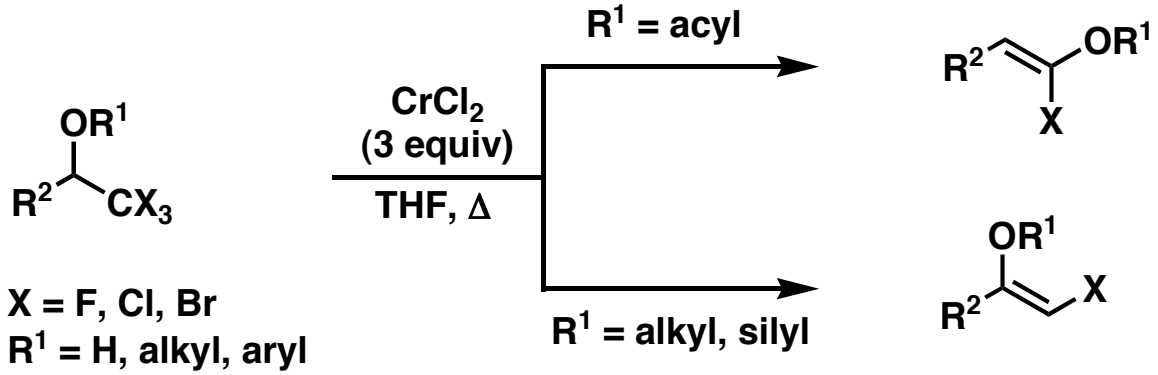
Stereoselective Transformations of Trihalomethylcarbinols Induced by Chromous Chloride



Bejot, R. Tisserand, S.; Reddy, L. M.; Barma, D. K.; Baati, R.; Falck, J. R.; Mioskowski, C.
Angew. Chem., Int. Ed. Engl. **2005**, *44*, 2008

Michel Grenon
April 2nd, 2005

Presentation Outline

- ***Some Aspects of Reactions Involving $CrCl_2$***

  Formation of organochromium(III) reagents

  Preparation of $CrCl_2$

  Reactions catalytic in CrX_2

- ***Earlier Work Performed by Falck and Mioskowski***

- ***Stereoselective Transformations of Trihalomethylcarbinols Induced by $CrCl_2$***

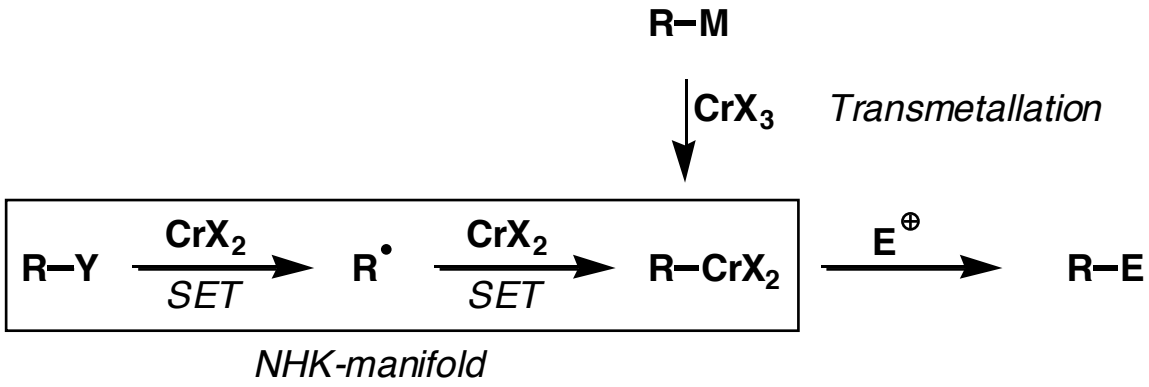
  Synthesis of (Z)-α-haloenol esters

  Synthesis of (Z)-β-chloroenol ethers

  Proposed mechanism for the rearrangement

Carbon-Carbon Bond Formations Involving Organochromium(III) Reagents

Reactivity of $CrCl_2$ in the preparation of organochromium (III) reagents



$CrCl_2$

Air-sensitive, hygroscopic pale gray powder (greenish lots may result in poor results)

Freshly prepared by reduction of $CrCl_3$ under a variety of conditions ($LiAlH_4$, Zn, Na amalgam, Mn, $LiBEt_3H$, Cr). Consider the acidity of the admixed salts produced when choosing.

Often use in large excess

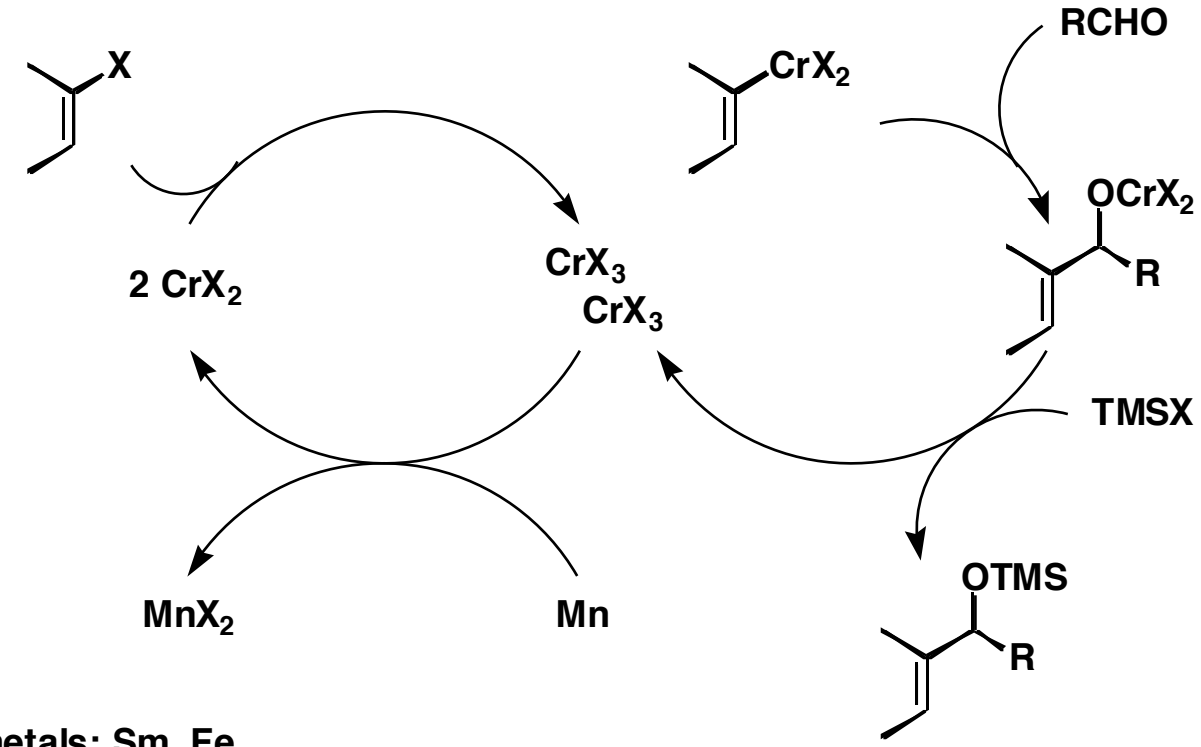
Propensity for oxidative insertion can be enhanced by donor ligands (TMEDA)

