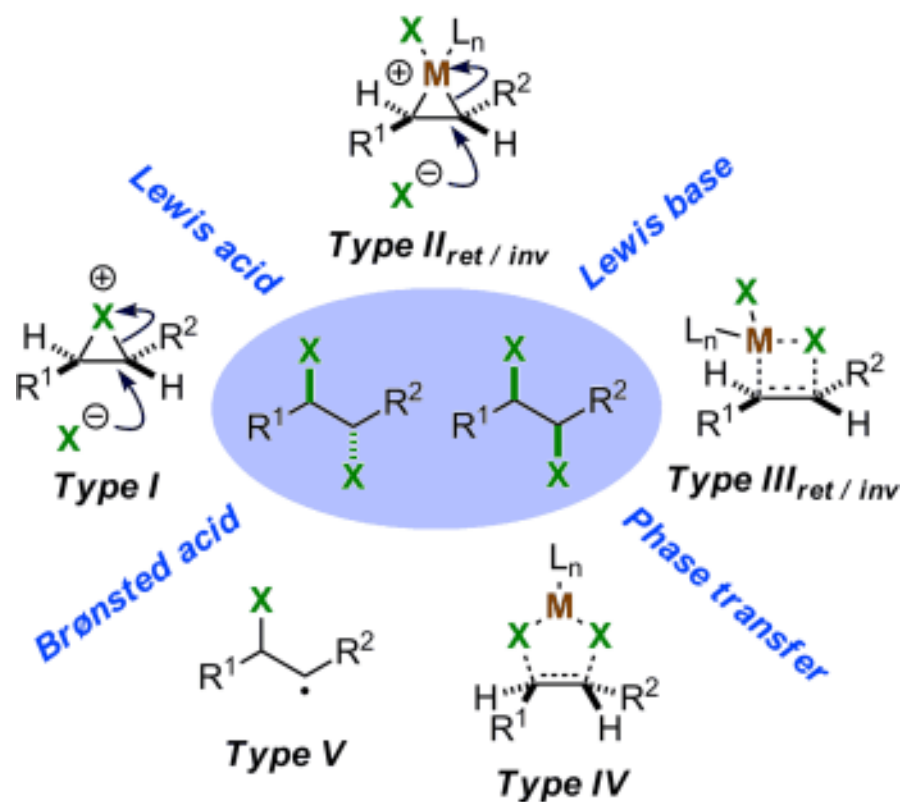


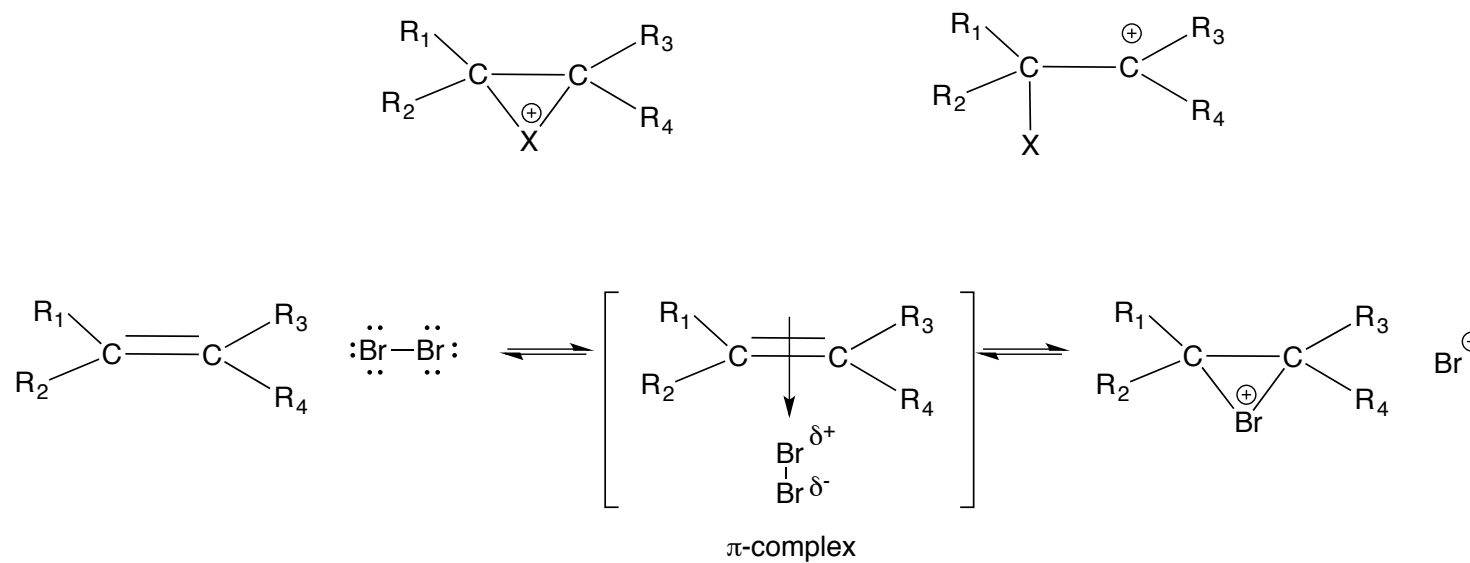
Catalytic, Stereoselective Dihalogenation of Alkenes



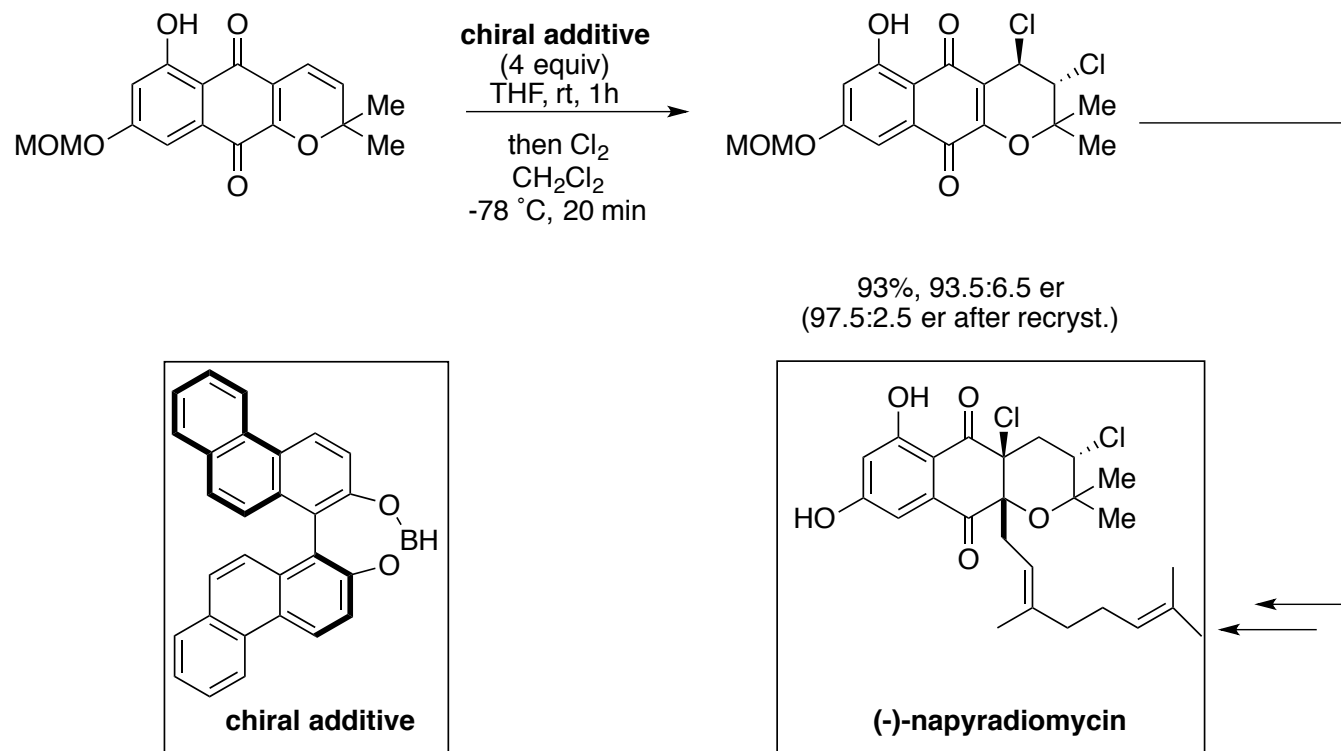
Topic Review
levgeniia Kovalova

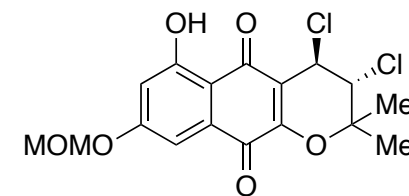
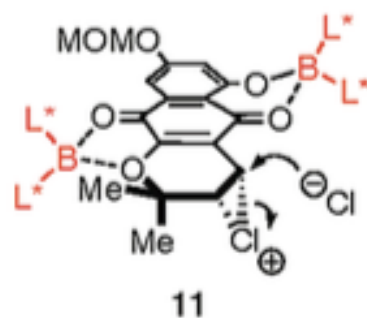
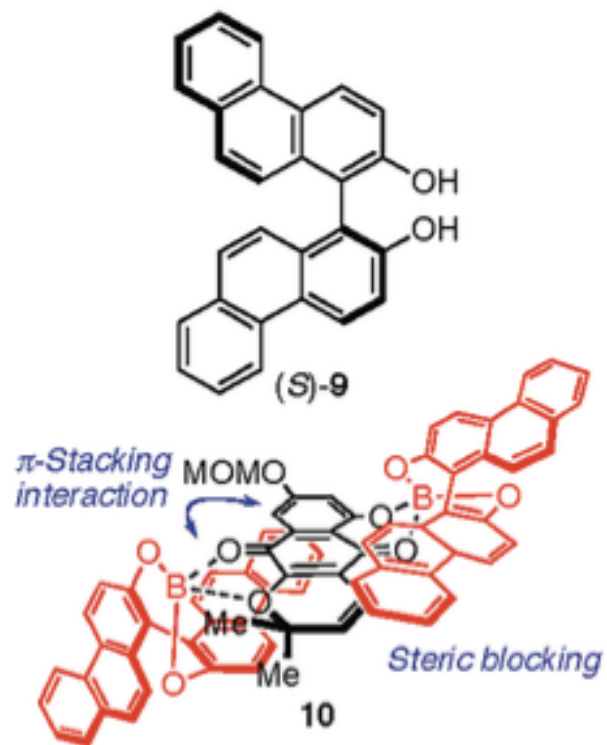
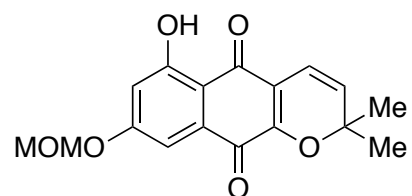
14. 04. 2016

Introduction

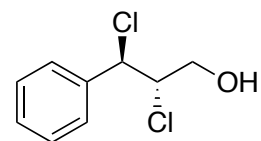
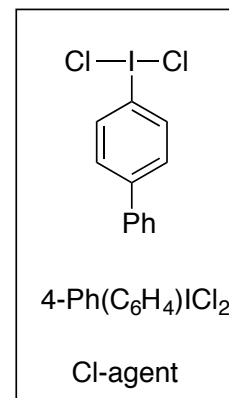
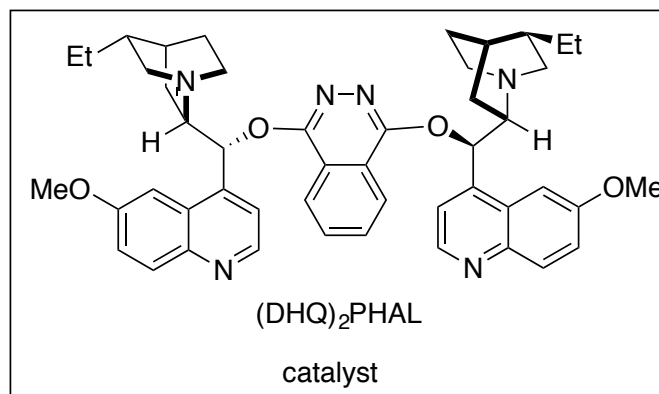
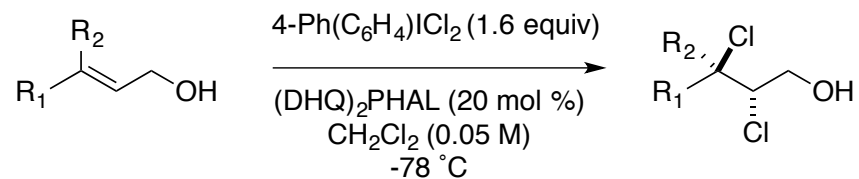


Enantioselective alkene dihalogenation in synthesis of natural product

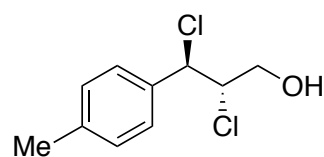




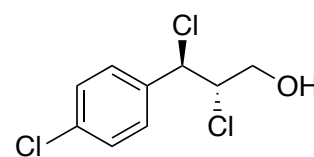
Enantioselective, catalytic alkene dihalogenation



