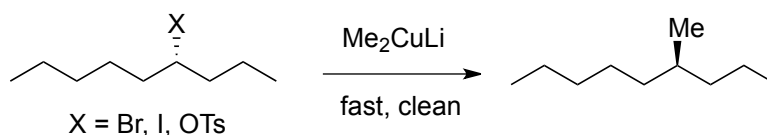


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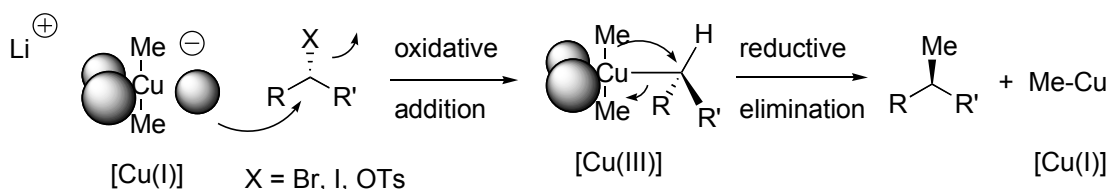
Topics Discussed on Nov. 2

Poor reactivity of organolithium or organomagnesium (Grignard) reagents in S_N2 reactions

Cuprates as carriers of very nucleophilic (= high carbon affinity) carbanions that are highly reactive in S_N2 reaction, e.g.:



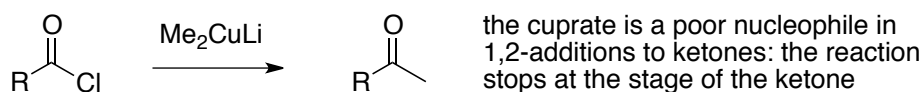
Possible mechanism of S_N2 reactions with cuprates:



Principle: cuprates are the reagents of choice in 1,4-additions and in S_N2 reactions; organolithiums and Grignards are the reagents of choice in carbonyl 1,2-addition reactions.

Poor reactivity of cuprates in nucleophilic 1,2-addition to carbonyls

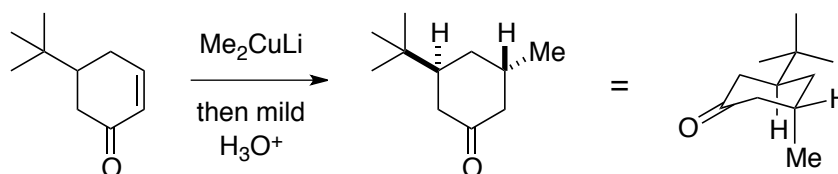
Ability of cuprates to convert acid chlorides into ketones (difficult / impossible to do with R-Li or R-MgX reagents) as a consequence of poor reactivity in 1,2-C=O addition:



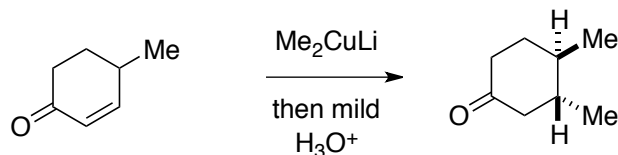
Stereochemical aspects of cuprate addition to cyclohexenones

Principle: the same effects that govern the stereochemical course of the alkylation of cyclohexanone enolates also control the stereochemical course of 1,4-addition of cuprates to cyclohexenones:

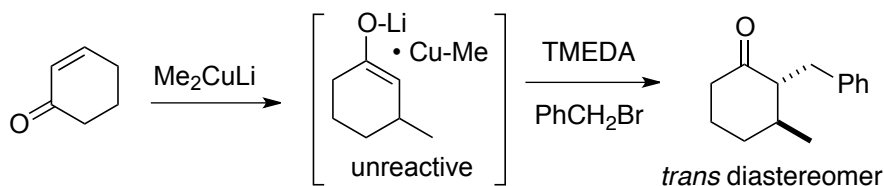
- Preferential axial attack in conformationally rigid cyclohexenones via a chair-like trans. state:



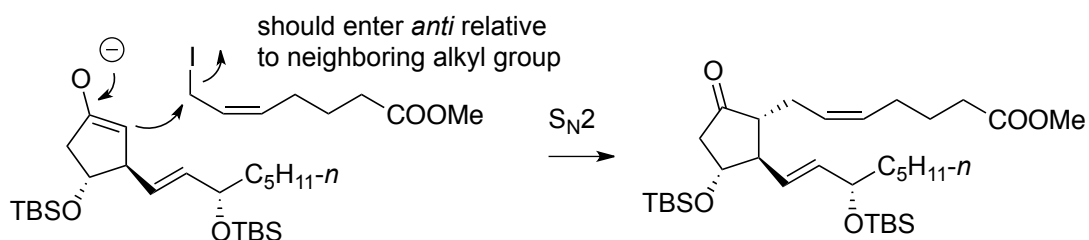
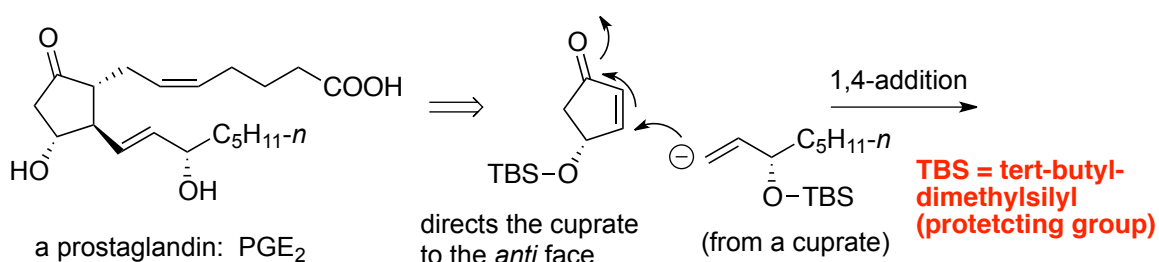
- Preferential attack *anti* to small alkyls in conformationally flexible cyclohexanone enolates:



and of course (notes of Oct 21) . . .



Application of cuprate technology in the chemical synthesis of biologically relevant substances: prostaglandins (important hormones):



Reminder: a dialkyl cuprate (e.g., lithium dimethyl cuprate) transfers **only one** of its two alkyl groups, because of the poor reactivity of simple monoalkyl copper(I) species

Problem: implementation of the above strategy requires a cuprate in which two vinyl "carbanions" are bound to the metal, but only one of them is usable. This is wasteful, because the carbanionic segment is itself the product of chemical synthesis

Requirement for technology that avoids the wasteful loss of one of the two alkyl ligands of a cuprate