SYNLETT
Spotlight 393

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

n-Butyllithium

Compiled by Hu Li

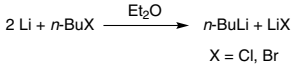
Hu Li was born in Xiaogan, Hubei province, P. R. of China, in 1986. He has graduated in chemical biology (National science base) and received his B.Sc. degree from Hubei University in 2010. Currently, he is working towards his Master/Ph.D. of science degree in chemistry under the supervision of Professor Pinaki S. Bhadury on the synthesis and application of chiral Brønsted acid in the Center for Research and Development of Fine Chemicals, Guizhou University.

Center for Research and Development of Fine Chemicals, State Key Laboratory Breeding Base of Green Pesticide and Agricultural Bioengineering, Key Laboratory of Green Pesticide and Agriculture Bioengineering, Ministry of Education, Guizhou University, Guiyang 550025, P. R. of China
E-mail: lhpesticide@163.com

Dedicated to my research supervisor Dr. Pinaki S. Bhadury

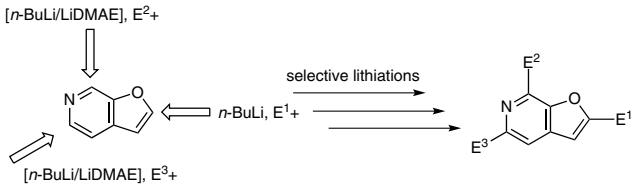
Introduction

n-Butyllithium (*n*-BuLi) is one of the most prominent organolithium reagents in the whole of synthetic chemistry,[1–3] and available as solutions in alkanes such as pentane, hexane, or heptane, which is usually encountered as a pale yellow solution. It is unstable towards air or moisture but stable in an atmosphere of nitrogen. It has been widely used in organic reactions, such as regioselective lithiation reaction,[4] reversible metathesis reaction,[5] Claisen rearrangement,[6] phospho-Fries rearrangement,[7] coupling reaction,[8] asymmetric deprotonation–electrophilic trapping reaction,[9] enantioselective hydroxyalkylation,[10] etc. In general, *n*-butyllithium is commercially available and can also be prepared readily by the reaction of 1-bromobutane or 1-chlorobutane with Li metal (Scheme 1).[11] An overview of the usage of *n*-BuLi in organic synthesis is presented below.

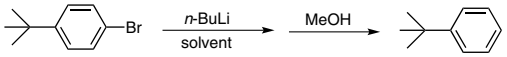


Scheme 1

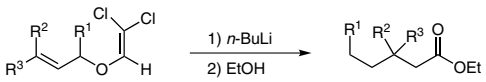
(A) Fort and co-workers described an efficient method for the synthesis of polysubstituted furo[2,3-*c*]pyridines via successive regioselective lithiations, using *n*-BuLi or [*n*-BuLi/LiDMAE] as base. For each step the products were obtained in moderate to excellent yields.[4]



(B) Bailey et al. reported mild and highly efficient experimental conditions for the reversible metathesis reaction known as the lithium–halogen exchange. The reaction products of 1-bromo-4-*tert*-butylbenzene with *n*-BuLi at 0 °C are obtained quantitative in heptane containing a small quantity of THF. Particularly, nettlesome side reactions, including coupling of aryllithium with the co-generated alkyl halide and formation of a benzyne intermediate via ortho-metalation of the aryl halide, are effectively avoided.[5]

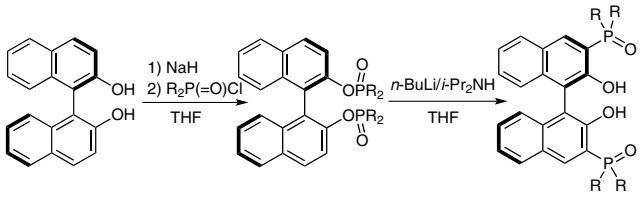


(C) Upon treatment with *n*-BuLi, a variety of allyl 1,1-dichlorovinyl ethers undergo rearrangement to furnish high yields of γ,δ-unsaturated esters after alcohol addition. A potential advantage of this method over other variants of the Claisen rearrangement is the ability to add a variety of alcohol nucleophiles to the proposed ketene intermediate, allowing the one-pot preparation of diverse esters of γ,δ-unsaturated carboxylic acids with high stereoselectivity.[6]

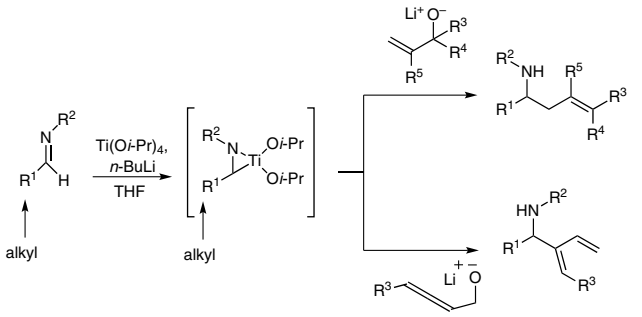


SYNLETT 2012, 23, 1407–1408
Advanced online publication: 14.05.2012
DOI: 10.1055/s-0031-1290685; Art ID: ST-2012-V0400-V