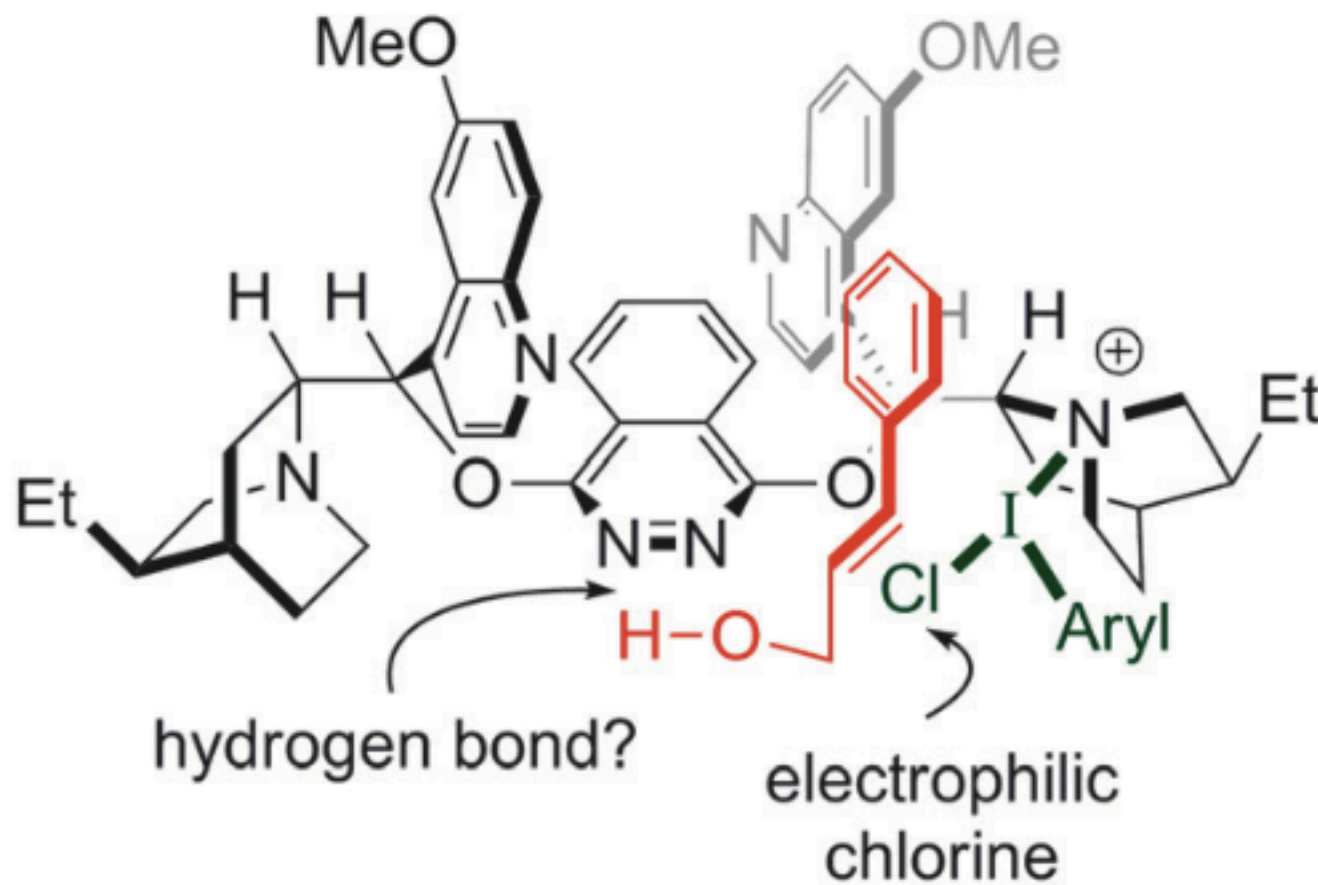
63%, er=90.5:9.5



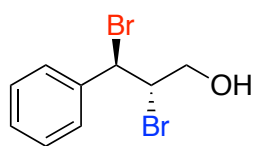
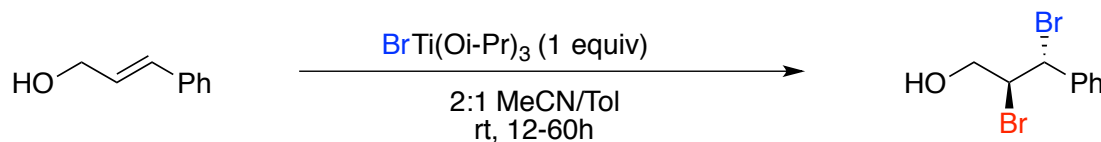
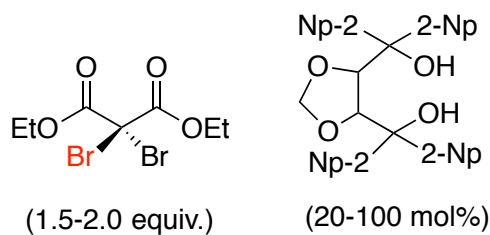
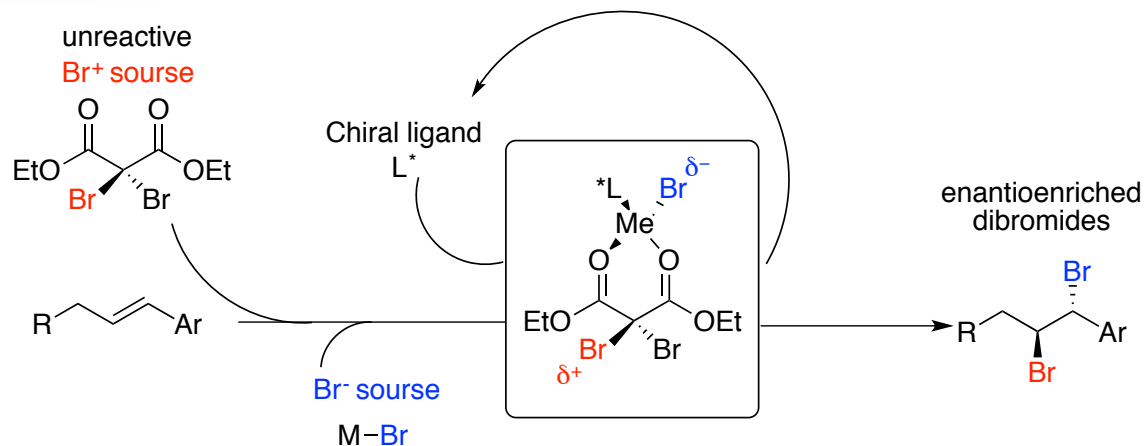
65%, er=72:28



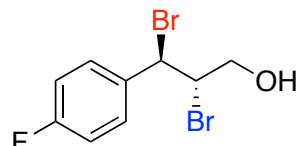
81%, er=85.5:14.5



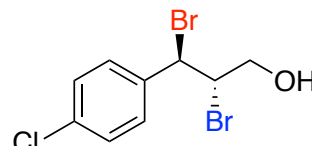
Enantioselective, catalytic alkene dibromination



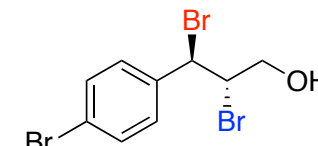
20 mol % of diol: 60%, ee=76%
100 mol % of diol: 63%, ee=86%



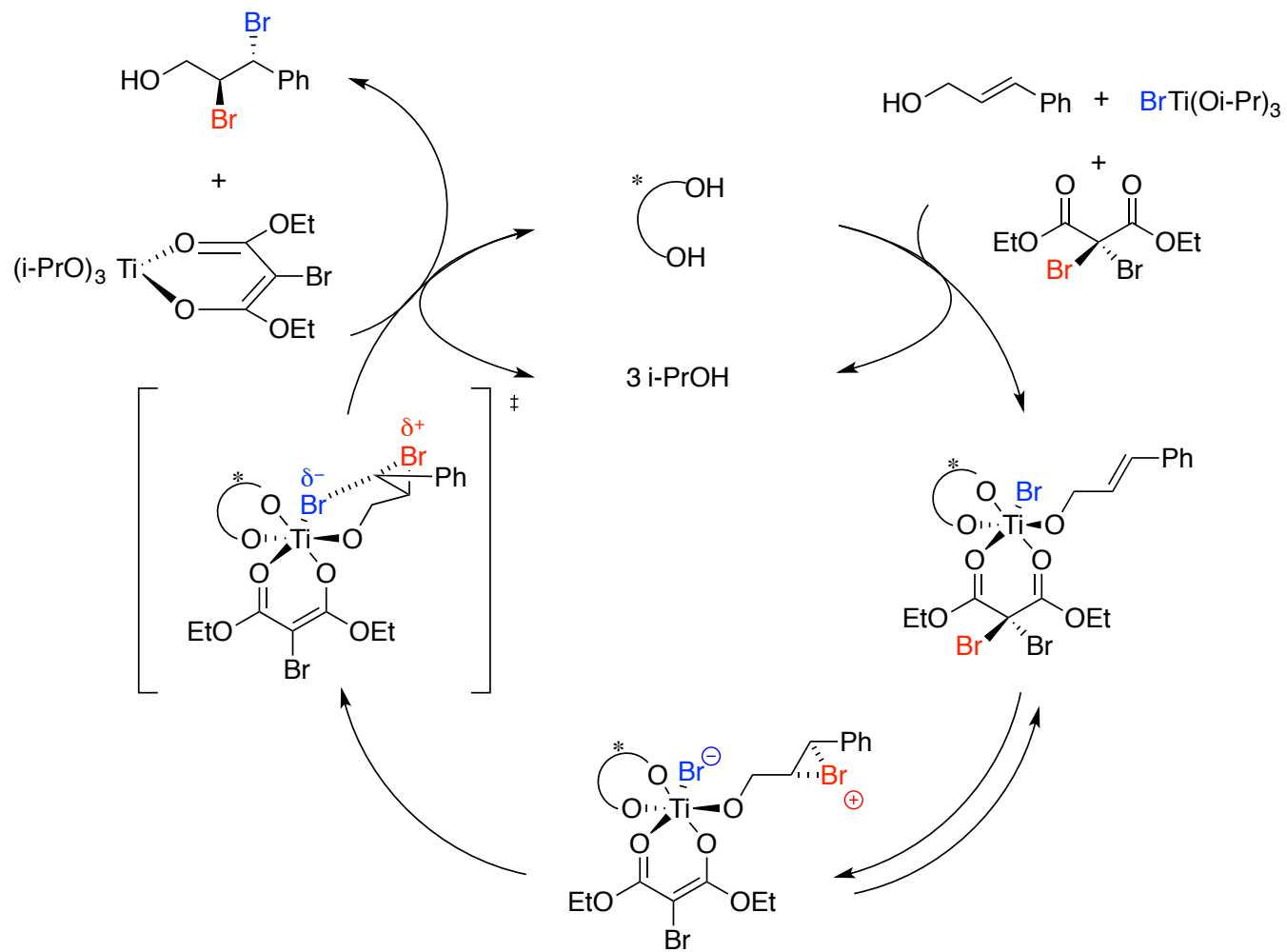
20 mol % of diol: 47%, ee=79%
100 mol % of diol: 65%, ee=88%



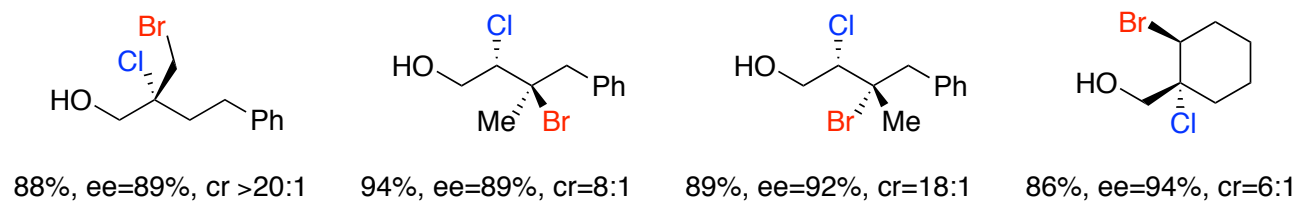
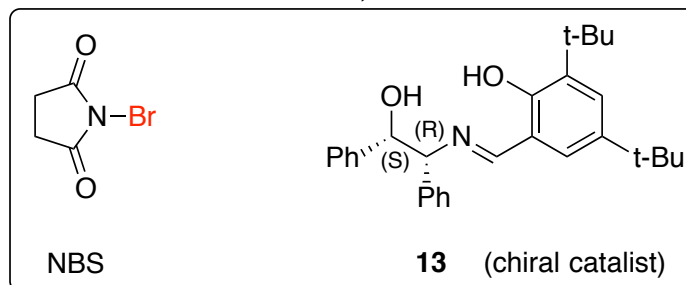
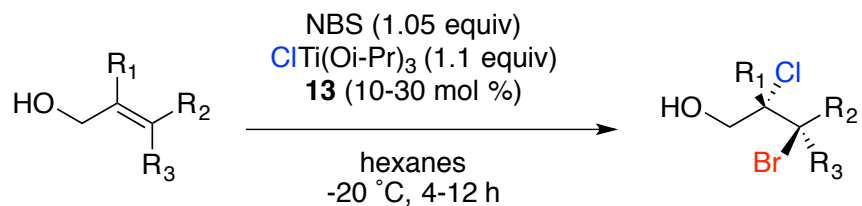
20 mol % of diol: 60%, ee=85%
100 mol % of diol: 64%, ee=90%

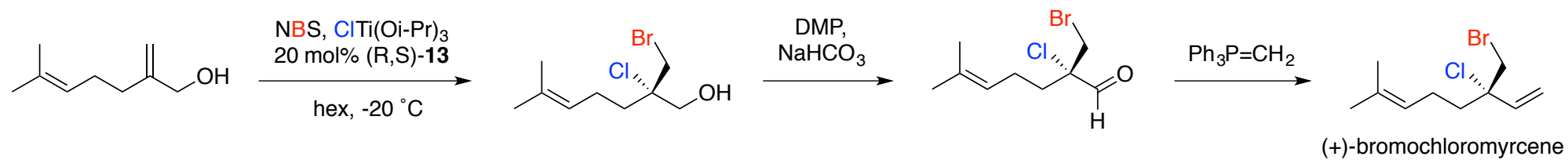
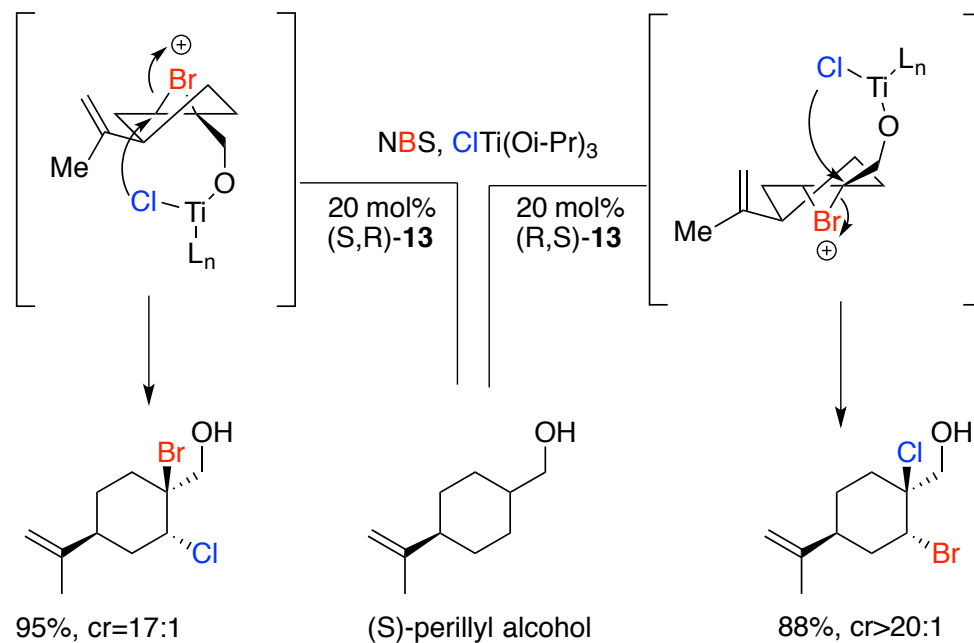


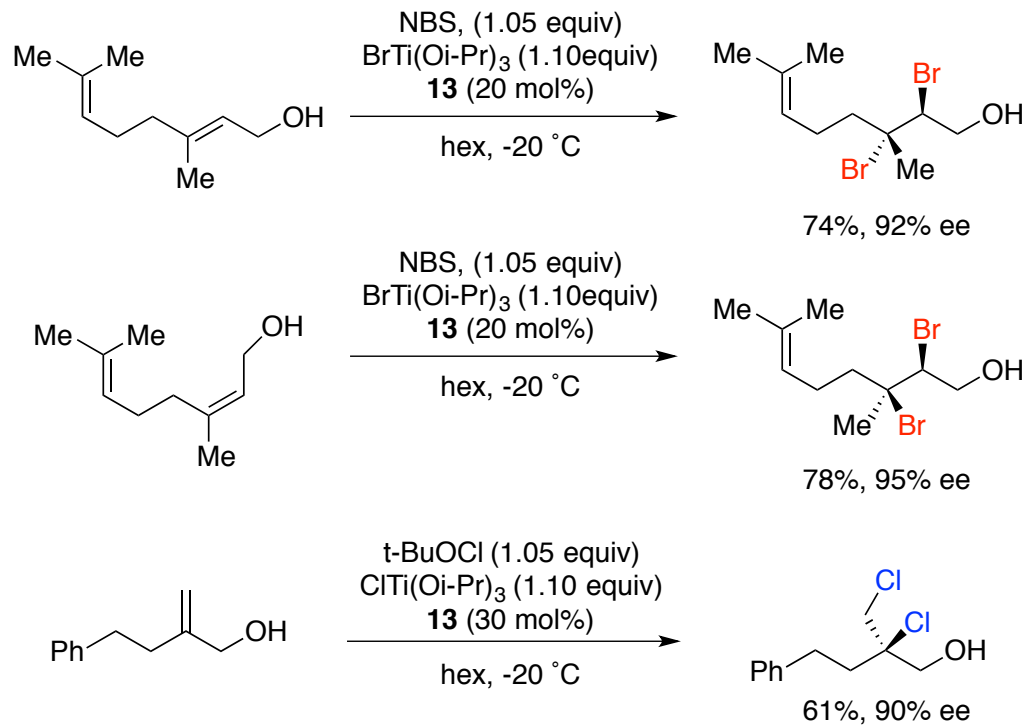
20 mol % of diol: 51%, ee=84%
100 mol % of diol: 64%, ee=90%



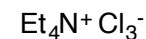
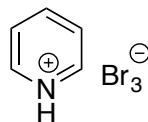
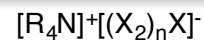
Enantioselective, catalytic alkene chlorobromination



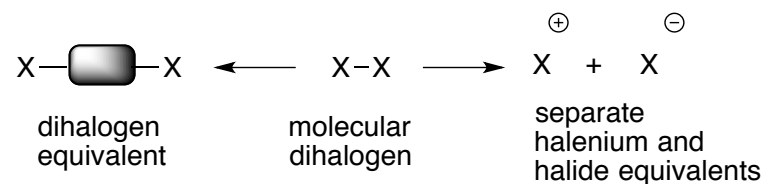
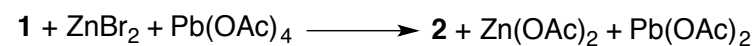
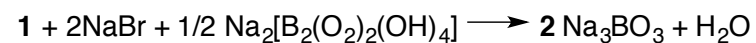
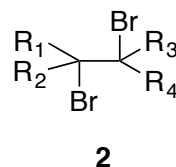
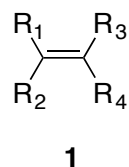




