Enantioselective Radical Reactions

Justin Potnick
March 12, 2004
Outline

• Introduction to Radical Reactions
• Atom Transfers
• Reductive Alkylations
• Fragmentations
• Tandem Addition-Trapping Reactions
• Oxidations
• Summary
Introduction

Typical radical reactions go through 3 steps

1. Generation of radical from non-radical species
2. Propagation/Chain transfer process
3. Termination
Radical Properties

• Short lived, highly reactive species; difficult to use

• Proceed under mild, neutral conditions
  – Radical reactions have been performed in aqueous media

• Compatible with many functional groups, inert toward
  -OH or -NH

• Early, reactant-like TS$^+$ allows for prediction of product
  stereochemistry from ground state structure

Creating Selectivity

- Chiral source must be present during reaction

1. Chiral source bound to achiral substrate (complex-controlled)

\[
\text{SUB} + \quad \text{LA}^* \quad \text{SUB} \quad \xrightarrow{A} \quad \text{LA}^* \quad \text{PROD}^* \quad \text{PROD}^* + \quad \text{LA}^*
\]

2. Chiral source bound to the reagent (reagent-controlled)

\[
\text{SUB} + \quad \text{H-M}_{R}^* \quad \xrightarrow{} \quad \left[ \text{SUB}^* - \text{H-M}_{R}^* \right]^{+} \quad \rightarrow \quad \text{SUB-H}^* + \quad \text{M}_{R}^*
\]
Outline

• Introduction to Radical Reactions
• Atom Transfers
  • Reductive Alkylations
  • Fragmentations
  • Tandem Addition-Trapping Reactions
• Oxidations
• Summary
Atom Transfer Reactions

- Typically involve transfer of a hydrogen or halogen atom
- Transfer of atom from a chain-transfer agent to a radical species to generate another radical

1. Chiral Lewis Acid
   ![Chiral Lewis Acid](image)

2. Chiral Reagent
   ![Chiral Reagent](image)
Enantioselective Atom Transfer

- Lewis acids have been used to enhance and catalyze radical reactions

- Conjugate addition followed by selective H-atom transfer

Radical Initiator

- Trialkylboranes give free alkyl radicals upon treatment with oxygen
- $\text{Et}_3\text{B}/\text{O}_2$ works as a radical initiator even at -78 °C
- Advantageous for stereoselective reactions: improved selectivities at lower temperatures
- Alternate methods of radical generation typically involve high temperatures

Initiation: $\text{Et}_3\text{B} + \text{O}_2 \rightarrow \text{Et}_2\text{BOO}^\cdot + \text{Et}^\cdot$

Propagation: $\text{R-I} + \text{Et}^\cdot \rightarrow \text{R}^\cdot + \text{Et-I}$

Enantioselective Atom Transfer

- Selectivity was dependent on concentration of reactants
  - Low ee at low concentration
  - Suggests uncomplexed radical reacting to give racemic product in competing background reaction

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-CH₂OMe</td>
<td>88</td>
<td>62 (R)</td>
</tr>
<tr>
<td>2</td>
<td>-CH₂OEt</td>
<td>84</td>
<td>65 (R)</td>
</tr>
<tr>
<td>3</td>
<td>-CH₂OBn</td>
<td>89</td>
<td>58 (R)</td>
</tr>
<tr>
<td>4</td>
<td>-Me</td>
<td>78</td>
<td>30 (R)</td>
</tr>
</tbody>
</table>

Acyclic Systems

• With previous cyclic system, selectivity is easier to control
• Acyclic systems require more control

1. The complexing chiral group must be fixed relative to the prochiral center
2. The chiral group must shield one face of the radical or alkene
3. Reactivity of the complex must exceed reactivity of the free substrate

Rotamer Control

- Rotamer control in radical transformations is important for selectivity
- Achiral auxiliaries can provide a handle to control rotamers of acyclic substrates
  - Oxazolidinone templates were chosen based on success of chiral auxiliaries in Lewis acid promoted free radical transformations
  - S-cis favored due to $A^{1,3}$ strain

Acyclic Rotamer Control

\[
\text{2-naph} \text{H}_N\text{OMe} \xrightarrow{\text{Mg(ClO}_4)_2, \text{ligand 1, } \text{RX, Bu}_3\text{SnH, Et}_3\text{B/O}_2} \text{2-naph} \text{H}_N\text{O} \text{R}
\]

\[
\text{CH}_2\text{Cl}_2, -78 \, ^\circ\text{C, 3h}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>RX</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>AcBr</td>
<td>76</td>
<td>80</td>
</tr>
<tr>
<td>2</td>
<td>MeOCH\text{2}Br</td>
<td>71</td>
<td>65</td>
</tr>
<tr>
<td>3</td>
<td>EtI</td>
<td>72</td>
<td>85 (R)</td>
</tr>
<tr>
<td>4</td>
<td>iBuI</td>
<td>76</td>
<td>79</td>
</tr>
<tr>
<td>5</td>
<td>iPrI</td>
<td>62</td>
<td>83 (R)</td>
</tr>
<tr>
<td>6</td>
<td>cHexI</td>
<td>62</td>
<td>55 (R)</td>
</tr>
<tr>
<td>7</td>
<td>tBuI</td>
<td>54</td>
<td>27 (R)</td>
</tr>
</tbody>
</table>