Fürstner, A. *Chem. Rev.* **1999**, *99*, 991

Carbon-Carbon Bond Formations Involving Organochromium(III) Reagents

Chromiun-catalyzed processes

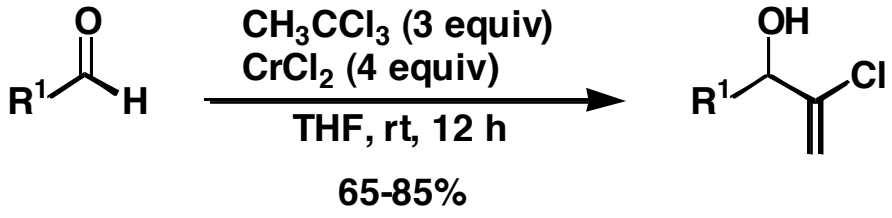
The formation of a O–Cr(III) bond serves as a thermodynamic driving force, that can be used to compensate for strain energy build up in the product being formed. It is essential to break the O–Cr(III) bond and reoxidize the chromium to have an effective catalytic system

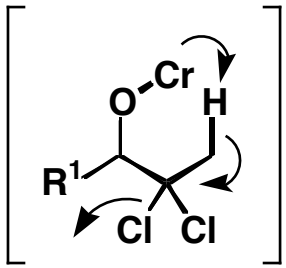


Other metals: Sm, Fe

Fürstner, A. *Chem. Rev.* **1999**, *99*, 991

α-Chlorovinylation: Synthesis of 2-Chloropropenyl and Propargyl Alcohols

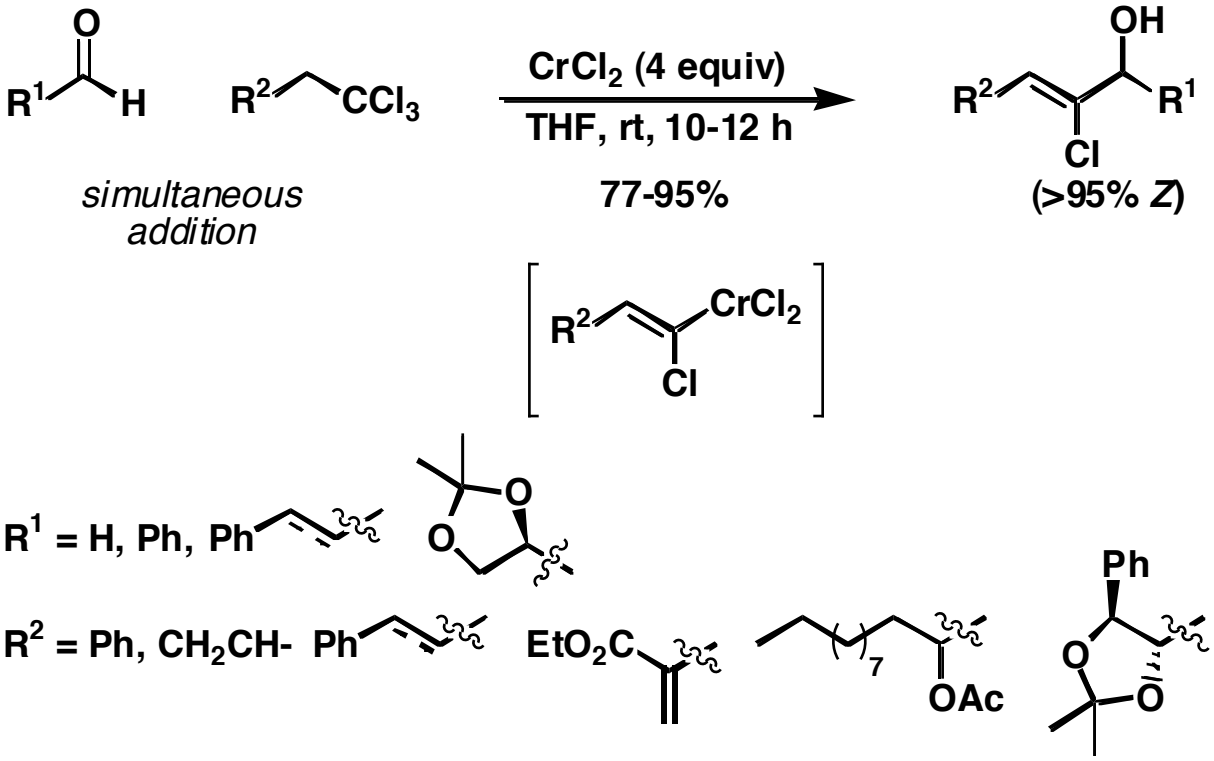




- Works with R^1 = alkyl, cycloalkyl, α,β-unsaturated, aromatic (electron-rich and deficient)
- Comparable results were obtained using a catalytic amount of $CrCl_2$ (70 mol%) with Mn powder (1.7 equiv) and TMSCl (2.4 equiv)
- Treatment with LDA at -78 °C affords the propargyl alcohols (89-96%)

