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# ***Activating Acids with Bases: Theory and Applications An Homage to G. N. Lewis***

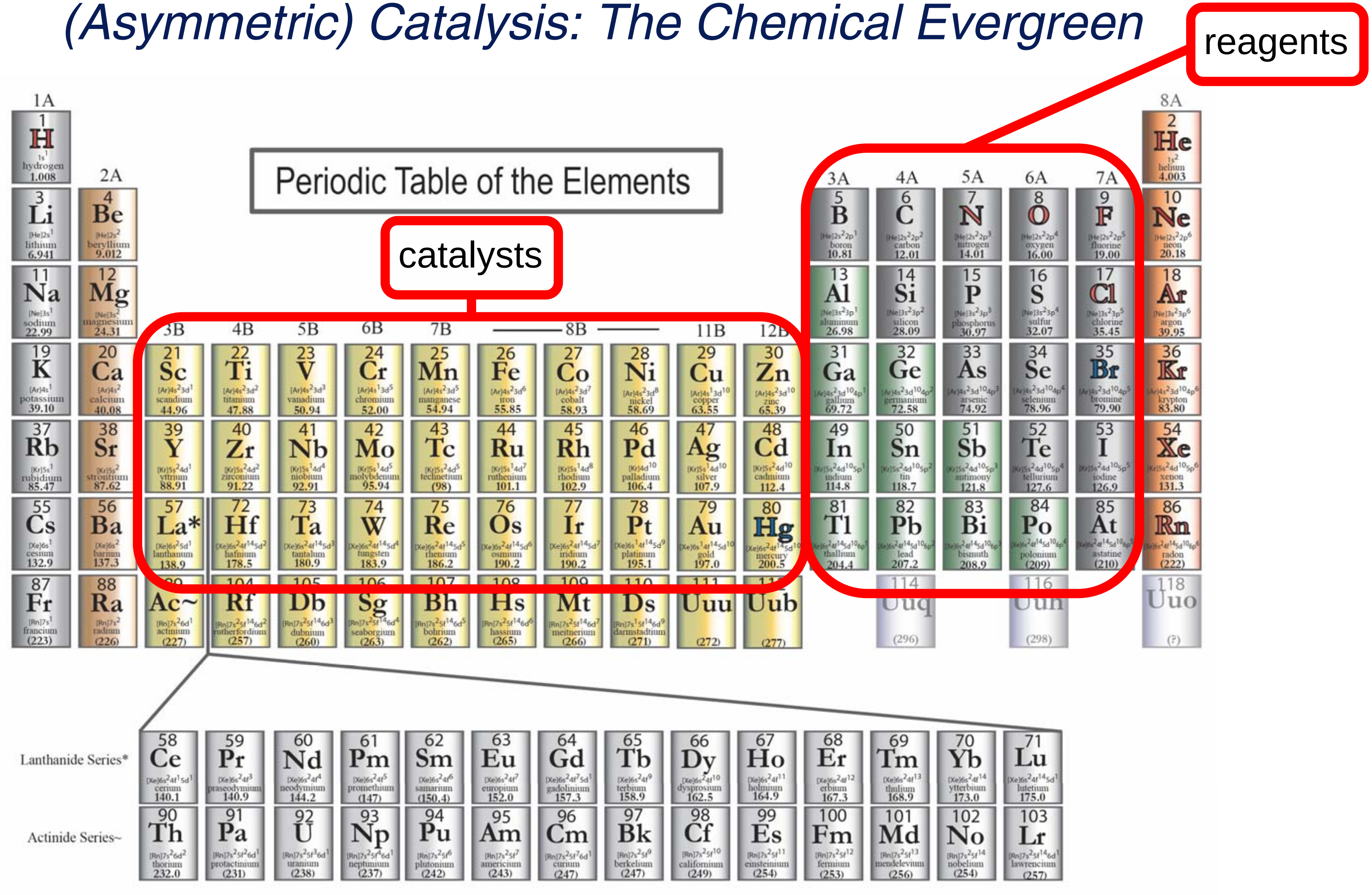
Ischia Advanced School
of Organic Chemistry 2006
Ischia, Italy

19-23 September 2006

QuickTime™ and a
Photo - JPEG decompressor
are needed to see this picture.