Conjugate Additions to $\alpha$-Methacrylates

\[ \text{MgBr}_2 \cdot \text{Et}_2\text{O}, \text{Ligand 1} \rightarrow \]

1. **$\text{MgBr}_2 \cdot \text{Et}_2\text{O}, \text{Ligand 1}$**
   - $i$-PrX, Bu$_3$SnH, Et$_3$B/O$_2$
   - CH$_2$Cl$_2$, -78 $^\circ$C
   - 80% yield, 65% ee

2. **$\text{MgBr}_2 \cdot \text{Et}_2\text{O}, \text{Ligand 1}$**
   - acetyl-X, Bu$_3$SnH, Et$_3$B/O$_2$
   - CH$_2$Cl$_2$, -78 $^\circ$C
   - 75% yield, 75% ee

3. **$\text{MgBr}_2 \cdot \text{Et}_2\text{O}, \text{Ligand 1}$**
   - R-X, Bu$_3$SnH, Et$_3$B/O$_2$
   - CH$_2$Cl$_2$, -78 $^\circ$C
   - 25-96% yield, 18-90% ee

4. **$\text{MgBr}_2 \cdot \text{Et}_2\text{O}, \text{Ligand 1}$**
   - acetyl-X, Bu$_3$SnH, Et$_3$B/O$_2$
   - CH$_2$Cl$_2$, -78 $^\circ$C
   - 55% yield, 22% ee

Achiral Napthosultam Template

\[
\begin{align*}
\text{O-SO} & \text{N} \\
\text{N} & \text{O} \\
\text{MgBr}_2 & \text{Et}_2O, \text{Ligand 1} \\
\text{R-X, Bu}_3\text{SnH, Et}_3\text{B/O}_2 \text{CH}_2\text{Cl}_2}
\end{align*}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Temp (°C)</th>
<th>LA (equiv.)</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>i-Pr</td>
<td>-78</td>
<td>none</td>
<td>&lt;5</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>i-Pr</td>
<td>-78</td>
<td>(1.0)</td>
<td>90</td>
<td>78</td>
</tr>
<tr>
<td>3</td>
<td>i-Pr</td>
<td>-78</td>
<td>(0.3)</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>4</td>
<td>i-Pr</td>
<td>-40</td>
<td>(0.3)</td>
<td>71</td>
<td>59</td>
</tr>
<tr>
<td>5</td>
<td>i-Pr</td>
<td>0</td>
<td>(0.3)</td>
<td>52</td>
<td>5</td>
</tr>
<tr>
<td>6*</td>
<td>i-Pr</td>
<td>-78</td>
<td>(0.3)</td>
<td>55</td>
<td>80</td>
</tr>
<tr>
<td>7</td>
<td>t-Bu</td>
<td>-78</td>
<td>(0.3)</td>
<td>84</td>
<td>89</td>
</tr>
<tr>
<td>8</td>
<td>c-Hex</td>
<td>-78</td>
<td>(0.3)</td>
<td>71</td>
<td>82</td>
</tr>
<tr>
<td>9</td>
<td>MeOCH₂</td>
<td>-78</td>
<td>(0.3)</td>
<td>89</td>
<td>90</td>
</tr>
</tbody>
</table>

*Ph₃SnH was used as H-atom donor

Predicted Transition State to Account for Selectivity

S-trans rotamer

Attack from re face

Attack occurs before any rotamer interconversion: precursor geometry imparts on product stereochemistry

[Chemical Structures and Reactions]

25-96% yield, 18-90% ee

α-Substituted β-Amino Acids

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>RX</th>
<th>Compd</th>
<th>LA mol %</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Isopropyl-I</td>
<td>1a</td>
<td>No LA</td>
<td>99</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>Isopropyl-I</td>
<td>1a</td>
<td>100</td>
<td>91</td>
<td>40</td>
</tr>
<tr>
<td>3</td>
<td>Cyclohexyl-I</td>
<td>1a</td>
<td>100</td>
<td>71</td>
<td>79</td>
</tr>
<tr>
<td>4</td>
<td>Cyclohexyl-I</td>
<td>1a</td>
<td>30</td>
<td>76</td>
<td>40</td>
</tr>
<tr>
<td>5</td>
<td>CH₃CH₂-I</td>
<td>1b</td>
<td>100</td>
<td>85</td>
<td>68</td>
</tr>
<tr>
<td>6</td>
<td>CH₃CH₂-I</td>
<td>1b</td>
<td>30</td>
<td>78</td>
<td>36</td>
</tr>
<tr>
<td>7</td>
<td>Cl(CH₂)₃(CH₃)₂C-Br</td>
<td>1b</td>
<td>100</td>
<td>72</td>
<td>98</td>
</tr>
<tr>
<td>8</td>
<td>Cyclopentyl-I</td>
<td>1b</td>
<td>100</td>
<td>86</td>
<td>94</td>
</tr>
<tr>
<td>9</td>
<td>Cyclohexyl-I</td>
<td>1b</td>
<td>100</td>
<td>95</td>
<td>88</td>
</tr>
<tr>
<td>10</td>
<td>Cyclohexyl-I</td>
<td>1b</td>
<td>30</td>
<td>86</td>
<td>90</td>
</tr>
<tr>
<td>11</td>
<td>1-adamantyl-I</td>
<td>1b</td>
<td>100</td>
<td>71</td>
<td>97</td>
</tr>
</tbody>
</table>

