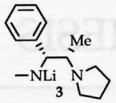
ABSTRACT

This thesis deals with investigations and development of chiral lithium amides for enantioselective deprotonations.

The chiral lithium amide **3** was found to deprotonate cyclohexene oxide **1** to yield 2-cyclohexen-1-ol (*S*)-**2** in 93% ee. NMR spectroscopic studies using ^{6}Li and ^{15}N labelled compounds revealed that chiral base **3** is a homodimer (**3**)$_2$ in THF solution. Kinetics showed that the rate limiting activated complex involved in the deprotonation is built from one dimer of the chiral lithium amide **3** and one molecule of **1**.



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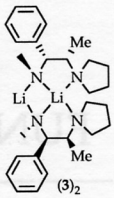
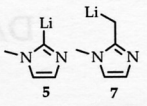


(3)$_2$

Lithiated 1-methylimidazole **5** and 1,2-dimethylimidazole **7** were found to change the homodimeric structure (**3**)$_2$ to mixed dimers of chiral lithium amide **3** and the lithiated imidazoles **5** or **7**. The additive DBU was found to be deprotonated by LDA to yield **9** which forms the mixed dimer **10** with **3**.



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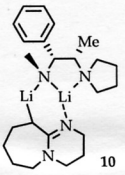


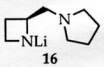
10

The use of these mixed dimers has been investigated in stoichiometric and catalytic enantioselective deprotonations. The lithiated imidazoles were found to be superior to LDA as catalyst regenerating bases.

Knowledge of the regioselectivity in the epoxide deprotonation is important for the mechanistic understanding. Using the natural abundance of deuterium in **1**, the regioselectivity of the deprotonations using chiral and achiral lithium amides has been studied using ^{2}H NMR spectroscopy. Homodimer (**3**)$_2$ was found to abstract the proton in the β-*syn* position. No evidence for β-*anti* or α-deprotonation was found.

Based on findings obtained from the activated complexes studied, novel lithium amide candidates were designed. Synthesis of new potent candidate bases and an efficient route to enantiopure (*S*)-5.7-spirodiamine **15a** and related compounds are reported. Deprotonation using chiral lithium amide **16** gave 87% ee of (*S*)-**2**.

15a



16

Keywords: Chiral lithium amides, NMR spectroscopy, mechanisms, enantioselective deprotonations, catalysis, natural abundance of deuterium, synthesis, (*S*)-5.7-spirodiamines.

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