

# Organolithium Compounds in Organic Synthesis Symposium

Gideon Fraenkel, Honorary Chairman

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**ICOS-OLS-1**      **William F. Bailey**  
*University of Connecticut, Connecticut, USA*

Asymmetric Cyclization of Achiral Organolithium

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**ICOS-OLS-2**      **Theodore Cohen**  
*University of Pittsburgh, Pennsylvania, USA*

Cyclizations of Organolithiums Prepared by Reductive Lithiation

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**Gideon Fraenkel**  
*The Ohio State University, USA*

Structure and Dynamic Behavior of Internally Solvated Organolithium compounds:  
Perturbation of Conjugation Effects

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**ICOS-OLS-4**      **Robert E. Gawley**  
*University of Arkansas, Arkansas, USA*

The Role of Organostannanes in the Generation of Chiral Organolithium  
Compounds

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**ICOS-OLS-5**      **Victor Snieckus**  
*Queen's University, Canada*

Lithium as a Conduit to Synthetic Aromatic Chemistry

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**ICOS-OLS-6**      **Miguel Yus**  
*Universidad de Alicante, Alicante, Spain*

Reactive Organolithiums by an Arene-catalyzed Lithiation

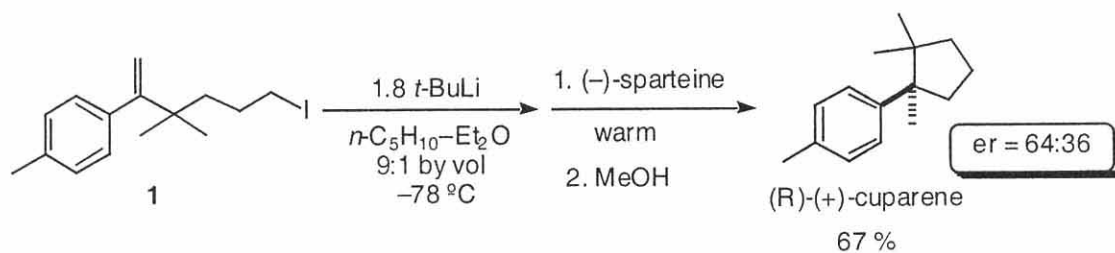
## Asymmetric Cyclization of Achiral Organolithiums

ICOS-OLS-1

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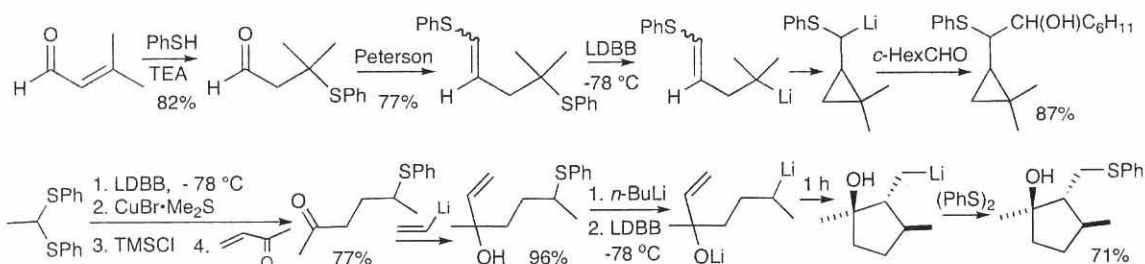
The 5-exo-trig cyclization of achiral olefinic organolithiums proceeds enantioselectively when conducted in the presence of a chiral ligand that serves to render the lithium atom stereogenic. Thus, for example, cyclization of the organolithium derived from **1** proceeds with modest enantiofacial selectivity when conducted in the presence of (-)-sparteine to deliver the natural sesquiterpene, (R)-(+)-cuparene, in good yield. Additional examples of the utility of this methodology will be discussed.



