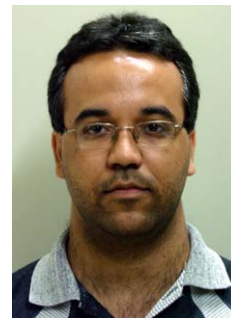


SYNLETT Spotlight 162

Synthetic Applications of Lithium Hydroxide

Compiled by Fernando de Carvalho da Silva



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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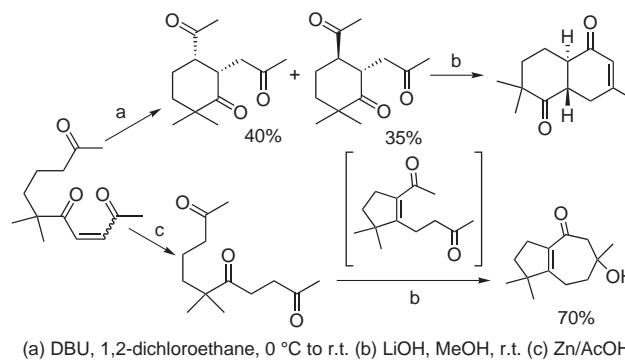
Introduction

Lithium hydroxide is a mild and efficient reagent used in several transformations in organic synthesis. It is used in tandem intramolecular aldol–aldol and sequential intramolecular Michael–aldol¹ reactions, as promoter of fragmentation reactions of optically active carbolactones providing γ -hydroxycyclohexenones and γ -butenolides,² in the synthesis of tropolones useful as bidentate ligands,³

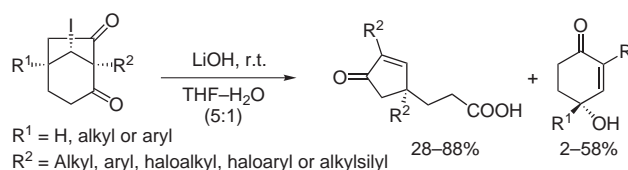
as promoter of glucosilation of 1-hydroxyindoles,⁴ in the stereoselective Michael addition of thiols to *N*-methacryloylcamphorsultam followed by hydrolysis of the sulfonamides,⁵ and it is applied in the deacylation of diazo-oxazolones.^{6,7} In addition, lithium hydroxide has been widely employed in Horner–Wadsworth–Emmons (HWE) reactions for preparation of α,β -unsaturated esters, α -unsaturated esters^{8,9} and α,β -unsaturated nitriles.¹⁰

Abstracts

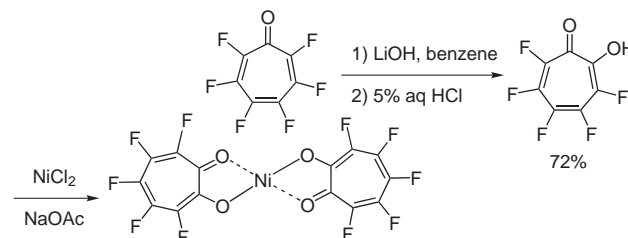
(A) Mischne reported a synthesis of [4.4.0] or [5.3.0] bicyclic frameworks achieved via sequential intramolecular Michael–aldol and tandem intramolecular aldol–aldol strategies, starting from acyclic precursors derived from β -ionone.¹



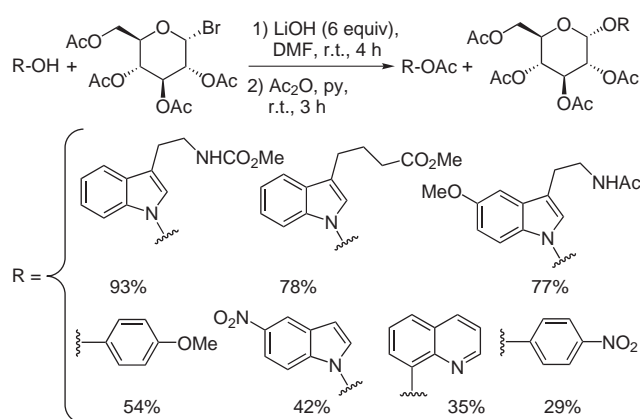
(B) Khim et al. reported that lithium hydroxide induced fragmentation in butenolides and γ -hydroxycyclohexenones. The addition of LiOH (2.0 equiv) to a solution of the carbolactone in THF–H₂O (5:1) at room temperature resulted in a mixture of the butenolides and γ -hydroxycyclohexenones in excellent yield.²