Falck, J. R.; Barma, D. K.; Mioskowski, C.; Schlama, T. *Tetrahedron Lett.* **1999**, *40*, 2091

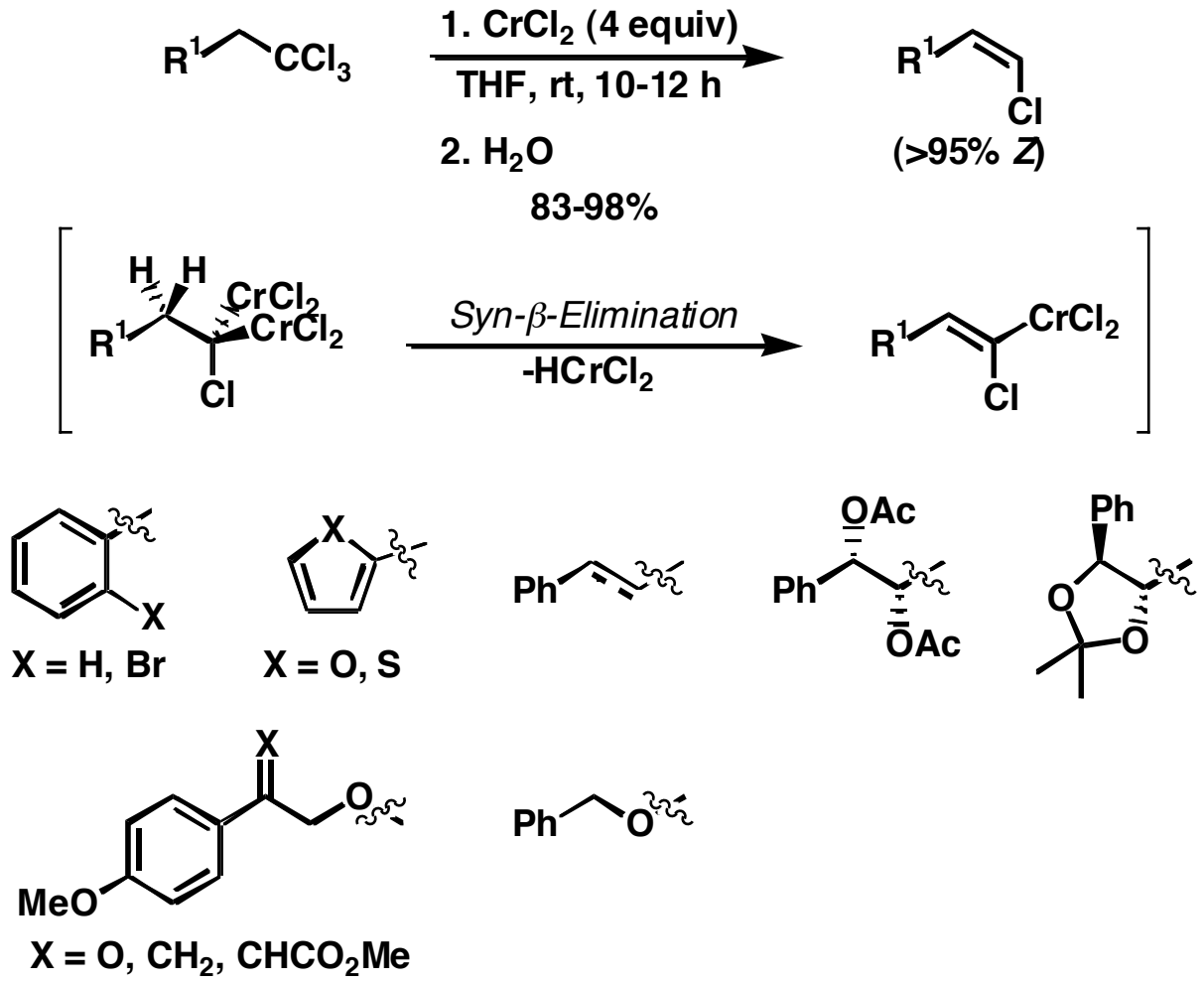
Chromium Vinylidene Carbenoids: Stereospecific Synthesis of (Z)-2-Chloroalk-2-enols



- **Barbier-type conditions can be used**
- **Catalytic system with Mn powder and TMSCl proved disappointing**
- **Addition to ketones were sluggish, even at 75-80 °C (10-15% yields)**

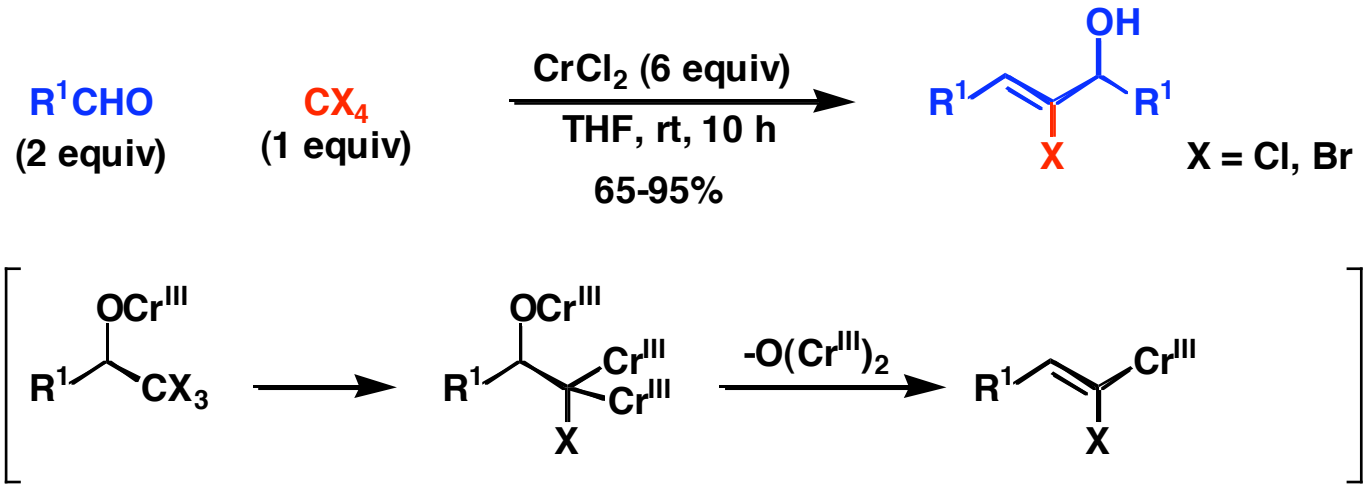
Barma, D. K.; Baati, R.; Valleix, A.; Mioskowski, C.; Falck, J. R. *Org. Lett.* **2001**, *3*, 4237

