SYNLETT
Spotlight 69

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

(*S*)-(–)-1-Amino-2-methoxypyrrolidine (SAMP) and (*R*)-(+)-1-Amino-2-methoxypyrrolidine (RAMP) as Versatile Chiral Auxiliaries

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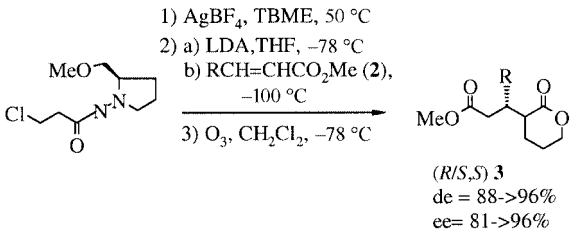
(*S*)-(–)-1-Amino-2-methoxypyrrolidine (SAMP) and (*R*)-(+)-1-amino-2-methoxypyrrolidine (RAMP) are commercially available chiral auxiliaries and have been successfully applied to asymmetric synthesis, especially bioactive natural product synthesis.[1] (*S*)-(–)-1-Amino-2-methoxypyrrolidine (SAMP) and (*R*)-(+)-1-amino-2-methoxypyrrolidine (RAMP) emerged as chiral auxiliaries for α-alkylation in various application during the total synthesis of various complex organic molecules. The α-alkylation generally proceeds via the α-alkylation of SAMP/RAMP hydrazones followed by 1,2-addition and reductive N-N bond cleavage.[2]

Recently SAMP/RAMP chiral auxiliaries was efficiently used as chiral auxiliaries in various important reactions, which includes the palladium catalyzed allylic substitution,[3] asymmetric synthesis of substituted β-formyl δ-lactones and furofuran lactones,[4] diastereo- and enantioselective synthesis of *syn*-2,3-disubstituted, 1,4-diketones,[5] diastereoselective electrophillic fluorination of enatiopure α-silylketones,[6] recemization free cleavage of ketones SAMP hydrazones,[7] diastereo-and enantioselective synthesis of various 1,2-anti *tert*-butyl sulfanyl amines,[8] asymmetric synthesis of γ-amino nitriles and γ-amino ketones[9] etc.

Abstracts

(A) An efficient method has recently been developed for the diastero- and enantioselective Michael addition of metalated lactones-SAMP hydrazones to enolates. The lactone esters (*S*/*R*,*S*)-**2** were synthesized in good overall yields (37–61%, two steps, high de, ee) by 1,2-addition of metalated lactone SAMP hydrazones to enolate Michael acceptors **2** and subsequent oxidative cleavage of the product of the hydrazones by ozonolysis. The present method represents a bifunctional building block for further synthetic applications.[10]



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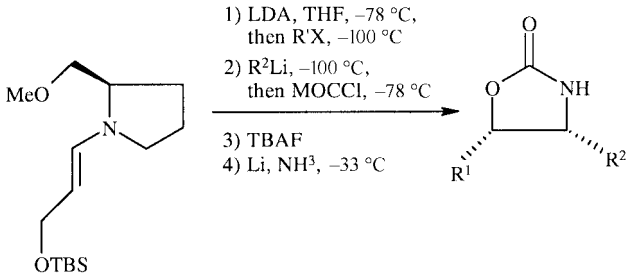
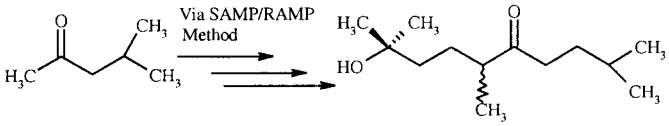
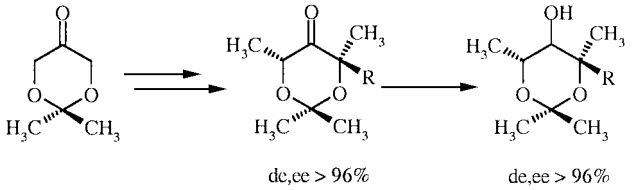
(B) Enders et al.[11] reported the short diastereo- and enantioselective synthesis of *cis*-4,5-disubstituted oxazolidin-2-ones using SAMP chiral auxiliary in a four step reaction sequence – α-alkylation, 1,2-addition with subsequent carbamate protection, cyclization and concluding with cleavage of the auxiliary. The title compounds are obtained in moderate yields and in excellent de and ee. The use of RAMP as auxiliary gave *cis*-(4*R*,5*S*) the enantiomer of SAMP gave *cis*-(4*S*,5*R*).



(C) SAMP/RAMP was used in the first asymmetric synthesis of (*S*)-and (*R*)-Stigmolane The stereogenic centre at the C-5 position of the pheromone was generated via SAMP/RAMP hydrazone methodology with high enantiomeric purity.[12]



(D) Very recently the asymmetric synthesis of protected 2-keto-1,3-diols and 1,2,3 triols bearing a quaternary stereogenic center starting from 2,2-dimethyl-1,3-dioxan-5-one was reported.[13] The stereogenic centers are generated by sequential α-alkylation using SAMP/RAMP hydrazone methodology and stereoselective reduction of the ketone generated with L-selectride. The key step in the synthesis was a subsequent third metalation and alkylation of intermediate to install the quaternary stereocentre. The products are obtained in good yields and high de and ee



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