TDC Part I
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Inorganic Chemistry

Department of Chemistry

L.S COLLEGE MUZAFFARPUR

B. R. A. BIHAR UNIVERSITY

Dr. Priyanka

TOPIC:- ORGANOLITHIUM REAGENT

Organolithium reagent

Organolithium reagents are organometallic compounds that contain carbon – lithium bonds. They are important reagents in organic synthesis, and are frequently used to transfer the organic group or the lithium atom to the substrates in synthetic steps, through nucleophilic addition or simple deprotonation

Organolithium reagents are used in industry as an initiator for anionic polymerization, which leads to the production of various elastomers. They have also been applied in asymmetric synthesis in the pharmaceutical industry.

Due to the large difference in electronegativity between the carbon atom and the lithium atom, the C-Li bond is highly ionic. This extremely polar nature of the C-Li bond makes organolithium reagents good nucleophiles and strong bases.These reagents are highly reactive, sometimespyrophoric, and should be handled with extreme caution.

chemists found that in comparison with Grignard reagents, organolithium reagents can often perform the same reactions with increased rates and higher yields, such as in the case of metalation.

Since then, organolithium reagents have surpassed Grignard reagents in usage.

Structure:

Although simple alkyllithium species are often represented as monomer RLi, they exist as aggregates (oligomers) or polymers. Their structures depend on the nature of organic substituent and the presence of other ligands.

Nature of carbon-lithium bond

A simplistic look at the large difference in electronegativity suggests the C-Li bond to be highly ionic.[Certain organolithium compounds possess properties such as solubility in nonpolar solvents that complicate the issue.

In allyl lithium compounds, the lithium cation coordinates to the face of the carbon π bond in an η-3 fashion instead of a localized, carbanionic center, thus, allyllithiums are often less aggregated than alkyllithiums.

In aryllithium complexes, the lithium cation coordinates to a single carbanion center through a Li-C σ type bond.

Solid state structure

Like other species consisting of polar subunits, organolithium species aggregate.

A basic building block toward constructing more complex structures is a carbanionic center interacting with a Li_3 triangle in an η- $_3$fashion.

In simple alkyllithium reagents, these triangles aggregate to form tetrahedron or octahedron structures. For example, methyllithium, ethyllithium and *tert*-butyllithium all exist in the tetramer $[RLi]_4$

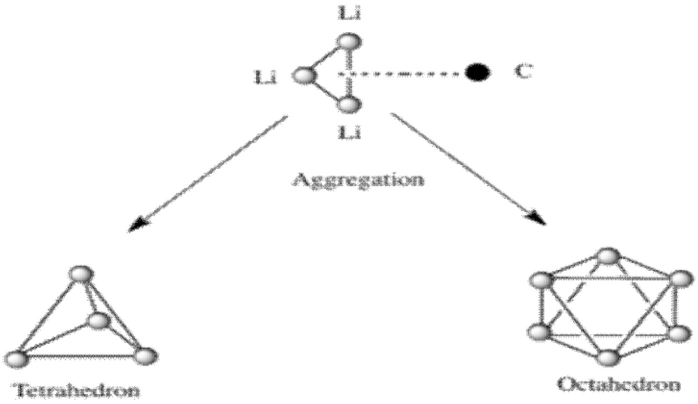


Figure 4: Tetrahedron and octrahedron metal cores formed by aggregation of the Li_3 triangle carbanion coordinate complex.

Another class of alkyllithium adopts hexameric structures, such as *n*-butyllithium, isopropyllithium, and cyclohexanyllithium. Common lithium amides, e.g. lithium bis(trimethylsilyl)amide, and lithium diisopropylamide are also subject to aggregation. Lithium amides adopt polymeric-ladder type structures in non- coordinating solvent in the solid state, and they generally exist as dimers in ethereal solvents.

Another important class of reagents is silyllithiums, extensively used in the synthesis of organometallic complexes and polysilanedendrimers.

In the solid state, most silyllithiums tend to form monomeric structures coordinated with solvent molecules such as THF, and only a few silyllithiums have been characterized as higher aggregates.

Reactivity and Applications

The C-Li bond in organolithium reagents is highly polarized. As a result, the carbon assumes most of the electron density in the bond and resembles a carbanion. Thus, organolithium reagents are strongly basic and nucleophilic.

