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Spotlight 120

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Lithium Bromide: A Versatile Reagent in Organic Synthesis

Compiled by Santosh Rudrawar

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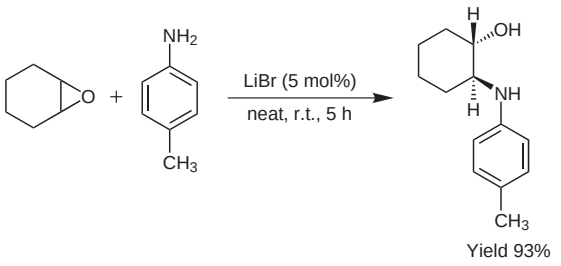
Introduction

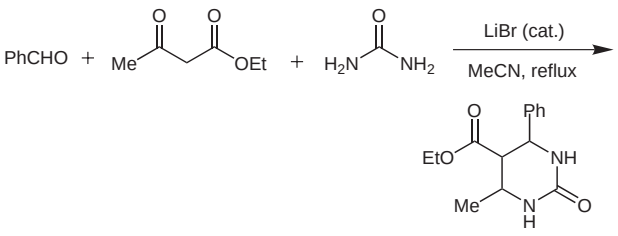
Lithium bromide is used as a sedative and a hypnotic (LD_{50} = 1800 mg/kg) in medicine and due to its highly hygroscopic property, it is widely used as an operating medium for air-conditioning and industrial drying systems. Since it is a stable and relatively safe compound, lithium bromide is used in various organic transformations such as Biginelli, Knoevenagel, and Wadsworth–Emmons reactions, brominations, dithioacetalizations, and dehydrohalogenations.

Abstract

(A) LiBr catalyzes the nucleophilic ring opening of epoxides with various aliphatic and aromatic amines to give β-amino alcohols. Aromatic and aliphatic amines react with cyclohexene oxides, providing exclusive formation of *trans*-2-aryl(alkyl)aminocycloalkanols in high yields. Excellent (98–100%) selectivity in favor of nucleophilic attack at the benzylic carbon of styrene oxide is observed with aromatic amines. The chelation effect of the Li^+ ion enables selective opening of the epoxide ring in 3-phenoxypropylene oxide in the presence of styrene oxide.[1]

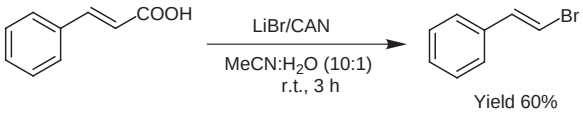


(B) The simple and direct method for the synthesis of dihydropyrimidinones, reported by Biginelli in 1893, involves the one-pot condensation of an aldehyde, an α,β-ketoester, and urea under strongly acidic conditions. LiBr catalyzes this three-component condensation reaction in refluxing acetonitrile to afford the corresponding dihydropyrimidinones in high yield, providing an improvement to the Biginelli reaction.[2]

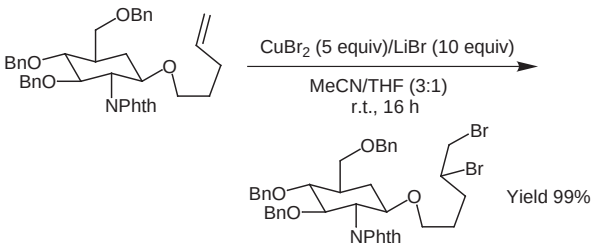


SYNLETT 2005, No. 7, pp 1197–1198
Advanced online publication: 14.04.2005
DOI: 10.1055/s-2005-865222; Art ID: V12105ST

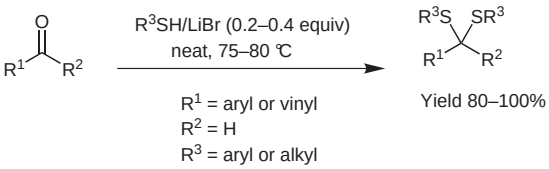
(C) Halodecarboxylation of α,β-unsaturated aromatic acids has been reported by using LiBr and ceric ammonium nitrate in acetonitrile–water at room temperature to afford the vinyl halides in moderate to good yield.[3]



(D) A mixture of copper(II) bromide and LiBr provides quantitative access to dibromides from alkenyl sugars that are resistant to straightforward reaction with molecular bromine. The mechanism predicts that the dibromide is created with *trans* stereochemistry. The success of $CuBr_2$/LiBr and the failure of Br_2 in this dibromination suggests that it is not an ordinary electrophilic addition.[4]



(E) Chemoselective dithioacetalization of aromatic and α,β-unsaturated aldehydes in the presence of other structurally different aldehydes and ketones was achieved efficiently in the presence of a catalytic amount of LiBr under solvent-free conditions. Because of the neutral reaction conditions, this method is compatible with acid-sensitive substrates.[5]



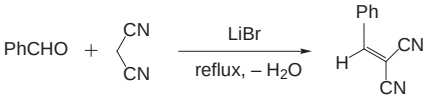
(F) Lithium bromide has a profound influence on the reactivity of SmI_2: it increases the reducing power of SmI_2 and promotes the pinacol coupling of cyclohexanone. The ability to simultaneously increase the reducing power of SmI_2 while decreasing the reduction potential of carbonyls may provide a method for selective reductive coupling of carbonyls in the presence of a more easily reduced functional group.[6]

Influence of LiBr on the reaction time and yield of Pinacol coupling of cyclohexanone.

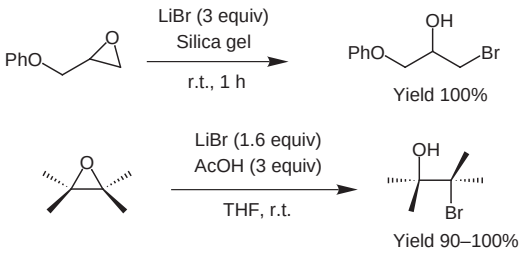
Equivalents[a]	Reaction time (min)	Isolated yield (%)
4	1	92
8	6	96
12	4	93

[a] Equivalents of LiBr based on the concentration of SmI_2.

(G) LiBr catalyzes the condensation of carbonyl compounds with active methylene compounds in the absence of solvent, to give the corresponding olefinic Knoevenagel products.[7]



(H) When treated at room temperature with LiBr adsorbed on silica gel, phenyl glycidyl ether was converted into the corresponding bromohydrin. For terminal epoxides, the ring-opening reaction was highly regioselective in giving the corresponding 1-halo-2-alkanols, demonstrating the predominant attack of the reagents from the less hindered side of the epoxides.[8] LiBr in the presence of acetic acid (pKa <13) reacts with epoxides regioselectively to give vicinol halohydrins in high yields under mild conditions, even when sensitive functional groups are present. The reaction is also highly stereoselective, as exemplified by the clean conversion of cyclohexene oxide to trans-2-halocyclohexanol.[9]



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