(-)-Spartheine 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. (-)-Spartheine is a chiral bidentate ligand with broad applicability. Hoppe was the first to use a mixture of alkylithium and (-)-spartheine (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 resolutions3 and deprotonations4 of phosphine-boranes, for asymmetric additions of alkylolithiums to imines,5 for asymmetric carbometallations of cinamyl derivatives,6 for palladium-catalyzed oxidative kinetic resolutions of secondary alcohols,7 and for enantioselective syntheses of ferrocenes with planar chirality.8

Abstracts

(A) Prochiral alkenylcarbamates are enantioselectively deprotonated using s-BuLi and (–)-spartheine. 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 (–)-spartheine 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, benzylaion with BnBr/NaH and hydrolysis afforded the aldehydes, which were reduced with NaBH4 to yield (S)- and (R)-2-benzyloxy-2-phenylethanol, respectively.12

Figure 1

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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.11

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-(diaryl)methylene-glycine t-butyester with isobutyraldehyde produced the corresponding erythro imine and threo oxazolidine with moderate enantioselectivities, which were separated and hydrolyzed to the epimeric β-hydroxy-(2R)-leucines.15

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.16

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

References