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Durch Katalysatoren bewirkte asymmetrische Synthese

*Biochem. Z.* **1912**, 687, 7–23.

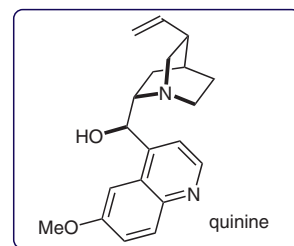
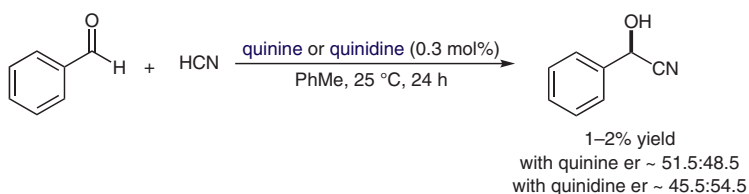
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Asymmetrische Synthesen mit Ketenen

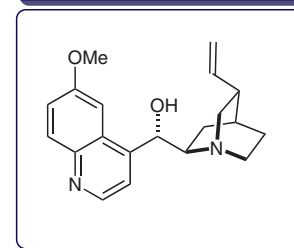
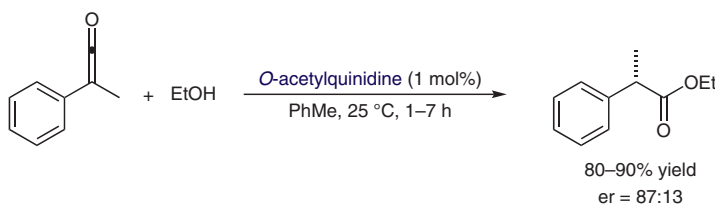
*Justus Liebigs Ann. Chem.* **1960**, 634, 9–22.

## Cinchona Alkaloids in Organic Catalysis

Bredig/Fiske (1912):



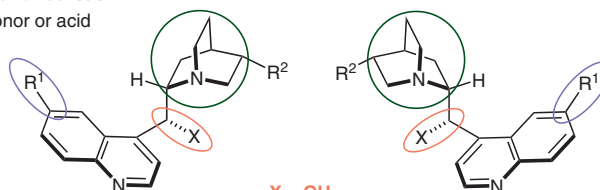
Pracejus (1960):



Active sites in cinchona alkaloids and their derivatives:

R<sup>1</sup> = i. a., OH or thioureas

1. H-bond donor or acid



X = OH

1. H-bond donor or acid  
2. metal coordinationX = NH<sub>2</sub> or further derivatizations  
(including inversion of C9-configuration)1. aminocatalysis  
2. H-bond donors (e.g. ureas, squaramides, amides)

Nitrogen of quinuclidine

1. metal-binding ability  
2. Brønsted base  
3. Lewis base catalyst  
4. N-alkylation:  
phase-transfer catalysis

**Significance:** In 1912, Bredig and Fiske published the first example of asymmetric (nonenzymatic) (organo)catalysis. They reported the addition of HCN to benzaldehyde catalyzed by the pseudo-enantiomeric alkaloids quinine and quinidine, with low but reproducible enantioselectivities. About four decades later, Pracejus, for the first time, achieved reasonable enantioselectivities (74% ee) by using O-acetylquinine as an organocatalyst. This groundwork paved the way to a variety of cinchona-alkaloid-catalyzed asymmetric transformations in industry and academia.

**Comment:** Cinchona alkaloids are among the most privileged asymmetry inducers in the area of enantioselective catalysis. They possess a chiral skeleton that is easily modifiable. In the last century, methodologies were developed in which they were used as chiral bases, as chiral Lewis base catalysts, in ligand-accelerated catalysis, or as quaternized ammonium salts in phase-transfer catalysis, among others. Current research continues to showcase their importance and utility in asymmetric catalysis, for example by incorporating other privileged organic catalophores such as thioureas.