Reasons for selectivity

• Radical reactions proceed through an early transition state that resembles starting complex

• H-atom transfer occurs rapidly on rotamer conformation timescale
  – Atom transfer or radical addition to a neutral molecule proceed at high rates: approximately $10^4$-$10^8$ dm$^3$M$^{-1}$s$^{-1}$
  – Geometry of starting material affects product stereochemistry

• Exploitation of relatively slow conformation changes is possible

Memory of Chirality

- Atom transfer occurs at a high rate
- Dependent on temperature and concentration of H-atom donor

Chiral Reagents

Reduction of $\alpha$-bromoketones

\[
\begin{align*}
\text{PhMe, -78 °C} & \quad \text{Et}_3\text{B/O}_2 \\
\text{SnMeH} + \text{PhBr}(\text{Ph}) & \quad \rightarrow \quad \text{PhMeH} \\
& \quad \text{30% yield, 41% ee}
\end{align*}
\]

Reduction of $\alpha$-bromoesters

\[
\begin{align*}
\text{Et}_2\text{O, -78 °C} & \quad \text{Et}_3\text{B/O}_2 \\
\text{SnH} + \text{PhBr}(\text{Me}) & \quad \rightarrow \quad \text{PhOMe} \\
& \quad \text{52% ee}
\end{align*}
\]

Hydrometallation of methyl methacrylate

\[
\begin{align*}
\text{AIBN, h} & \quad \text{or Et}_3\text{B/O}_2 \\
\text{SnH} + \text{CH}_3\text{CO}_2\text{Me} & \quad \rightarrow \quad \text{SnHCO}_2\text{Me} \\
\text{R} & \quad \text{61% yield, 3/1 dr} \\
\text{R} = \text{H} & \quad \text{a} \\
\text{R} = \text{TMS} & \quad \text{b} \\
\text{Tin-Hydride} & \quad \text{c}
\end{align*}
\]

Hydrosilylation of Alkenes

\[
\begin{align*}
1a & \xrightarrow{\text{Ph}_3\text{SiH, TBHN (0.05 eq.)}} 1 \ (0.05 \text{ eq.), } 60^\circ \text{C} \\
1b & \xrightarrow{\text{Ph}_3\text{SiH, TBHN (0.05 eq.)}} 1 \ (0.05 \text{ eq.), } 60^\circ \text{C} \\
1c & \xrightarrow{\text{Ph}_3\text{SiH, TBHN (0.05 eq.)}} 1 \ (0.05 \text{ eq.), } 60^\circ \text{C} \\
1d & \xrightarrow{\text{Ph}_3\text{SiH, TBHN (0.05 eq.)}} 1 \ (0.05 \text{ eq.), } 60^\circ \text{C} \\
\end{align*}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Thiol</th>
<th>Solvent</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a</td>
<td>Dioxane</td>
<td>88</td>
<td>80</td>
</tr>
<tr>
<td>2</td>
<td>1a</td>
<td>Benzene</td>
<td>92</td>
<td>86</td>
</tr>
<tr>
<td>3</td>
<td>1a</td>
<td>Hexane/Dioxane (5:1)</td>
<td>93</td>
<td>87</td>
</tr>
<tr>
<td>4</td>
<td>1b</td>
<td>Hexane/Dioxane (5:1)</td>
<td>90</td>
<td>95</td>
</tr>
<tr>
<td>5</td>
<td>1c</td>
<td>Hexane/Dioxane (4:1)</td>
<td>73</td>
<td>85</td>
</tr>
<tr>
<td>6</td>
<td>1d</td>
<td>Hexane/Dioxane (4:1)</td>
<td>87</td>
<td>94</td>
</tr>
</tbody>
</table>

Halogen Atom Transfer

- Addition of R-X to C-C double bond
- Good atom economy
- Product has halide group, allowing for further functionalization
- Reaction can be slow for R \ ? EWG

\[
R-X \xrightarrow{\text{initiation}} R^\cdot + R'R \quad \rightarrow \quad R_{R'}^\cdot \quad \rightarrow \quad R_{R'}X^\cdot + R^\cdot
\]

