Lithium Bromide[1]

LiBr

[7550-35-8] BrLi (MW 86.85)
InChI = 1/BrH.Li/h1H;/q;+1/p-1/fBr.Li/h1h;/q-1;m
InChIKey = AMXOYNBUYSYVKV-PMQAFHISCD

(source of nucleophilic bromide;[2] mild Lewis acid;[1] salt effects in organometallic reactions;[1] epoxide opening[1])

Physical Data: mp 550 °C; bp 1265 °C; *d* 3.464 g cm^{-3}.
Solubility: 145 g/100 mL H_2O (4 °C); 254 g/100 mL H_2O (90 °C); 73 g/100 mL EtOH (40 °C); 8 g/100 mL MeOH; sol ether, glycol, pentanol, acetone; slightly sol pyridine.
Form Supplied in: anhyd white solid, or as hydrate.
Purification: dry for 1 h at 120 °C/0.1 mmHg before use; or dry by heating in vacuo at 70 °C (oil bath) for 24 h, then store at 110 °C until use.
Handling, Storage, and Precautions: for best results, dry before use in anhyd reactions.

Original Commentary

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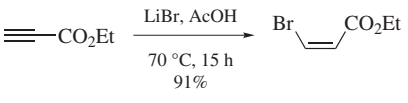
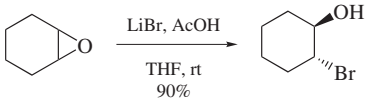
Alkyl and Alkenyl Bromides. LiBr has been extensively used as a source of bromide in nucleophilic substitution and addition reactions. Interconversion of halides[2] and transformation of alcohols to alkyl bromides via the corresponding sulfonate[3] or trifluoroacetate[4] have been widely used in organic synthesis. Primary and secondary alcohols have been directly converted to alkyl bromides upon treatment with a mixture of ***Triphenylphosphine***, ***Diethyl Azodicarboxylate***, and LiBr.[5]

(*Z*)-3-Bromopropenoates and -propenoic acids have been synthesized stereoselectively by the reaction of LiBr and propiolates or propiolic acid (eq 1).[6]

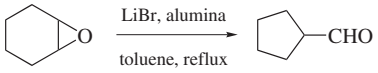


(1)

Heterolytic Cleavage of C–X Bonds. In the presence of a Lewis acid, LiBr acts as a nucleophile in the opening of 1,2-oxiranes to produce bromohydrins (eq 2).[7] In the absence of an external Lewis acid or nucleophile, epoxides generally give rise to products resulting from ring-contraction reactions (eq 3).

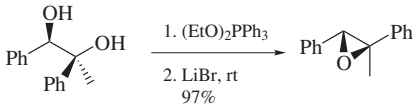


(2)



(3)

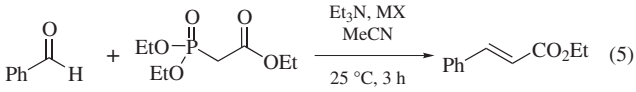
LiBr-mediated decomposition of dioxaphospholanes results in the exclusive formation of the epoxide, whereas the thermal decomposition produces a mixture of products (eq 4).[8]



(4)

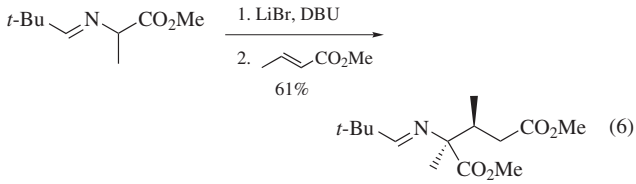
Protection of alcohols as their MOM ethers can be achieved using a mixture of ***Dimethoxymethane***, LiBr, and ***p-Toluenesulfonic Acid***.[9]

Bifunctional Reagents. Activated α-bromo ketones are smoothly converted into the corresponding silyl enol ethers when treated with a mixture of LiBr/R_3N/***Chlorotrimethylsilane***.[10] Aldehydes are converted into the corresponding α,β-unsaturated esters using ***Triethyl Phosphonoacetate*** and ***Triethylamine*** in the presence of LiBr (eq 5).[11,12] Similar conditions were extensively used in the asymmetric cycloaddition and Michael addition reactions of *N*-lithiated azomethine ylides (eq 6).[13]



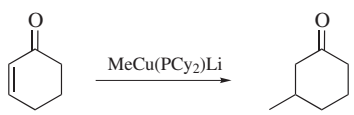
(5)

MX = LiCl, 77%; LiBr, 93%; $MgCl_2$, 15%; $MgBr_2$, 71%



(6)

Additive for Organometallic Transformations. The addition of LiBr and ***Lithium Iodide*** was shown to enhance the rate of organozinc formation from primary alkyl chlorides, sulfonates, and phosphonates, and ***Zinc*** dust.[14] Beneficent effects of LiBr addition have also been reported for the Heck-type coupling reactions[15] and for the nickel-catalyzed cross-couplings of alkenyl and α-metalated alkenyl sulfoximines with organozinc reagents.[16] The addition of 2 equiv of LiBr significantly enhances the yield of the conjugate addition products in reactions of certain organocopper reagents (eq 7).[17]