G. N. Lewis (1875-1946)

# *(Asymmetric) Catalysis: The Chemical Evergreen*

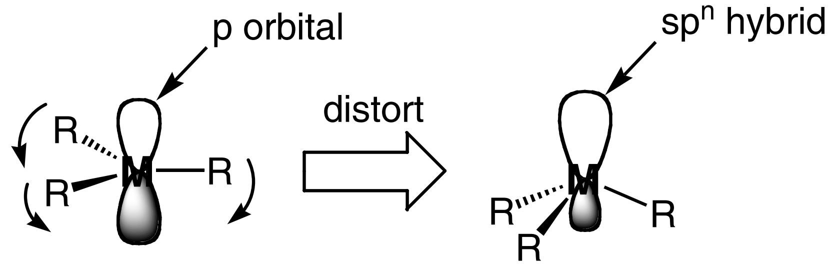


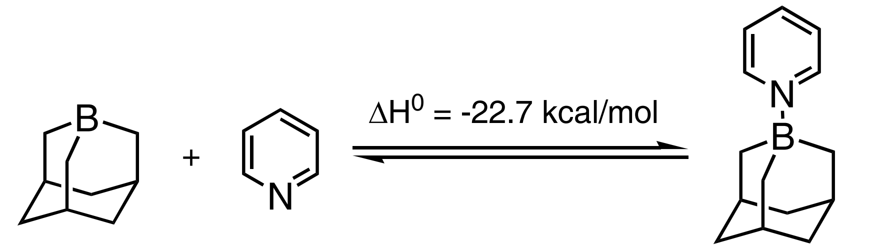
## *Opportunities for Catalysis in the Main Group?*

- Lewis Acidity:
  - B(+3), Al(+3), Ga(+3), In(+3)
  - Si(+4), Sn(+2, +4), Pb(+4)
  - P(+5), Sb(+3, +5), Bi(+3, +5)
  - O(+2), S(+2, +4, +6), Se(+2, +4, +6), Te(+2, +4, +6)
  - F(+1), Cl(+1, +3, +5, +7), Br(+1, +3, +5, +7), I(+1, +3, +5, +7)
- Catalyzed Chemical Processes
  - Carbonyl addition reactions (aldol, allylation, ene)
  - Acetal addition reactions
  - Friedel-Crafts reactions
  - Conjugate addition reactions
  - Azomethine addition reactions
  - Epoxide opening reactions
  - Cycloadditions ([4+2], hetero [4+2], [3+2]), Electrocyclic reactions
  - Sigmatropic (and other) rearrangements

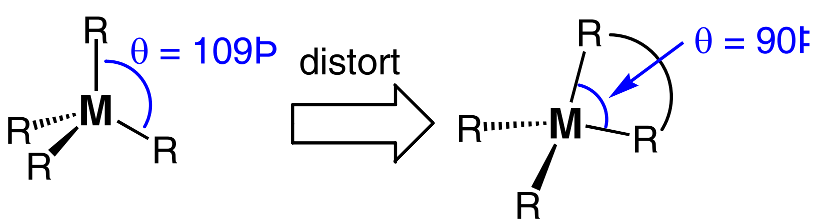
# *Strategies for Modulating Lewis Acidity: Structural*

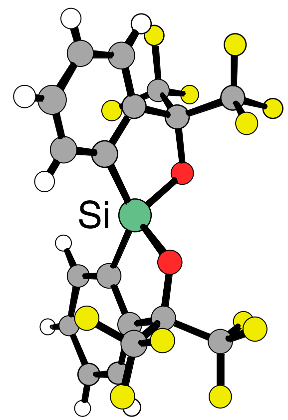
structural perturbations ("strain-release Lewis acidity")

