

SYNLETT Spotlight 258

Lithium Aluminum Hydride: A Powerful Reducing Agent

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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

Lithium aluminum hydride (LiAlH_4) is a powerful reducing agent used in organic synthesis¹ and is commonly abbreviated as LAH. It is more powerful than the related reagent sodium borohydride because of the relatively weaker Al–H bond compared to the B–H bond. It reduces a vast number of functional groups. For example, it converts esters,^{2a,b} carboxylic acids^{2c} and carbonyl compounds^{2d} into the corresponding alcohols; α,β -unsaturated ketones are reduced to allylic alcohols.^{2e} When epoxides are reduced using LAH, the reagent attacks the less hindered end of the epoxide, usually producing a secondary or tertiary alcohol. Epoxycyclohexanes are reduced to give axial alcohols preferentially.^{2f} Using LAH, amines can be prepared by the reduction of amides,^{2g,h} oximes,²ⁱ nitriles, nitro compounds or alkyl azides. LAH does not

reduce simple alkenes, arenes, or alkynes; but alkynes can be reduced if an alcohol group is nearby.^{2j}

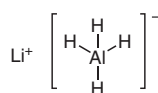


Figure 1

Preparation

Treatment of lithium hydride with an ethereal solution of AlCl_3 produces the new ether-soluble compound, LAH.³ Addition of further quantities of AlCl_3 yields a mild reducing agent, aluminum hydride (AlH_3).⁴

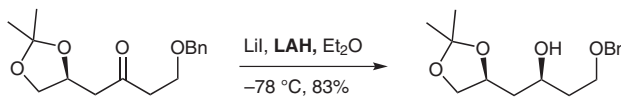


Figure 2

Abstracts

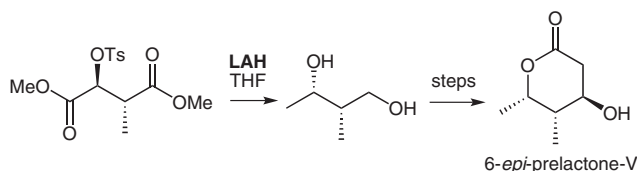
(A) Stereoselective reduction

Various *syn*-1,3-diols were prepared conveniently by reduction of β -alkoxy ketones with LiI and LAH (*syn/anti* selectivity up to >99:1). Here the coordination of LiI gives rise to a *syn*-selective reducing agent as a consequence of the intervention of a Li^+ -containing six-membered chelation.⁵



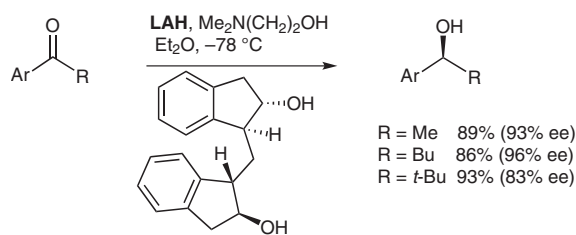
(B) Reductive removal of a tosylated hydroxy group/epoxide formation/epoxide opening

LAH is also employed in a highly chemo- and regioselective reduction of 2-tosyloxy esters, followed by epoxide formation via an $\text{S}_{\text{N}}2$ mechanism and reductive opening of the epoxide.⁶

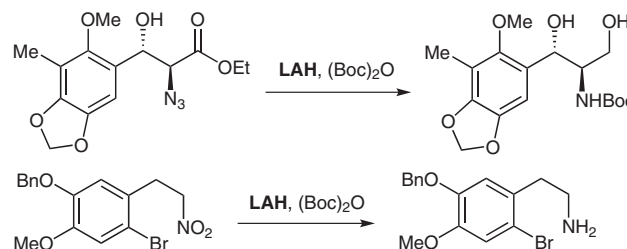


(C) *Enantioselective reduction of ketones by modified LAH*

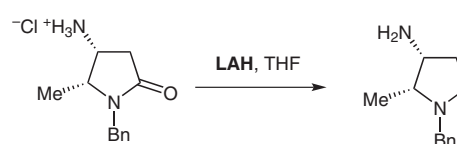
Highly enantioselective reduction of ketones by chiral-diol modified LAH was successfully demonstrated, with good yields and high ee.⁷

(D) *Synthesis of amines*

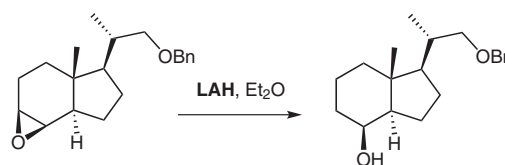
LAH is a powerful reducing agent, it reduces azide and nitro functionalities into the corresponding amines in a one-pot process.⁸

(E) *Reduction of amides*

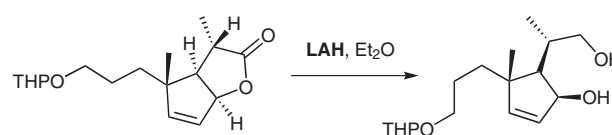
LAH reduces both cyclic and acyclic amides to the corresponding amines.⁹

(F) *Epoxide ring opening*

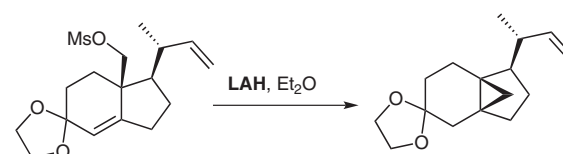
LAH attacks the epoxide at the less hindered side and produces the alcohols.¹⁰

(G) *Reduction of lactones*

LAH reduces lactones to the corresponding diols.¹¹

(H) *Formation of cyclopropane derivatives*

A homoallylic mesylate, when subjected to LAH, provided the cyclopropane derivative through homoallylic π -participation.¹²



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