(7)

LiBr (0 equiv), 61%
LiBr (2 equiv), 96%

Finally, concentrated solutions of LiBr are also known to alter significantly the solubility and the reactivity of amino acids and peptides in organic solvents.[18]

First Update

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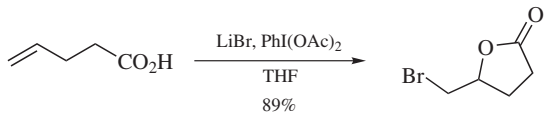
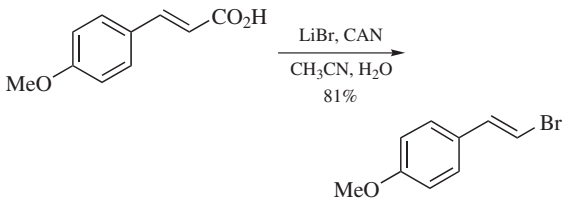
A recent review highlights the synthetic utility of lithium bromide.[19]

Alkyl and Alkenyl Bromides. The combination of LiBr with an oxidant has been employed as a source of electrophilic bromine. The reagent combination LiBr/(diacetoxyiodo)benzene monobrominates electron rich aromatic and heteroaromatic compounds, converts γ,δ-unsaturated carboxylic acids to bromomethyl butyrolactones (eq 8) and dibrominates olefins.[20]



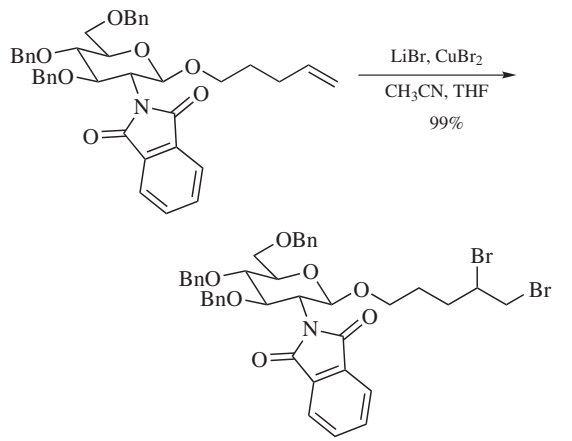
(8)

Vinyl bromides are produced by oxidative halodecarboxylation of α,β-unsaturated carboxylic acids using LiBr in the presence of cerium(IV) ammonium nitrate (eq 9).[21] The same reagent combination brominates electron rich aryl compounds.[22]



(9)

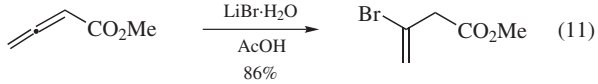
Dibromination of *n*-pentenyl glycosides occurred in high yield using a combination of LiBr/copper(II) bromide; for these substrates lower yields were observed with $CuBr_2$ alone or with a variety of other reagents (eq 10).[23]



(10)

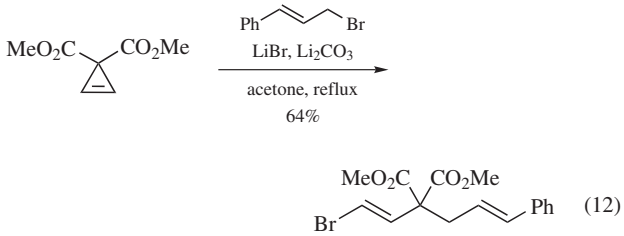
Alternative reagents	Yields (%)
Br_2	10
Br_2/Et_4NBr	20
NBS/Et_4NBr	85

Allenes functionalized with electron withdrawing groups are hydrohalogenated across the α,β carbon-carbon double bond with LiBr (or lithium chloride) and acetic acid, yielding vinyl bromides (eq 11).[24] Dibromination of allenes to substituted 2, 3-dibromoprop-1-enes occurs upon treatment with LiBr, catalytic palladium(II) acetate, 1,4-benzoquinone, and acetic acid.[25]



(11)

Lithium chloride, sodium iodide, and LiBr open methylenecyclopropanes to homoallylic halides in the presence of acetic acid,[26] whereas substituted internal cyclopropenes give ring-opened, alkylated adducts when treated with LiBr (or sodium iodide) and an alkyl halide electrophile (eq 12).[27]



(12)

The combination of LiBr and Amberlyst 15 resin converts α,β-epoxy ketones to α-bromo-α,β-unsaturated ketones,[28] while allylic epoxides are ring-opened to halohydrins.[29]