Yield: 5-15%
best ee approx. 40%

Atom Transfer Radical Cyclizations

- Transfer of halogen atom from one C to another followed by ring formation
- Halogen atom is retained in the product
- Can be promoted or catalyzed by Lewis acids
Radical Cyclizations

\[
\begin{align*}
\text{1a} \quad n = 1, R_1 = R_2 = \text{Me} \\
\text{1b} \quad n = 2, R_1 = \text{Et}, R_2 = \text{H} \\
\text{1c} \quad n = 2, R_1 = \text{H}, R_2 = \text{Et} \\
\text{1d} \quad n = 2, R_1 = R_2 = \text{Me}
\end{align*}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substr</th>
<th>Catalyst (equiv.)</th>
<th>Solvent</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a</td>
<td>1.1</td>
<td>CH\textsubscript{2}Cl\textsubscript{2}</td>
<td>7.5</td>
<td>68</td>
<td>71</td>
</tr>
<tr>
<td>2</td>
<td>1a</td>
<td>1.1</td>
<td>toluene</td>
<td>5</td>
<td>67</td>
<td>94</td>
</tr>
<tr>
<td>3\textsuperscript{a}</td>
<td>1a</td>
<td>0.3</td>
<td>toluene</td>
<td>7</td>
<td>68</td>
<td>92</td>
</tr>
<tr>
<td>4\textsuperscript{a}</td>
<td>1b</td>
<td>0.3</td>
<td>toluene</td>
<td>12</td>
<td>58 (1/1)\textsuperscript{b}</td>
<td>74/87\textsuperscript{c}</td>
</tr>
<tr>
<td>5\textsuperscript{a}</td>
<td>1c</td>
<td>0.3</td>
<td>toluene</td>
<td>9.5</td>
<td>81 (1/1.4)\textsuperscript{b}</td>
<td>74/95\textsuperscript{c}</td>
</tr>
<tr>
<td>6</td>
<td>1d</td>
<td>1.1</td>
<td>toluene</td>
<td>7.5</td>
<td>62</td>
<td>93</td>
</tr>
<tr>
<td>7\textsuperscript{a}</td>
<td>1d</td>
<td>0.5</td>
<td>toluene</td>
<td>7.5</td>
<td>53</td>
<td>94</td>
</tr>
</tbody>
</table>

\textsuperscript{a} MS 4Å added; \textsuperscript{b} ratio of 2b:2c; \textsuperscript{c} ee for 2b/2c

Tandem Atom Transfer Cyclizations

![Chemical structures](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>T (°C)</th>
<th>Solvent</th>
<th>Product</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a</td>
<td>-78</td>
<td>CH₂Cl₂</td>
<td>2a</td>
<td>41</td>
<td>13</td>
</tr>
<tr>
<td>2</td>
<td>1a</td>
<td>-78</td>
<td>CH₂Cl₂</td>
<td>2a</td>
<td>24</td>
<td>33</td>
</tr>
<tr>
<td>3</td>
<td>2a</td>
<td>-40</td>
<td>toluene</td>
<td>2b</td>
<td>23</td>
<td>82</td>
</tr>
<tr>
<td>4</td>
<td>2a</td>
<td>-20</td>
<td>toluene</td>
<td>2b</td>
<td>16</td>
<td>84</td>
</tr>
</tbody>
</table>

- Sets four stereocenters in one step with a single diastereomer observed

Outline

• Introduction to Radical Reactions
• Atom Transfers
• Reductive Alkylations
• Fragmentations
• Tandem Addition-Trapping Reactions
• Oxidations
• Summary
Reductive Alkylation

- Addition to carbon-carbon or carbon-heteroatom multiple bonds, followed by trapping with an H-atom source
  - Conjugate additions
  - Addition to imines
  - Cyclizations

- Catalysis is possible with the use of Lewis acids

\[ \begin{align*}
  &\text{Initiator} \\
  &\text{H-atom source} \\
  &R''YR'X
\end{align*} \]

\[ \begin{align*}
  &\text{R''YR''O} \\
  &\text{H} \\
  &\text{R''YR''O} \\
  &\text{R''YR''O} \\
\end{align*} \]

\[ \begin{align*}
  &\text{Y = C or N}
\end{align*} \]
Conjugate Additions

\[
\text{LA, Chiral Ligand 1, } \text{CH}_2\text{Cl}_2, -78 \, ^\circ\text{C}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>LA</th>
<th>Ligand (eq)</th>
<th>Temp (°C)</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MgI(_2)</td>
<td>1a (1.0)</td>
<td>-78</td>
<td>88</td>
<td>82 (R)</td>
</tr>
<tr>
<td>2</td>
<td>MgI(_2)</td>
<td>1a (0.5)</td>
<td>-78</td>
<td>86</td>
<td>79 (R)</td>
</tr>
<tr>
<td>3</td>
<td>MgI(_2)</td>
<td>1b (1.0)</td>
<td>-78</td>
<td>88</td>
<td>47 (S)</td>
</tr>
<tr>
<td>4</td>
<td>Zn(OTf)(_2)</td>
<td>1b (1.0)</td>
<td>-78</td>
<td>88</td>
<td>61 (S)</td>
</tr>
<tr>
<td>5</td>
<td>MgI(_2)</td>
<td>1c (1.0)</td>
<td>-78</td>
<td>88</td>
<td>93 (R)</td>
</tr>
<tr>
<td>6</td>
<td>MgI(_2)</td>
<td>1c (0.3)</td>
<td>-78</td>
<td>91</td>
<td>97 (R)</td>
</tr>
<tr>
<td>7</td>
<td>MgI(_2)</td>
<td>1c (0.3)</td>
<td>-20</td>
<td>93</td>
<td>95 (R)</td>
</tr>
<tr>
<td>8</td>
<td>MgI(_2)</td>
<td>1c (0.3)</td>
<td>25</td>
<td>87</td>
<td>93 (R)</td>
</tr>
<tr>
<td>9</td>
<td>Zn(OTf)(_2)</td>
<td>1c (1.0)</td>
<td>-78</td>
<td>-</td>
<td>53 (R)</td>
</tr>
</tbody>
</table>