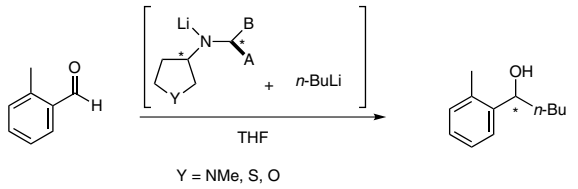
(D) *n*-BuLi together with *i*-Pr_2NH has been used in the preparation of bifunctional BINOL ligands bearing phosphine oxides [$P(=O)R_2$], phosphonates [$P(=O)(OR)_2$], or phosphoramides [$P(=O)(NR_2)_2$] at the 3,3′-positions via a phospho-Fries rearrangement as key step. This method has an advantage with regard to yield and purification in comparison with a coupling method that uses halide compounds, expensive diphenylphosphine oxide [$Ph_2P(=O)H$], and palladium or nickel catalysts.[7]



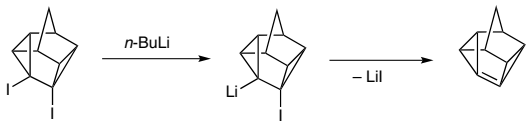
(E) Tarselli and Micalizio described a successful procedure for the coupling of aliphatic imines with allylic and allenic alkoxides enabled by a unique reactivity profile of Ti(IV) isopropoxide/*n*-BuLi compared to well-known Ti(IV) isopropoxide/RMgX systems. This coupling proceeds with moderate to excellent yields.[8]



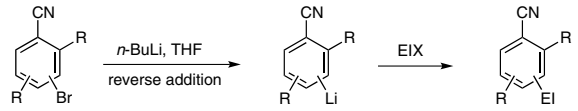
(F) An enantioselective hydroxyalkylation of *o*-tolualdehyde and 3-aminotetrahydrofurans (or 3-aminopyrrolidines, 3-aminotetrahydrothiophenes) in the presence of *n*-BuLi and lithium amides gives the target product 1-*o*-tolylpentan-1-ol in good yield and moderate ee.[10]



(G) The highly pyramidalized alkene pentacyclo-[4.3.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]non-4-ene was successfully synthesized with *n*-BuLi via dehalogenation of vicinal dihalides. The method has proven to be reliable for the synthesis of a variety of strained alkenes.[12]



(H) Luliński et al. found that lithiated benzonitriles can be generated in high yields from reactions of bromobenzonitriles with *n*-BuLi in THF under standard cryogenic conditions (ca. –70 °C, even up to –60 °C). The reverse addition mode is employed to reduce significantly side reactions.[13]



References

(1) Coldham, I.; Dufour, S.; Haxell, T. F. N.; Patel, J. J.; Sanchez-Jimenez, G. *J. Am. Chem. Soc.* **2006**, *128*, 10943.
(2) Eddy, N. A.; Morse, P. D.; Morton, M. D.; Fenteany, G. *Synlett* **2011**, 699.
(3) Posaneschi, F.; Sejberg, J. J. P.; Blain, C.; Ng, W. H.; Eric, O. Aboagye E. O.; Spivey, A. C. *Synlett* **2011**, 241.
(4) Chartoire, A.; Comoy, C.; Fort, Y. *J. Org. Chem.* **2010**, *75*, 2227.
(5) Bailey, W. F.; Mark, R. Luderer M. R.; Jordan, K. P. *J. Org. Chem.* **2006**, *71*, 2825.
(6) Christopher, A.; Brandes, D.; Kelly, S.; Minehan, T. *Org. Lett.* **2006**, *8*, 451.
(7) Hatano, M.; Miyamoto, T.; Ishihara, K. *J. Org. Chem.* **2006**, *71*, 6474.
(8) Tarselli, M. A.; Micalizio, G. C. *Org. Lett.* **2009**, *11*, 4596.
(9) Genet, C.; Canipa, S. J.; O'Brien, P.; Taylor, S. *J. Am. Chem. Soc.* **2006**, *128*, 9336.
(10) Duguet, N.; Petit, S. M.; Marchand, P.; Harrison-Marchand, A.; Maddaluno, J. *J. Org. Chem.* **2008**, *73*, 5397.
(11) Brandsma, L.; Verkruijsse, H. D. *Preparative Polar Organometallic Chemistry I*; Springer: Berlin, Heidelberg, **1987**.
(12) Mark, A. Forman M. A.; Moran, C.; Herres, J. P.; Stairs, J.; Chopko, E.; Pozzessere, A.; Kerrigan, M.; Kelly, C.; Lowchyj, L.; Salandria, K.; Gallo, A.; Loutzenhiser, E. *J. Org. Chem.* **2007**, *72*, 2996.
(13) Luliński, S.; Zajac, K. *J. Org. Chem.* **2008**, *73*, 7785.