Stereospecific Synthesis of (Z)-1-Chloro-1-alkenes and (Z)-1-Chloro-2-alkoxy-1-alkenes



Baati, R.; Barma, D. K.; Krishna, U. M.; Mioskowski, C.; Falck, J. R. *Tetrahedron Lett.* **2002**, *43*, 959

Three-component Synthesis of 2-Haloalk-2-(Z)-enols via Tandem Haloalkylidenation/Aldehyde Addition



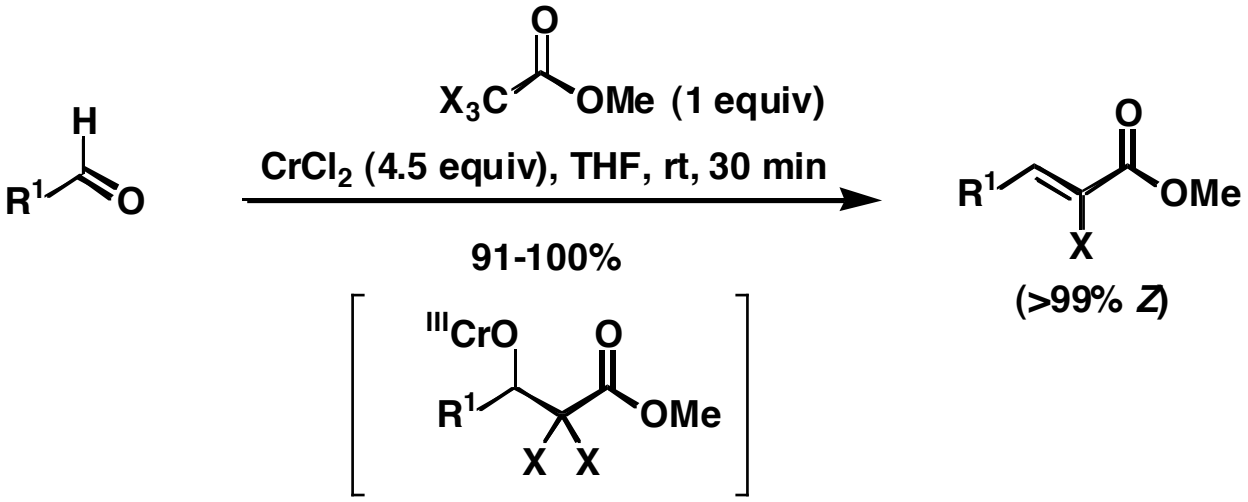
- **A catalytic system using Mn powder to recycle the Cr^{III} proved disappointing**
- **Pre-incubation of CX_4 with $CrCl_2$ optimal for aliphatic aldehydes**
- **Barbier-type conditions used for aromatic aldehydes**

Baati, R.; Barma, K. T.; Falck, J. R.; Mioskowski, C. *Tetrahedron Lett.* **2002**, *43*, 2179

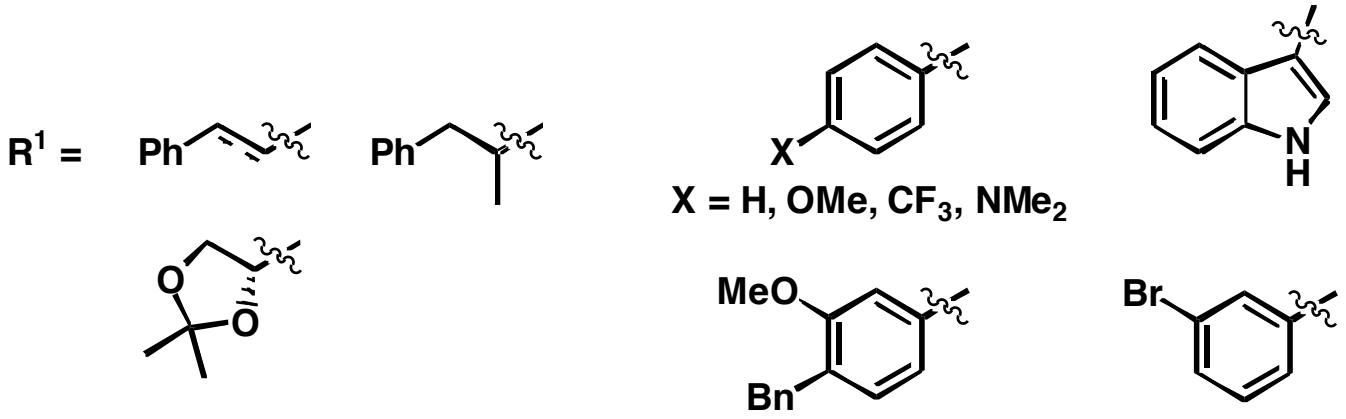
- **A two-step process to prepare similar compounds for which both R^1 groups are different using $HCCl_3$ and a base instead of CX_4 and $CrCl_2$**

