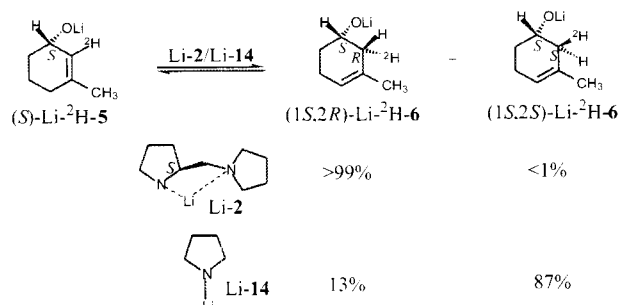


ABSTRACT

Lithium amide catalysed isomerisation of an allylic lithium alkoxide to a homoallylic lithium alkoxide has been shown to be induced upon changing the solvent from tetrahydrofuran (THF) to a more sterically demanding solvent, e.g. diethyl ether (DEE) or 2,5-dimethyltetrahydrofuran (2,5-DMTHF). This thesis deals with the elucidation of the stereochemistry and other mechanistic aspects of such a 1,3-proton transfer. Proper substrates have been designed and synthesised.

Isomerisation of (*S*)-Li-²H-5 in 2,5-DMTHF catalysed by Li-2 is found to exclusively yield the deuterium labelled homoallylic alkoxide (1*S*,2*R*)-Li-²H-6, i.e. the abstracted proton has been delivered to C2 *anti* with respect to the alkoxide group.



The decisive stereochemical influence of the 1-pyrrolidinylmethyl group in this isomerisation has been shown by the use of the lithium amide lacking this substituent, i.e. Li-14. With this catalyst a reversal of the stereochemistry is observed. The main homoallylic lithium alkoxide product is (1*S*,2*S*)-Li-²H-6 (87%) and the diastereoisomer (1*S*,2*R*)-Li-²H-6 is formed in 13%. Thus, the abstracted proton has delivered mainly *syn* to the oxygen.

Further stereochemical insights have been obtained by ¹H/²H exchange experiments using Li-14 as catalyst in the isomerisation of (1*S*,2*R*)-²H-6; Li-2 as catalyst in the isomerisation of the substrate with inverted stereochemistry at C1, i.e. (1*R*,2*R*)-²H-6 and isomerisation of racemic Li-5 by Li-14 in the presence of [*N*-²H]pyrrolidin, i.e. ²H-14.

Studies of reaction complexes in the 1,3-proton transfer have been performed by NMR spectroscopy and kinetics. Different complexes of the allylic lithium alkoxide and the lithium amide in the initial state have been detected. Deaggregation occurs on going from reagents to activated complexes. Possible mechanisms for the exchange and isomerisation reactions are discussed.

Keywords: allylic alcohol, deuterium labelling, homoallylic alcohol, isomerisation, kinetics, lithium alkoxides, chiral lithium amide, mechanism, 1,3-proton transfer, NMR spectroscopy, stereochemistry, stereoselective.

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