vitamins, agrochemicals, pharmaceuticals, colorants, organic semiconductors and many more.

An example is the synthesis of pigments, i.e. water-insoluble non-ionic colorants applied to hydrophobic fibers (cellulose acetate, polyester, and nylon) from aqueous dispersions. These MDN-condensed pigments produce deeper colors and shades with better fastness to washing, light, and perspiration on application to polyester and nylon fabrics when compared to their uncondensed analogs.[6] Two common pigments derived from MDN are Yellow 90[7] and Blue 354[8] (Figure 1a). Nonlinear optical (NLO) compounds are another class of molecules that can be synthesized from MDN. They are characterized by their capacity to modulate their refractive index or polarization according to electric field or light intensity fluctuations. These properties make such compounds indispensable in fields such as telecommunications and optical information processing. An example is the aniline derivative in Figure 1b; ((*E*)-2-(3-(4-aminostyryl)-5,5-dimethylcyclohex-2-enylidene) malononitrile).[9] The three mentioned examples (Yellow 90 Blue 354 and the aniline derivative) are synthesizable through a Knoevenagel condensation. The Knoevenagel condensation is a common reaction in organic synthesis in which MDN can take part: it is reacted with either an aldehyde or a ketone in the presence of a base to give an α,β-unsaturated nitrile (**1**, Scheme 2).[10]

[1] Javahershenas et al. *Ultrason. Sonochem.* **2024**, 102, 106741.
[2] Hassan et al. **2015**, *IJISR*, 16, 1, 11-46.
[3] Patent publication number: CN104945278.
[4] Patent publication number: CN112724041.
[5] Patent publication number: CN116143657.
[6] Lams et al. *J. Text.* **2014**, 3.
[7] Patent publication number: US3909198.
[8] Patent publication number: GB2026528.
[9] Koleva et al. *Cent. Eur. J. Chem.* **2008**, 6, 592-599.
[10] Verdía et al. *Molecules*, **2011**, 16, 6, 4379-4388.

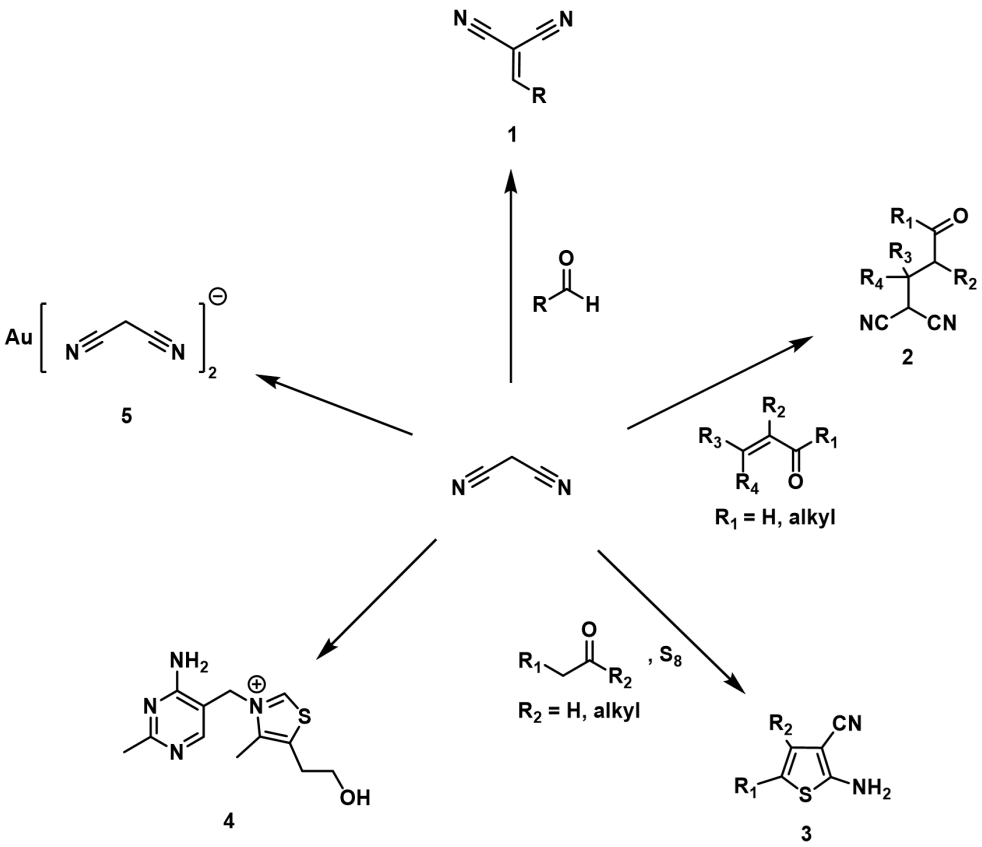
Figure 1. Example molecules derived from MDM: a) Common cyano pigments; b) Structure (aniline derivative) of a nonlinear optical (NLO) molecule.



