Synthesis of Levamisole


Oxazoline-Based Organocatalyst for Enantioselective Strecker Reactions: A Protocol for the Synthesis of Levamisole

Significance: Levamisole (Ergamisol®) is an antihelminthic that is currently used to treat worm infestations in livestock. The synthesis of levamisole depicted features an asymmetric Strecker reaction of N-benzhydryl aldimine 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-benzhydryl aldimines 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.