Dihalogenating Reagents

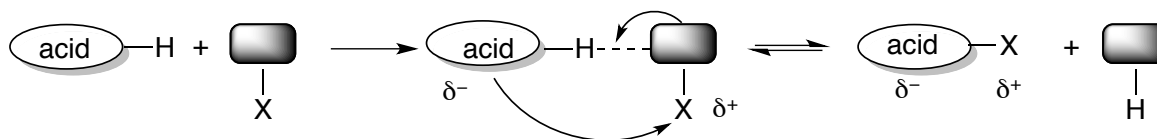


Mioskowski's reagent
slow release of Cl₂ on storage

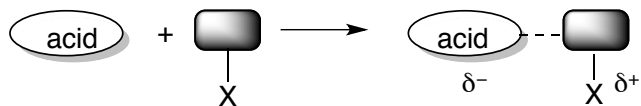


Catalysis problem

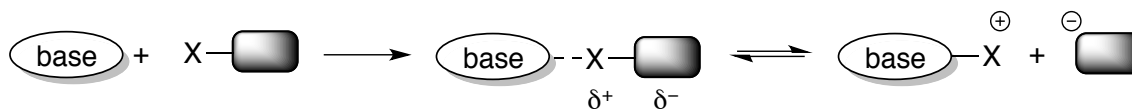
Brønsted acid



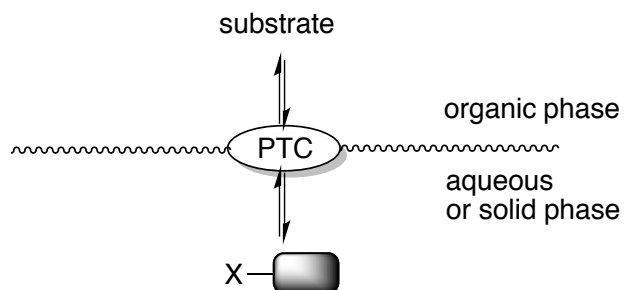
Lewis acid



Lewis base

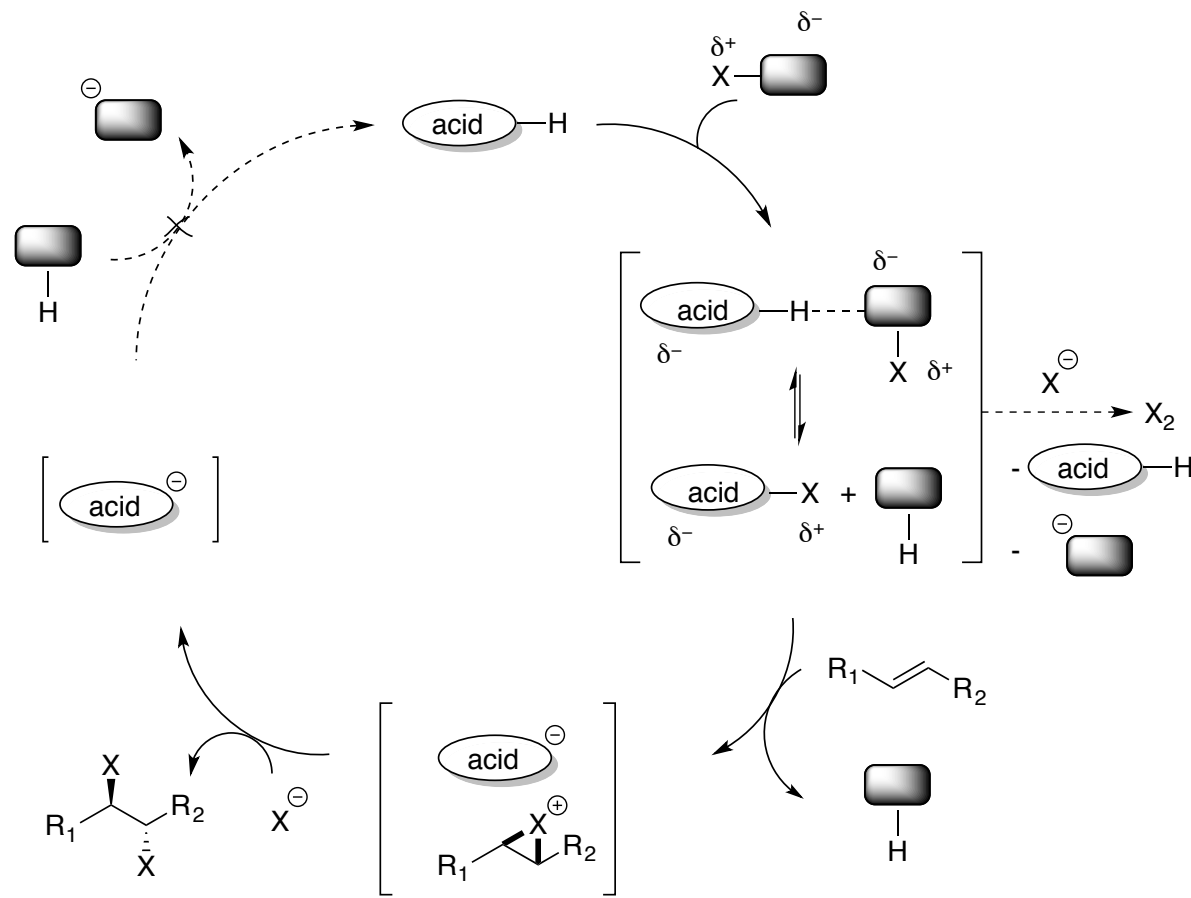


Phase transfer



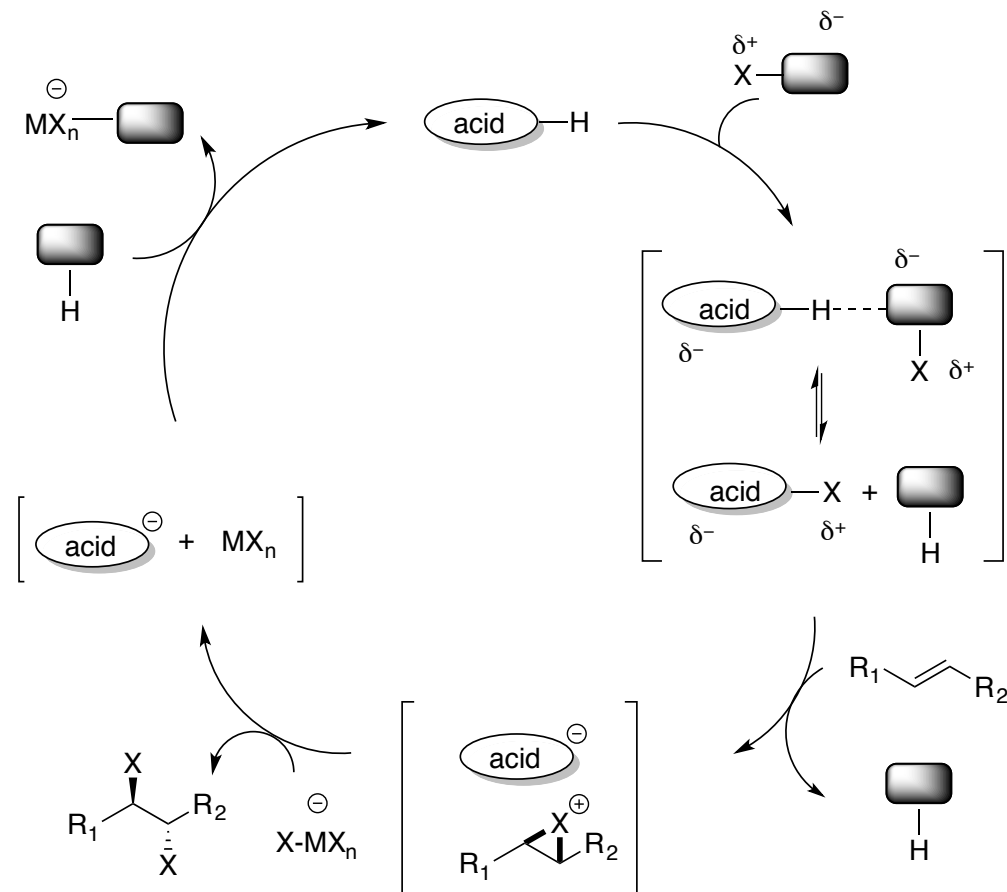
Brønsted acid catalysis

Brønsted acid catalyzed alkene dihalogenation using separate X⁺ and X⁻ sources



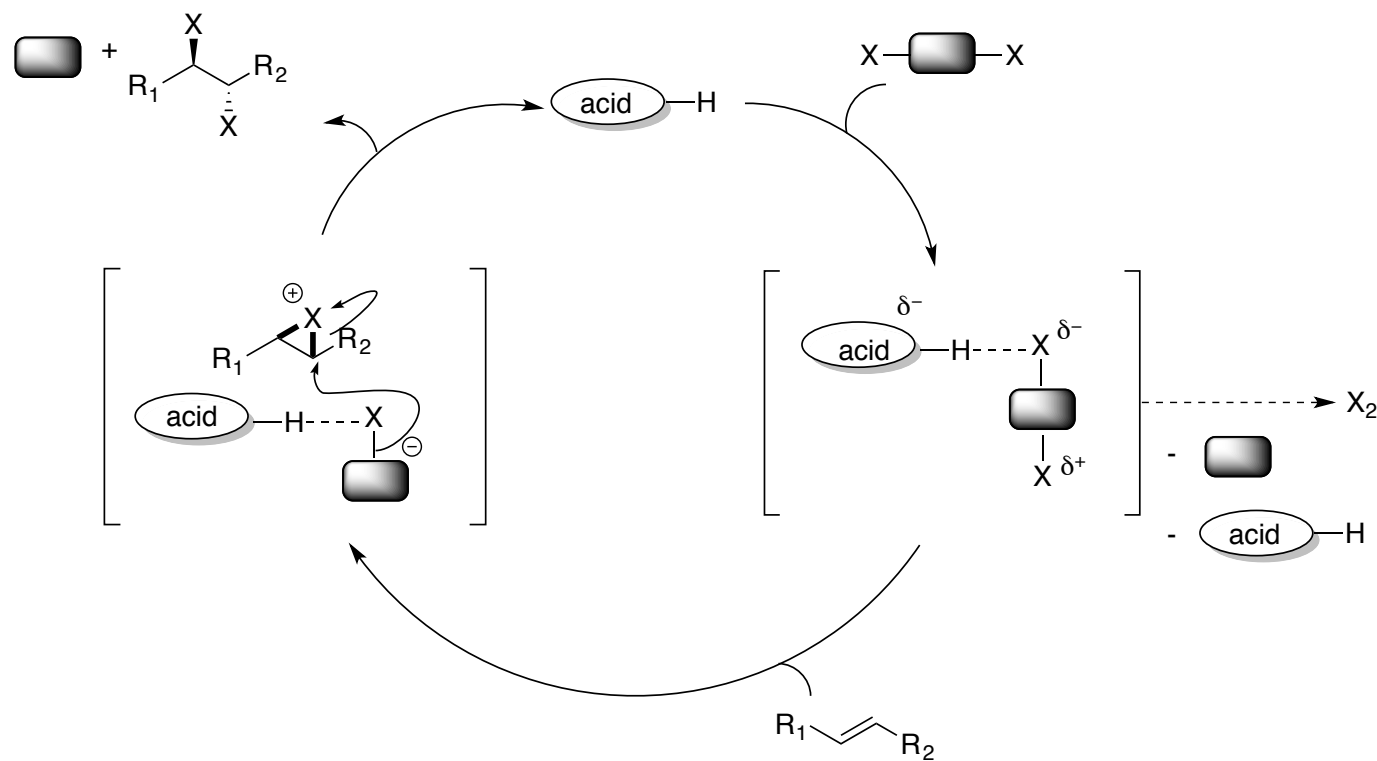
Brønsted acid catalysis

Brønsted acid catalyzed alkene dihalogenation using an X⁺ reagent combined with a complex anion of the halide as an X⁻ source



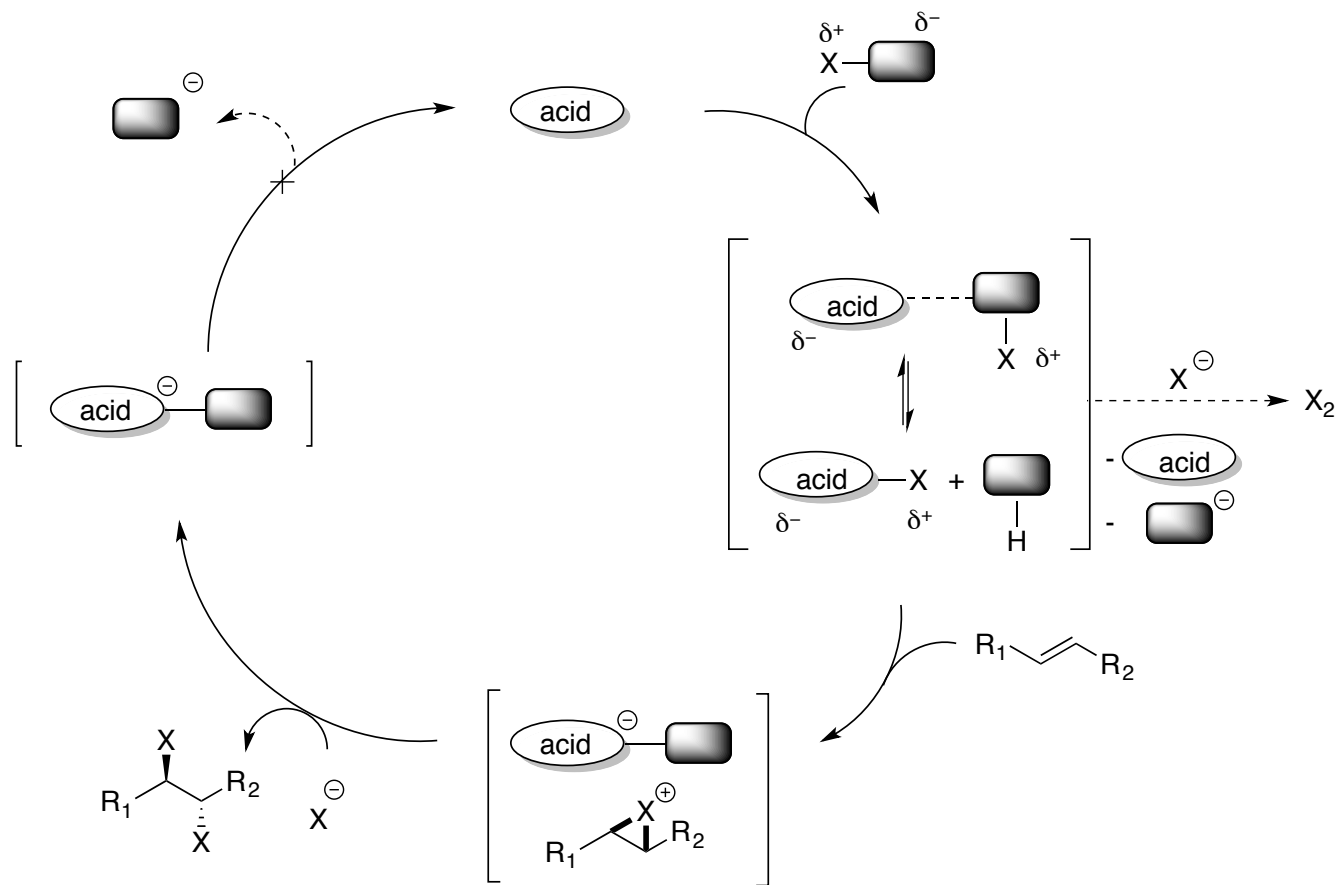
Brønsted acid catalysis

Brønsted acid catalyzed alkene dihalogenation using a dihalogen equivalent as a single reagent