Besides the Knoevenagel condensation there are four other reactions requiring MDM to be highlighted:

- MDN in a Michael addition: in the presence of a base, MDN is deprotonated at the symmetric center of the β carbon of an α,β-unsaturated carbonyl to create a 1,4-dinitrile compound (**2**).[11]
- The Gewald reaction is a chemical reaction that involves the formation of a thiophene ring from MDN, a ketone or an aldehyde, elemental sulfur, and a base (**3**). Thiophenes are heterocyclic compounds with various biological and industrial applications.[12]
- One of the most important roles that MDN plays in industry, however, is as starting material for the synthesis of thiamine (vitamin B1) (**4**)[13], a water-soluble vitamin essential for the growth and well-being of animals as antineuritic.
- Finally, MDN can also be used as a leaching agent for gold (**5**).[14]

Scheme 2. Applications of MDN.



[11] Flores-Reyes et at. *RSC Adv*. **2023**, 13, 16091–16125.

[12] Huang et al. *Mol. Divers*. **2011**, 15, 3–33.

[13] Zhao et al. *Org. Process Res. Dev*. **2012**, 16, 57–60.

[14] Heinen et al. *Malononitrile extraction of gold from ores*. Vol. 7464. US Department of Interior, Bureau of Mines, **1970**.

A specific application for MDN is the synthesis of photo-cross-linkable liquid crystalline polymers, materials endowed with optical and mechanical properties that can be controlled by light. These polymers can form covalent bonds when exposed to ultraviolet radiation.[15]

MDN has also been employed in the synthesis of donor–acceptor heterocyclic compounds, which have potential uses in ultra-fast and ultrasensitive molecular electronic devices and ultra-high density data storage. These structures contain an electron-donating group and an electron-withdrawing group connected by a conjugated bridge.[16]

Malononitrile (MDN) proves to be an exceptionally versatile and valuable building block in organic synthesis. Its unique reactivity, due to its structure, facilitates the creation of a wide range of essential compounds across various industries. By continuing to explore its reaction with other derivatives and applications, MDN's role in advancing scientific research and industrial processes will only become more prominent.

Acknowledgments

This work was funded by Arxada AG, Peter Merian-Strasse 80, 4052 Basel, Switzerland.

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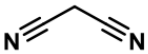
Our offer



MDN

- **Waste free synthesis of MDM**
- **Experienced process control experts for high temperature reactions**
- **Usage of MDN for derivatization**
- ***Focus on what matters to you***

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MDN	
CAS number	109-77-3
Chemical formula	$C_3H_2N_2$
Molar mass	66.063 g/mol
Appearance	Colorless or white solid
Density	1.049 g/cm³
Boiling point	220.1 °C; 428.1 °F; 493.2 K
Melting point	32 °C; 89 °F; 305 K
Solubility in water	13% at 20°C

Safety remarks: Due to its high solubility in water, MDN is a cyanogenic toxicant[17] (LD50 = 66 mg/kg)[18] and a water pollutant. When released in the environment, it could be completely converted to HCN and interfere with animal tissue metabolism.[19-20-21] Also, the presence of cyanide can inhibit the aerobic glycolysis in tissue and the respiration of the brain, kidney and liver, which even further causes several serious symptoms, such as irritation of the eyes and skin, dizziness, headaches, dyspnoea, convulsions, nausea, and vomiting.[22] Thus, when working with MDN, an effective method for its real-time monitoring of biological and environmental samples is essential.

[15] Dhameliya et al. *RSC Adv*. **2020**, 10, 32740-32820.
[16] Lu et al. *J. Chem. Crystallogr*. **2006**, 36, 10.
[17] Zhifen et al. *Toxicol. Mech. Methods*, **2003**, 13, 4, 241-245.
[18] Rao et al. *FCT*. **2013**, 59, 595-609.
[19] Henderson, Richard. *Science*, **1968**, 159, 3814, 482-482.
[20] Stern et al. *J. Biochem*. **1952**, 52, 1, 114.
[21] Punte et al.*Toxicol. Appl. Pharmacol*. **1962**, 4, 5, 656-662.
[22] Karalliedde et al. *Public Health*, **2000**, 114, 4, 238-248.

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