**Conjugate Additions**

![Chemical reaction](image)

LA, Chiral Ligand 1, CH₂Cl₂, -78 °C

<table>
<thead>
<tr>
<th>Entry</th>
<th>LA</th>
<th>Ligand (eq)</th>
<th>Temp (°C)</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MgI₂</td>
<td>1a (1.0)</td>
<td>-78</td>
<td>88</td>
<td>82 (R)</td>
</tr>
<tr>
<td>2</td>
<td>MgI₂</td>
<td>1a (0.5)</td>
<td>-78</td>
<td>86</td>
<td>79 (R)</td>
</tr>
<tr>
<td>3</td>
<td>MgI₂</td>
<td>1b (1.0)</td>
<td>-78</td>
<td>88</td>
<td>47 (S)</td>
</tr>
<tr>
<td>4</td>
<td>Zn(OTf)₂</td>
<td>1b (1.0)</td>
<td>-78</td>
<td>88</td>
<td>61 (S)</td>
</tr>
<tr>
<td>5</td>
<td>MgI₂</td>
<td>1c (1.0)</td>
<td>-78</td>
<td>88</td>
<td>93 (R)</td>
</tr>
<tr>
<td>6</td>
<td>MgI₂</td>
<td>1c (0.3)</td>
<td>-78</td>
<td>91</td>
<td>97 (R)</td>
</tr>
<tr>
<td>7</td>
<td>MgI₂</td>
<td>1c (0.3)</td>
<td>-20</td>
<td>93</td>
<td>95 (R)</td>
</tr>
<tr>
<td>8</td>
<td>MgI₂</td>
<td>1c (0.3)</td>
<td>25</td>
<td>87</td>
<td>93 (R)</td>
</tr>
<tr>
<td>9</td>
<td>Zn(OTf)₂</td>
<td>1c (1.0)</td>
<td>-78</td>
<td>-</td>
<td>53 (R)</td>
</tr>
</tbody>
</table>

Achiral Additives

- Achiral additives were used in an attempt to increase selectivity

![Chemical Structure]

<table>
<thead>
<tr>
<th>Entry</th>
<th>R$^1$</th>
<th>1 (equiv)</th>
<th>Additive</th>
<th>R</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H</td>
<td>1.0</td>
<td>none</td>
<td>t-Bu</td>
<td>88</td>
<td>9 (S)</td>
</tr>
<tr>
<td>2</td>
<td>H</td>
<td>1.0</td>
<td>2b</td>
<td>t-Bu</td>
<td>78</td>
<td>52 (S)</td>
</tr>
<tr>
<td>3</td>
<td>Ph</td>
<td>1.0</td>
<td>none</td>
<td>t-Bu</td>
<td>80</td>
<td>3 (S)</td>
</tr>
<tr>
<td>4</td>
<td>Ph</td>
<td>1.0</td>
<td>2b</td>
<td>t-Bu</td>
<td>96</td>
<td>88 (R)</td>
</tr>
<tr>
<td>5</td>
<td>Ph</td>
<td>1.0</td>
<td>2b</td>
<td>i-Pr</td>
<td>86</td>
<td>82 (R)</td>
</tr>
<tr>
<td>6</td>
<td>Ph</td>
<td>1.0</td>
<td>2c</td>
<td>i-Pr</td>
<td>98</td>
<td>29 (S)</td>
</tr>
<tr>
<td>7</td>
<td>Ph</td>
<td>0.25</td>
<td>2b</td>
<td>i-Pr</td>
<td>92</td>
<td>80 (R)</td>
</tr>
</tbody>
</table>

## Pyrazole Template

![Pyrazole Template Structure](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Ligand (equiv)</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>i-Pr</td>
<td>1.0</td>
<td>76</td>
<td>51 (S)</td>
</tr>
<tr>
<td>2</td>
<td>i-Pr</td>
<td>0.3</td>
<td>84</td>
<td>39 (S)</td>
</tr>
<tr>
<td>3</td>
<td>Et</td>
<td>1.0</td>
<td>80</td>
<td>39 (R)</td>
</tr>
<tr>
<td>4</td>
<td>cyclohexyl</td>
<td>1.0</td>
<td>81</td>
<td>81</td>
</tr>
<tr>
<td>5</td>
<td>cyclohexyl</td>
<td>0.3</td>
<td>76</td>
<td>39</td>
</tr>
</tbody>
</table>

