

# ORGANOMETALLIC CHEMISTRY

## Lithium Technology

- Substitute for Commercial Lithium Reagents
- Major Cost Reduction
- Higher Yields and Selectivity
- Tailor-made Applications

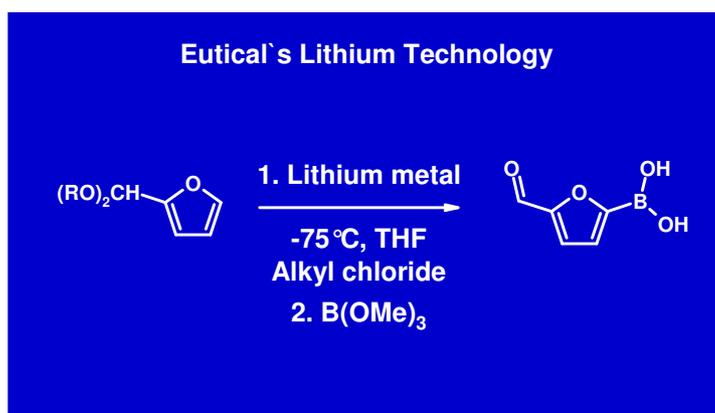
### Euticals's Lithium Technology

Euticals has developed a new technology for lithiation that allows for the general substitution of commercially available butyl lithium, other alkyl lithiums or lithium amides with lithium metal. The traditional lithiation reagents are characterized by their difficulty in handling and use, higher price and in some cases low selectivity.

Euticals lithium technology consists of two different chemical approaches:

### Substitution of Aromatic Chlorine by Lithium:

These methods have been developed to a level where almost quantitative yield and selectivity can be achieved. As these reactions are often performed under cryogenic conditions, this technology tolerates a wide range of functional groups, in some instances even labile groups like CN, CO<sub>2</sub>H or CO<sub>2</sub>R.



### In Situ Metallation with Lithium Metal:

Almost all reactions formerly run using butyl lithium, LDA or other commercially available reagents can be conducted in a very effective manner using this newly developed method. The *in situ* generation of an organometallic base by addition of an alkyl chloride to a mixture of substrate and lithium metal, in a suitable solvent, has several unique advantages. Besides economic considerations, the method allows a tailoring of the reaction conditions by using numerous kinds of alkyl chlorides. These lithium technologies have been developed to a very high level of performance. In almost all of the applications evaluated so far, a significant increase in yields (sometimes approaching 100%) and most often higher product purities have been found. As a general comment, handling of lithium metal in etheral solvents bears significant risks, as this alkali metal can react vigorously with the solvent. As a result of having the necessary cryogenic equipment and extensive process development and upscaling work done, Euticals is able to safely work with these technologies even on production volume of up to 13 m<sup>3</sup> at temperatures between -100°C and up to 0°C and under cGMP and non-cGMP conditions.

### General Substitution method for n-Butyllithium