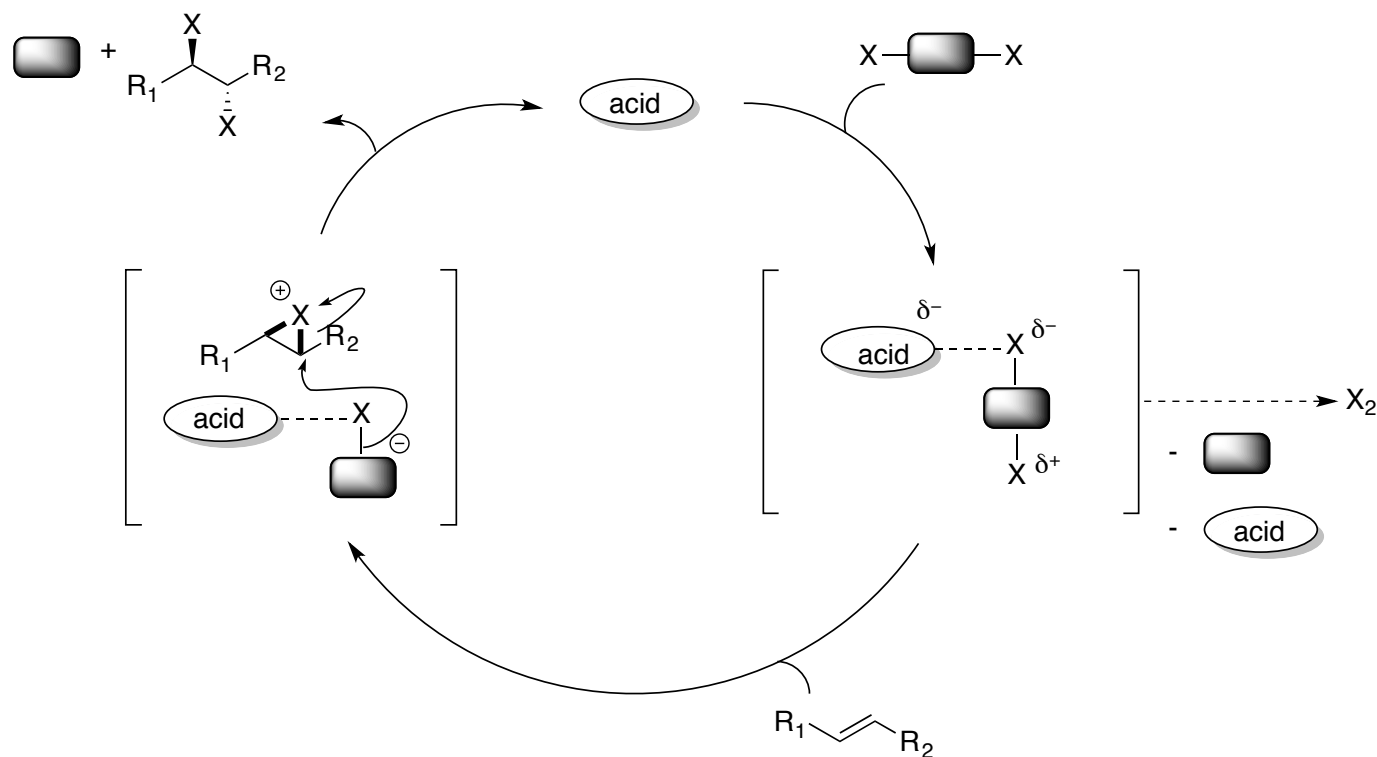
Lewis acid catalysis

Lewis acid catalyzed alkene dihalogenation using separate X⁺ and X⁻ sources



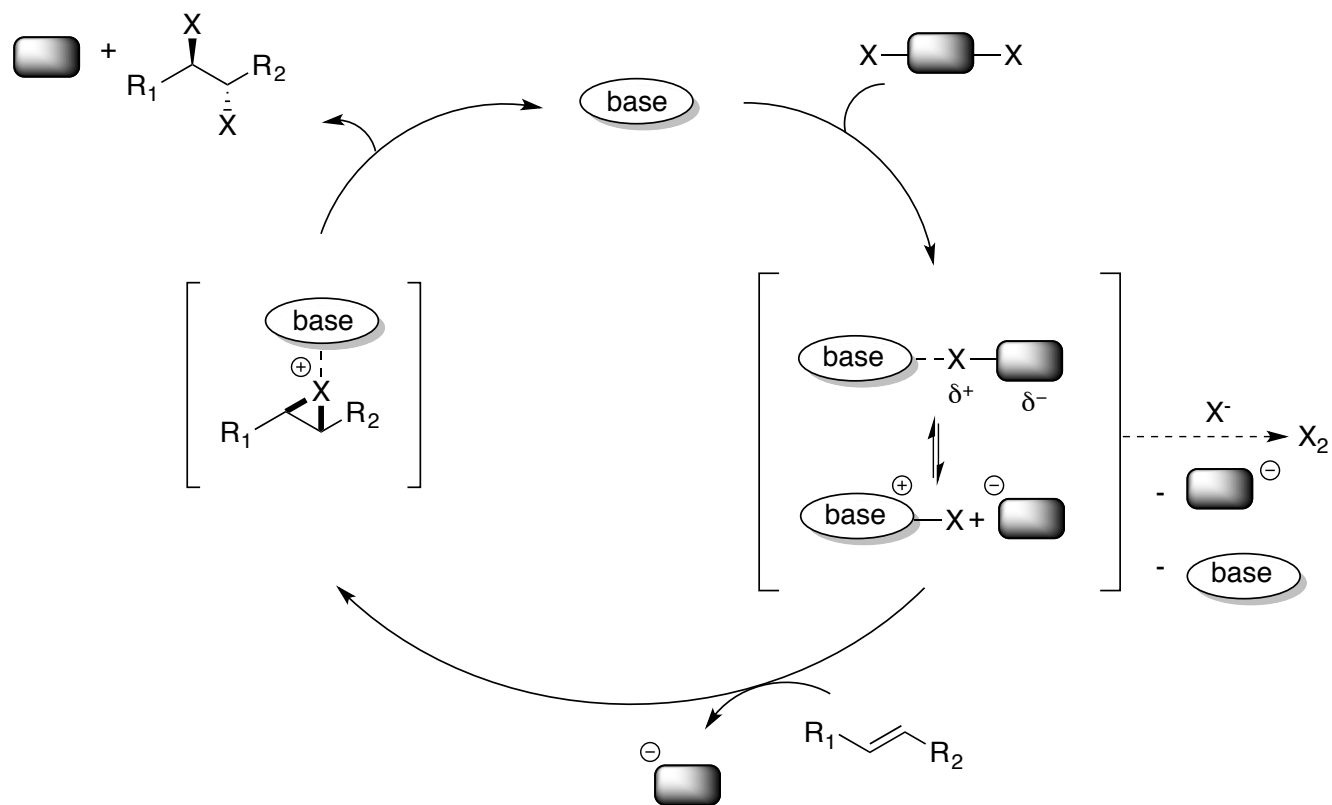
Lewis acid catalysis

Lewis acid catalyzed alkene dihalogenation using a dihalogen equivalent as a single reagent



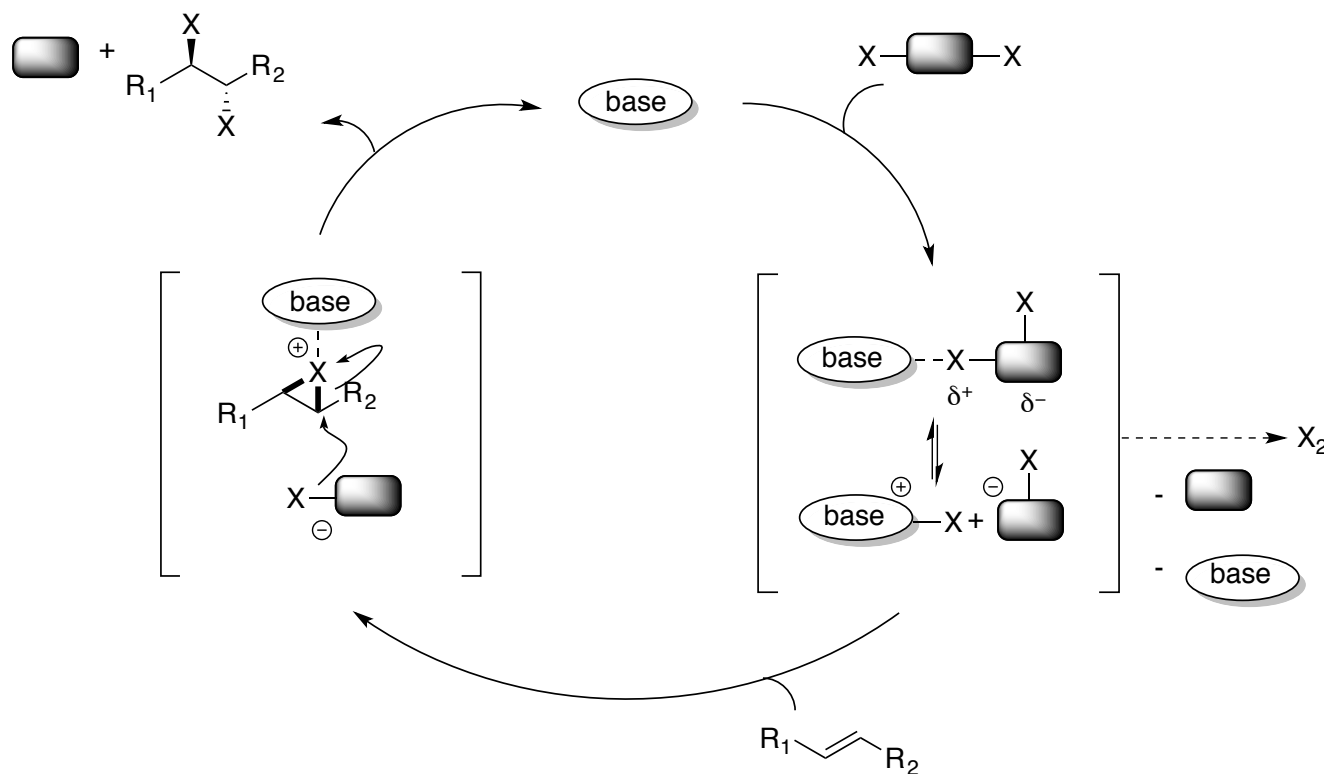
Lewis base catalysis

Lewis base catalyzed alkene dihalogenation using separate X⁺ and X⁻ sources



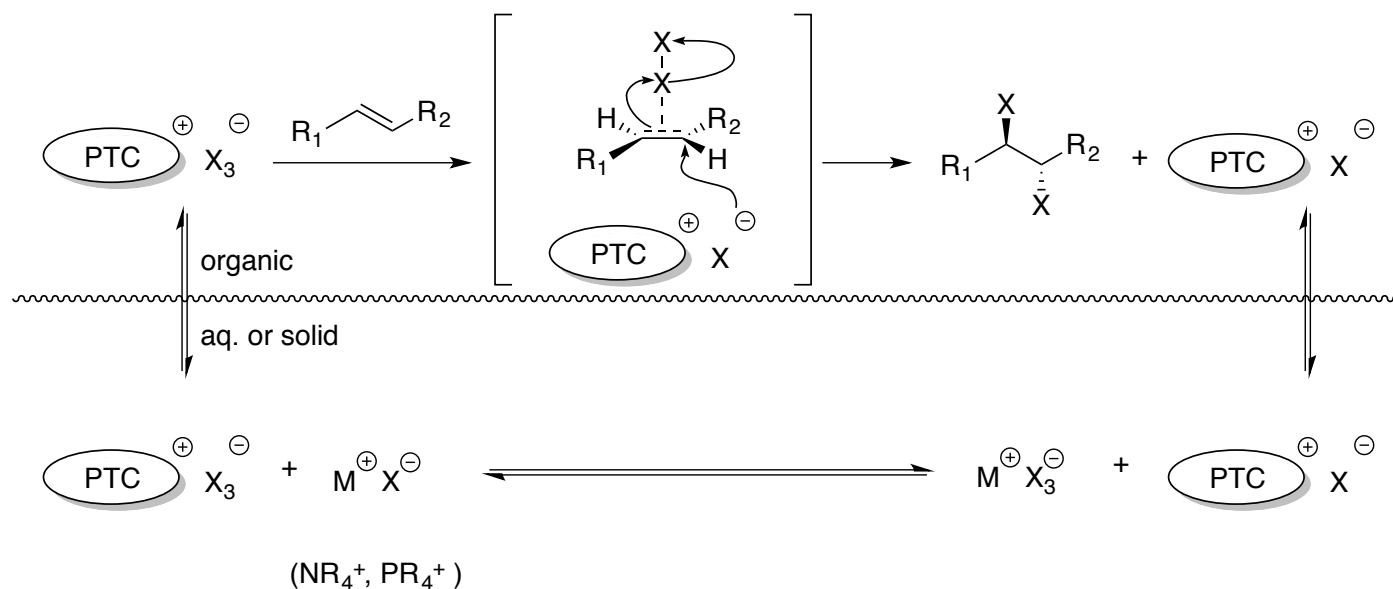
Lewis base catalysis

Lewis base catalyzed alkene dihalogenation using a dihalogen equivalent as a single reagent



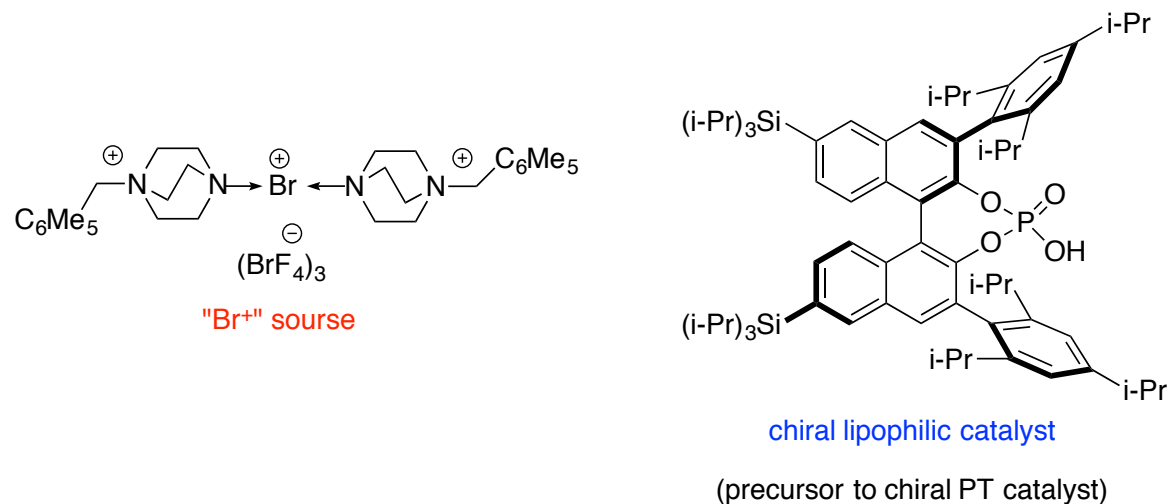
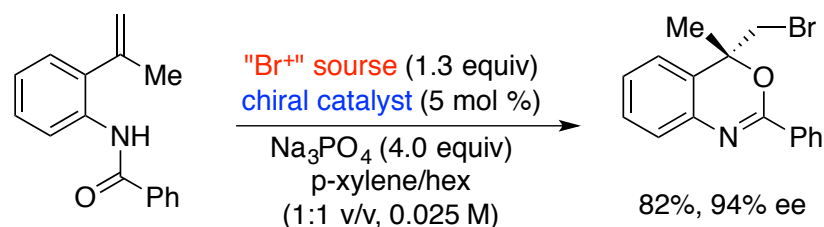
Phase Transfer Catalysis

Cationic phase transfer-catalyzed alkene dihalogenation

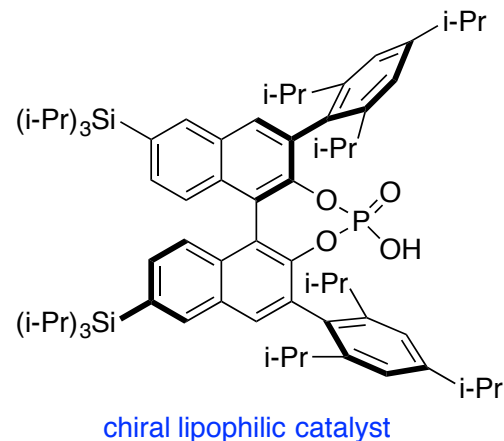
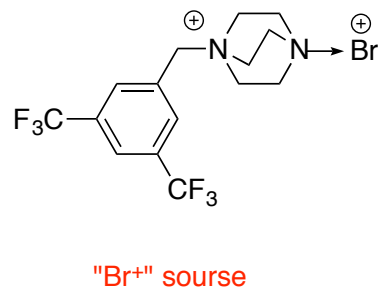
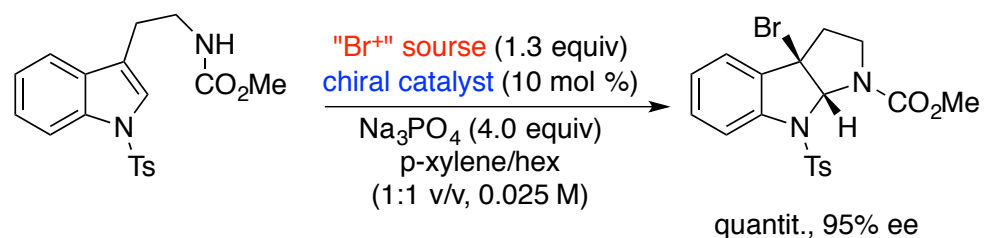


