Asymmetric Conjugate Addition of Cyanide to Give Quaternary Stereocenters

Significance: Enantioselective conjugate additions to \( \beta,\beta \)-disubstituted enones are highly desirable, but challenging reactions. Recent progress has been made in the use of carbon-based nucleophiles, such as alkyl and aryl. However, high-yielding enantioselective additions of cyanide are unknown. Extending on their previous work with cyanide additions (J. Am. Chem. Soc. 2008, 130, 6072), the authors present the first general catalytic, asymmetric conjugate addition of cyanide to form quaternary stereocenters. A strontium(II) source and a novel chiral ligand produce a catalyst giving excellent yields and enantioselectivities with as low as 0.5 mol% loading.

Comment: The combination of 2,6-dimethylphenol and TBSCN is proposed to slowly generate HCN in situ as the stoichiometric cyanide source. Under the reaction conditions, cyano hydrins (1,2-addition products) undergo retro-cyanation, explaining why complete selectivity is observed for the irreversibly formed 1,4-addition product. Insight into the nature of the catalyst is gained through ESI-MS studies, where a complex containing a Sr/ligand ratio of 3:5 is observed as the major component.

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