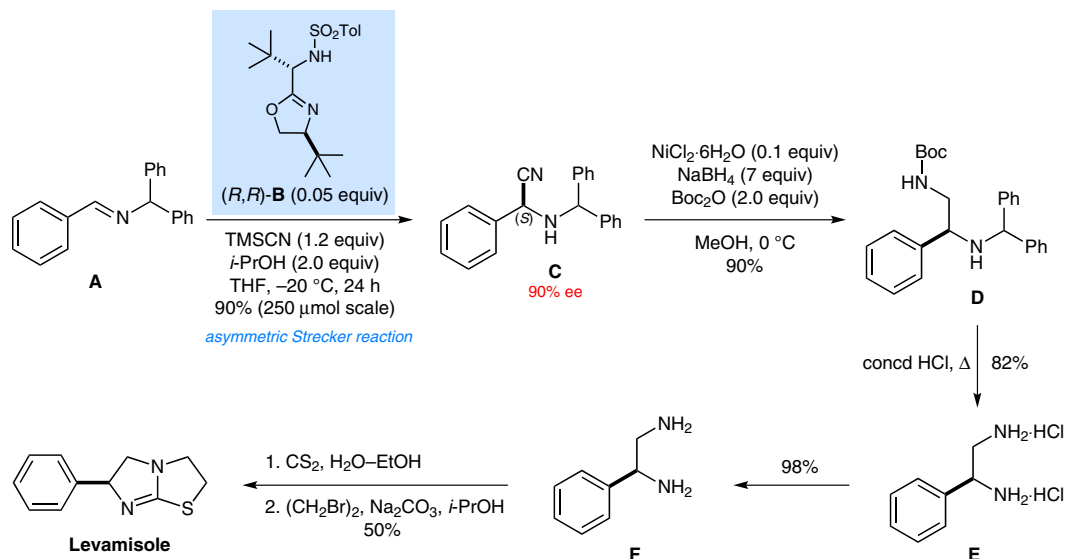


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Oxazoline-Based Organocatalyst for Enantioselective Strecker Reactions: A Protocol for the Synthesis of Levamisole
Chem. Eur. J. **2013**, *19*, 14224–14232.

Synthesis of Levamisole



Scope of the substrates in the asymmetric Strecker reaction catalyzed by (S,S)-B:

X	Yield (%)	ee (%)
Me	90	94
OMe	93	96
F	78	91
Cl	90	82
Br	93	80
NO_2	90	82

R	Yield (%)	ee (%)
Bn	90	91
CH_2Bn	90	87
<i>t</i> -Bu	91	93
<i>i</i> -Bu	94	90
Hex	90	71
CH=CHPh	93	90

Other substrates and yields:

- Pyridine derivative: 85% (60% ee)
- Thiophene derivative: 94% (82% ee)

Significance: Levamisole (Ergamisol®) is an antihelmintic that is currently used to treat worm infestations in livestock. The synthesis of levamisole depicted features an asymmetric Strecker reaction of *N*-benzhydrylaldimine **A** with trimethylsilyl cyanide catalyzed by oxazoline **(R,R)-B** (5 mol%) as the key step. The chiral α -aminonitrile intermediate **C** was generated in 90% yield and 90% ee.

Comment: A study of the scope of the asymmetric Strecker reaction (18 examples) revealed that both alkyl and aryl *N*-benzhydrylaldimines participate in the reaction to give the corresponding α -aminonitriles in good yield and generally >80% ee with some exceptions being shown in the box above. For a previous synthesis of levamisole based on asymmetric diamination of styrenes, see: C. Röben et al. *Angew. Chem. Int. Ed.* **2011**, *50*, 9478.

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Synfacts 2014, 10(1), 0007 Published online: 13.12.2013
DOI: 10.1055/s-0033-1340326; Reg-No.: K07213SF