The Knoevenagel Condensation

Significance: Between 1896 and 1898, Emil Knoevenagel reported that primary and secondary amines, their respective salts, and ammonia (but not tertiary amines) are efficient catalysts for the aldol condensation of β-keto esters or malonates with either aldehydes or ketones. The reaction proceeds under mild conditions, is scalable, tolerates a wide range of substrates, and delivers the corresponding α,β-unsaturated esters in good to excellent yields in an atom-economic fashion. Decarboxylation of malonic acid-derived products selectively provides (E)-cinnamic acid derivatives.

Comment: More than 120 years ago, Knoevenagel had already recognized the catalytic nature of the added amine. His discovery therefore arguably signifies the starting point of aminocatalysis. The proposal of iminium-type intermediates (Schiff’sche Körper or Schiff-type intermediates) had a great influence on later studies that ultimately led to the systematic development of aminocatalysis. As the Knoevenagel condensation is a reliable, efficient, and scalable method for the formation of C–C bonds, it is still widely used in both academia and industry.