

Lithium Iodide¹



[10377-51-2] **LiI** (MW 133.84)

InChI = 1/H1.Li/h1H;/q;+1/p-1/f1.Li/h1h;/q-1;m

InChIKey = HSZCZNFUXUDYRKD-IABDHUKHCQ

(ester cleavage and decarboxylation;² source of nucleophilic iodide;³ mild Lewis acid;¹ salt effects in organometallic reactions;¹ epoxide opening⁴)

Physical Data: mp 449 °C; bp 1180 °C; *d* 4.076 g cm⁻³.

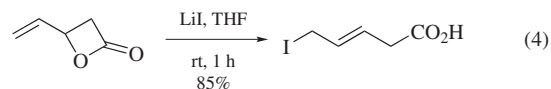
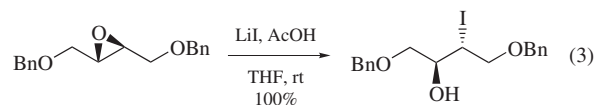
Solubility: 165 g/100 mL H₂O (20 °C); 433 g/100 mL H₂O (80 °C); 251 g/100 mL EtOH (20 °C); 343 g/100 mL MeOH (20 °C); 43 g/100 mL acetone (18 °C); very sol NH₄OH.

Form Supplied in: anhydrous white solid or as the hydrate.

Preparative Method: the anhydrous salt of high purity can be prepared from lithium hydride and iodine in ether.⁵

Purification: crystallized from hot H₂O (0.5 mL g⁻¹) by cooling in CaCl₂-ice or from acetone. LiI is dried for 2 h at 120 °C (0.1 mmHg, P₂O₅) before use.

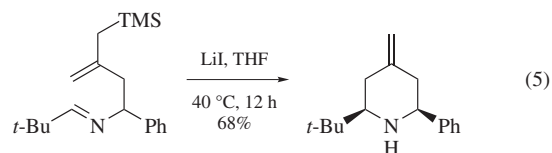
Handling, Storage, and Precautions: for best results, LiI should be dried prior to use in anhydrous reactions.



Alkyl and Alkenyl Iodides. LiI has been used as a source of iodide in nucleophilic substitution and addition reactions. Primary alcohols have been directly converted to alkyl iodides upon treatment with a mixture of **Triphenylphosphine**, **Diethyl Azodicarboxylate**, and LiI.³ Tertiary alcohols can be converted into tertiary alkyl iodides upon treatment with **Hydrogen Iodide** in the presence of LiI.¹²

(*Z*)-3-Iodopropenoates and -propenoic acids have been synthesized stereoselectively by the reaction of LiI and propiolates or propiolic acid.¹³

C–C Bond Forming Reactions. LiI was shown to efficiently catalyze the Michael addition of β -dicarbonyl compounds,¹⁴ and the intramolecular allylsilane addition to imines to produce 4-methylenepiperidine derivatives (eq 5).¹⁵

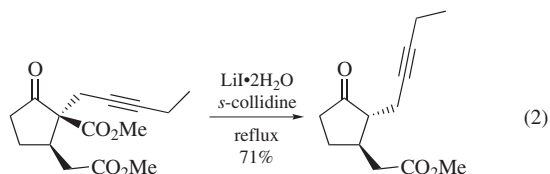
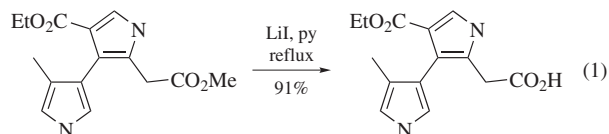


Original Commentary

André B. Charette

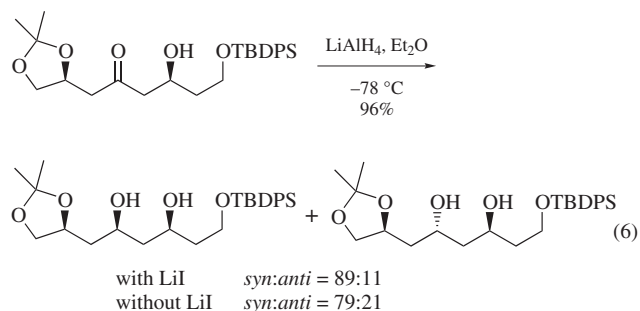
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Heterolytic C–X Bond Cleaving Reactions. In the presence of amine bases, LiI has been extensively used as a mild reagent for the chemoselective cleavage of methyl esters (eq 1).⁶ Decarboxylation of methyl esters usually occurs when an electron-withdrawing group is present at the α -position of the ester (eq 2).⁷ Ester-type glycosyl linkages of acidic tri- and diterpenes can also be selectively cleaved under these conditions.⁸ Aryl methyl ethers can be demethylated to afford the corresponding phenols upon heating with LiI and *s*-collidine.⁹



