SYNLETT Spotlight 359

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research.

(S)-(+-)1-(2-Pyrrolidinylmethyl)-pyrrolidine

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Introduction

Last decade witnessed an explosive growth in asymmetric organocatalysis. A large number of organocatalysts have been developed by different research groups. (S)-(+-)1-(2-Pyrrolidinylmethyl)pyrrolidine (CAS: 51207-66-0) is a versatile organocatalyst, which is commercially available or can be easily prepared from commercially available Cbz-(L)-proline (Scheme 1).1 It is known to catalyze many organic reactions, for example, the asymmetric aldol reaction,2,3 Michael reaction,4–7 Mannich reaction,8 and the domino reaction.9 It is also used as a chiral ligand/additive in metal-mediated stereoselective organic syntheses.10,11

Abstracts

(A) The direct homoaldol reaction of ethyl pyruvate was reported to be catalyzed by (S)-(+-)1-(2-pyrrolidinylmethyl)pyrrolidine (1) and trifluoroacetic acid. The use of the polymer-supported acid facilitated the removal of 1. The base allowed the lactonization of the aldol adduct and the isolation of the isotetronic acid derivative in its hydroxyl-free form.2c

(B) The trifluoroacetic acid salt of 1 catalyzed the intramolecular aldol reaction of a series of tricarbonyl compounds wherein the keto group acted as an electrophile. This resulting bicyclo[4.3.0]nonene derivatives were formed in high yield and enantioselectivity (81–89% ee).

(C) The direct conjugate addition of an a-amino ketone to nitroolefins was reported to be catalyzed by 1.5 The adducts are formed in high yield and ee’s (89–97%). One of such addition product was converted into a pyrrolidine skeleton.
The catalyst I/TFA (3:1) combination catalyzed the direct addition of alkyl methyl ketones to β-dimethylphenylsilylmethylene malonate exclusively via the COMe terminus. The adducts are formed in high yield and excellent enantioselectivity (99.6% ee).\(^6\) These addition products thus obtained can easily undergo deethoxy-carbonylation to give β-silylated keto esters with excellent synthetic potential.

(E) The catalyst I/TFA combination is used for the synthesis of chiral 1,4-dihydropyridazines from 1,2-diaza-1,3-dienes and aryl-acetaldehydes. The ee values ranged from 25% to 75%.\(^7\)

(F) The first organocatalytic enantioselective Mannich reaction of ketimines and unmodified aldehydes was investigated using I.\(^8\) The reaction leads to the generation of a chiral quaternary center. The α,α-disubstituted amino acid derivatives were produced in good yield and very high optical purities (83–98% ee). The reaction was also catalyzed by l-proline, but produced the opposite diastereoisomer of the Mannich product. Quantum mechanical calculations provided a good explanation for the opposite diastereoselectivities of catalyst I and L-proline.\(^9\)

(G) The domino reaction between 2-mercaptobenzaldehyde or salicylaldehyde derivatives and α,β-unsaturated cyclic ketones were catalyzed by I with excellent chemoselectivity to give the corresponding tetrahydrothioxanthenones or tetrahydroxanthenones with high enantioselectivity.\(^10\)

**References**


