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-4,4-dimethyl-1,3-oxazolidine and N-Boc-allylamines.2 Furthermore, it was used for dynamic resolutions1 and deprotonations2 of phosphine-boranes, for asymmetric additions of alkyl lithiums 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.

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 enantio-meric 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 MgBr2 increased the diastereomeric ratio to 90:10. Separation of the diastereomers, benzyla- tion with BnBr/NaH and hydrolysis afforded the aldehydes, which were reduced with NaBH4 to yield (S)- and (R)-2-benzyloxy-2-phenylethan-1-ol, respectively.12
(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. Enantioselective conversion up to 88% have been obtained.

(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.

(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-(diphenylmethene)glycine t-butylester with isobutyraldehyde produced the corresponding erythro imine and threo ozoxazolidine with moderate enantioselectivities, which were separated and hydrolyzed to the epimeric β-hydroxy-(2R)-leucines.

(F) (–)-Sparteine provides remarkable stereocontrol in the de-symmetrization 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.

(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.

References