Baati, R.; Barma, K. T.; Falck, J. R.; Mioskowski, C. *Tetrahedron Lett.* **2002**, *43*, 2183

Stereoselective Preparation of (Z)-α-Haloacrylates via $CrCl_2$-Mediated Olefination with Trihaloacetates

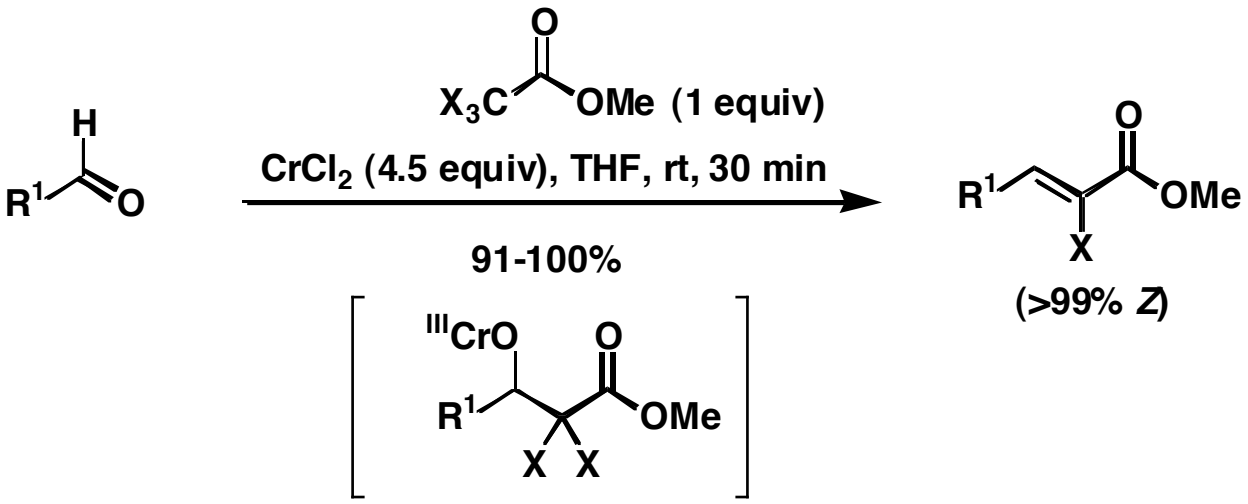


Reformatsky-type adduct



Barma, D. K.; Kundu, A.; Zhang, H.; Mioskowski, C.; Falck, J. R.
J. Am. Chem. Soc. **2003**, *125*, 3218

Stereoselective Preparation of (Z)-α-Haloacrylates via $CrCl_2$-Mediated Olefination with Trihaloacetates

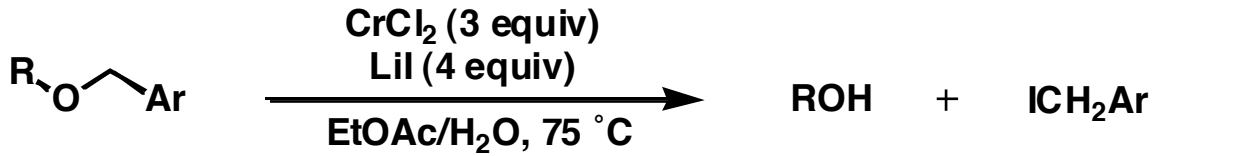


Reformatsky-type adduct

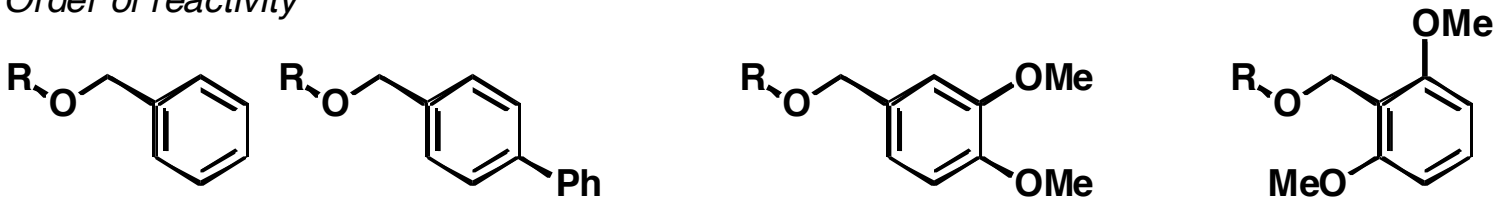
- **To prepare the α-fluoroacrylates, need to use FBr_2CCO_2Et**
- **Can use catalytic amounts of $CrCl_2$ (50 mol%) with Mn powder (4 equiv) and TMSCl (6 equiv)**
- **The dihalohydrins can be isolated under conditions of limiting $CrCl_2$ and at lower temperature (2.5 equiv, 0 ˚C)**

Barma, D. K.; Kundu, A.; Zhang, H.; Mioskowski, C.; Falck, J. R.
J. Am. Chem. Soc. **2003**, *125*, 3218