Other Lewis Acids

- Lanthanide Lewis acids can be used


Aldol-Type Products

- β-Alkoxy groups prone to elimination with ionic nucleophiles
- Nucleophilic radical addition avoids this

\[
\text{OCOPh} \quad \text{O} \quad \text{N} \quad \text{O}
\]

Addition to Imines

\[
\text{MeO}_2\text{C} = \text{NOBn} + \text{MgBr}_2, 1, \text{i-Prl}, \text{Bu}_3\text{SnH} \quad \text{CH}_2\text{Cl}_2, \text{Et}_3\text{B}, -78^\circ \text{C} \rightarrow \text{MeO}_2\text{C} - \text{NOBn} \\
97\% \text{Yield}, 52\% \text{ee} (R)
\]


\[
\text{EtO}_2\text{C} = \text{NOBn} \quad \text{i-Prl}, 2, \text{Et}_3\text{B/O}_2 \quad \text{CH}_2\text{Cl}_2, \text{r.t.} \rightarrow \text{EtO}_2\text{C} - \text{NHOBn} \\
56\% \text{Yield}, 15\% \text{ee}
\]


\[
\text{Cu(1)(H}_2\text{O})_2(\text{OTf})_2 \quad \text{i-Prl, Et}_3\text{B/O}_2 \quad \text{CH}_2\text{Cl}_2, 25^\circ \text{C} \rightarrow \text{HN} - \text{i-Pr} \\
66\% \text{Yield}, 95\% \text{ee} (R)
\]

Enantioselective 5-Exo Cyclization

![Chemical structures and reactions](image)

53% Yield, 77% ee


- Cyclization using “memory of chirality”

Outline

• Introduction to Radical Reactions
• Atom Transfers
• Reductive Alkylations
• Fragmentations
• Tandem Addition-Trapping Reactions
• Oxidations
• Summary
Fragmentation Reactions

1. Addition of radical to a neutral molecule

2. β-elimination of resultant radical to generate terminal olefin

\[
\begin{align*}
\text{R}^1 \text{R}^1 \text{X} & \quad + \quad \text{乙烯} \text{Z} & \quad \rightarrow & \quad \text{R}^1 \text{R}^1 \text{Z} \quad + \quad \text{X-Z}
\end{align*}
\]

\[
\begin{align*}
\text{R}^1 \text{R}^1 \text{Z} & \quad + \quad \text{乙烯} & \quad \rightarrow & \quad \text{R}^1 \text{R}^1 \text{Z} \quad + \quad \text{乙烯}
\end{align*}
\]

\[
\begin{align*}
\text{X} = \text{halide}; \quad \text{Z} = \text{Sn(Bu)}_3, \text{Si(Me)}_3, \text{Si(Si(Me)}_3)_3
\end{align*}
\]
Fragmentation Reactions

\[
\begin{align*}
R^1\text{Br} & 
\overset{\text{MX}_2, 1, \text{Et}_3\text{B/O}_2}{\xrightarrow{\text{CH}_2\text{Cl}_2, -78 \degree C}} 
\text{R}^1\text{O} \text{N} \text{O} 
\end{align*}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>(\text{MX}_2)</th>
<th>(\text{Z})</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(\text{Zn(OTf)}_2)</td>
<td>(\text{SnBu}_3)</td>
<td>84</td>
<td>42</td>
</tr>
<tr>
<td>2</td>
<td>(\text{Zn(OTf)}_2)</td>
<td>(\text{SiMe}_3)</td>
<td>88</td>
<td>90</td>
</tr>
<tr>
<td>3</td>
<td>(\text{MgI}_2)</td>
<td>(\text{SiMe}_3)</td>
<td>86</td>
<td>68</td>
</tr>
</tbody>
</table>


\[
\begin{align*}
\text{O} \text{N} \text{O} & 
\overset{\text{SnBu}_3}{\xrightarrow{\text{Me}_3\text{Al/2, Et}_3\text{B/O}_2}} 
\text{O} \text{N} \text{O} 
\end{align*}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>(R)</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(\text{Me})</td>
<td>93</td>
<td>34</td>
</tr>
<tr>
<td>2</td>
<td>(\text{H})</td>
<td>90</td>
<td>32</td>
</tr>
</tbody>
</table>

Fragmentation Reactions

Fragmentation Reactions

Fragmentation Reactions of $\alpha$-Iodolactones

- Single point binding chiral Lewis acid

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Additive</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Me</td>
<td>None</td>
<td>72</td>
<td>27</td>
</tr>
<tr>
<td>2</td>
<td>Me</td>
<td>Et$_2$O</td>
<td>84</td>
<td>81</td>
</tr>
<tr>
<td>3</td>
<td>CH$_2$OEt</td>
<td>Et$_2$O</td>
<td>85</td>
<td>85</td>
</tr>
<tr>
<td>4</td>
<td>CH$_2$OBn</td>
<td>Et$_2$O</td>
<td>76</td>
<td>91</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Entry</th>
<th>2 (eq.)</th>
<th>LA (eq.)</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>Me$_3$Al (2)</td>
<td>76</td>
<td>51</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>i- Bu$_3$Al (2)</td>
<td>75</td>
<td>43</td>
</tr>
<tr>
<td>3</td>
<td>0.5</td>
<td>Me$_3$Al (2)</td>
<td>72</td>
<td>54</td>
</tr>
<tr>
<td>4</td>
<td>0.5</td>
<td>i- Bu$_3$Al (2)</td>
<td>72</td>
<td>37</td>
</tr>
</tbody>
</table>