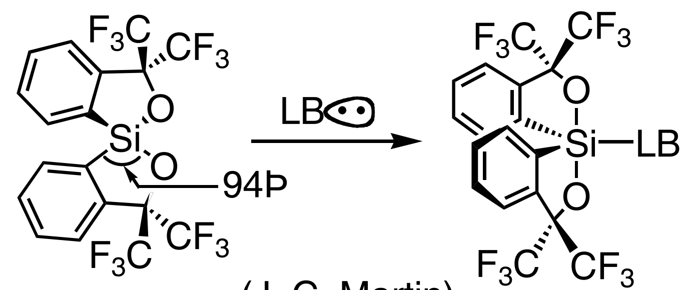


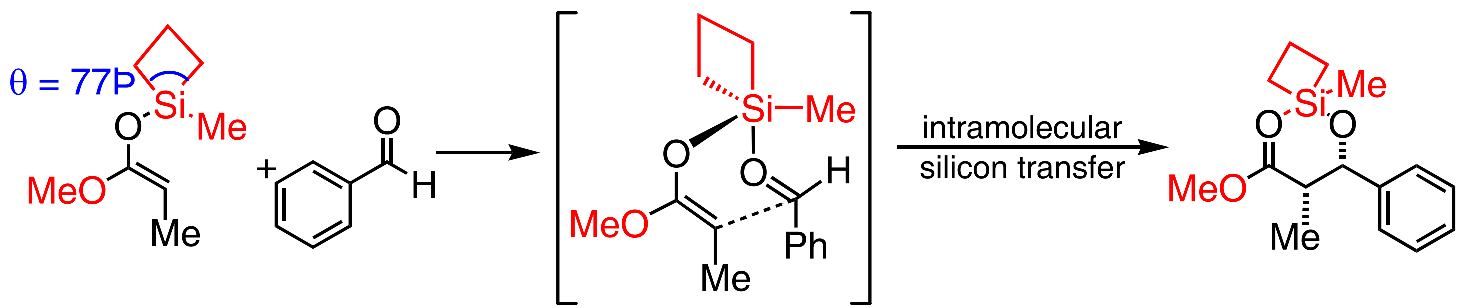

(Mihkailov)



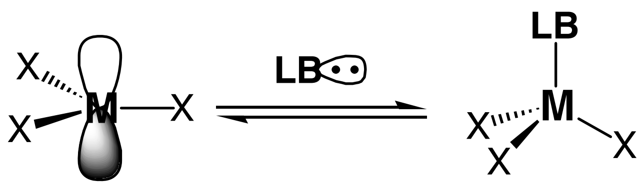



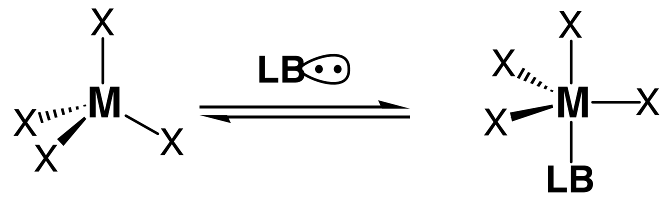

(J. C. Martin)



# *Strategies for Modulating Lewis Acidity: Electronic*

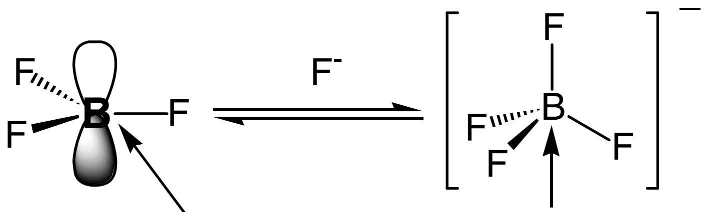
## electronic perturbations (electrophilic)




Binding equilibrium becomes more favorable as electron deficiency at **M** increases: X = $NR_2$ < OR < halide < TfO ~$Tf_2N$