Differential Cleavage of Arylmethyl Ethers induced by Chromous Chloride

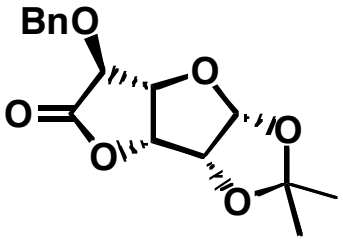


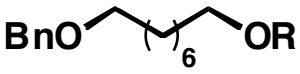
Order of reactivity



less reactive ⟶ *more reactive*

Functional group selectivity



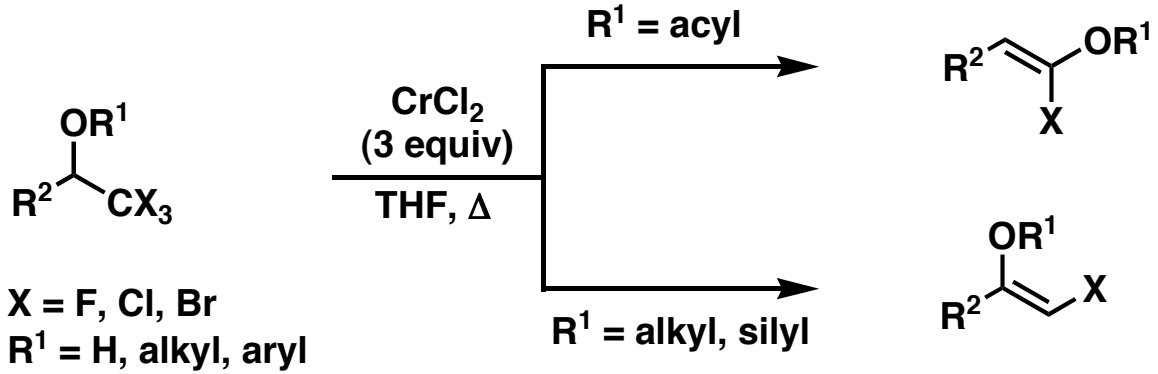


R = Me, THP, PMP, TBDPS **1° and 2° allylic ethers**

▷ No isomerization of *cis*-alkenes

Falck, J. R.; Barma, D. K.; Baati, R.; Mioskowski, C. *Angew. Chem., Int. Ed. Engl.* **2001**, *40*, 1281

Stereoselective Transformations of Trihalomethylcarbinols Induced by Chromous Chloride



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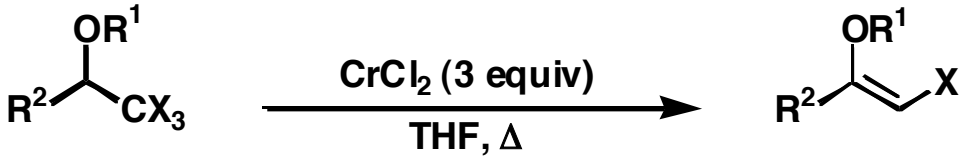
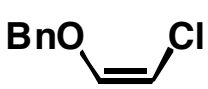
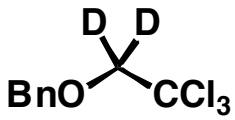
Michel Grenon
April 2nd, 2005

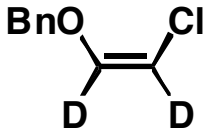
Stereoselective Transformations of Trihalomethylcarbinols induced by Chromous Chloride

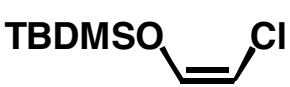
Conversion of Trichloromethylcarbinol ethers into (Z)-α-haloenol ethers

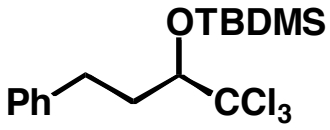


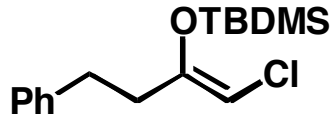


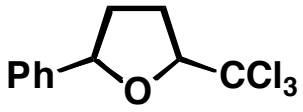


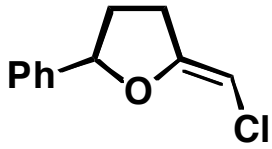












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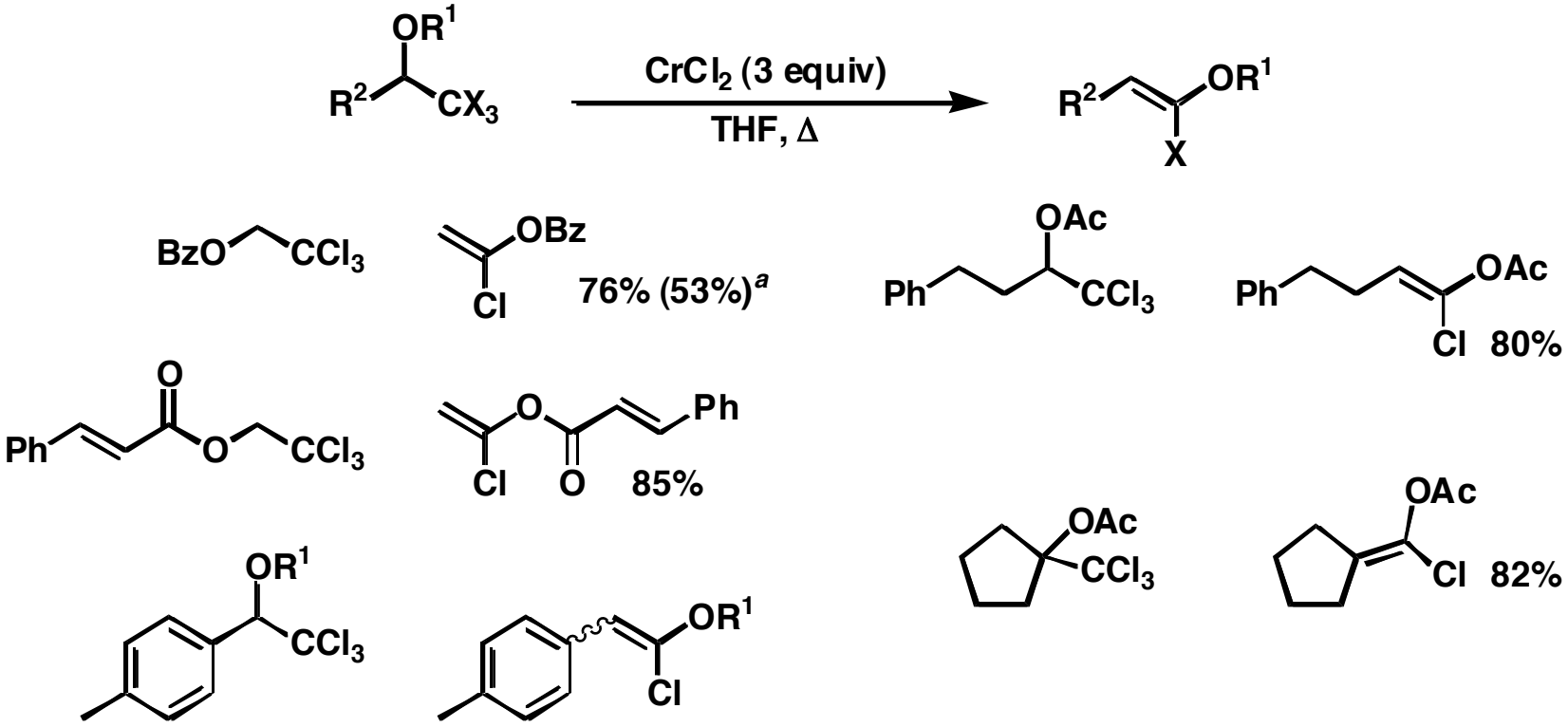
Conversion of Trichloromethylcarbinol esters into (Z)-α-haloenol esters