Phase Transfer Catalysis

Enantioselective halocyclization *via* chiral anion phase transfer catalysis

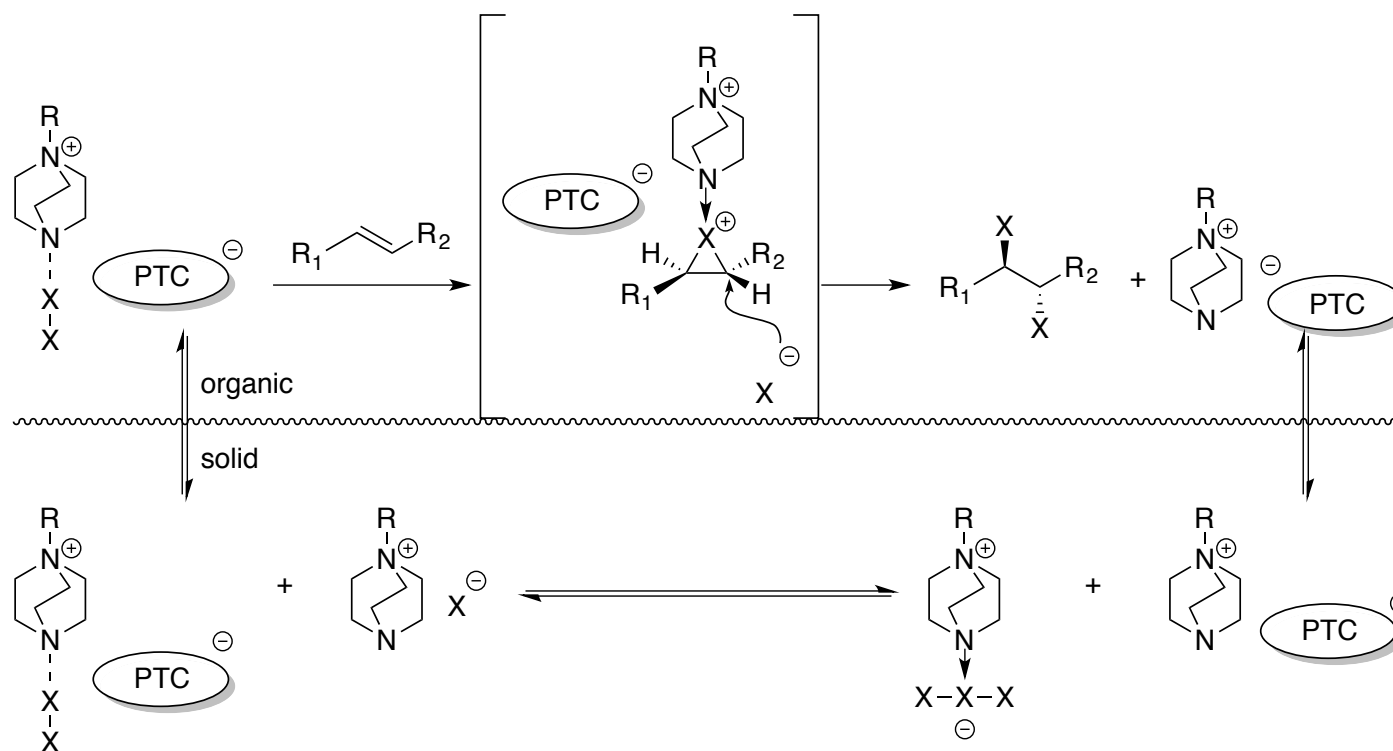


Phase Transfer Catalysis

Enantioselective halocyclization *via* chiral anion phase transfer catalysis

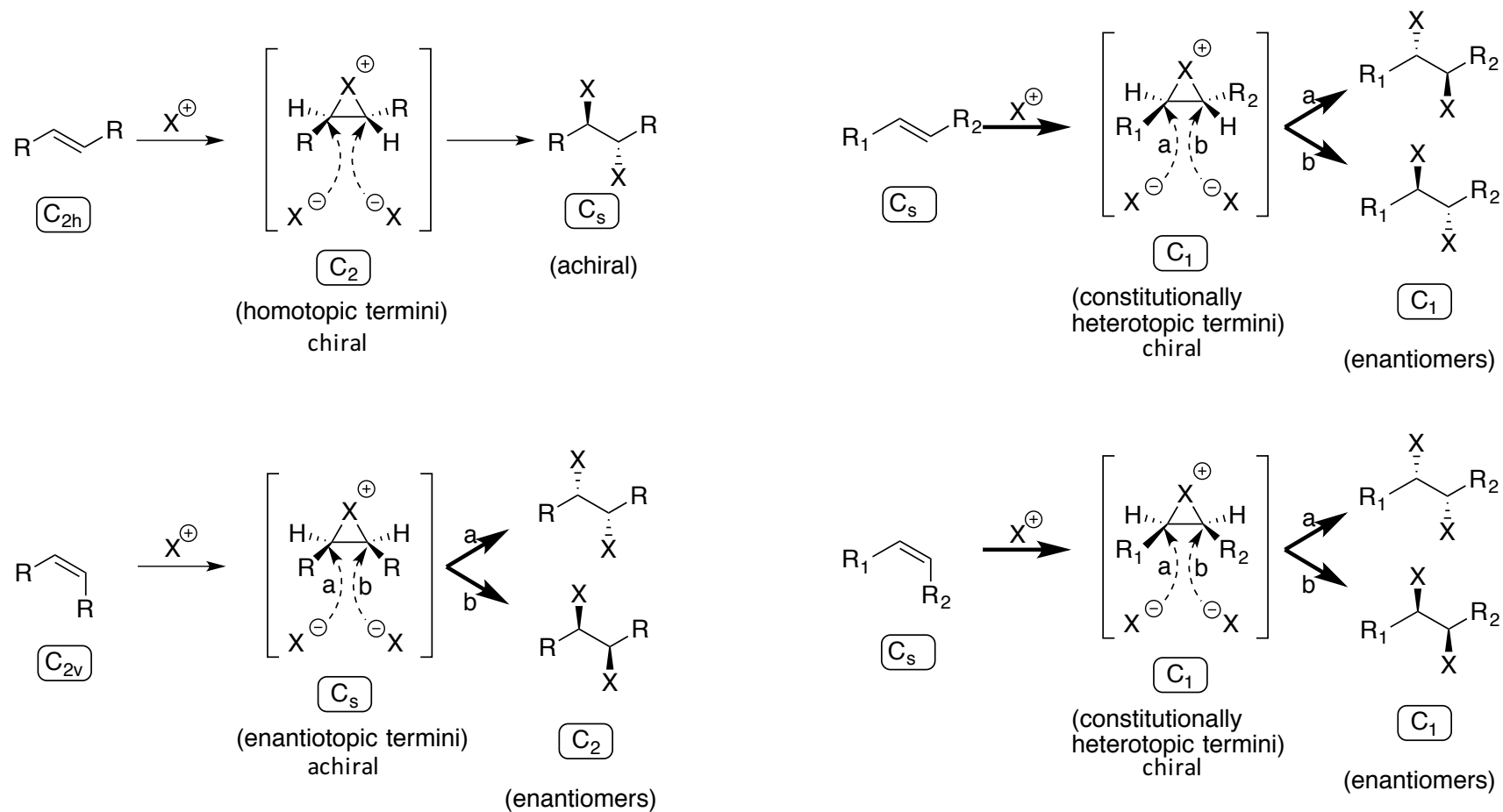
Phase Transfer Catalysis

Anionic phase transfer-catalyzed alkene dihalogenation



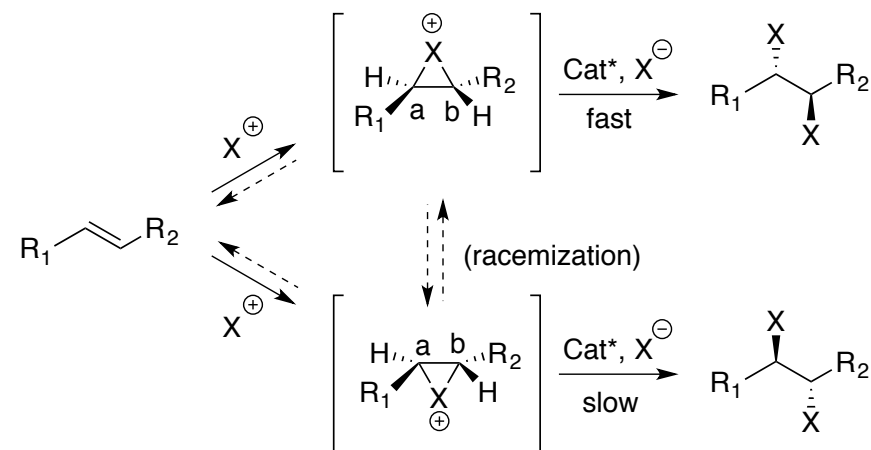
Symmetry-based alkene dihalogenation *via* haliranium ions

(Enantiodetermining steps highlighted with bold arrows)

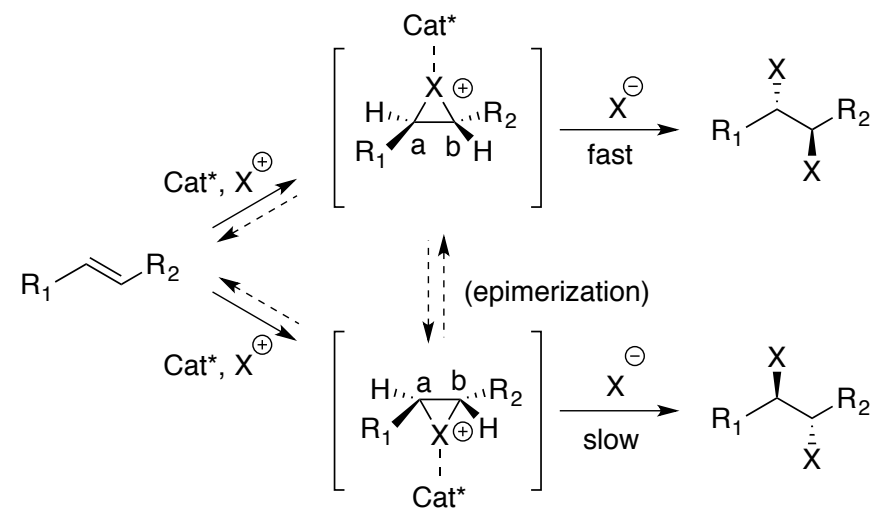


Enantiodetermining nucleophilic attack of halide ion by kinetic resolution of halonium ions

Dynamic kinetic resolution (with substrate- or catalyst-controlled halide attack at carbon "a")

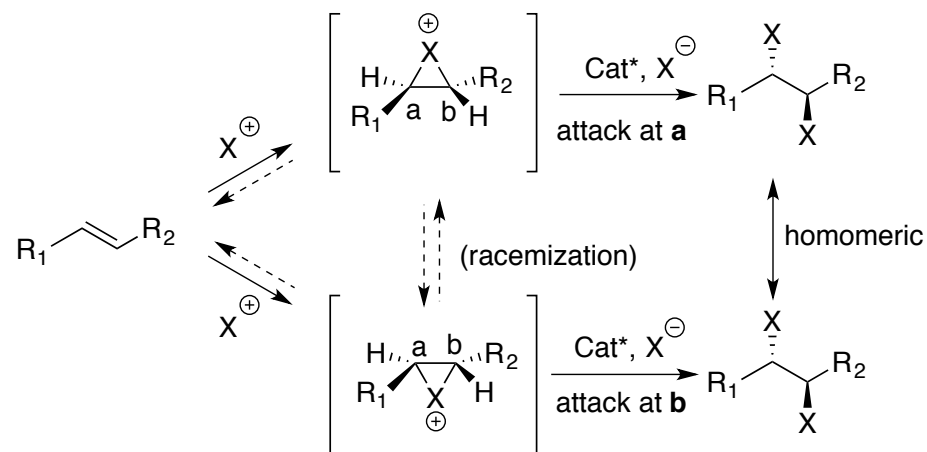


Dynamic kinetic asymmetric transformation (type 1) (with substrate- or catalyst-controlled halide attack at carbon "a")



Enantiodetermining nucleophilic attack of halide ion

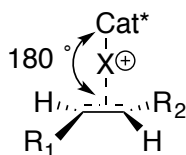
Regiodivergent (enantioconvergent) reaction of a racemic mixture



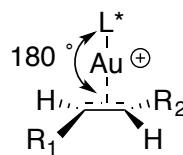
Enantiodetermining haliranium ion formation

For haliranium ion formation to be enantiodetermining, two conditions must be met:

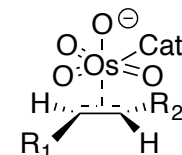
- 1) the halenium ion transfer to the olefin from the "X⁺" source must be **irreversible**
- 2) the haliranium ion thus produced must be configurationally stable prior to its nucleophilic trapping (it must **not racemize**).



Difficult to predict stereochemical information *via* σ^* orbital

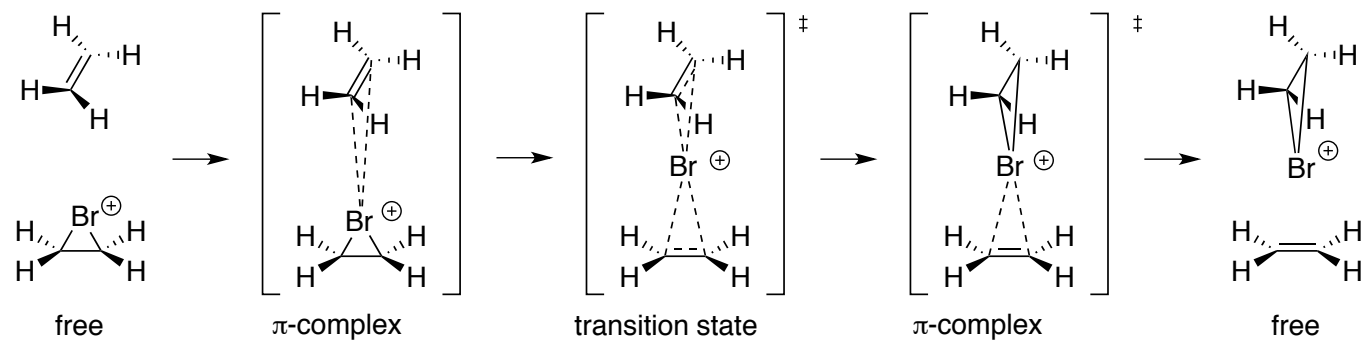


Au^(I) complexes have linear coordination geometry



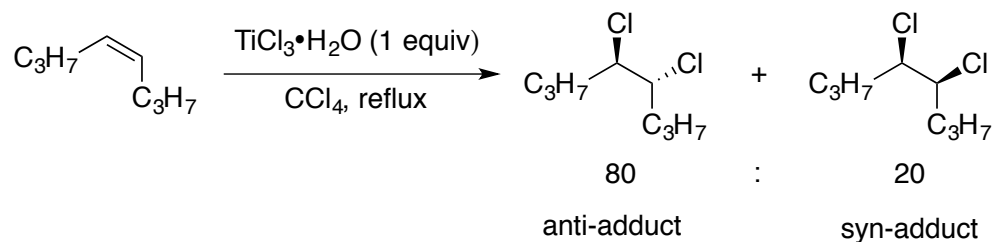
Access to π^* orbital allows to have better stereochemical interaction between Cat* and alkene

