SYNLETT
# Spotlight 63

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

## (–)-Sparteine in Asymmetric Synthesis

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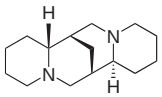
### Introduction

Asymmetric synthesis represents a challenging topic in modern organic chemistry. The asymmetric deprotonation of a prochiral carbon by a chiral base offers attractive access to a chiral carbanion, which may react to give enantioenriched products. (–)-Sparteine is a chiral bidentate ligand with broad applicability. Hoppe was the first to use a mixture of alkyllithium and (–)-sparteine (Figure 1) for very effective asymmetric deprotonations.[1] Beak examined enantioselective deprotonations of *N*-Boc-pyrrolidines and *N*-Boc-allylamines.[2] Furthermore, it was used for dynamic resolutions[3] and deprotonations[4] of phosphine-boranes, for asymmetric additions of alkyllithiums to imines,[5] for asymmetric carbometallations of cinnamyl derivatives,[6] for palladium-catalyzed oxidative kinetic resolutions of secondary alcohols,[7] and for enantioselective syntheses of ferrocenes with planar chirality.[8]

The title compound is an alkaloid, which can be isolated from certain *papilionaceous* plants such as *Scotch broom*.[9] Its antipode is also naturally occurring but can be obtained far less easily. An 18 steps asymmetric total synthesis of (+)-sparteine starting from norbornadiene has been reported.[10] A (+)-sparteine surrogate is readily available from (–)-cytisine.[11]

(–)-Sparteine is commercially available as a free base or as the sulfate-pentahydrate. The chiral ligand can usually be recovered from the reaction mixtures by alkaline extraction.

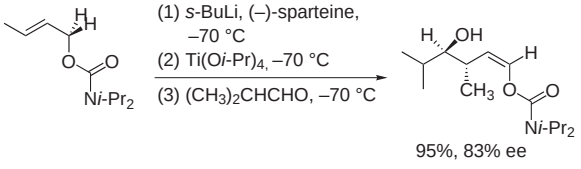



(–)-sparteine

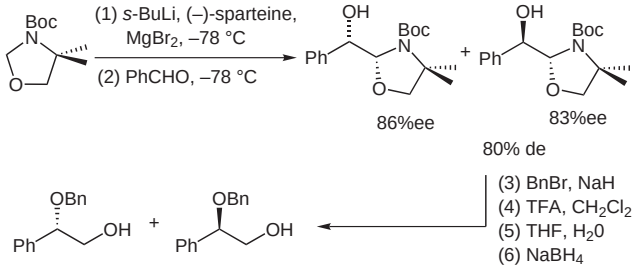
**Figure 1**

### Abstracts

(A) Prochiral alkenylcarbamates are enantioselectively deprotonated using *s*-BuLi and (–)-sparteine. After transmetalation with Ti(*i*-PrO)$_4$ the titanium complex adds to aldehydes under 1,3-chirality transfer to yield homoaldol adducts with good enantiomeric excesses.[1]




(B) In the presence of (–)-sparteine 2-lithiated *N*-Boc-4,4-dimethyl-1,3-oxazolidine can be used as a chiral formyl anion equivalent. Deprotonation with *s*-BuLi in the presence of the chiral ligand followed by the addition of benzaldehyde yielded the *syn* and *anti* diastereomers (*syn*:*anti* = 46:54) with about 85% ee. The addition of $MgBr_2$ increased the diastereomeric ratio to 90:10. Separation of the diastereomers, benzylation with BnBr/NaH and hydrolysis afforded the aldehydes, which were reduced with $NaBH_4$ to yield (*S*)- and (*R*)-2-benzyloxy-2-phenylethanol, respectively.[12]

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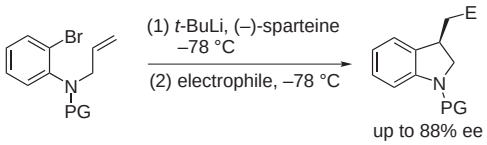
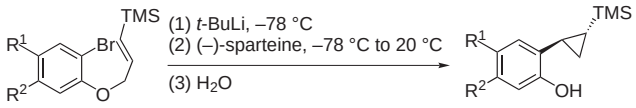
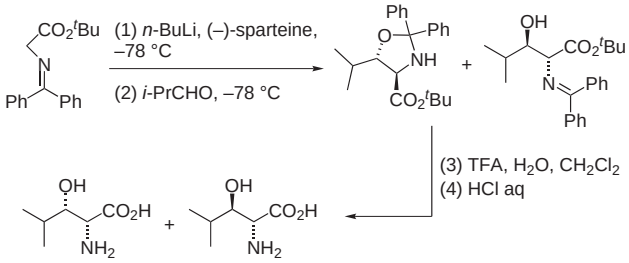
(C) On treatment with *t*-BuLi and (–)-sparteine *N*-protected *N*-allyl-2-bromo-anilines undergo intramolecular carbolithiation to afford chiral 3-substituted indolines. The lithiumintermediate can be scavenged by several electrophiles such as methanol, DMF, or 1,2-dibromotetrafluoroethane. Enantiomeric excesses up to 88% have been obtained.[13]



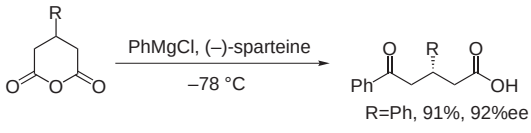

(D) Treatment of several allyl 2-lithioaryl ethers with *t*-BuLi and (–)-sparteine furnished after tandem carbolithiation/elimination new chiral cyclopropanes with moderate to good enantioselectivities.[14]



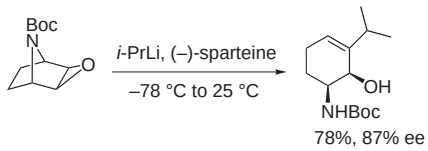

(E) The asymmetric synthesis of β-hydroxy-α-amino acids is another topic, which takes advantage of (–)-sparteine. Reaction of the lithium salt of *N*-(diphenylmethylene)glycine *t*-butylester with isobutyraldehyde produced the corresponding *erythro* imine and *threo* oxazolidine with moderate enantioselectivities, which were separated and hydrolyzed to the epimeric β-hydroxy-(2*R*)-leucines.[15]




(F) (–)-Sparteine provides remarkable stereocontrol in the desymmetrization of anhydrides with carbon nucleophiles such as Grignard reagents. Several 3-substituted glutaric anhydrides were opened with phenylmagnesium chloride to yield the corresponding ketoacids in good enantiomeric excesses.[16]




(G) *N*-Boc protected epoxides derived from azabicycloalkenes have been converted to aminoalcohols by organolithium-induced alkylative ring-opening. The protocol is also suitable for the generation of cycloalkenediols from oxabicycloalkenes.[17]

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