R^1 = Ac, 75% (87:13)

R^1 = Bz, 84% (78:22)

[a] Catalytic $CrCl_2$, excess Mn powder

Bejot, R. Tisserand, S.; Reddy, L. M.; Barma, D. K.; Baati, R.; Falck, J. R.; Mioskowski, C. *Angew. Chem., Int. Ed. Engl.* **2005**, *44*, 2008

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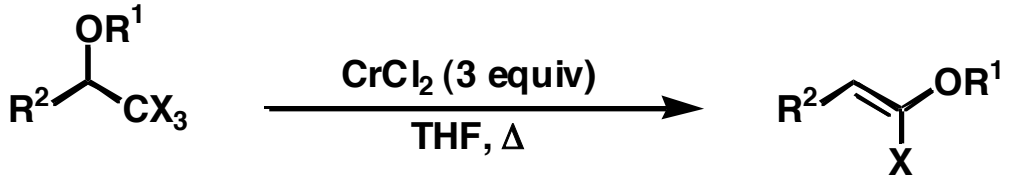
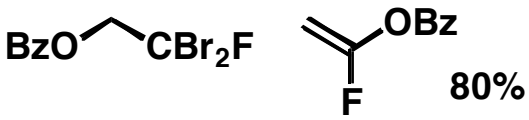
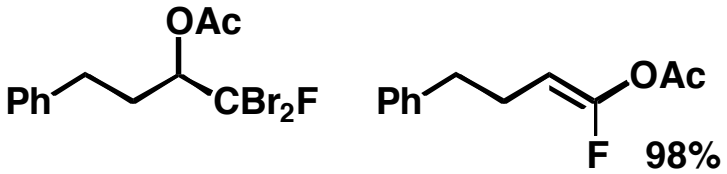
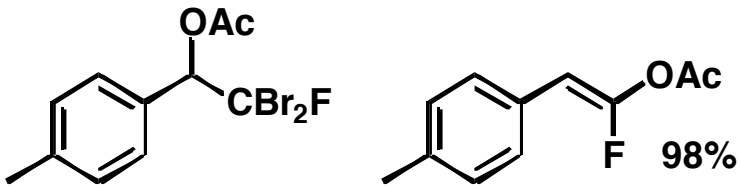
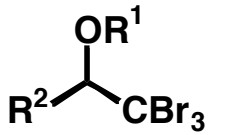