1,2-Oxiranes are readily opened by LiI and a Lewis acid to produce iodohydrins (eq 3).⁴ Conversely, 1-oxaspiro[2.2]pentanes and 1-oxaspiro[3.2]hexanes give rise to bond migration products.¹⁰ β -Vinyl- β -propiolactone is efficiently opened by LiI to produce the corresponding substituted allyl iodide (eq 4).¹¹

LiI as an Additive for Organometallic-mediated Transformations.¹⁶ The *syn/anti* selectivity in the reduction of β -alkoxy ketones is drastically increased by the addition of LiI (eq 6).¹⁷



The addition of **Lithium Bromide** and LiI was shown to enhance the rate of organozinc formation from primary alkyl chlorides, sulfonates, and phosphonates, and zinc dust.¹⁸ Beneficial effects of LiI addition have also been reported for Heck-type coupling reactions¹⁹ and in conjugate addition to chiral vinyl sulfoximines.²⁰

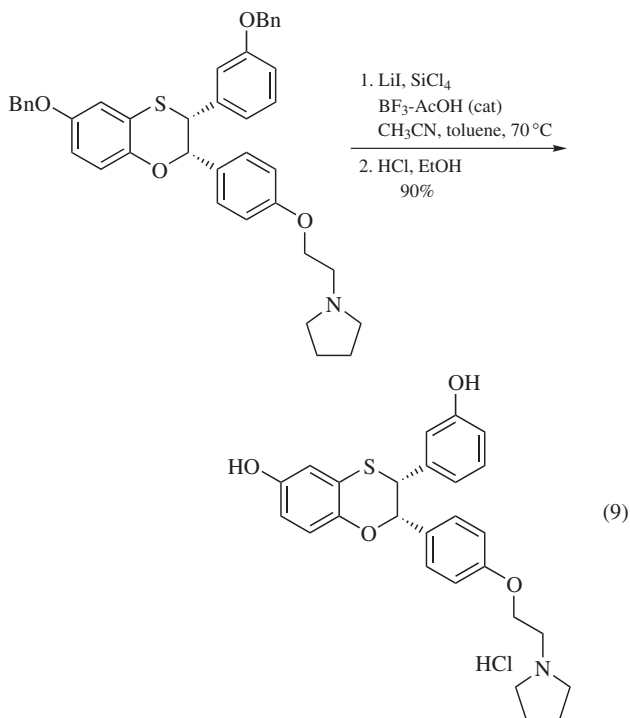
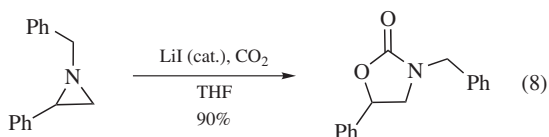
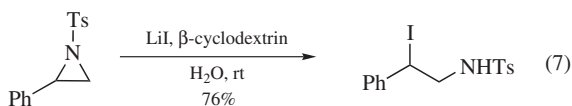
The (*E*)/(*Z*) alkenic ratio in Wittig-type alkenations was shown to be dependent on the amount of Li salt present.²¹

Reduction of α -Alkoxy carbonyl Derivatives. α -Halo ketones are reduced to the corresponding ketones upon treatment with a mixture of LiI and *Boron Trifluoride Etherate*.²²