## Cyclizations of Organolithiums Prepared by Reductive Lithiation ICOS-OLS-2

*Theodore Cohen, University of Pittsburgh, Pittsburgh, Pennsylvania, U.S.A.*

Since its introduction in 1978, the reductive lithiation of phenyl thioethers using aromatic radical-anions has become one of the most versatile methods known for generating organolithiums. This assertion will be amply demonstrated by the preparation of a large variety of alkene-bearing phenyl thioethers that can be reductively lithiated to organolithiums capable of intramolecular carbolithiation of the alkene to produce 3-, 4-, 5-, 6-membered rings bearing the useful -CHYL*i>*i group, where Y is H, SPh, or, in some cases, alkyl. The organolithiums to be cyclized can be primary, secondary, or tertiary alkylolithiums, allyllithiums, or vinylolithiums. The ease of preparation of the reductive lithiation thioether substrates will be emphasized. The remarkable effect of lithium oxyanionic groups at various positions, but especially at the allylic or homoallylic position with respect to the alkene acceptor, in accelerating the cyclization and strongly controlling its stereochemistry, will be demonstrated and rationalized. Two examples are below:



## The Role of Organostannanes in the Generation of Chiral Organolithium Compounds

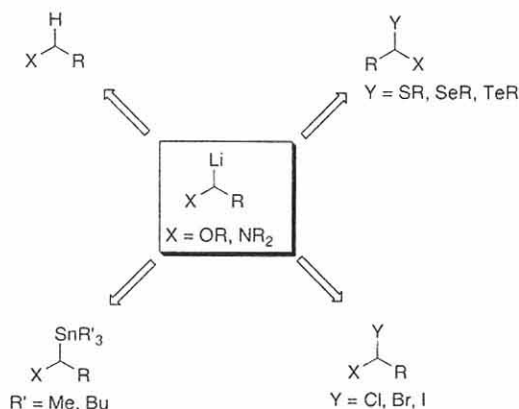
ICOS-OLS-4

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Functionalized organolithium compounds having a stereogenic metal-bearing carbon atom can be prepared by a number of routes, as shown in the figure. The tin-lithium exchange reaction offers advantages over other routes in many instances. For example, the reaction is stereoretentive ( $S_E2ret$ ). As a result, preparation of configurationally stable, chiral, nonracemic organolithiums reduces to methods of preparation of scalemic organostannanes. Tin-lithium exchange is also useful in accessing organolithiums that are not available by deprotonation. Finally, tin-lithium exchange can usually be achieved in the absence of ligands that can interfere with subsequent transmetalations and dynamic resolutions.



A summary of new methods for the preparation of functionalized, chiral organostannanes (methods that do not involve deprotonation) will be presented, along with recent results on the solution dynamics of  $\alpha$ -aminoorganostannanes and structural influences on the tin-lithium exchange reaction.

## Lithium as a Conduit to Synthetic Aromatic Chemistry ICOS-OLS-5

### Victor Snieckus

The simple link between the Directed *ortho* Metalation (DoM) reactions, the rich cross coupling chemistry of B, Mg, and Zn (**1**) and the enabling Directed remote Metalation chemistry (**2**) has allowed the development of new regiospecific strategies in aromatic synthesis. Recent results from our laboratories will be described.



Anctil, E.; Snieckus, V. In Diederich, F.; de Meijere, A. Ed. *Metal-Catalyzed Cross-Coupling Reactions*, 2<sup>nd</sup> Ed., **2004**, 761-813, Whistler, M.C.; MacNeil, S.; Snieckus, V.; Beak, P. *Angew. Chem. Int. Ed.* **2004**, *43*, 2206-2225 and Macklin, T.; Snieckus, V. In Dyker, Ed. *Handbook of C-H Transformations*, Wiley-VCH; New York, **2005**, p 106-119.

## Reactive organolithiums by an arene-catalyzed lithiation

ICOS-OLS-6

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Very reactive organolithium intermediates, such as functionalized organolithium compounds **1** [*Curr. Org. Chem.* **2003**, 867] or dilithium synthons **2** [*Curr. Org. Chem.* **2005**, 459] can be easily generated by an arene-catalyzed lithiation [*The Chemistry of Organolithium Compounds.* **2004**, Chapter 11] starting from heterocyclic compounds **3** [*Pure Appl. Chem.* **2003**, 1453] or dichlorinated materials **4** [*Chem. Rev.* **2002**, 4009], respectively, working in the last case under Barbier-type reaction conditions [*Recent Res. Devel. Org. Chem.* **1997**, 397]. The generated lithiated species (**1,2**) react in situ with different electrophiles giving the corresponding polyfunctionalized molecules in one only synthetic operation. In the case of using carbonyl compounds as electrophiles, the obtained hydroxy compounds are easily cyclized to give a series of polycyclic and spiro ethers of preparative interest.