## electronic perturbations (nucleophilic?)



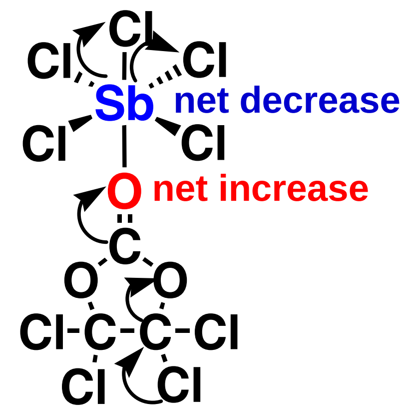

electron deficient
MP2: q(au) +0.990

*more electron deficient!!*
MP2: q(au) +1.070

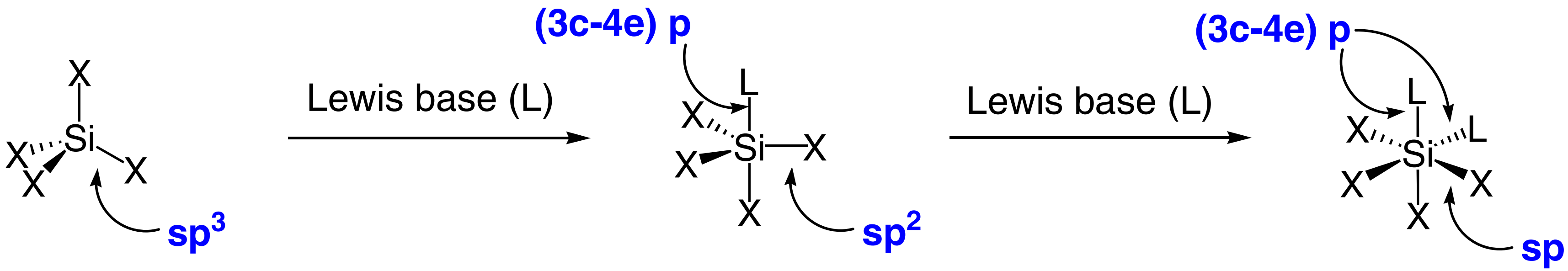
C. Cramer, private communication

## Gutmann's Fourth Rule "spillover effect"

"…although a donor-acceptor interaction will result in a net transfer of electron density from a donor species to an acceptor species, it will, in the case of polyatomic species, actually lead to a net **increase** of electron density at the donor atom of the donor species and to a net **decrease** of electron density at the acceptor atom of the acceptor species."



# *Structure, Bonding and Charge Distribution in Hypercoordinate Silicon Compounds*




tetrahdral ($T_d$)

formal bond order: 1.0

Si-Cl 2.039 Å

| X | Si charge | X charge |
|---|---|---|
| Cl | **+0.178** | - 0.045 |

tbp ($C_{3v}$)

formal bond order (apical): 0.75

formal bond order (basal): 0.83

| X | L | Si charge | X charge |
|---|---|---|---|
| Cl | Cl | **+0.279** | -0.430(a), -0139(b) |

octahedron ($D_{4h}$ or $C_{2v}$)

formal bond order: 0.66

Si-Cl 2.273 Å

| X | L | Si charge | X charge |
|---|---|---|---|
| Cl | Cl | **+0.539** | -0.423 |

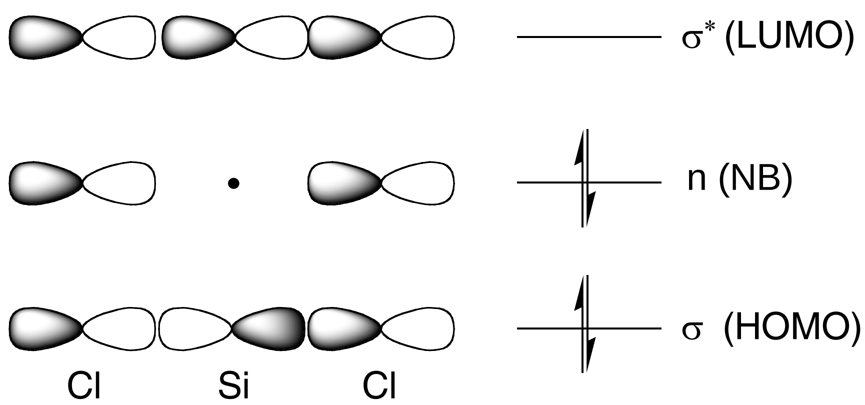
1. Coordination by both neutral and anionic ligands results in a decrease in the electron density at the central silicon atom and an increase in electron density on the ligands.

2. Hypervalent bonding is highly ionic in character and dissociation can be facile.

3. Hypervalent bonds favor electronegative ligands, sp bonds favor electropositive ligands

M. Gordon, *J. Phys. Chem.* **1990**, *94*, 8125

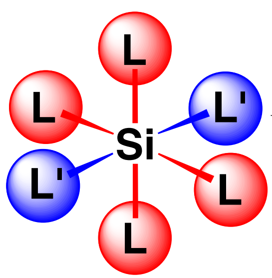
# The Hypervalent 3-Center/4 Electron Bond





