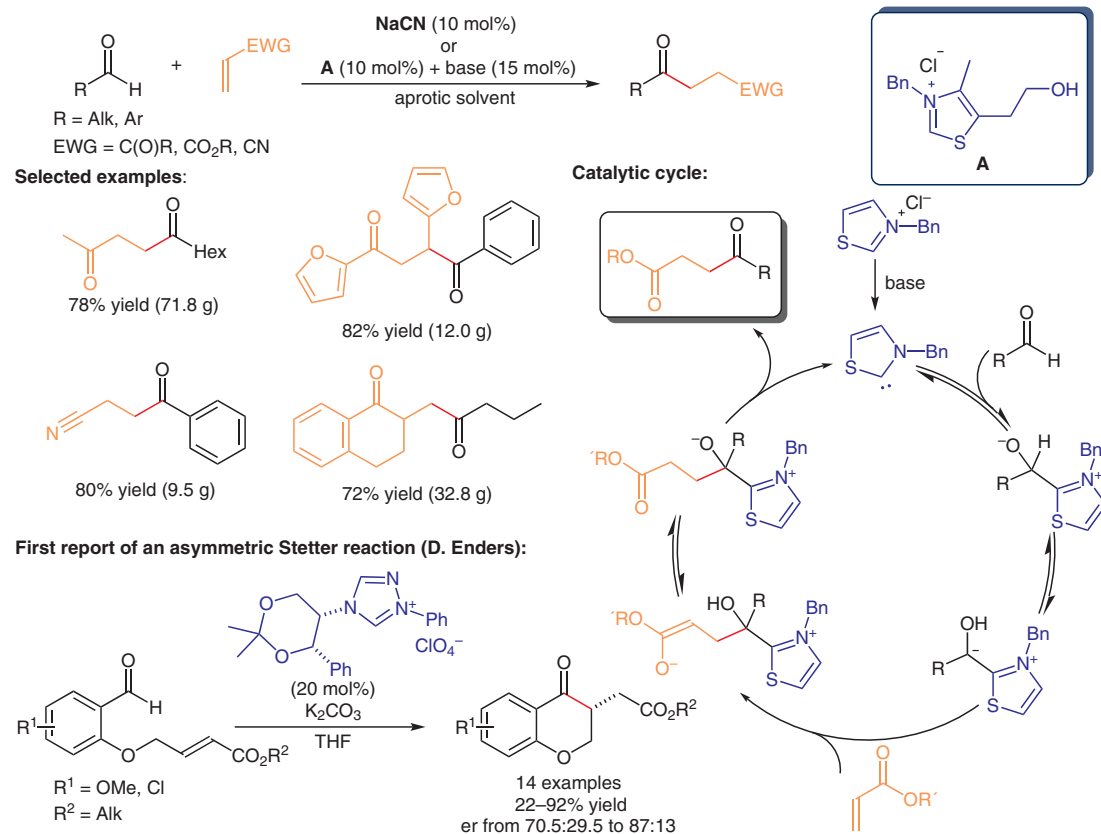


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Catalyzed Addition of Aldehydes to Activated Double Bonds – A New Synthetic Approach

Angew. Chem. Int. Ed. **1976**, 15, 639–647.

The Stetter Reaction



Significance: In 1976, Hermann Stetter reported the catalytic conjugate addition of aromatic or aliphatic aldehydes to Michael acceptors. Cyanide or thiazolium salts (essential for aliphatic substrates) catalyze the umpolung of aldehydes, permitting nucleophilic addition of in situ generated acyl-carbanion equivalents to α,β -unsaturated ketones. This method is scalable, proceeds under mild conditions, and represents an efficient 1,4-disconnection to form C–C-bonds, furnishing a broad range of important products, such as 1,4-diketones, 4-keto carboxylic acids, or 4-keto nitriles.

Comment: The utility and applicability of this methodology was rapidly recognized by the scientific community. For example, Trost and co-workers applied the Stetter reaction in the total synthesis of *rac*-hirsutic acid C (*J. Am. Chem. Soc.* **1979**, 101, 1284) shortly after the initial report. Enders and co-workers utilized a chiral triazolium salt (*Helv. Chim. Acta* **1996**, 79, 1899) for the first asymmetric intramolecular Stetter reaction, providing enantio-enriched chromanones. To the present day, 1,4-dicarbonyl compounds and their analogues are frequently synthesized in both academia and industry by employing the Stetter reaction.