Asymmetric Conjugate Addition of Cyanide to Give Quaternary Stereocenters

Category

**Metal-Catalyzed
Asymmetric
Synthesis and
Stereoselective
Reactions**

Key words

conjugate cyanation

quaternary
stereocenters

strontium

SYNFACT
of the month

Selected examples:

Reversibility of 1,2-cyanation:

Significance: Enantioselective conjugate additions to β,β -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.

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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, cyanohydrins (1,2-addition products) undergo retrocyanation, 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.