hypervalent bonds formed from the $p_y$ and $p_z$ orbitals

covalent bonds from sp-hybrids obtained from $p_x$ and s-orbitals

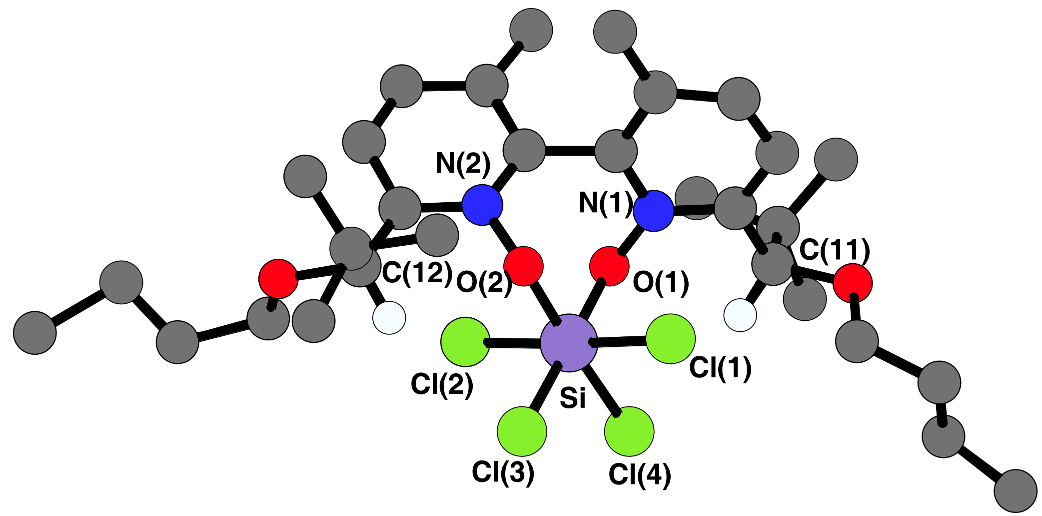



binding site for **s-donors**

binding site for **s-acceptors**

— hypervalent (3c-4e) bonds ($p_x$ and $p_z$ orbitals)

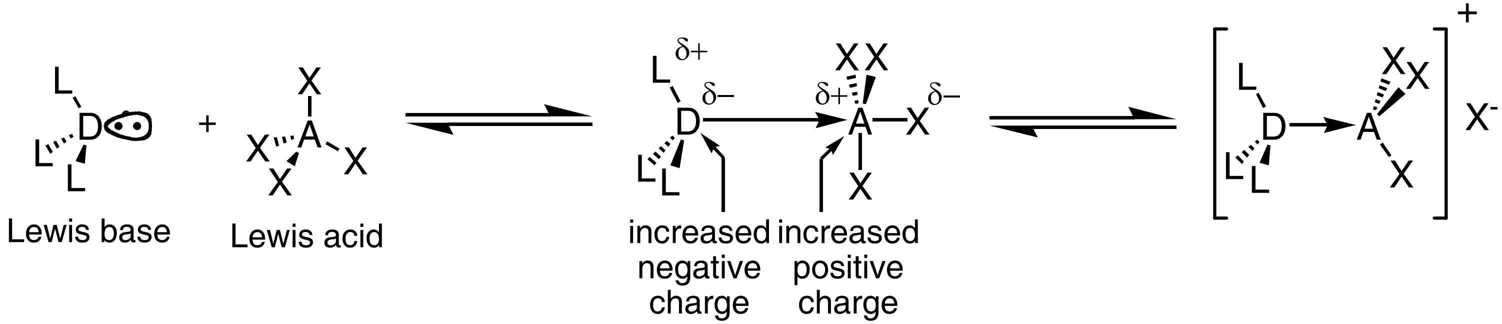
— covalent bonds ($p_y$ and s orbitals)



