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 alkylolithium 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 alkylolithiums 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 homoalaldol 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 MgBr2 increased the diastereomeric ratio to 90:10. Separation of the diastereomers, benzylaition 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 indoles. The lithium intermediate 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-(diphenylmethyleneglycine t-butylester with isobutyaldehyde 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 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 azabicyclocalkenes have been converted to aminoalkohols by organolithium-induced alkylative ring-opening. The protocol is also suitable for the generation of cycloalkenediols from oxabicyclocalkenes.17

References


