

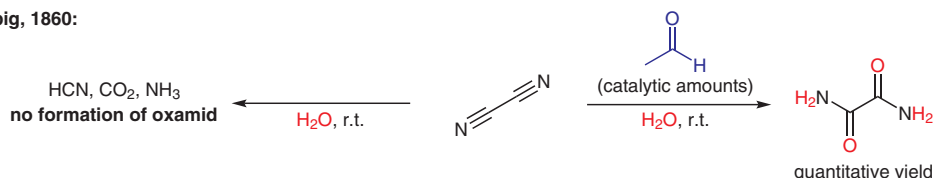
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Über die Bildung des Oxamids aus Cyan

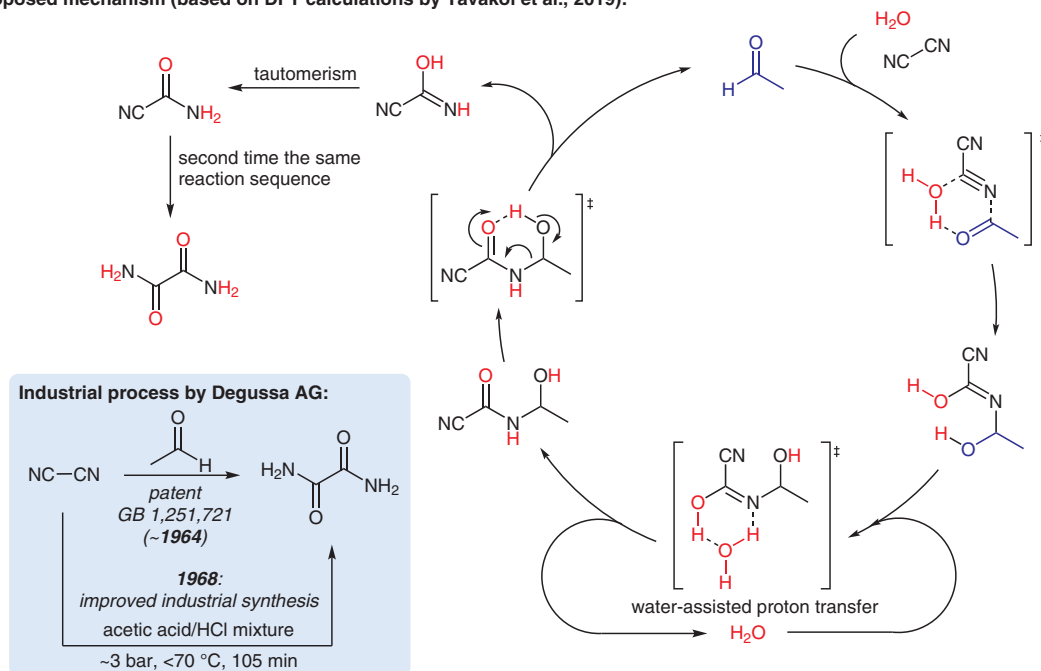
*Justus Liebigs Ann. Chem.* **1860**, 113, 246–247.

# Carbonyl Catalysis: Acetaldehyde-Catalyzed Synthesis of Oxamide by Hydrolysis of Cyanogen

Liebig, 1860:



Proposed mechanism (based on DFT calculations by Tavakol et al., 2019):



**Significance:** In 1860, Liebig discovered that acetaldehyde acts as an organocatalyst in the hydrolysis of cyanogen. The absence of acetaldehyde during the reaction led to a complex mixture, whereas addition of catalytic amounts yielded the hydrolysis product, oxamide, in a quantitative reaction. Nearly 100 years later, Degussa improved Liebig's oxamide synthesis and made it practical on an industrial scale. Furthermore, these seminal contributions by Liebig recently inspired other research groups to recognize the potential of aldehydes to catalyze transformations, thereby contributing to the emerging field of carbonyl catalysis (see for example: S. Chitale et al. *Chem. Commun.* **2016**, 52, 13147; A. J. Wagner et al. *ACS Cent. Sci.* **2017**, 3, 322; Y. E. Liu et al. *J. Am. Chem. Soc.* **2016**, 138, 10730, and J. Chen et al. *Science* **2018**, 360, 1438).

**Comment:** Liebig concluded that acetaldehyde acted in a similar way to ferments (enzymes), so this is arguably among the first organocatalytic transformations. The mechanism is relatively complex because several activation modes of the catalyst are possible. In 1929, Langenbeck (*Justus Liebigs Ann. Chem.* **1929**, 469, 16) started mechanistic investigations and proposed a mechanism in which acetaldehyde is enolized and nucleophilically attacks cyanogen in the first step. However, Tavakol and co-workers (*Comput. Theor. Chem.* **2019**, 1154, 37) performed DFT calculations that excluded Langenbeck's mechanism and suggested the simultaneous addition of water and acetaldehyde followed by a water-assisted proton transfer and tautomerism as the most likely mechanism. Accordingly, acetaldehyde acts as an organic Lewis acid.

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 Synfacts 2019, 15(12), 1432 Published online: 18.11.2019  
 DOI: 10.1055/s-0039-1691095; Reg-No.: B10119SF