**Allylation Using an Acyclic Template**

![Chemical Structure]

**Table**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ligand</th>
<th>LA</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>Et$_3$Al</td>
<td>68</td>
<td>60</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>Et$_3$Al</td>
<td>80</td>
<td>64</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>Mg(OTf)$_2$</td>
<td>65</td>
<td>52</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>Mg(OTf)$_2$</td>
<td>41</td>
<td>83</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>Mg(OTf)$_2$</td>
<td>64</td>
<td>50</td>
</tr>
</tbody>
</table>

Outline

- Introduction to Radical Reactions
- Atom Transfers
- Reductive Alkylations
- Fragmentations
- Tandem Addition-Trapping Reactions
- Oxidations
- Summary
Tandem Radical Reactions

- Addition of a radical to a neutral molecule followed by trapping of the resultant radical
- Potential of forming two stereogenic centers

\[ R^1 - I + \text{Z} \rightarrow R^1 Z \]

- Downside is possibility of reactive byproduct formed

\[ Z = \text{Sn(Bu)}_3, \text{Si(Me)}_3, \text{Si(Si(Me)}_3)_3 \]
Enantioselective Tandem Addition

\[ R-I + \text{Acrylate} + \text{SnBu}_3 \xrightarrow{\text{Zn(OTf)}_2, \text{Ligand 2}} \text{Product} + \text{Bu}_3\text{Sn-I} \]

<table>
<thead>
<tr>
<th>Entry</th>
<th>R (equiv.)</th>
<th>Acrylate:M:L*</th>
<th>Solvent</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>c-hexyl (10)</td>
<td>1:1:1</td>
<td>CH(_2)Cl(_2)</td>
<td>62</td>
<td>50</td>
</tr>
<tr>
<td>2</td>
<td>c-hexyl (10)</td>
<td>1:1:1</td>
<td>Et(_2)O</td>
<td>90</td>
<td>64</td>
</tr>
<tr>
<td>3</td>
<td>c-hexyl (10)</td>
<td>1:2:2</td>
<td>Et(_2)O</td>
<td>61</td>
<td>80</td>
</tr>
<tr>
<td>4</td>
<td>c-hexyl (1.5)</td>
<td>1:1:1.2</td>
<td>CH(_2)Cl(_2)/pent 6:4</td>
<td>62</td>
<td>68</td>
</tr>
<tr>
<td>5</td>
<td>c-hexyl (1.5)</td>
<td>1:2:2.4</td>
<td>CH(_2)Cl(_2)/pent 6:4</td>
<td>92</td>
<td>72</td>
</tr>
<tr>
<td>6</td>
<td>t-Bu (5)</td>
<td>1:1:1.2</td>
<td>CH(_2)Cl(_2)/pent 6:4</td>
<td>78</td>
<td>88</td>
</tr>
<tr>
<td>7</td>
<td>t-Bu (5)</td>
<td>1:1:1.2</td>
<td>CH(_2)Cl(_2)/pent 6:4</td>
<td>92</td>
<td>90</td>
</tr>
<tr>
<td>8</td>
<td>t-Bu (5)</td>
<td>1:2:2.1</td>
<td>Et(_2)O</td>
<td>55</td>
<td>88</td>
</tr>
</tbody>
</table>

**Tandem Reaction vs. Fragmentation**

Higher selectivity of tandem reaction pathway may be due to catalysis of background reaction by tin bromide byproduct


<table>
<thead>
<tr>
<th>Entry</th>
<th>Precursor</th>
<th>LA eq.</th>
<th>3a</th>
<th>3b</th>
<th>3c</th>
<th>3d</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>0.6</td>
<td>84</td>
<td>76</td>
<td>62</td>
<td>56</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>1.0</td>
<td>90</td>
<td>78</td>
<td>69</td>
<td>61</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>2.0</td>
<td>90</td>
<td>80</td>
<td>75</td>
<td>67</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>0.6</td>
<td>64</td>
<td>43</td>
<td>36</td>
<td>25</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>1.0</td>
<td>74</td>
<td>58</td>
<td>50</td>
<td>42</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td>2.0</td>
<td>76</td>
<td>64</td>
<td>53</td>
<td>46</td>
</tr>
</tbody>
</table>
Lanthanide Lewis Acids

