

Mujahid Alam, *Synlett*, **2003**, 1755

Due to the number of errors found in the Spotlight article 69 after publication the article is reprinted on the following pages.

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-methoxymethylpyrrolidine (SAMP) and (R)-(+)-1-Amino-2-methoxymethylpyrrolidine (RAMP) as Versatile Chiral Auxiliaries

Compiled by M. Mujahid Alam



M. Mujahid Alam was born in Hyderabad. He completed his Bachelor's degree in 1996 and Master's degree in chemistry in 1999 from Osmania University, Hyderabad, A. P. India. He then joined the Indian Institute of Chemical Technology (IICT) Hyderabad, as a research assistant. At present he is working under the supervision of Dr. Adapa Srinivas Rao, on his PhD in the area of organic chemistry, in particular metal catalyzed organic reactions.

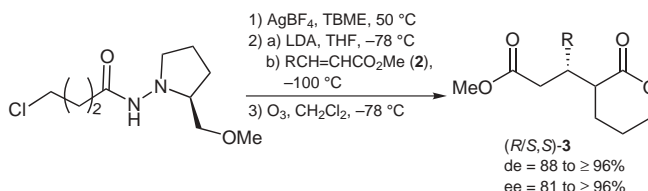
Inorganic Chemistry Division, Indian Institute of Chemical Technology, Hyderabad - 500007, India
Fax +91(40)27160921; E-mail: mujahid1206@yahoo.com

(S)-(-)-1-Amino-2-methoxymethylpyrrolidine (SAMP) and (R)-(+)-1-amino-2-methoxymethylpyrrolidine (RAMP) are commercially available chiral auxiliaries and have been successfully applied to asymmetric synthesis, especially bioactive natural product synthesis.¹ (S)-(-)-1-Amino-2-methoxymethylpyrrolidine (SAMP) and (R)-(+)-1-amino-2-methoxymethylpyrrolidine (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

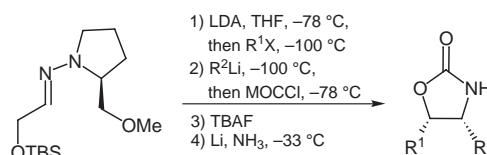
Recently SAMP/RAMP chiral auxiliaries were efficiently used as chiral auxiliaries in various important reactions, which includes the palladium catalyzed allylic substitution,³ asymmetric synthesis of substituted β -formyl δ -lactones and furofuran lactones,⁴ diastereo- and enantioselective synthesis of *syn*-2,3-disubstituted, 1,4-diketones,⁵ diastereoselective electrophilic fluorination of enantiopure α -silylketones,⁶ racemization free cleavage of ketone SAMP hydrazones,⁷ diastereo- and enantioselective synthesis of various 1,2-*anti* *tert*-butylsulfanyl amines,⁸ asymmetric synthesis of γ -amino nitriles and γ -amino ketones⁹ etc.

Abstracts

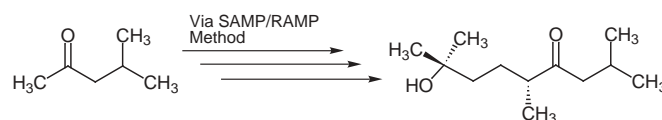
(A) An efficient method has recently been developed for the diastereo- and enantioselective Michael addition of metalated lactone SAMP hydrazones to enoates. The lactone esters (*R/S,S*)-**3** were synthesized in good overall yields (37–61%, two steps, high de, ee) by 1,2-addition of metalated lactone SAMP hydrazones to enoate 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



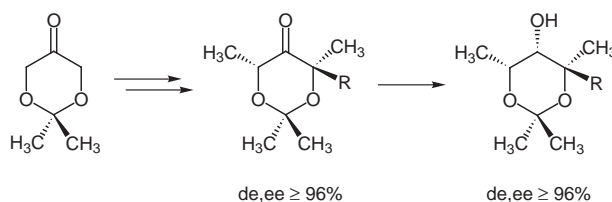
(B) Enders et al.¹¹ reported the short diastereo- and enantioselective synthesis of *cis*-4,5-disubstituted oxazolidin-2-ones using SAMP chiral auxiliary in a four step reaction sequence – α -alkylation, 1,2-addition with subsequent carbamate protection, cyclization and concluding with cleavage of the 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*)-Stigmolone. 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 stereocenter. The products are obtained in good yields and high de and ee.



References

- (1) (a) Enders, D.; Thiebes, C. *Pure. Appl. Chem.* **2001**, 73, 573. (b) Enders, D. In *Asymmetric Synthesis*; Morrison, J.-D., Ed.; Academic: New York, **1984**, Vol. 3, 275. (c) Enders, D.; Klatt, M. In *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; Wiley: Chichester, **1995**, Vol. 1, 178. (d) Enders, D.; Fey, P.; Kipphardt, H. *Org. Synth.* **1987**, 65, 173. (e) Job, A.; Janeck, C. F.; Bettray, W.; Peters, R.; Enders, D. *Tetrahedron* **2002**, 58, 2253.
- (2) (a) Enders, D.; Eichenauer, H. *Tetrahedron Lett.* **1977**, 18, 191. (b) Enders, D.; Reinhold, U. *Tetrahedron: Asymmetry* **1997**, 8, 1895. (c) Enders, D.; Lochtman, R.; Meiers, M.; Müller, S.; Lazny, R. *Synlett* **1998**, 1182. (d) Enders, D.; Thiebes, C. *Synlett* **2000**, 1745. (e) Enders, D.; Kirchhoff, J. H. *Synthesis* **2000**, 2099.
- (3) Mino, T.; Imiya, W.; Yamashita, M. *Synlett* **1997**, 583.
- (4) Enders, D.; Vazquez, J.; Raabe, G. *Eur. J. Org. Chem.* **2000**, 893.
- (5) Enders, D.; Müller, P.; Klein, D. *Synlett* **1998**, 43.
- (6) Enders, D.; Faure, S.; Potthoff, M.; Runsink, J. *Synthesis* **2001**, 2307.
- (7) Enders, D.; Hundertmark, T.; Lazny, R. *Synlett* **1998**, 721.
- (8) Enders, D.; Schaadt, A. *Synlett* **2002**, 498.
- (9) Enders, D.; Janeck, C. F.; Runsink, J. *Synlett* **2000**, 641.
- (10) Enders, D.; Teschner, P.; Gröbner, R.; Raabe, G. *Synthesis* **1999**, 237.
- (11) Enders, D.; Kallfass, U.; Nolte, B. *Synlett* **2002**, 33.
- (12) Enders, D.; Ridder, A. *Synthesis* **2000**, 1848.
- (13) Enders, D.; Nührling, A.; Runsink, J.; Raabe, G. *Synthesis* **2001**, 1406.