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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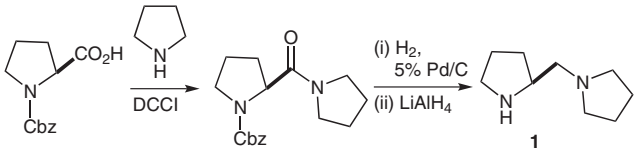
Introduction

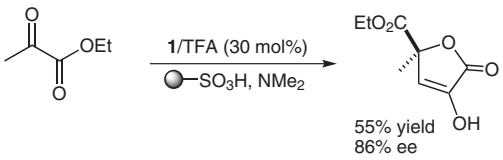
Last decade witnessed an explosive growth in asymmetric organocatalysis. A large number of organocatalysts have been developed by different research groups. (*S*)-(+)-1-(2-Pyrrolidinylmethyl)pyrrolidine (CAS: 51207-66-0) is a versatile organocatalyst, which is commercially available or can be easily 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]



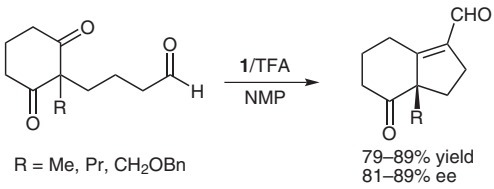
Scheme 1

Abstracts

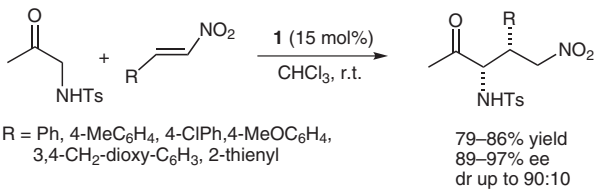
(A) The direct homoaldol reaction of ethyl pyruvate was reported to be catalyzed by (*S*)-(+)-1-(2-pyrrolidinylmethyl)pyrrolidine (**1**) and trifluroacetic acid. The use of the polymer-supported acid facilitated the removal of **1**. The base allowed the lactonization of the aldol adduct and the isolation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



(B) The trifluoroacetic acid salt of **1**[3] 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 α-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.



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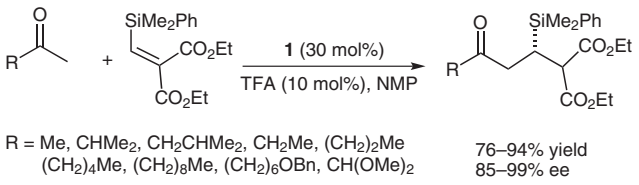
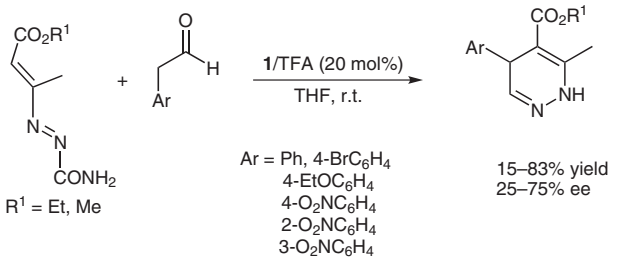
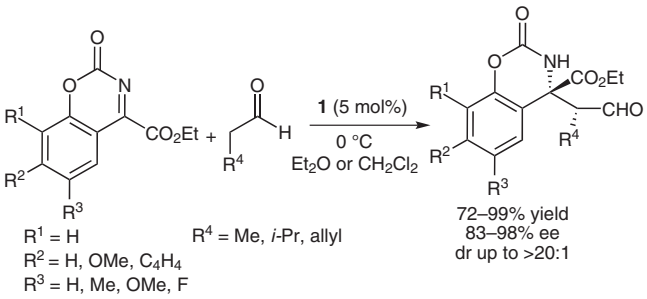
(D) The catalyst **1**/TFA (3:1) combination catalyzed the direct addition of alkyl methyl ketones to β-dimethyl(phenyl)silylmethylene malonate exclusively via the COMe terminus. The adducts are formed in high yield and excellent enantioselectivity (99.6% ee).[6] These addition products thus obtained can easily undergo deethoxycarbonylation to give β-silylated keto esters with excellent synthetic potential.



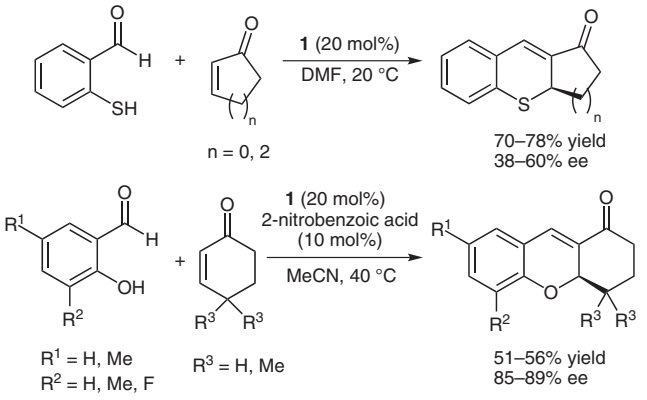
(E) The catalyst **1**/TFA combination is used for the synthesis of chiral 1,4-dihydropyridazines from 1,2-diaza-1,3-dienes and arylacetaldehydes. The ee values ranged from 25% to 75%.[7]



(F) The first organocatalytic enantioselective Mannich reaction of ketimines and unmodified aldehydes was investigated using **1**.[8a] 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 **1** and L-proline.[8b]



(G) The domino reaction between 2-mercaptobenzaldehyde or salicyaldehyde derivatives and α,β-unsaturated cyclic ketones were catalyzed by **1** with excellent chemoselectivity to give the corresponding tetrahydrothioxanthenones or tetrahydroxanthenones with high enantioselectivity.[9a,b]



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