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

Fernando de Carvalho da Silva was born in Rio de Janeiro/RJ, Brazil in 1979. He received his Industrial Chemistry degree from Universidade Federal Fluminense, Niterói/RJ, Brazil in 2002. He is currently in the final stages of his PhD studies under the supervision of Prof. Vitor F. Ferreira and Prof. Maria Cecília B. V. de Souza. His research interests focus on the synthesis of diazo compounds, β -enaminones and triazoles derived from carbohydrates.

Instituto de Química, Universidade Federal Fluminense, UFF, CEP: 24020-150 Niterói, Rio de Janeiro, Brazil
Fax +55(21)26292136; E-mail: gqofermando@yahoo.com.br

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*-methacryloylcampforsultam followed by hydrolysis of the sulfonamides,⁵ and it is applied in the deacylation of diazo-oxazolidones.^{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 Ac_2O and pyridine.⁴

(E) Tsai et al. showed that lithium base (LiOH) promotes stereoselective Michael addition of thiols to *N*-methacryloylcamphorsultam 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– H_2O gave the corresponding optically active β -thioester without racemization, and camphorsultam 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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