Alkene-to-alkene bromiranium ion transfer

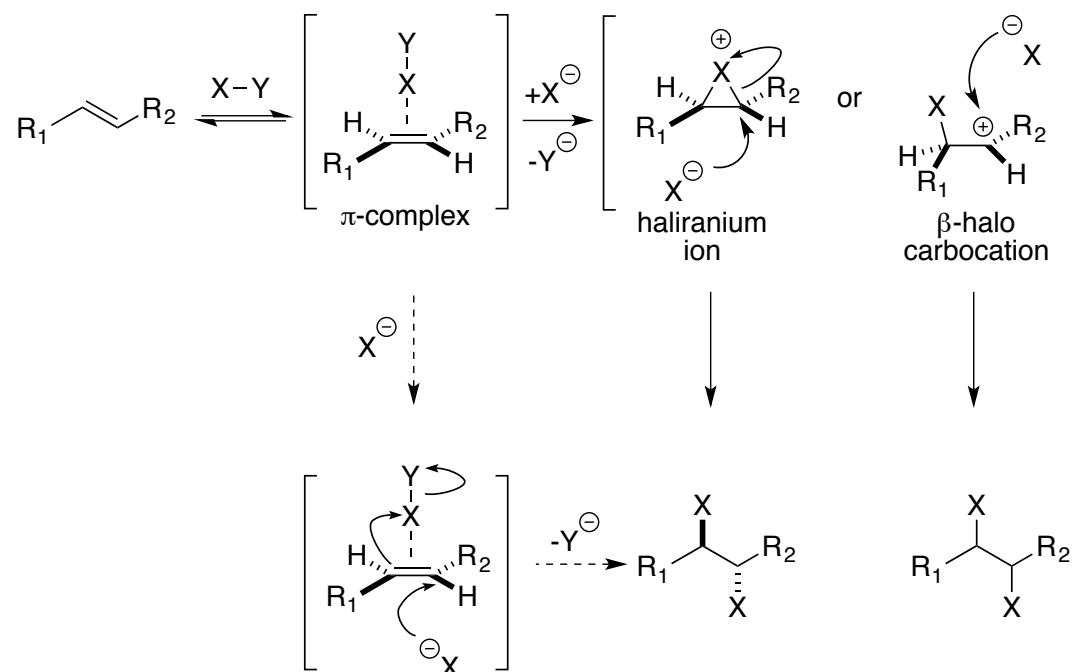


Alkene dihalogenation with main group halides as reagent or catalysts

Group IIIa (B, Al, Ga, In, Tl) Halides



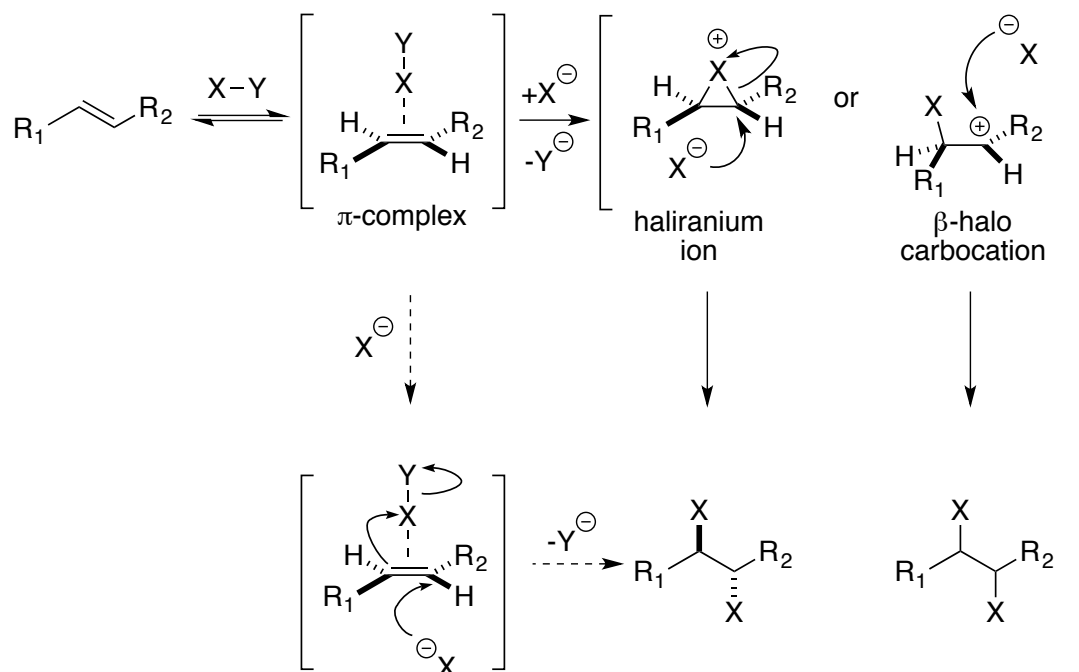
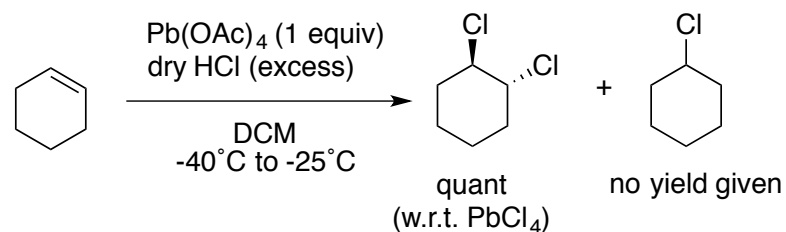
5% combined yield (w.r.t. TiCl₃)
(plus 33% of hydrochlorinated products)



Alkene dihalogenation with main group halides as reagent or catalysts

Group IVa (C, Si, Ge, Sn, Pb) Halides

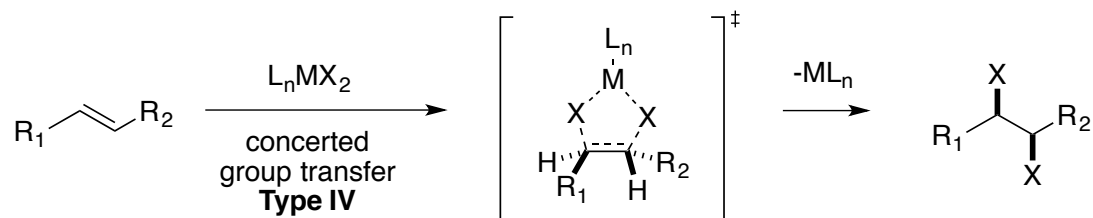
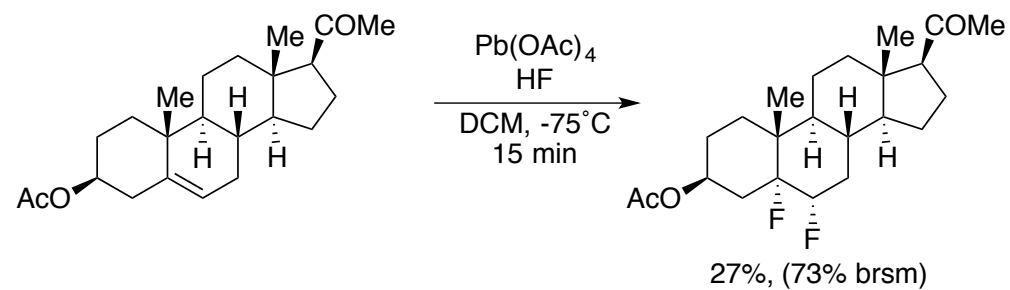
Only PbCl₄ has power to dichlorinate alkenes.



Alkene dihalogenation with main group halides as reagent or catalysts

Group IVa (C, Si, Ge, Sn, Pb) Halides

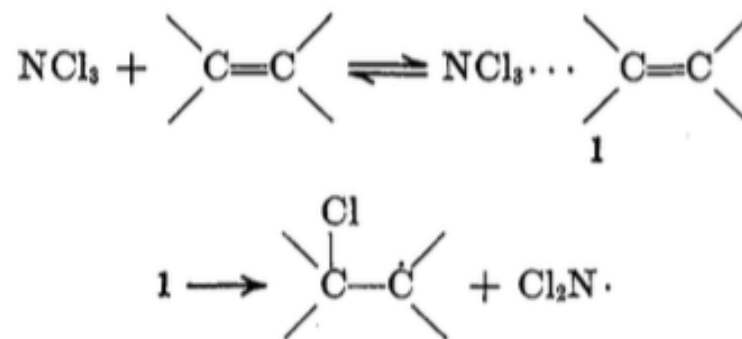
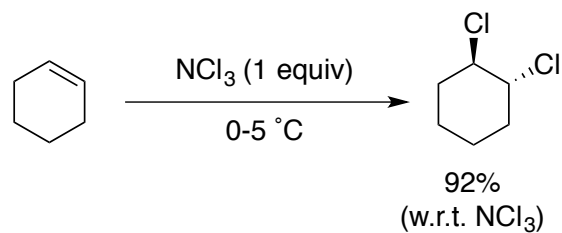
Difluorination



Alkene dihalogenation with main group halides as reagent or catalysts

Group Va (N, P, As, Sb, Bi) Halides

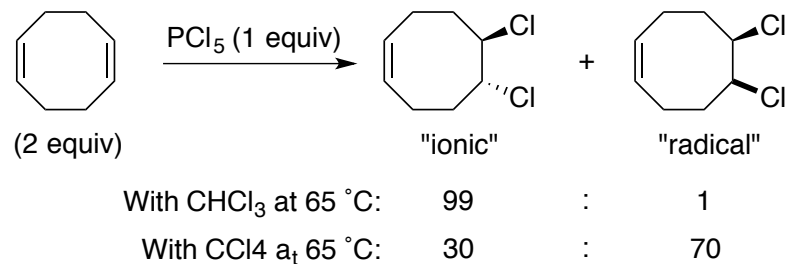
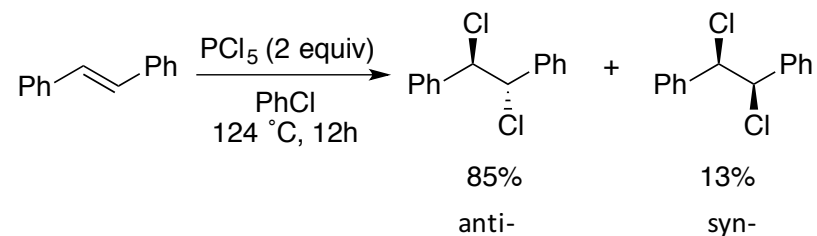
Nitrogen



Alkene dihalogenation with main group halides as reagent or catalysts

Group Va (N, P, As, Sb, Bi) Halides

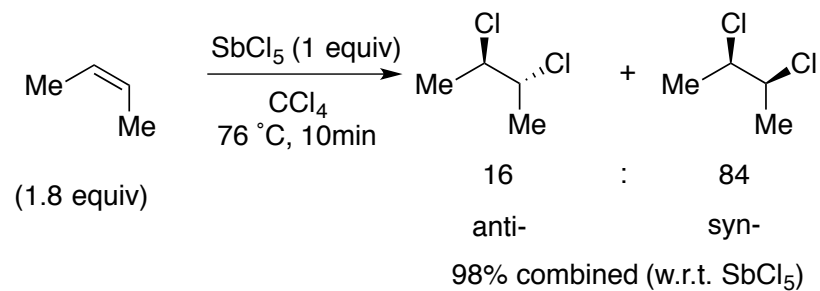
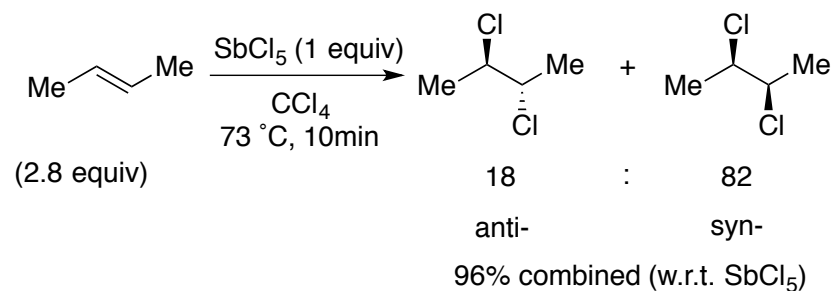
Phosphorus



Alkene dihalogenation with main group halides as reagent or catalysts

Group Va (N, P, As, Sb, Bi) Halides

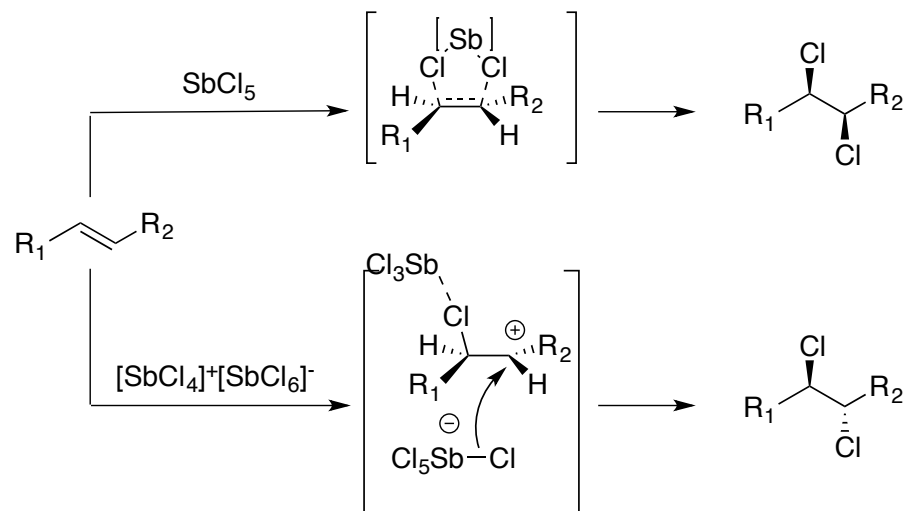
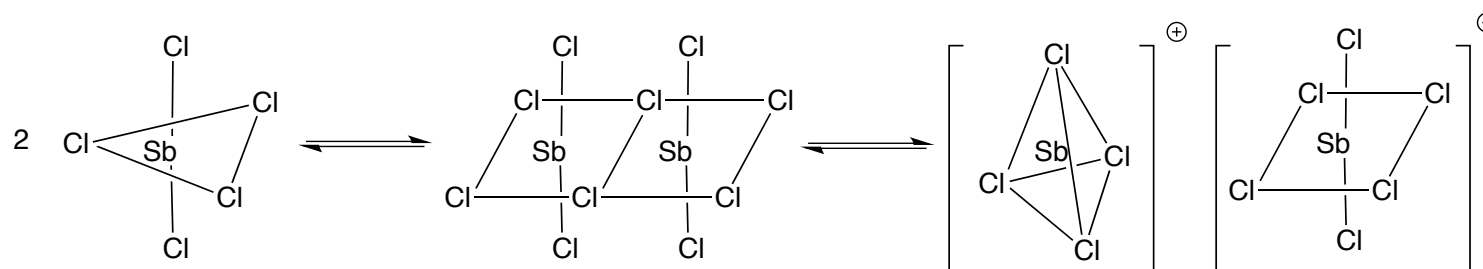
Antimony



Equilibria of SbCl₅ in CCl₄

Group Va (N, P, As, Sb, Bi) Halides

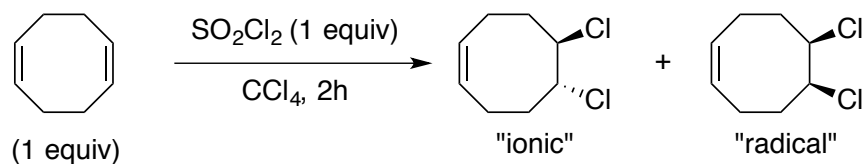
Antimony



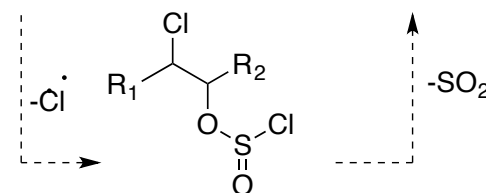
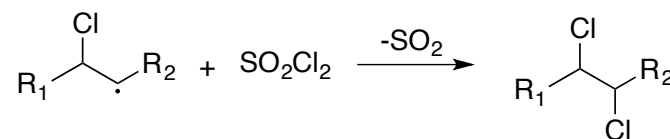
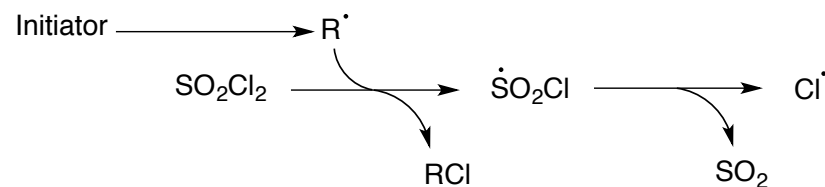
Alkene dihalogenation with main group halides as reagent or catalysts

Group VIa (O, S, Se, Te, Po) Halides

Sulfur



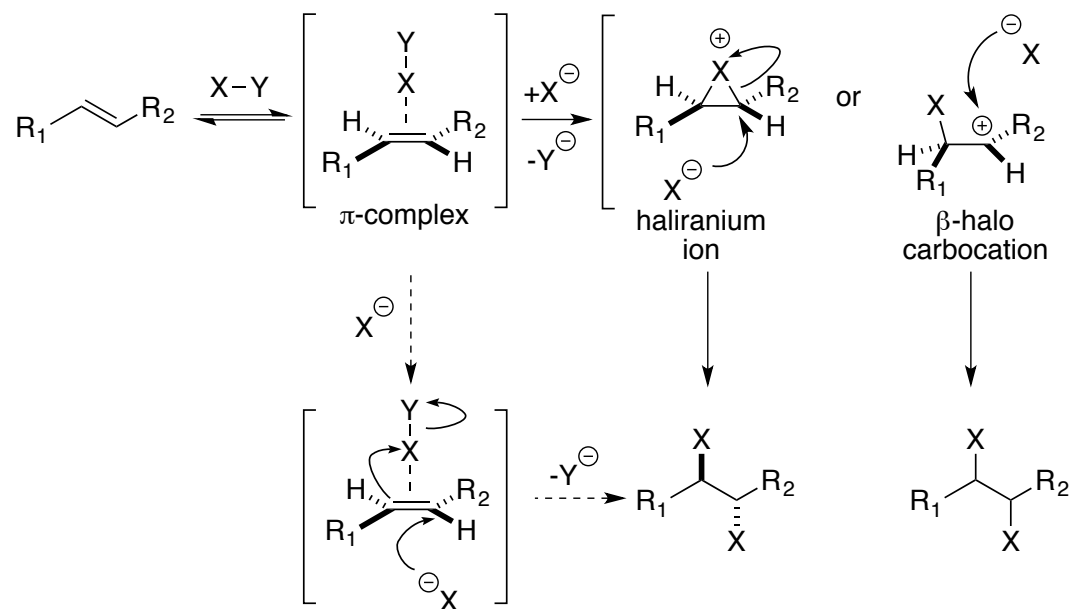
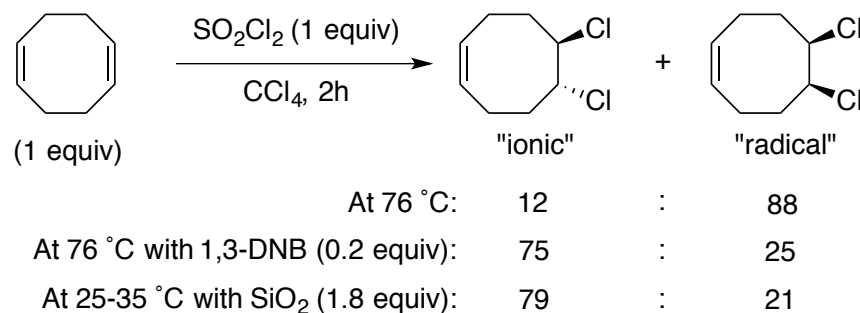
	At 76 °C:	12	:	88
	At 76 °C with 1,3-DNB (0.2 equiv):	75	:	25
	At 25-35 °C with SiO ₂ (1.8 equiv):	79	:	21