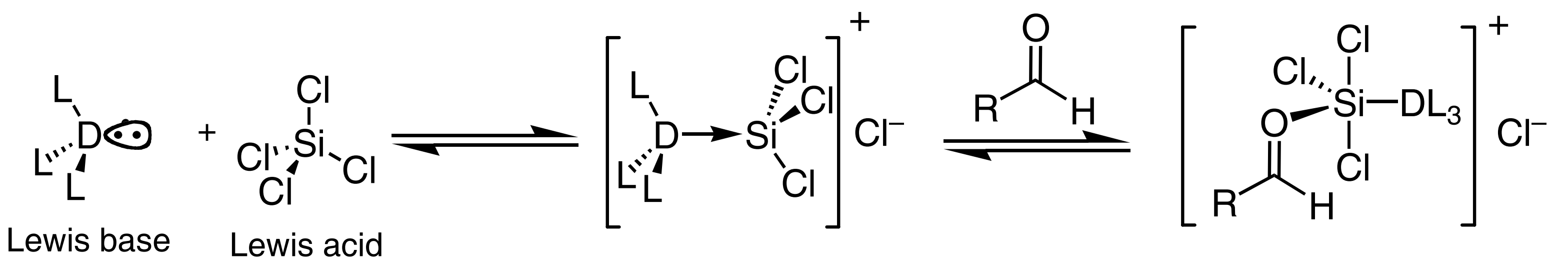

Si-Cl(1)/Cl(2): 2.180 Å

Si-Cl(3)/Cl(4): 2.197 Å

# *Lewis Base Activation of Lewis Acids*

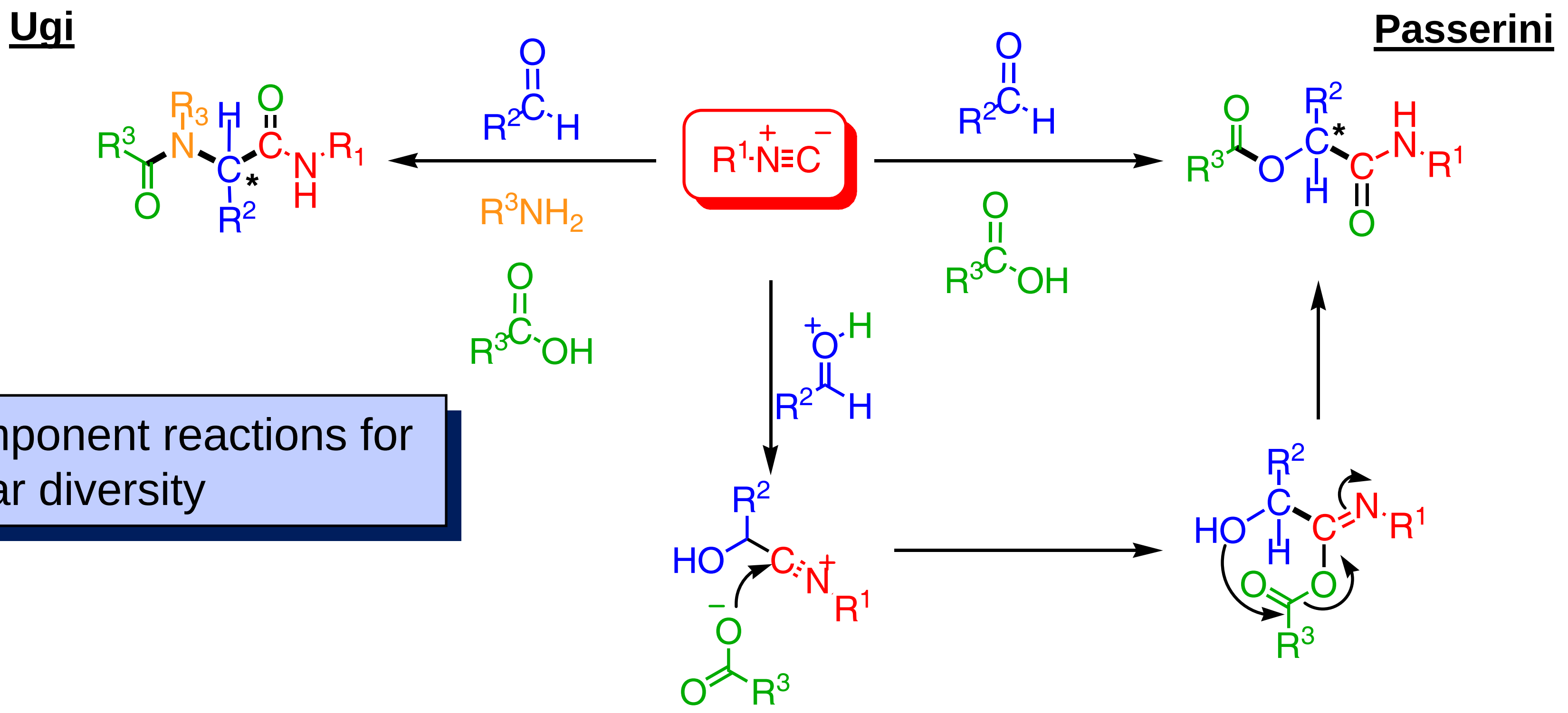



- The kinetically significant (strong) Lewis acid is generated only in the presence of the Lewis base thus negating the achiral background reaction.
- Reactions can be run with a stoichiometric amount of the weak Lewis acid
    - •Increased rates
    - •Product inhibition is minimized




Other electrophiles: enals, enones, azomethines, epoxides, nitrones, nitroalkenes
Pro Nucleophiles: Nu-Si$R_3$ = allylsilanes (stannanes) enol silanes, silyl ketene acetals, etc.