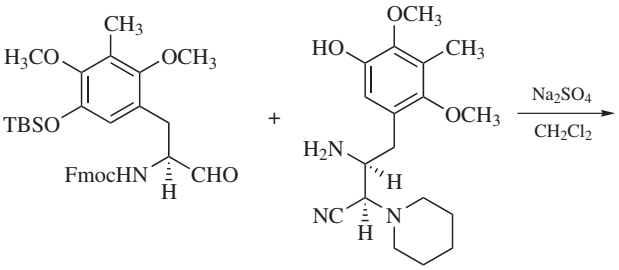
Heterolytic Cleavage of C–X Bonds. Lithium bromide catalyzes the opening of epoxides by aliphatic amines and anilines at ambient temperature under solvent-free conditions.[30] In the presence of carbon dioxide (atmospheric pressure), LiBr catalyzes conversion of epoxides to cyclic carbonates.[31]

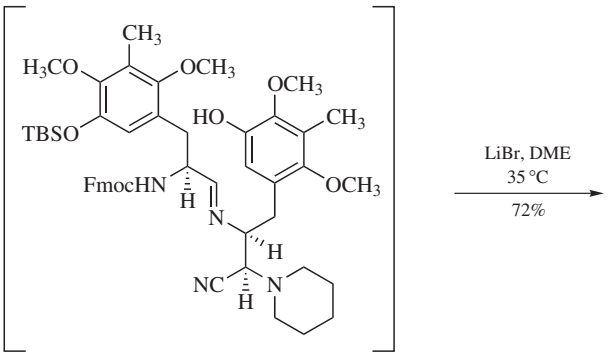
Selective cleavage of one alkoxycarbonyl group of *N*, *N*-dicarbamoyl-protected amines was achieved by means of LiBr in refluxing acetonitrile.[32]

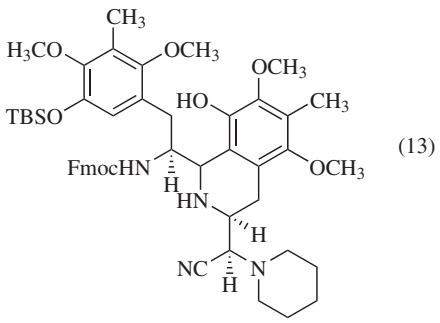
Weak Lewis Acid. Lithium bromide is used as a mild Lewis acid in a variety of reactions. For example, this reagent was used in the Pictet-Spengler cyclization of a highly functionalized imine (eq 13).[33] In this reaction, carbon-carbon bond formation occurs without reaction or loss of stereochemical integrity of the α-amino nitrile functionality.

Lithium bromide catalyzes the one-pot condensation of aldehydes, β-keto esters, and ureas to form dihydropyrimidinones (Biginelli reaction, eq 14).[34] LiBr is also a suitable Lewis acid for promotion of the one-pot Bischler-Möhlau indole synthesis (eq 15).[35]

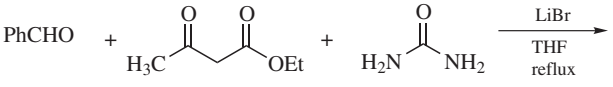
LiBr interacts with and can influence the reactivity of enolates and other basic species. For instance, LiBr demonstrated a beneficial effect on enantioselectivity in asymmetric alkylation of ketones[36] and lactams[37] using a chiral lithium amide base. In the cyclopropanation of α,β-unsaturated amides and esters by allylic ylides, the combination of LiBr and sodium hexamethyldisilazide results in a reversal of diastereoselectivity when compared to the use of potassium hexamethyldisilazide (eq 16).[38]

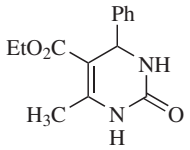






99% ee (13)





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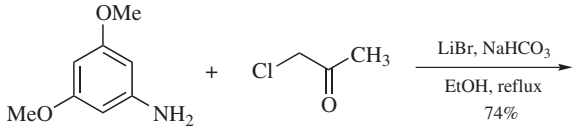

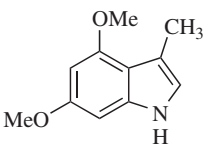

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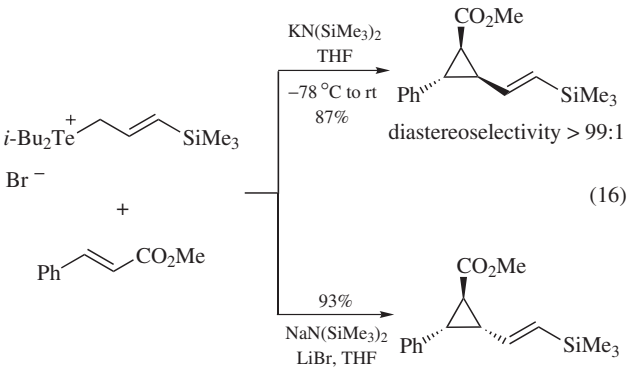

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