Organolithium reagent as nucleophile

Carbolithiation reactions

As nucleophiles, organolithium reagents undergo carbolithiation reactions, whereby the carbon-lithium bond adds across a carbon-carbon double or triplebond, forming new organolithium species. This reaction is the most widely employed reaction of organolithium compounds.

Addition to carbonyl compounds

Nucleophilic organolithium reagents can add to electrophilic carbonyl double bonds to form carbon-carbon bonds. They can react with aldehydes and ketones to produce alcohols.

Organolithium reagents are also superior to Grignard reagents in their ability to react with carboxylic acids to form ketones.

A more common way to synthesize ketones is through the addition of organolithium reagents to Weinreb amides (N-methoxy-N-methyl amides). This reaction provides ketones when the organolithium reagents is used in excess

Organolithium reagents can also react with carbon dioxide to form carboxylic acids.

S_N2 type reactions

Organolithium reagents can serve as nucleophiles and carry out S_N2 type reactions with alkyl or allylic halides

Although they are considered more reactive than Grignards reactions in alkylation, their use is still limited due to competing side reactions such as radical reactions or metal-halogen exchange.

Organolithium reagents can also carry out nucleophilic attacks with epoxides to form alcohols.

Organolithium reagent as base

Organolithium reagents provide a wide range of basicity. *tert*-Butyllithium, with three weakly electron donating alkyl groups, is the strongest base commercially available (pKa = 53).

Some commonly used lithium bases are alkyllithium species such as *n*-butyllithium and lithium dialkylamides ($LiNR_2$).

Metalation

Metalation with organolithium reagents, also known as lithiation or lithium-hydrogen exchange, is achieved when a basic organolithium species, most commonly an alkyllithium, abstracts a proton and forms a new organolithium species.

$R\text{-}H + R'Li \rightarrow RLi + R'H$

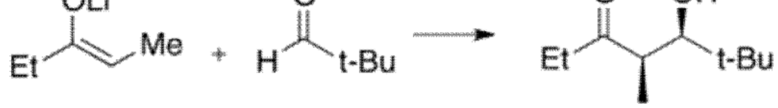
Common metalation reagents are often butyllithiums. *tert*-Butyllithium and *sec*-butyllithium are generally more reactive and have better selectivity than *n*-butyllithium Metalation is a common way of preparing versatile organolithium reagents.

Superbase

Addition of potassium alkoxide to alkyllithium greatly increases the basicity of organolithium species.The most common “superbase” can be formed by addition of KOtBu to butyllithium, often abbreviated as “LiCKOR”reagents. These “superbases” are highly reactive and often stereoselective reagents.

Lithium enolates

Lithium enolates are formed through deprotonation of a proton α to the carbonyl group by an organolithium species. Lithium enolates are widely used as nucleophiles in carbon-carbon bond formation reactions such as aldol condensation



and alkylation. They are also an important intermediate in the formation of silyl enol ether.

Lithium-Halogen exchange

Lithium halogen exchange is a metathesis reaction between an organohalide and organolithium species.

$$\text{R-Li} + \text{R'-X} \longrightarrow \text{R-X} + \text{R'-Li}$$

The rate of lithium halogen exchange is extremely fast. It is usually faster than nucleophilic addition and can sometimes exceed the rate of proton transfer.

Lithium-halogen exchange is very useful in preparing new organolithium reagents. The trend of exchange rates usually follows I > Br> Cl, while alkyl- and arylfluoride are generally not reactive toward organolithium reagents. Lithium halogen exchange is kinetically controlled.

Transmetalation

Organolithium reagents are often used to prepare other organometallic compounds via transmetalation. Organocopper, organotin, organosilicon, organoboron, organophosphorus, organocerium and organosulfur compounds are frequently prepared by reacting organolithium reagents with appropriate electrophiles.

$$\text{R-M} + n\text{-BuLi} \longrightarrow \text{R-Li} + n\text{-BuM}$$

Organolithium can also be used in to prepare organozinc compounds through transmetalation with zinc salts.

Preparation

Most simple alkyllithium reagents, and common lithium amides are commercially available in a variety of solvents and concentrations.

Reaction with lithium metal

Reduction of alkyl halide with metallic lithium can afford simple alkyl and aryl organolithium reagents.

$$\text{R-X} + 2\text{Li} \longrightarrow \text{R-Li} + \text{Li-X}$$

Industrial preparation of organolithium reagents is achieved using this method by treating the alkyl chloride with metal lithium containing 0.5-2% sodium.