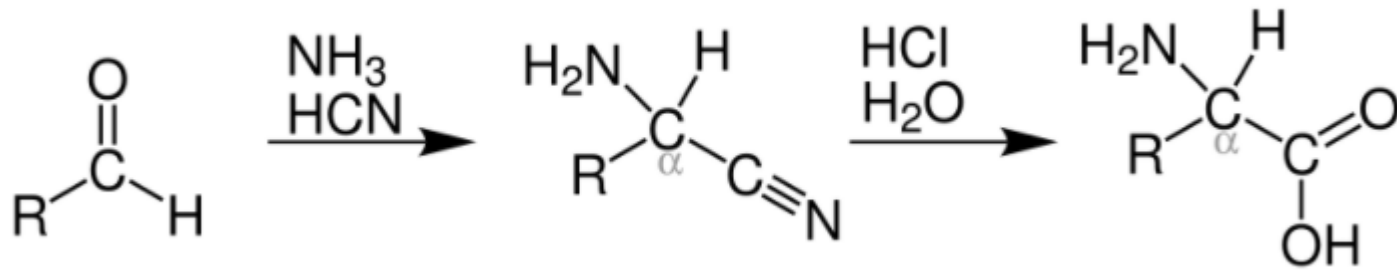
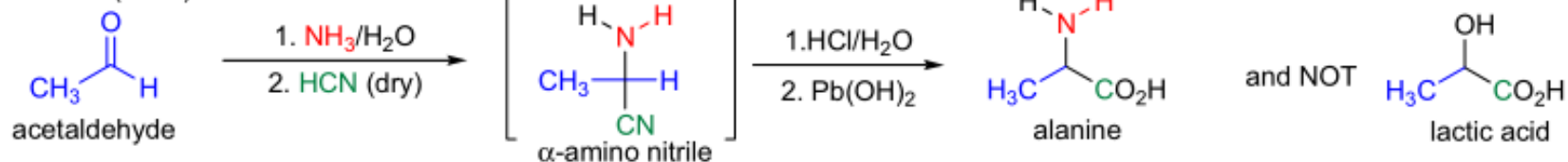


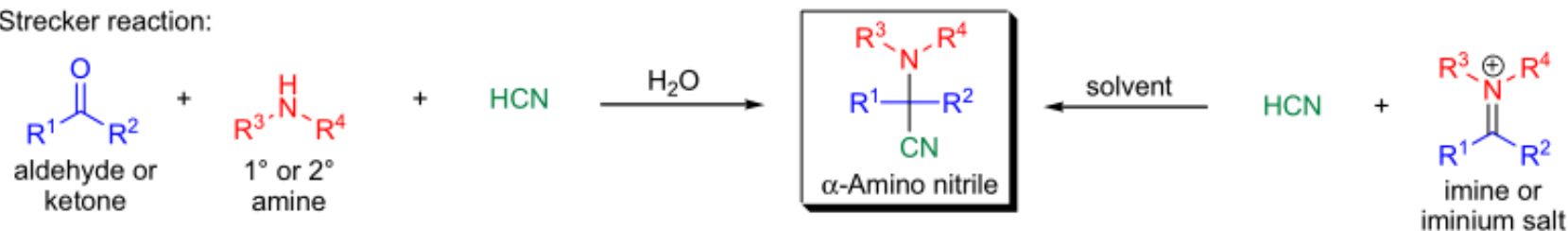
STRECKER REACTION (Strecker amino acid synthesis)



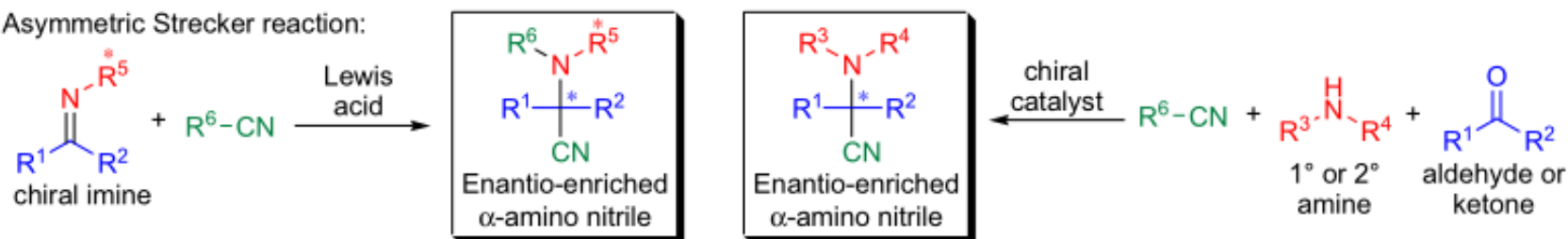
Strecker (1850):



Strecker reaction:

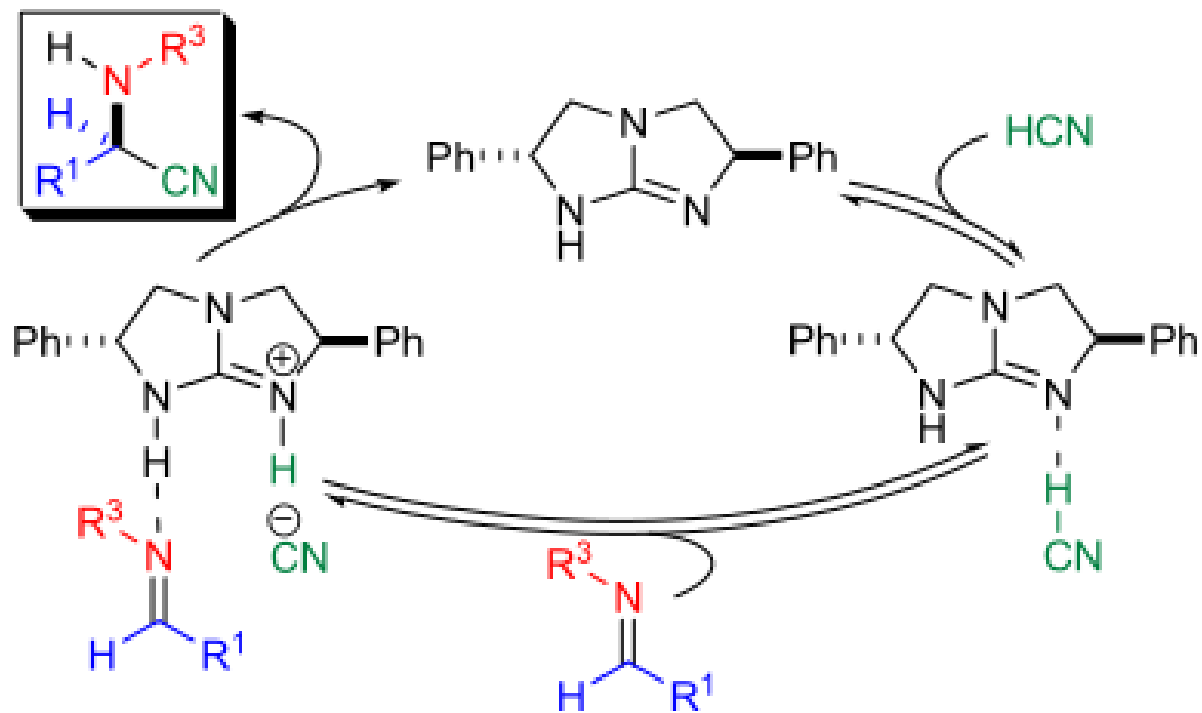


Asymmetric Strecker reaction:



R^1 = alkyl, aryl, heteroaryl; R^2 = H, alkyl, aryl, heteroaryl; R^{3-4} = H, alkyl, aryl, heteroaryl; R^5 = group having a chiral center;
 R^6 = H, TMS; chiral catalyst: chiral metal catalyst or organocatalyst

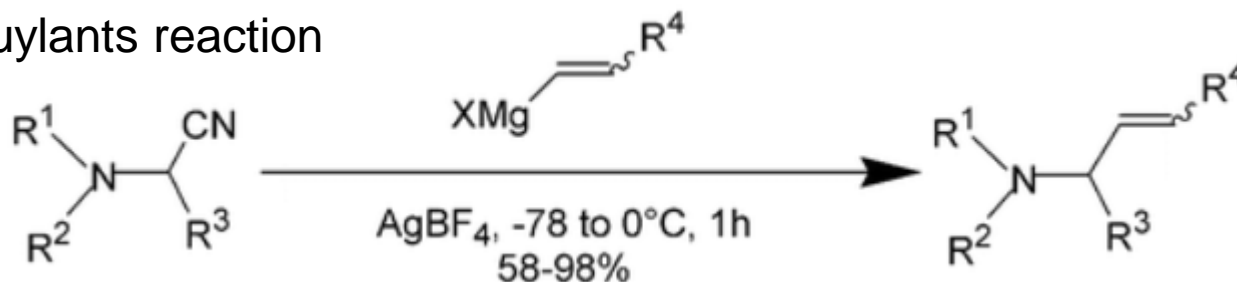
Mechanism in the presence of an organocatalyst (Corey, 1999):



