Abstract

Several chiral amines have been synthesised from common amino acids and used as ligands in the asymmetric 1,2-addition of alkyllithiums to aldehydes. The influence of the substituents on the enantioselectivity of the reaction has been investigated as well as the structure of the mixed complexes between the lithiated chiral amines and *n*-butyllithium in solution using low temperature NMR techniques. A transition state structure has been proposed for the reaction in coordinating ethers which is consistent with the dimeric mixed complex found in solution and the stereochemical outcome of the addition reaction. The chiral amines with chelating sulfide groups were found to be the most efficient at inducing asymmetry with enantiomeric excesses of 99% and 95% for the addition of *n*-butyllithium and methyllithium to benzaldehyde at –116 °C, respectively.

The chiral amines were also used in the 1,2-addition of functionalized organolithium compounds (lithioacetonitrile, lithium acetylides and phenyllithium) to aldehydes at low temperature yielding synthetically more versatile products. Again the chiral amines with the sulfide groups proved the most efficient with enantiomeric excesses ranging from decent, 75% in the addition of lithioacetonitrile to benzaldehyde, to excellent, 95% in the addition of phenyllithium to cyclohexanecarboxaldehyde. The lithium acetylides of phenylacetylene and 1-pentyne afforded enantiomeric excesses of 87% and 82% respectively, in the addition to benzaldehyde at –116 °C. Extensive low temperature NMR studies of the mixed complexes between the chiral lithium amides and lithioacetonitrile revealed a great diversity of solution structures depending on the structure of the chiral lithium amide and the solvent. Dimeric and trimeric structures were found with both *N*-lithiated ketenimines and bridged lithioacetonitrile with the negative charge delocalised.

Mixed dimeric complexes between chiral lithium amides and chiral sodium amides were prepared, as shown by low temperature NMR studies, and used in the asymmetric deprotonation of cyclohexene oxide. A significantly higher initial rate of the reaction was found for the mixed metal complexes compared to the respective homo complexes of the lithium and sodium amides.

Several ^{15}N labelled chiral lithium amides were synthesised and the influence of the solvation at lithium on the $^{1}J(^{6}Li,^{15}N)$ coupling constant was investigated. After studying the $^{1}J(^{6}Li,^{15}N)$ coupling constant of several mixed lithium amide dimers as well as the mixed complexes with *n*-butyllithium in both coordinating and non-coordinating solvents it was concluded that the magnitude of the coupling constant indeed is dependent on the solvation at lithium. However, the coupling constant alone is not enough to reliably predict the solvation at lithium as structural differences of the lithium amide, particularly differences between internally coordinating groups, seem to affect the magnitude of the coupling constant as well.

Keywords: Enantioselective 1,2-additions, enantioselective deprotonations, chiral lithium amides, NMR spectroscopy, mixed alkali metal amides, $^{1}J(^{6}Li,^{15}N)$ coupling constant.