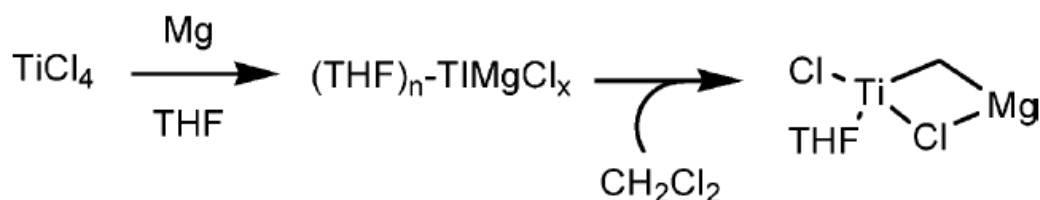


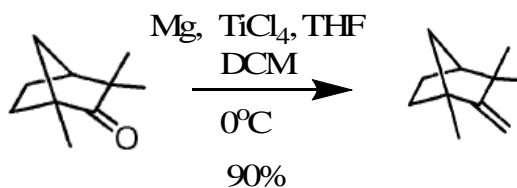
Dichloromethylation activation: Methylenation and cyclopropanation.

Methylenations and cyclopropanations usually use expensive or dangerous reagents such as CH_2Br_2 or diazomethane. Dichloromethane has never been reported for metal-based methylenations or cyclopropanations on account of its extreme stability. Insertion into the highly unactivated C-Cl bond has been achieved by the use of bimetallic Mg-TiCl₄ species forming a carbenoid which is ambiphilic in nature yet highly selective.

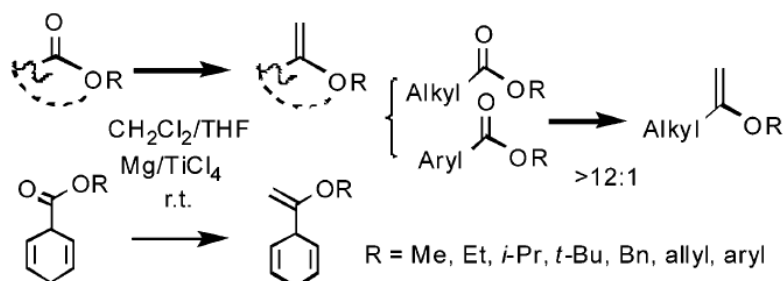


- DCM is inert to Mg and low-valent Ti additions so the bimetallic nature of the species is crucial.
- the addition of THF is very important for the carbenoid's reactivity, yields were poor with other electron donors.

Methylenation of ketones, aldehydes and esters *via* a nucleophilic Schrock type carbene



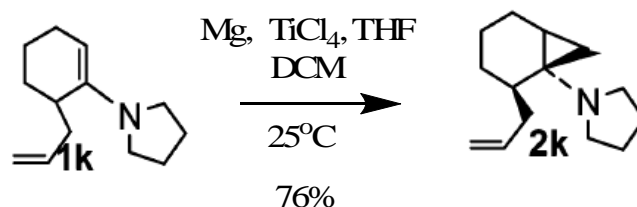
- Methylenation occurs even in very hindered ketones and aldehydes, where Tebbe or Wittig reagents fail.¹
- Reaction occurs with an excess of TiCl₄ and Mg (typically 2eq and 8eq)
- Ketones and aldehydes can be methylenated in the presence of esters, amides and sulfones at 0°C. However at room temperature esters can be methylenated to give vinyl ethers. A wide range of esters including *tert*-butyl and benzoate are tolerated, as well as aromatic and aliphatic carbonyls.²



Cyclopropanation of enamines *via* an electrophilic Fischer-type carbene

As well as being nucleophilic in nature the Mg-TiCl₄ DCM carbenoid also displays electrophilic properties and will cyclopropanate enamines.³

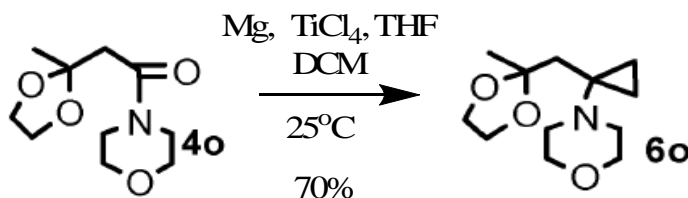
- Usual methods of cyclopropanation of alkenes with *gem*-dibromides promoted by Cu or Cu-Zn fail for enamines.
- The reaction occurs in the presence of catalytic TiCl₄ and an excess of Mg (typically 0.3eq and 10 eq)
- The reaction occurs with good chemo- and stereoselectivity



Cyclopropanation of amides – ambiphilicity in action!

The ambiphilic nature of these carbenoids can be exploited in the cyclopropanation of amides.⁴

- The carbenoid first reacts with the amide in a nucleophilic sense, and then with the enamine in an electrophilic sense.
- The reaction occurs with a sub-stoichiometric amount of TiCl₄ and excess of Mg (typically 0.8 eq and 8 eq)
- The variety of carbenoid species that are possible make the exact mechanism unclear, and a titanacyclopropane complex cannot be ruled out as the active species.
- The reaction is again quite chemoselective and a broad range of functional groups are tolerated



¹ *Org.Lett.* **2004**, 6, 4961.

² *Org.Lett.* **2004**, 6, 4965

³ *Org.Lett.* **2006**, 8, 2261

⁴ *Org.Lett.* **2006**, 8, 2265