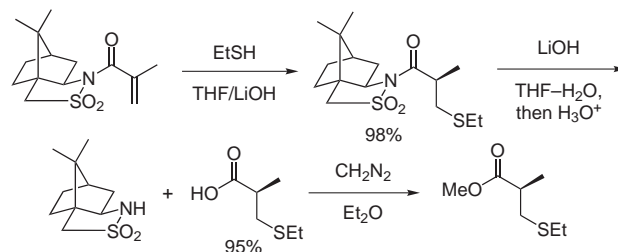
(C) Lemal and co-workers showed that anhydrous lithium hydroxide in benzene transforms tropone into pentafluorotropolone, which functions as a bidentate ligand (72% yield).³



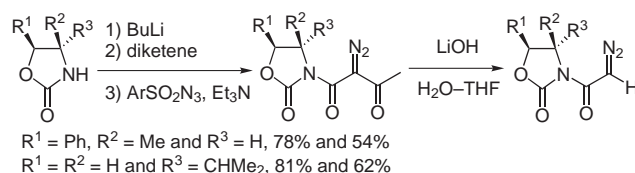
(D) Yamada et al. reported a lithium hydroxide promoted glucosidation of 1-hydroxyindoles with 2,3,4,6-tetra-*O*-acetyl- α -D-glucopyranosyl bromide followed by acetylation with Ac₂O and pyridine.⁴



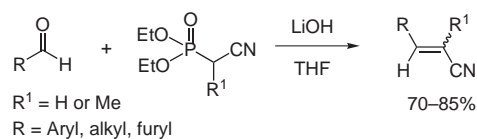
(E) Tsai et al. showed that lithium base (LiOH) promotes stereoselective Michael addition of thiols to *N*-methacryloylcamporsultam and produced the corresponding addition products with a diastereomeric ratio of 66–90%. Hydrolysis of the Michael product with three equivalents of lithium hydroxide in THF–H₂O gave the corresponding optically active β -thioester without racemization, and camporsultam was recovered quantitatively.⁵



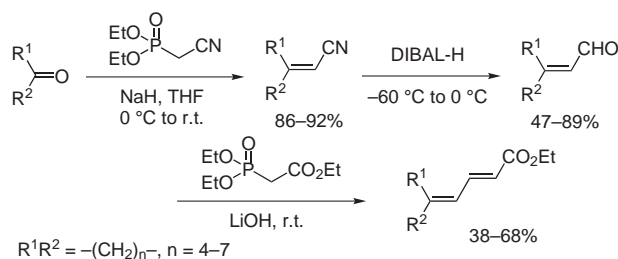
(F) Lithium hydroxide promotes selective deacylation of diazo-oxazolidones resulting in *N*-diazoacetyl derivatives.^{6,7}



(G) Lattanzi et al. showed a mild and practical procedure of LiOH-promoted HWE olefination, in which aldehydes were reacted with α -cyano phosphonates, yielding α,β -unsaturated nitriles. The reaction conditions are tolerated by functionalized ketones and the exclusive formation of (*E*)- γ -hydroxy α,β -unsaturated nitriles was observed.¹⁰



(H) Karagiozov and Abbott reported a stereoselective synthesis of α,β -unsaturated esters achieved via HWE reaction of β,β -disubstituted α,β -unsaturated aldehydes. Thus, aldehydes undergo olefination with phosphonate carbanion generated from triethyl phosphonoacetate and lithium hydroxide to give (*E*)- α,β -unsaturated esters in excellent selectivity.⁹



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