First Update

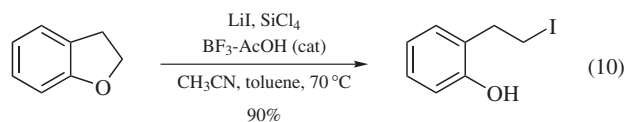
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Heterocyclic C–X Bond Cleaving Reactions. LiI has been employed in a variety of ring-opening reactions of aziridines and their derivatives. The conversion of *N*-arylsulfonylaziridines to β -haloamine derivatives was conducted using lithium halides (LiI, as well as lithium chloride or lithium bromide) and β -cyclodextrin in water (eq 7).²³ *N*-Arylsulfonylaziridines react with isocyanates in the presence of LiI to form imidazolidinones.²⁴ Aziridines are converted to oxazolidinones upon treatment with catalytic LiI and carbon dioxide (eq 8).²⁵

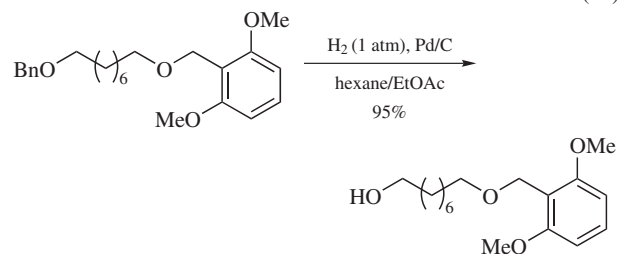
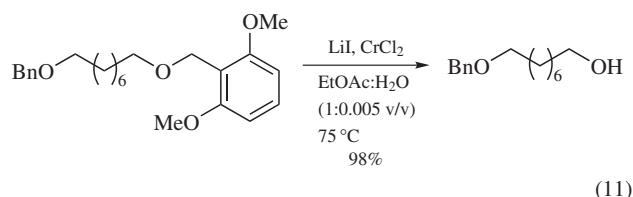


Combinations of LiI and other Lewis acidic reagents are useful in the *O*-dealkylation of ethers. Aryl methyl, allyl, and benzyl ethers are cleaved to phenols using LiI/tetrachlorosilane in the

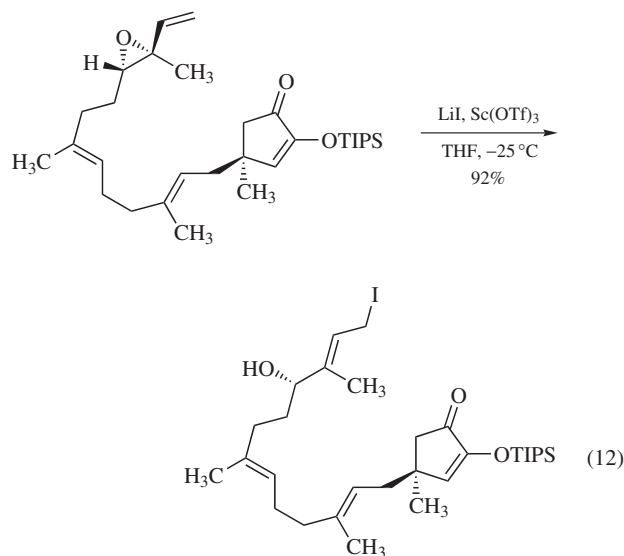
presence of catalytic boron trifluoride-acetic acid (eq 9). Cyclic ethers yield ring-opened alkyl iodides under these conditions (eq 10). LiI/boron tribromide/acetic acid was more reactive than iodotrimethylsilane in the debenzoylation of the dibenzoyloxydihydrobenzoxathiin substrate of eq 9, providing a higher yield and improved impurity profile.²⁶



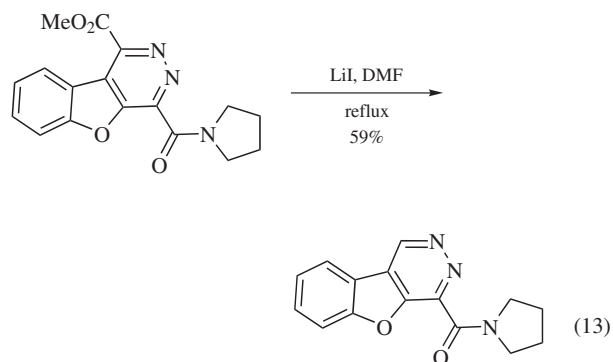
LiI/chromium(II) chloride in moist ethyl acetate cleaves benzylic ethers; the preference of this reagent combination for electron rich aryl ethers with coordinating functionality results in the selective cleavage of 2,6-dimethoxybenzyl ethers in the presence of other benzyl ethers, enabling orthogonal deprotection of bis-protected diols (eq 11).²⁷



