

# SYNLETT Spotlight 63

## (-)-Sparteine in Asymmetric Synthesis

Compiled by Thorben Schütz



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

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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.<sup>1</sup> Beak examined enantioselective deprotonations of *N*-Boc-pyrrolidines and *N*-Boc-allylamines.<sup>2</sup> Furthermore, it was used for dynamic resolutions<sup>3</sup> and deprotonations<sup>4</sup> of phosphine-boranes, for asymmetric additions of alkyllithiums to imines,<sup>5</sup> for asymmetric carbometallations of cinnamyl derivatives,<sup>6</sup> for palladium-catalyzed oxidative kinetic resolutions of secondary alcohols,<sup>7</sup> and for enantioselective syntheses of ferrocenes with planar chirality.<sup>8</sup>

The title compound is an alkaloid, which can be isolated from certain *papilionaceous* plants such as *Scotch broom*.<sup>9</sup> 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.<sup>10</sup> A (+)-sparteine surrogate is readily available from (-)-cytisine.<sup>11</sup>

(-)-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.

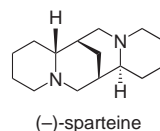
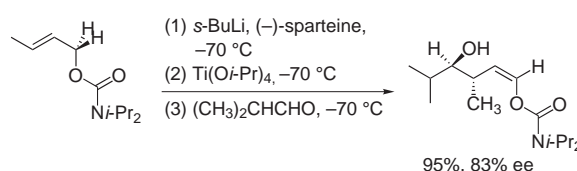


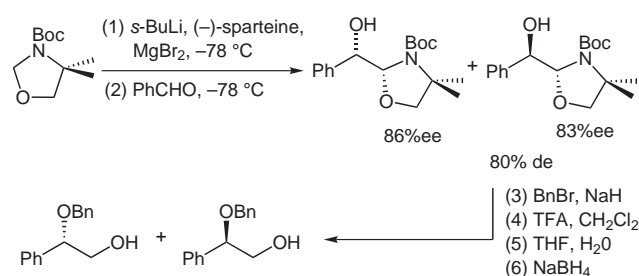
Figure 1

### Abstracts

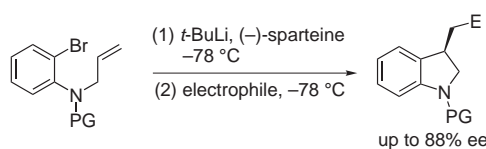
(A) Prochiral alkenylcarbamates are enantioselectively deprotonated using *s*-BuLi and (-)-sparteine. After transmetalation with Ti(*i*-PrO)<sub>4</sub> the titanium complex adds to aldehydes under 1,3-chirality transfer to yield homoaldol adducts with good enantiomeric excesses.<sup>1</sup>



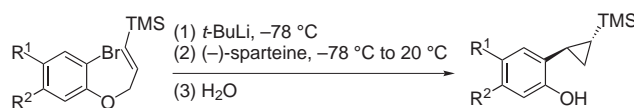
(B) In the presence of (-)-sparteine 2-lithiated *N*-Boc-4,4-dimethyl-1,3-oxazolidine can be used as a chiral formyl anion equivalent. Deprotonation with *s*-BuLi in the presence of the chiral ligand followed by the addition of benzaldehyde yielded the *syn* and *anti* diastereomers (*syn:anti* = 46:54) with about 85% ee. The addition of MgBr<sub>2</sub> 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<sub>4</sub> to yield (*S*)- and (*R*)-2-benzyloxy-2-phenylethanol, respectively.<sup>12</sup>



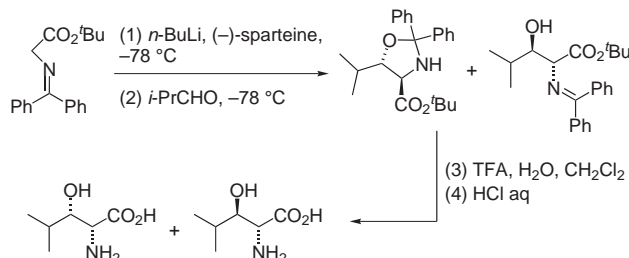
(C) On treatment with *t*-BuLi and (–)-sparteine *N*-protected *N*-allyl-2-bromo-anilines undergo intramolecular carbolithiation to afford chiral 3-substituted indolines. The lithium intermediate can be scavenged by several electrophiles such as methanol, DMF, or 1,2-dibromotetrafluoroethane. Enantiomeric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



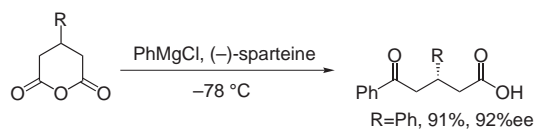
(D) Treatment of several allyl 2-lithioaryl ethers with *t*-BuLi and (–)-sparteine furnished after tandem carbolithiation/elimination new chiral cyclopropanes with moderate to good enantioselectivities.<sup>14</sup>



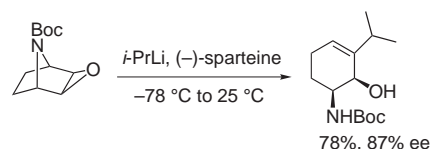
(E) The asymmetric synthesis of  $\beta$ -hydroxy- $\alpha$ -amino acids is another topic, which takes advantage of (–)-sparteine. Reaction of the lithium salt of *N*-(diphenylmethylene)glycine *t*-butylester with isobutyraldehyde produced the corresponding *erythro* imine and *threo* oxazolidine with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



(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.<sup>16</sup>



(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.<sup>17</sup>



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