# *Catalytic Enantioselective Passerini Reaction*



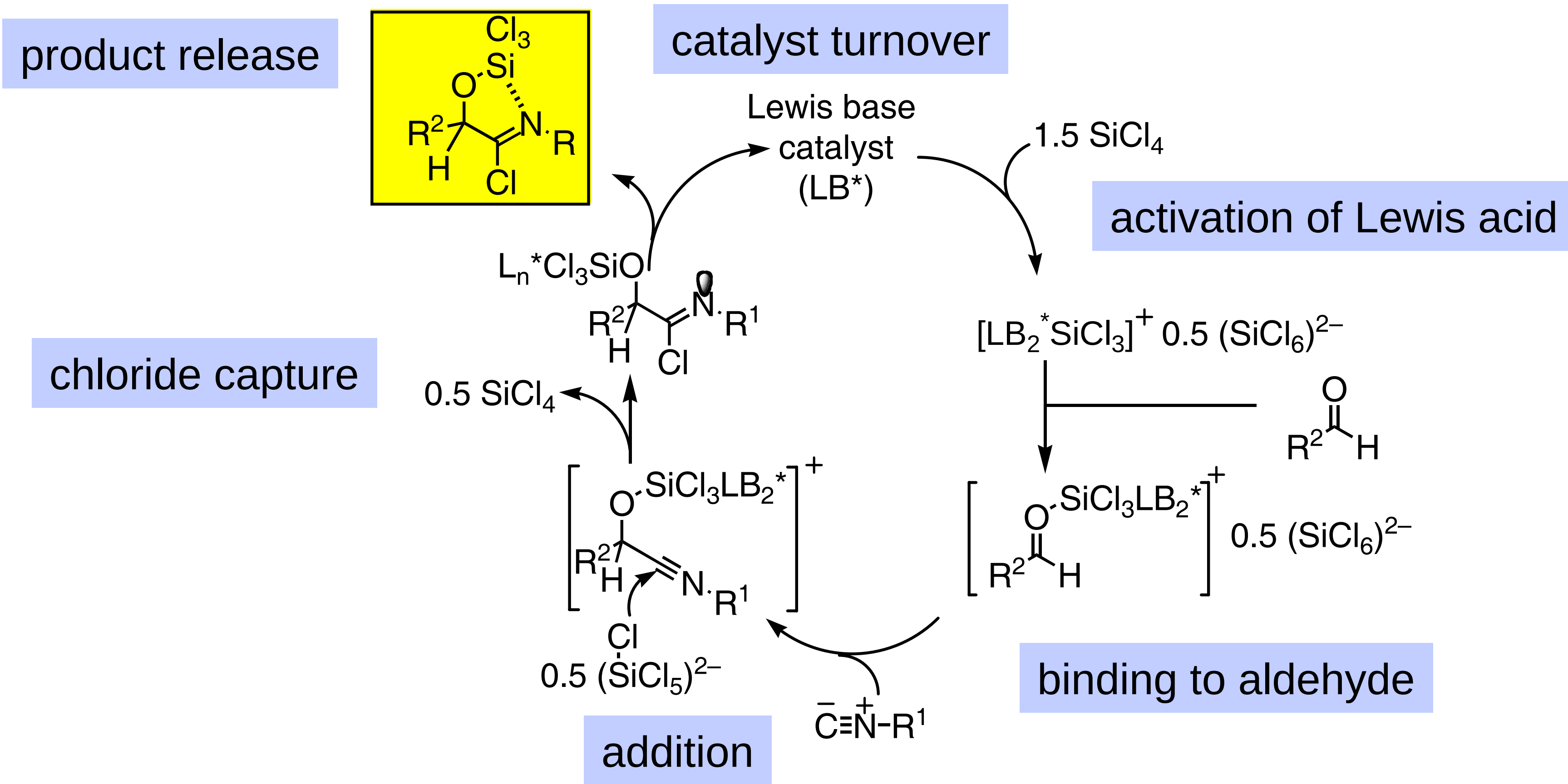

multicomponent reactions for molecular diversity

Isocyanide bears divalent carbon atom with electrophilic and nucleophilic properties

Up to four new bonds and one stereocenter created in very useful $\alpha$–acyloxy amides

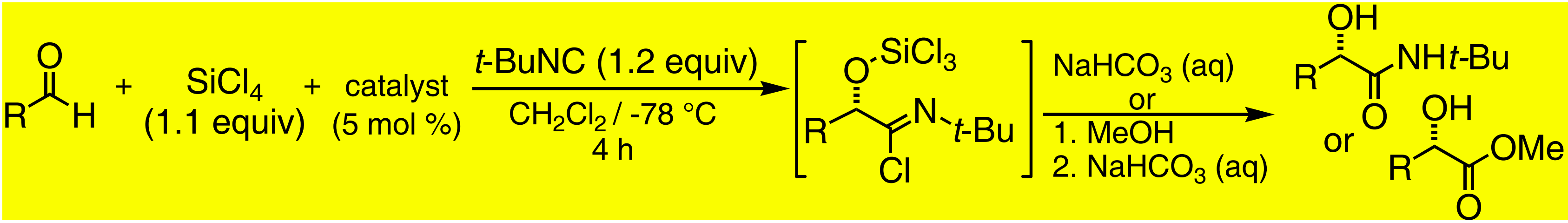
Auxiliary-based approaches but no examples of catalytic enantioselective process!!