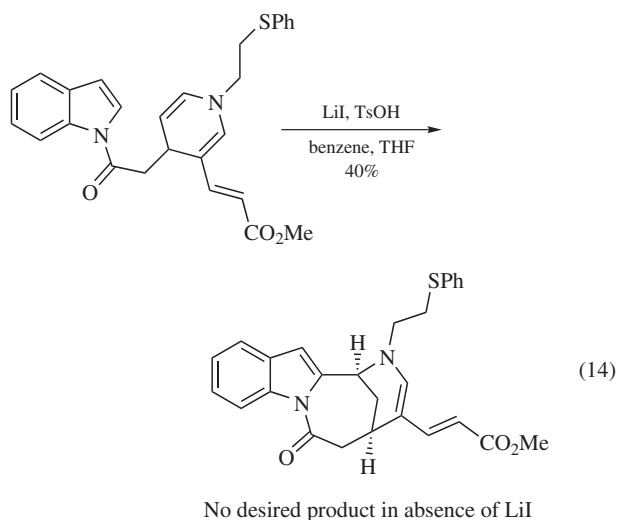
The stereoselective ring opening of an allylic epoxide to an (*E*)-allylic iodide was achieved using a combination of LiI and scandium trifluoromethanesulfonate (eq 12).²⁸ In contrast, 9-bromo-9-borabicyclo[3.3.1]nonane furnished the corresponding (*Z*)-allylic bromide selectively. LiI transforms 2,3-epoxy alcohols to 1-iodo-2,3-diols upon heating in DME.²⁹ α,β -Epoxy ketones³⁰ and allylic epoxides³¹ are deoxygenated to α,β -unsaturated ketones and dienes, respectively, with LiI and Amberlyst 15 resin.



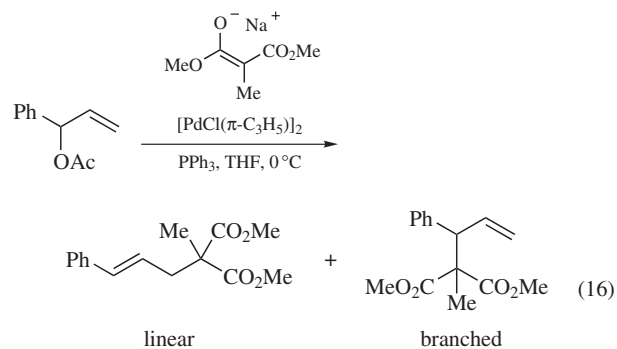
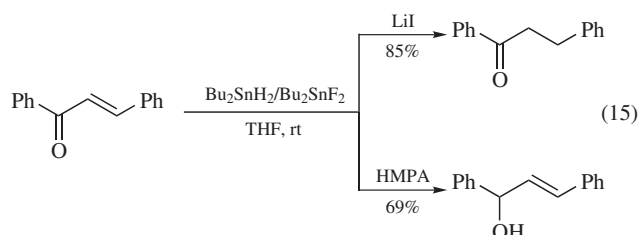
Dealkoxycarbonylation of 1-carbomethoxypyridazines occurred upon refluxing with LiI in DMF (eq 13).³²



C–C Bond Forming Reactions. LiI displayed a beneficial effect on the acid-promoted intramolecular cyclization of 1,4-dihydropyridines (eq 14).³³ In this case, reversible trapping of an iminium ion by iodide was proposed to shift the reaction equilibrium away from an unproductive fragmentation pathway.



LiI as an Additive for Organometallic-mediated Transformations. Diastereoselectivity in the cyclization of 5-hexenyl-lithiums was shown to be influenced by LiI.³⁴ As an additive in the reduction of α,β -unsaturated ketones by $\text{Bu}_2\text{SnH}_2/\text{Bu}_2\text{SnF}_2$, LiI has a dramatic effect on the selectivity for 1,2- versus 1,4-reduction (eq 15).³⁵ Catalytic LiI improves regioselectivity in favor of the linear isomer in the palladium-catalyzed alkylation of allylic acetates (eq 16).³⁶



Additive	Yield (%)	Linear:Branched
None	96	77:23
LiI (10 mol %)	99	100:0

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