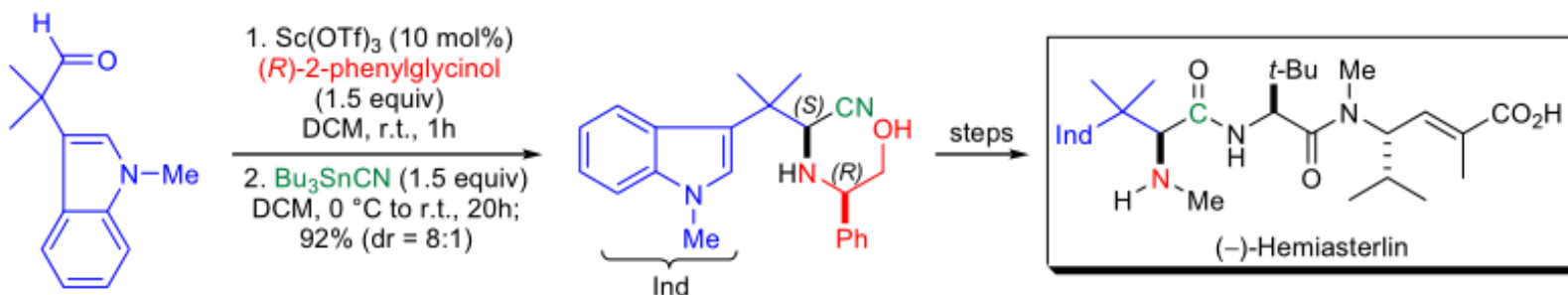
General features

- 1) The transformation is a one-pot three-component coupling;
- 2) Due to the extreme toxicity of HCN, various alkali cyanides (e.g., **KCN**, **NaCN**) in buffered aqueous media are used;
- 3) Both **aldehydes and ketones** are good substrates;
- 4) Hydrolysis of α -amino nitriles gives α -amino acids, reduction with metal hydrides affords 1,2-diamines, while strong bases can deprotonate at the α -carbon (if $R^2 = H$) and the resulting carbanion can be trapped with a variety of electrophiles (**umpolung**);
- 5) Upon treatment with heavy metal salts (e.g., $AgNO_3$), Brønsted or Lewis acids, α -amino nitriles undergo a loss of cyanide ion to form iminium ions, which can be trapped with various nucleophiles.

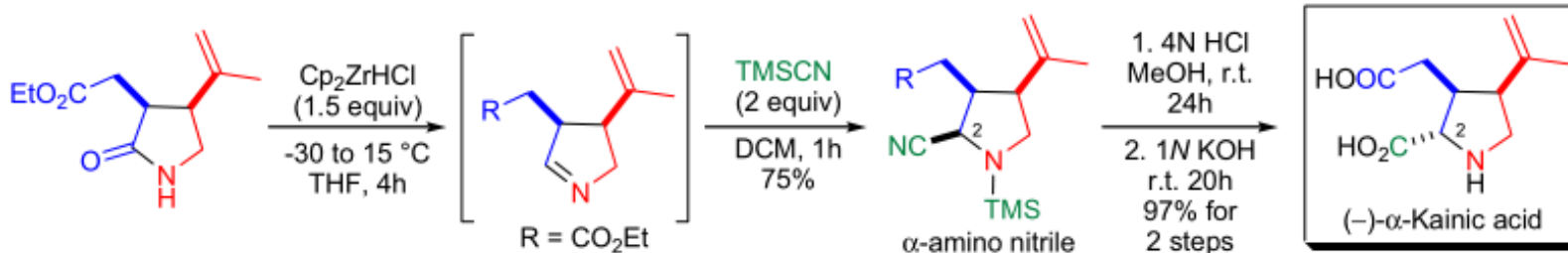
Bruylants reaction



The enantioselective total synthesis of (-)-hemiasterlin, a marine tripeptide with cytotoxic and antimetabolic activity, was achieved by E. Vedejs and co-workers.⁵⁵ The *asymmetric Strecker reaction* was used to construct the key tetramethyltryptophan subunit. The aldehyde substrate was first converted to the corresponding chiral imine with (*R*)-2-phenylglycinol under scandium triflate catalysis. The addition of tributyltin cyanide resulted in the formation of α -amino nitriles as an 8:1 mixture of diastereomers. Subsequently the cyano group was converted to a primary amide, and the chiral auxiliary was removed under catalytic hydrogenation conditions.



In the laboratory of B. Ganem, the asymmetric total synthesis of (-)- α -kainic acid was accomplished starting from very simple precursors. A highly stereoselective *zirconium-mediated Strecker reaction* was used to install the α -amino acid moiety of the natural product. The five-membered lactam substrate was treated with excess Schwartz reagent at low temperature which generated the corresponding cyclic imine *in situ*. This cyclic imine was not isolated but was immediately reacted with cyanotrimethylsilane to afford the all *cis* α -amino nitrile. In order to convert this intermediate to kainic acid, the cyano group was first converted by the *Pinner reaction* to a methyl ester. The resulting diester was hydrolyzed with aqueous KOH solution to give the corresponding dicarboxylic acid with complete epimerization at C2.



Benzoin condensation



R = aryl, heteroaryl, 3° alkyl, C(=O)-alkyl; catalyst: NaCN, KCN, thiazolium salt, NHC (*N*-heterocyclic carbenes)

STETTER REACTION

Stetter & Schreckenber (1973):