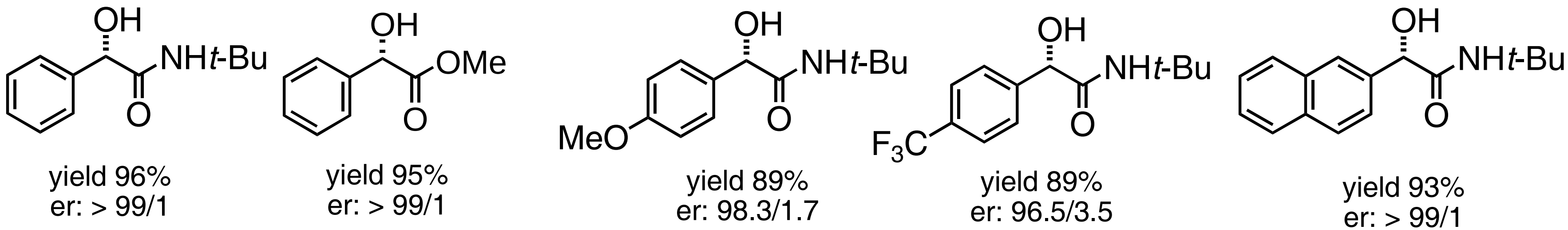
# *Passerini Reaction: Lewis Base Activation of Lewis Acid*

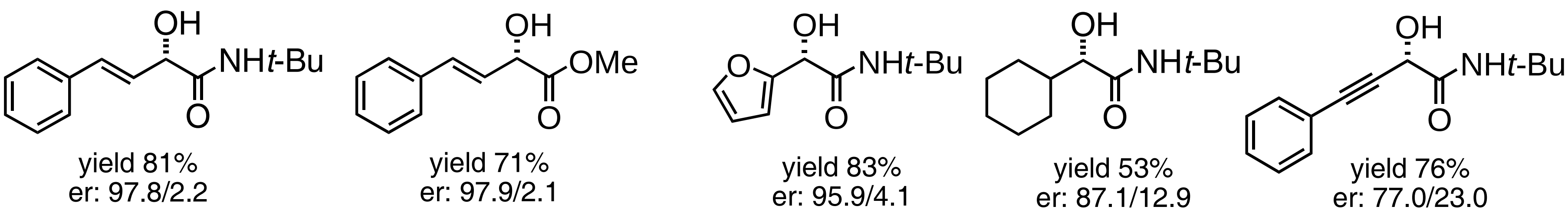


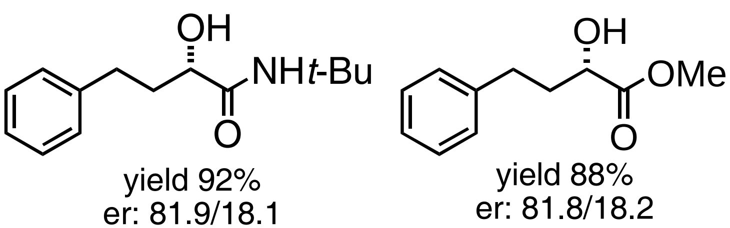

- •activated silyl cation preferentially binds carbonyl substrate, instead of the isocyanide
- •attenuated Lewis acidity of the silicon center in imidoyl chloride results facile turnover
- •catalyst turnover becomes the release of the Lewis base, instead of the Lewis acid

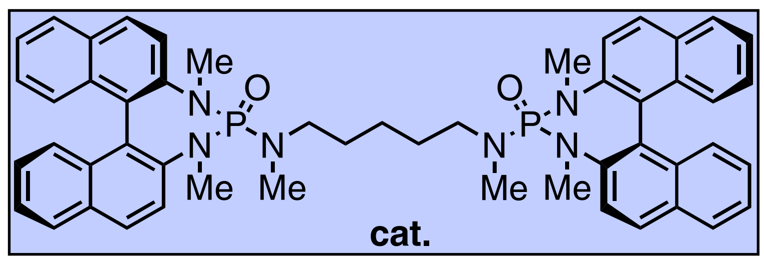
# *Catalytic Enantioselective Passerini Reaction: Aldehyde Survey*



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*Funding*

National Science Foundation
Eastman Kodak Company
Boehringer Ingelheim Pharmaceuticals
Ministry of Science and Education (Japan)
GlaxoSmithKline (UK)
Pharmacia Corporation
Abbott Laboratories