Alkene dihalogenation with main group halides as reagent or catalysts

Group VIa (O, S, Se, Te, Po) Halides

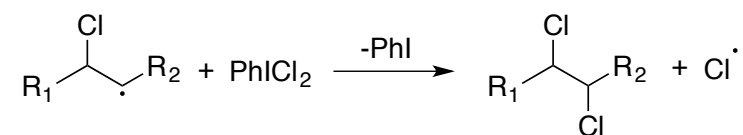
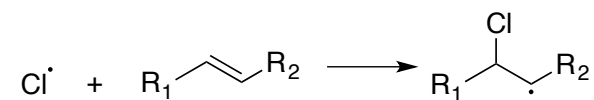
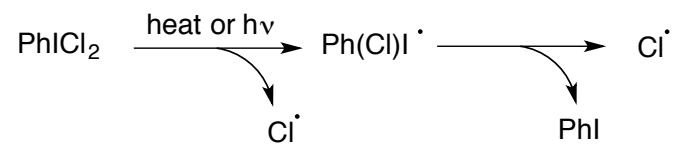
Sulfur



Alkene dihalogenation with main group halides as reagent or catalysts

Group VIIa (F, Cl, Br, I) Halides (except dihalogens)

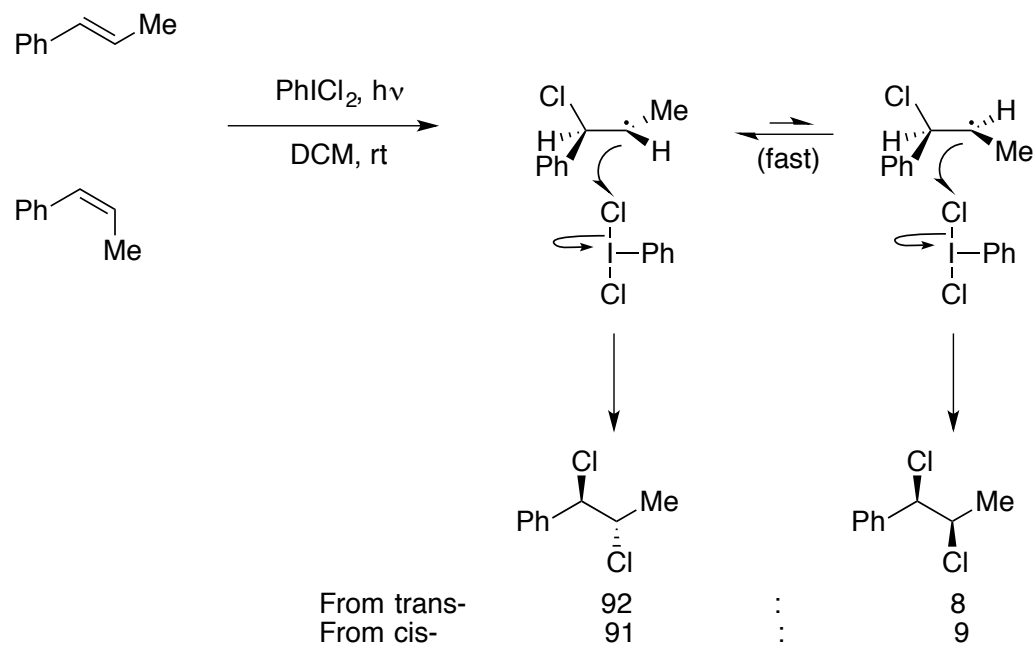
Iodine



Alkene dihalogenation with main group halides as reagent or catalysts

Group VIIa (F, Cl, Br, I) halides (except dihalogens)

Iodine

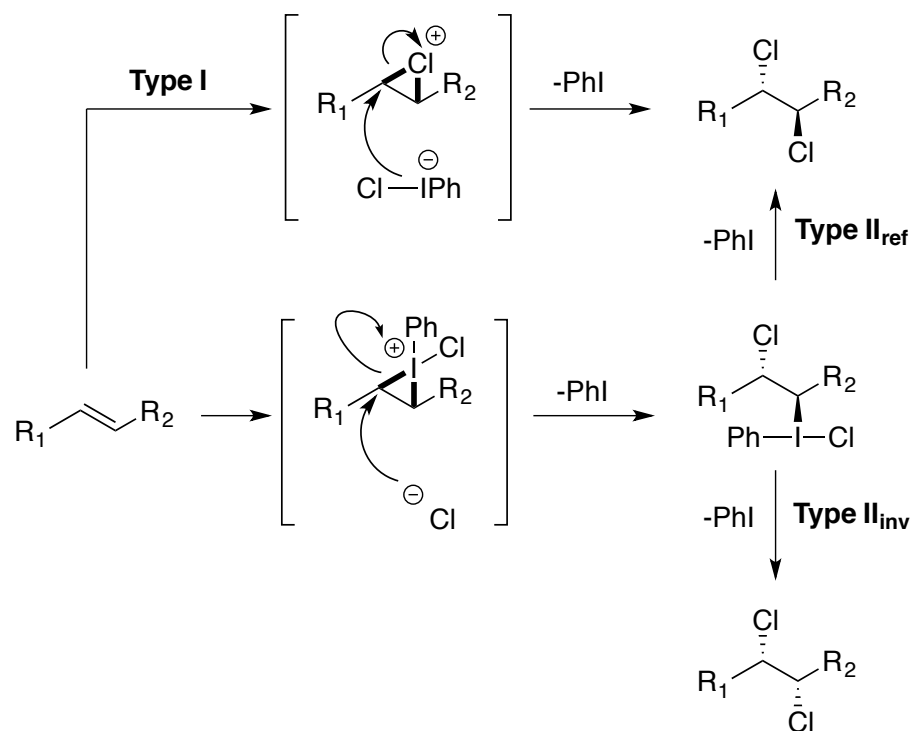


Alkene dihalogenation with main group halides as reagent or catalysts

Group VIIa (F, Cl, Br, I) halides (except dihalogens)

Iodine

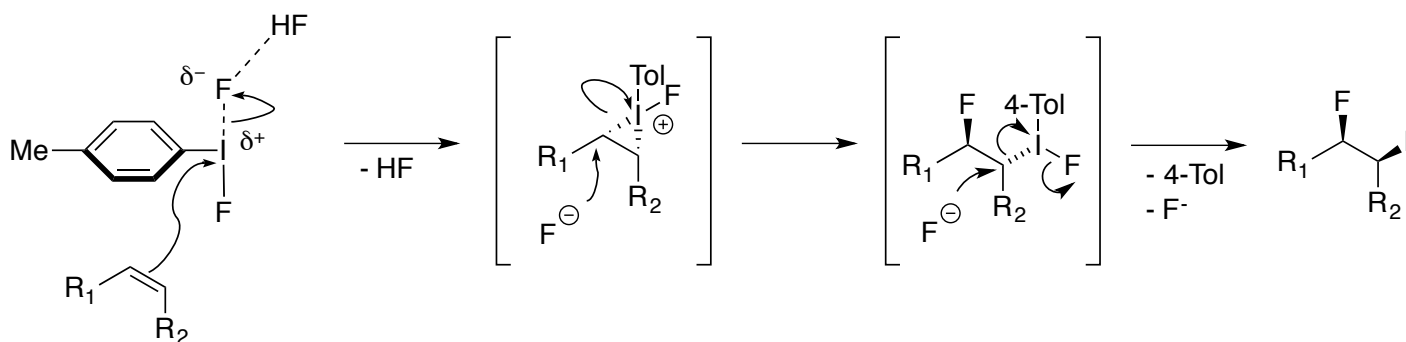
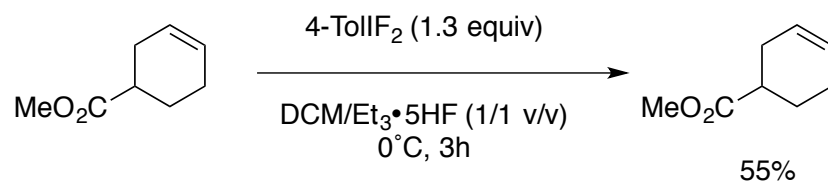
Possible reaction pathways for the ionic dichlorination of alkenes with PhICl_2



Alkene dihalogenation with main group halides as reagent or catalysts

Group VIIa (F, Cl, Br, I) halides (except dihalogens)

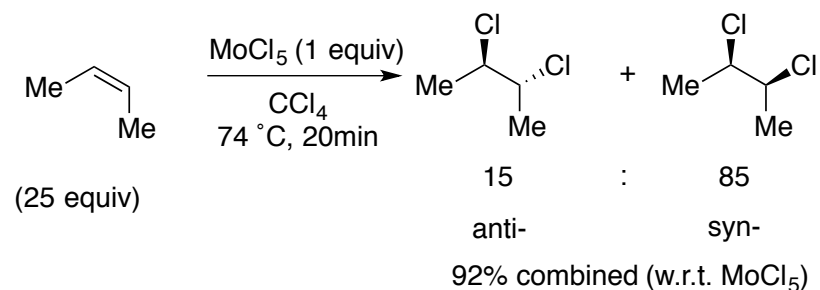
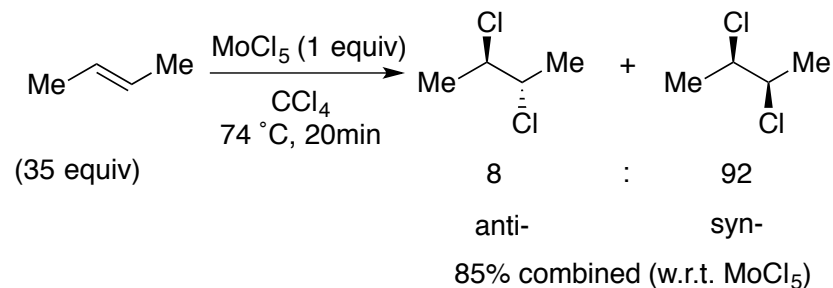
Difluorination



Alkene dihalogenation with transition metal halides as reagent or catalysts

Group VI (Cr, Mo, W,) metal halides

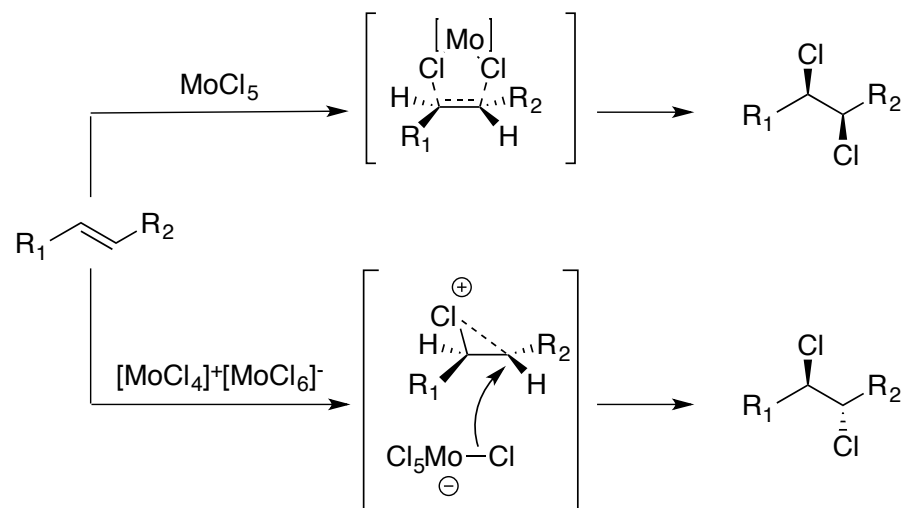
Molybdenum



Alkene dihalogenation with transition metal halides as reagent or catalysts

Group VI (Cr, Mo, W,) metal halides

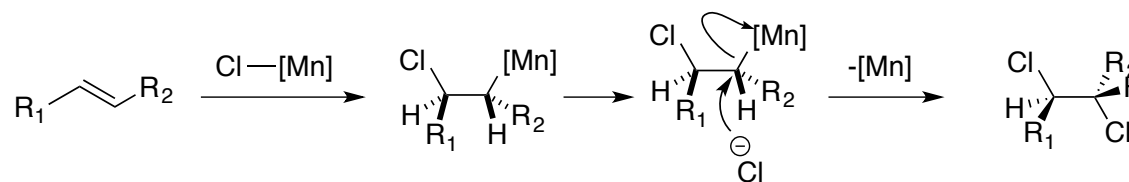
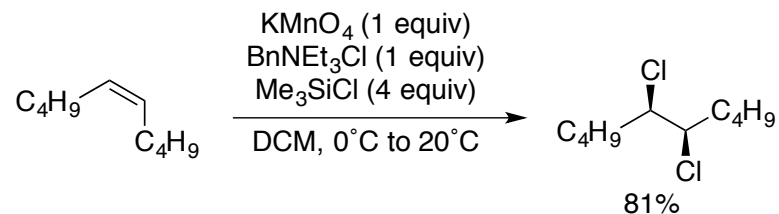
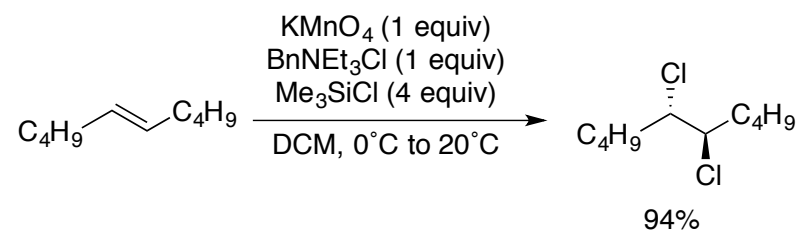
Mechanism for the formation of *syn*- and *anti*-dichlorination products



Alkene dihalogenation with transition metal halides as reagent or catalysts

Group VII (Mn, Tc, Re,) metal halides

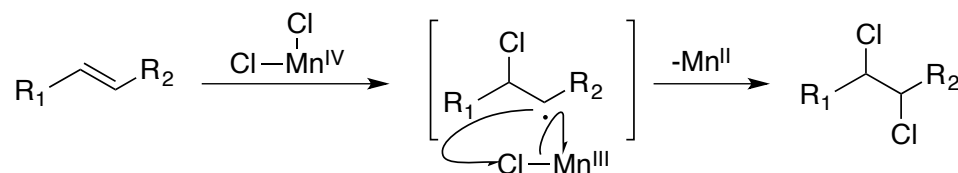
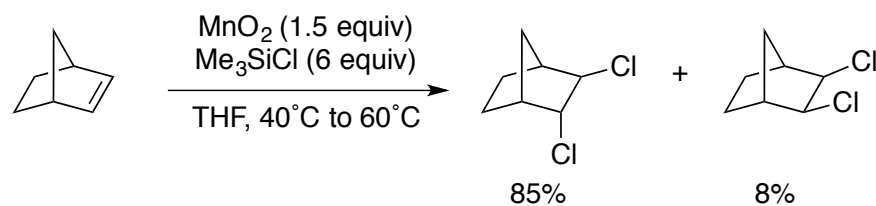
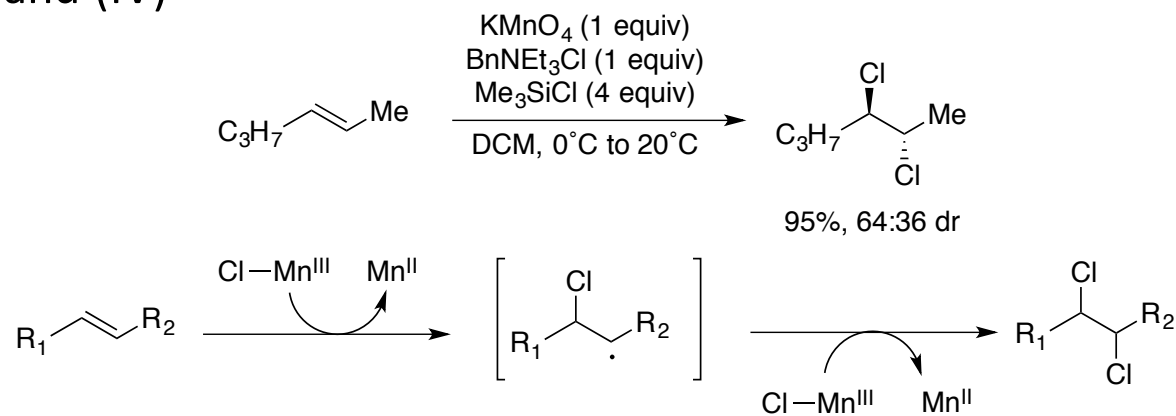
Manganese (VII)