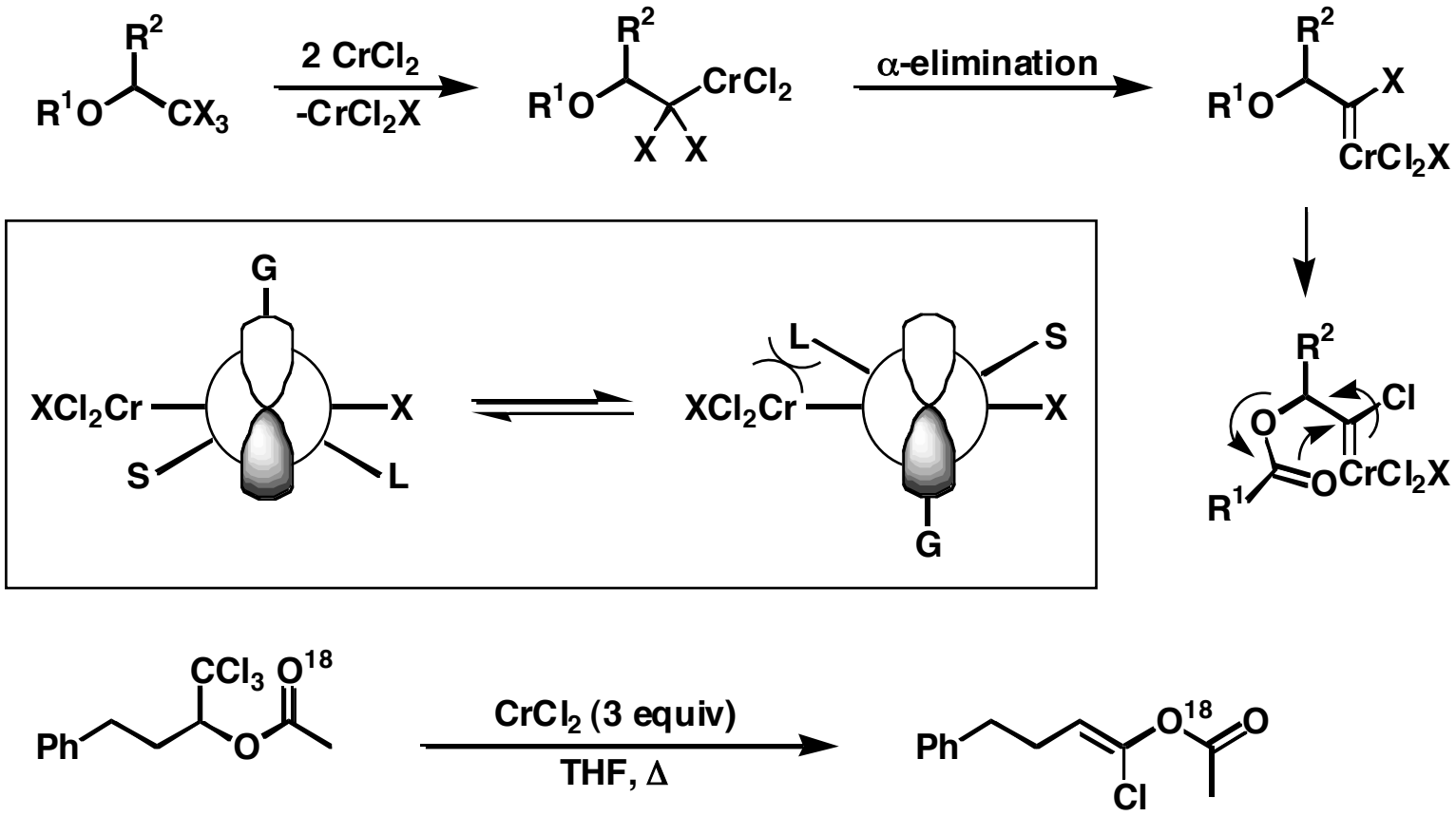
complex mixtures

unreactive

Bejot, R. Tisserand, S.; Reddy, L. M.; Barma, D. K.; Baati, R.; Falck, J. R.; Mioskowski, C. *Angew. Chem., Int. Ed. Engl.* **2005**, *44*, 2008

Stereoselective Transformations of Trihalomethylcarbinols induced by Chromous Chloride

Proposed mechanism for the rearrangement of trichloromethylcarbinol esters and ethers



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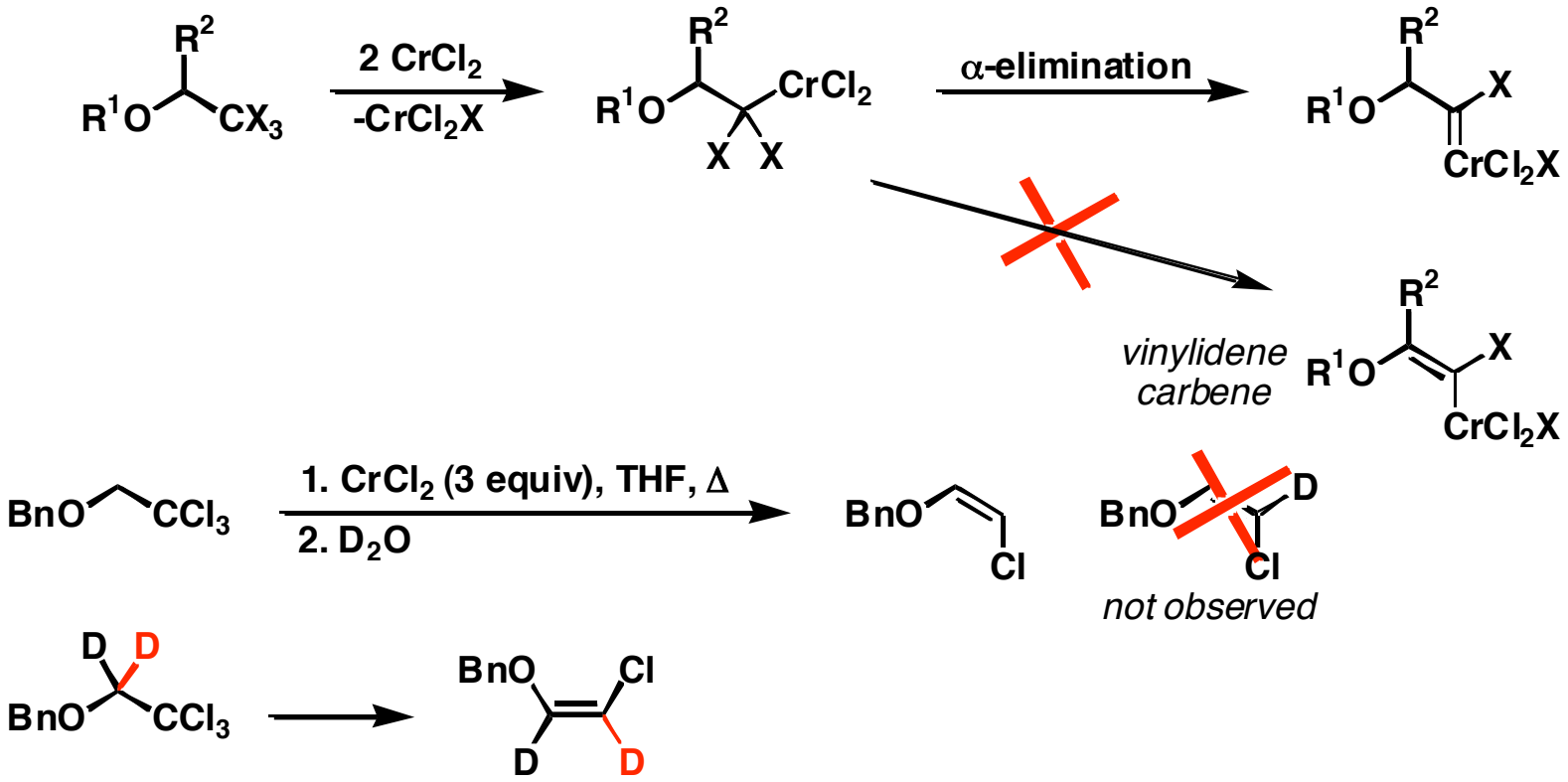

The intermediacy of a chromium vinylidene carbene for other processes has been observed;
Baati, R.; Barma, D. K.; Falck, J. R.; Mioskowski, C. *J. Am. Chem. Soc.* **2001**, *123*, 9196

Bejot, R. Tisserand, S.; Reddy, L. M.; Barma, D. K.; Baati, R.; Falck, J. R.; Mioskowski, C. *Angew. Chem., Int. Ed. Engl.* **2005**, *44*, 2008