Alkene dihalogenation with transition metal halides as reagent or catalysts

Group VII (Mn, Tc, Re,) metal halides

Manganese (III) and (IV)

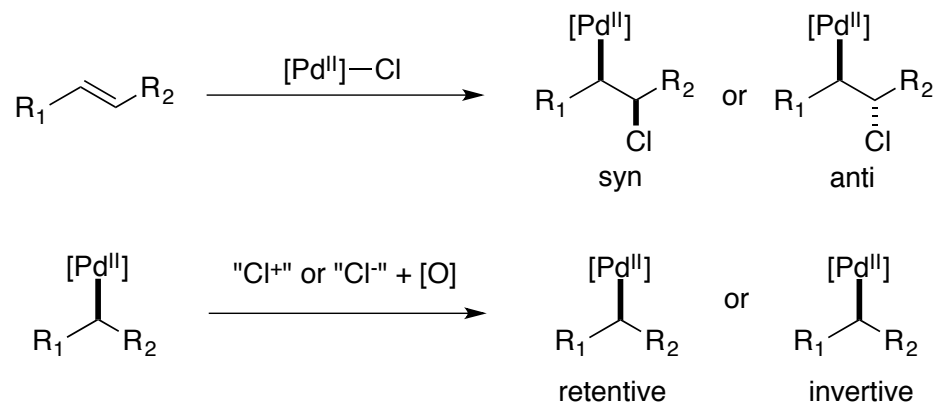


Alkene dihalogenation with transition metal halides as reagent or catalysts

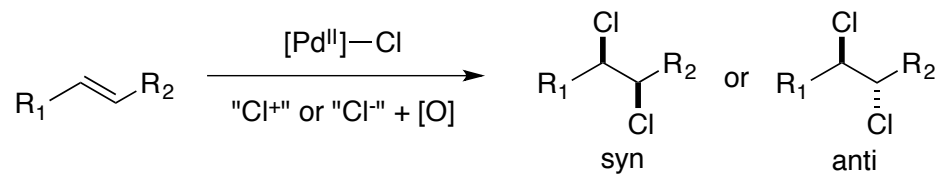
Group 10 (Ni, Pd, Pt,) metal halides

Palladium

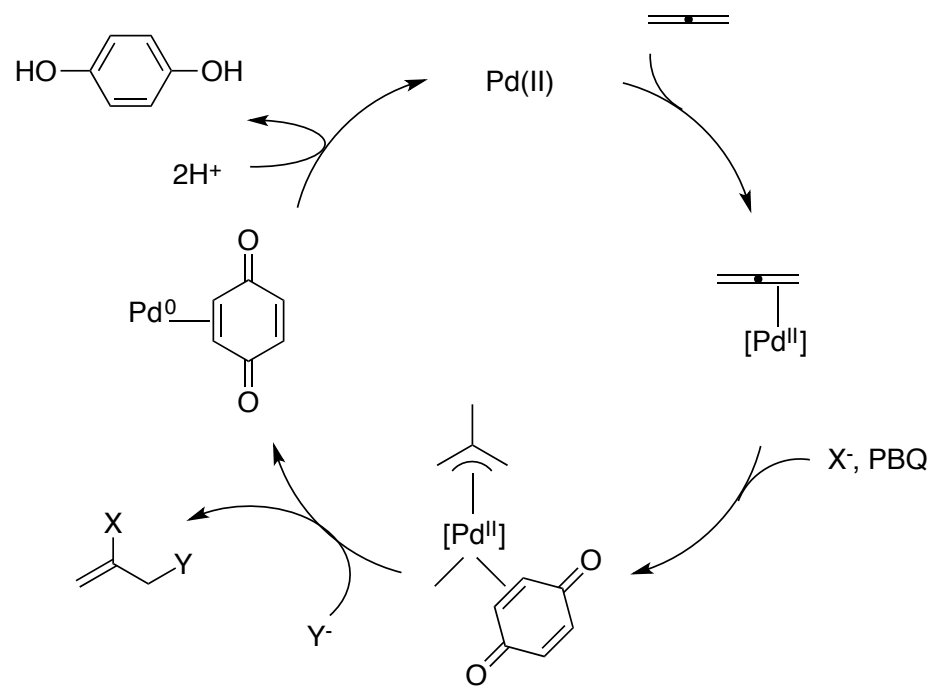
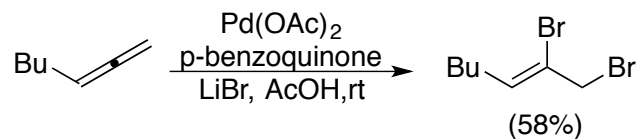
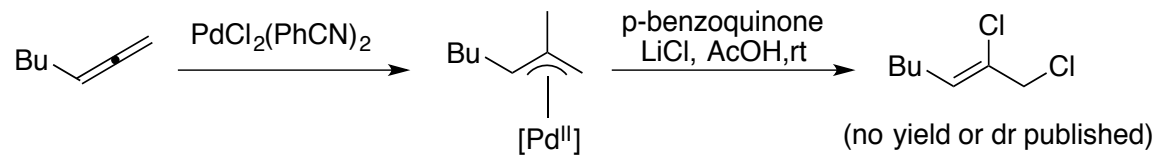
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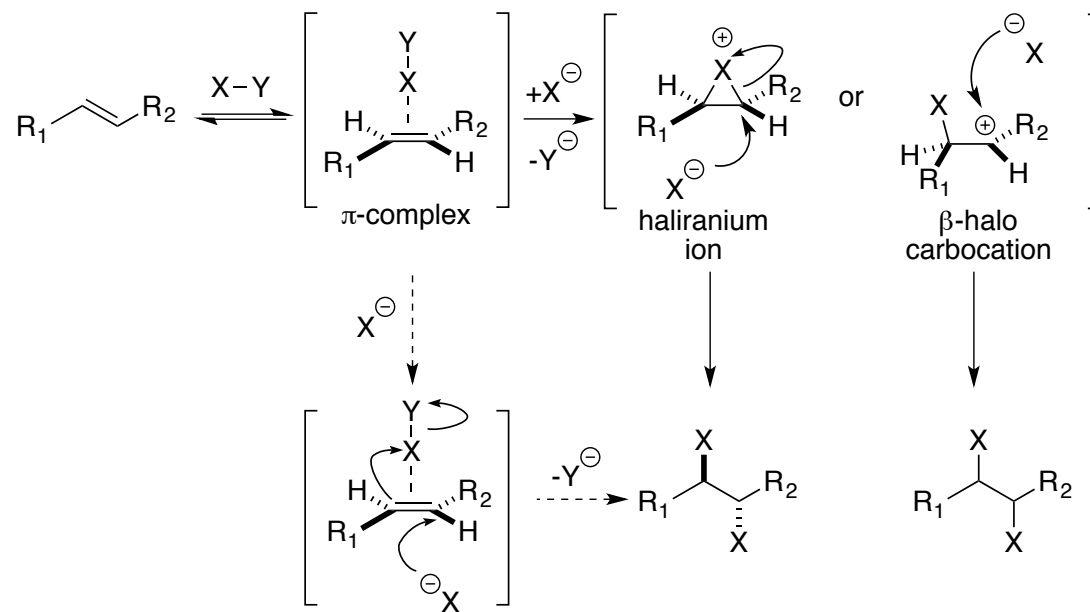
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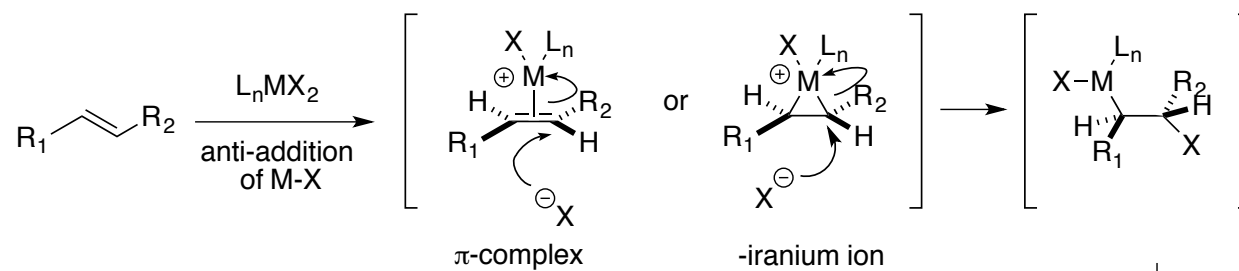
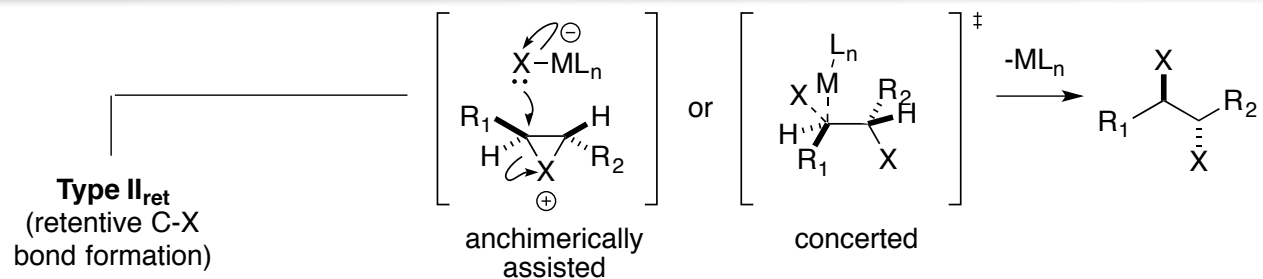


Alkene dihalogenation with transition metal halides as reagent or catalysts

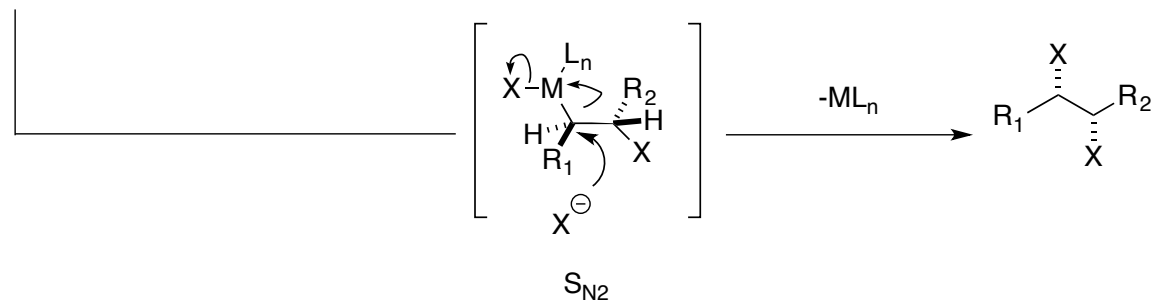


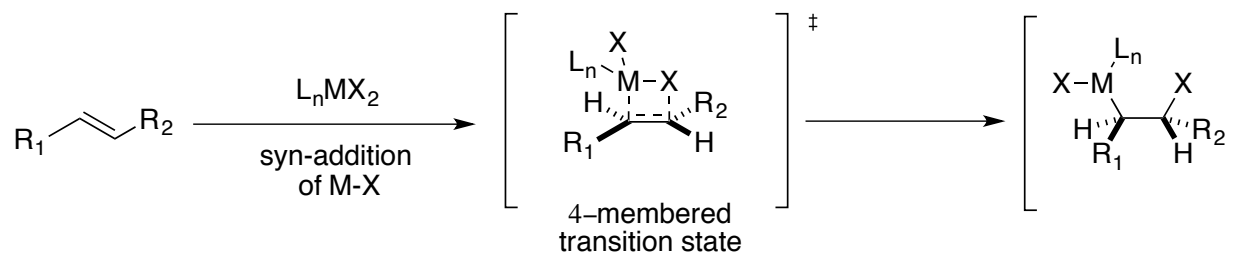
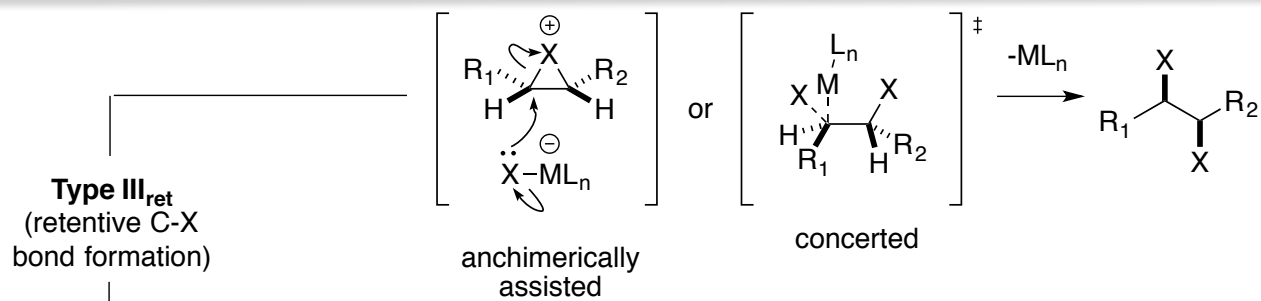
Thank you for your attention!



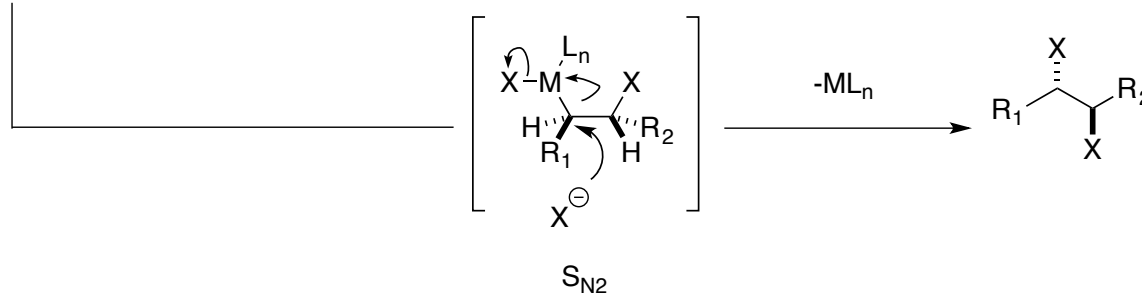


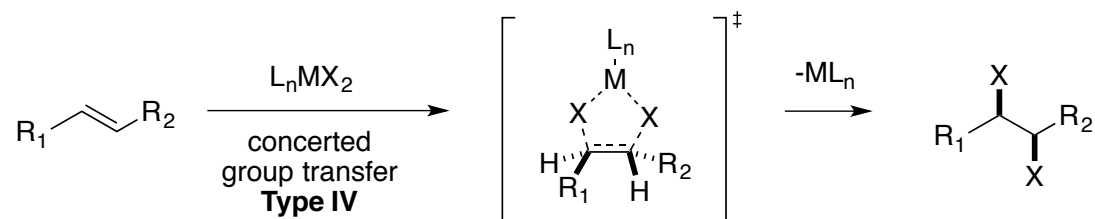
Type II_{inv}
(invertive C-X bond formation)



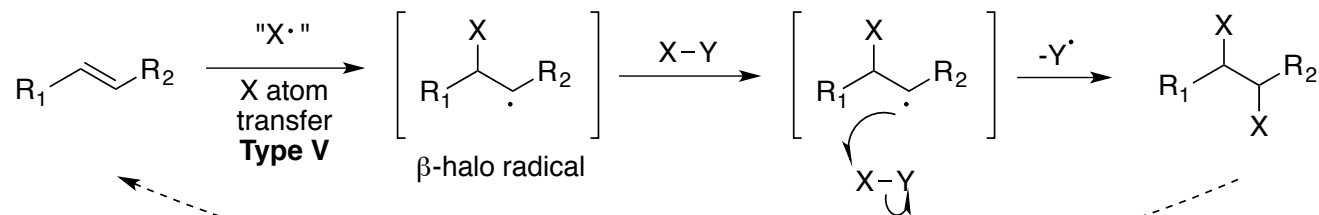


Type III_{inv}
(invertive C-X bond formation)





Radical Type V



chain reaction if $\text{Y}\cdot = \text{X}\cdot$ or $\text{Y}\cdot \rightarrow \text{X}\cdot + \text{Y}'$