- Lanthanide triflates are generally air and moisture stable
- Strong Lewis acidity
- Ionic radii of lanthanide metals increase in a small and regular manner: easy to modify chiral environment

\[
\begin{align*}
R-I + \text{enantiopure \text{N,N,N-triethyl-N'-(2-pyridyl)ethylenediamine}} + \text{SnBu}_3 & \rightarrow \text{Y(OTf)}_3 \text{ (30 mol\%)} \\
& \text{Chiral Ligand 1} \\
& \text{CH}_2\text{Cl}_2, \text{Et}_3\text{B/O}_2, -78^\circ \text{C}
\end{align*}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ClCH_2^-</td>
<td>56</td>
<td>42</td>
</tr>
<tr>
<td>2</td>
<td>Et</td>
<td>61</td>
<td>70</td>
</tr>
<tr>
<td>3</td>
<td>n-Pr</td>
<td>57</td>
<td>60</td>
</tr>
<tr>
<td>4</td>
<td>n-Bu</td>
<td>41</td>
<td>38</td>
</tr>
<tr>
<td>5</td>
<td>i-Pr</td>
<td>50</td>
<td>56</td>
</tr>
<tr>
<td>6</td>
<td>t-Bu</td>
<td>40</td>
<td>24</td>
</tr>
<tr>
<td>7</td>
<td>c-Hex</td>
<td>53</td>
<td>31</td>
</tr>
</tbody>
</table>

Allylation of an $\alpha$-Sulfonyl Radical

\[
\begin{align*}
\text{Ar} &= 2-(1\text{-benzylbenzimidazolyl}) \\
\text{Entry} & \quad \text{Allylstannane} & \quad \text{Time (min)} & \quad \text{Yield (\%)} & \quad \text{ee (\%)} \\
1 & \text{AllylBu$_3$Sn} & 120 & 35 & 80 \\
2 & \text{AllylPh$_3$Sn} & 180 & 49 & 16 \\
3 & \text{AllylBu$_2$Sn} & 120 & 74 & 50 \\
4 & \text{AllylBu$_2$Sn (5 eq.)} & 50 & 86 & 78 \\
5 & \text{AllylBu$_2$Sn (10 eq.)} & 20 & 80 & 84
\end{align*}
\]

Control of $\alpha$ and $\beta$ carbon selectivity

![Chemical Structure](image)

Lewis Acid, 1, $R^1X$

$Et_3B/O_2, CH_2Cl_2, -78^\circ C$

$Sn(R^2)_3$

$R^2 = Bu$ or $Ph$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Sub.</th>
<th>$R^1X$</th>
<th>LA (0.3 eq.)</th>
<th>Yield (%)</th>
<th>dr</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>EtI</td>
<td>MgI$_2$</td>
<td>79</td>
<td>32:1</td>
<td>77</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>c-HexI</td>
<td>MgI$_2$</td>
<td>80</td>
<td>60:1</td>
<td>92</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>t-Bul</td>
<td>MgI$_2$</td>
<td>84</td>
<td>99:1</td>
<td>97</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>t-Bul</td>
<td>Cu(OTf)$_2$</td>
<td>90</td>
<td>99:1</td>
<td>-96</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>c-HexI</td>
<td>Mg(ClO$_4$)$_2$</td>
<td>83</td>
<td>4:1</td>
<td>62</td>
</tr>
<tr>
<td>6</td>
<td>4</td>
<td>EtI</td>
<td>Mg(ClO$_4$)$_2$</td>
<td>83</td>
<td>7:1</td>
<td>66</td>
</tr>
<tr>
<td>7</td>
<td>4</td>
<td>t-Bul</td>
<td>Mg(ClO$_4$)$_2$</td>
<td>85</td>
<td>19:1</td>
<td>92</td>
</tr>
<tr>
<td>8</td>
<td>4</td>
<td>t-Bul</td>
<td>Cu(OTf)$_2$</td>
<td>66</td>
<td>50:1</td>
<td>-83</td>
</tr>
</tbody>
</table>

Control of $\alpha$ and $\beta$ carbon selectivity

![Chemical structure]

Lewis Acid, 1, $R^1X$
Et$_3$B/O$_2$, CH$_2$Cl$_2$, -78 $^\circ$C

<table>
<thead>
<tr>
<th>Entry</th>
<th>Sub.</th>
<th>$R^1X$</th>
<th>LA (0.3 eq.)</th>
<th>Yield (%)</th>
<th>dr</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>EtI</td>
<td>MgI$_2$</td>
<td>79</td>
<td>32:1</td>
<td>77</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>c-HexI</td>
<td>MgI$_2$</td>
<td>80</td>
<td>60:1</td>
<td>92</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>t-Bul</td>
<td>MgI$_2$</td>
<td>84</td>
<td>99:1</td>
<td>97</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>t-Bul</td>
<td>Cu(OTf)$_2$</td>
<td>90</td>
<td>99:1</td>
<td>-96</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>c-HexI</td>
<td>Mg(ClO$_4$)$_2$</td>
<td>83</td>
<td>4:1</td>
<td>62</td>
</tr>
<tr>
<td>6</td>
<td>4</td>
<td>EtI</td>
<td>Mg(ClO$_4$)$_2$</td>
<td>83</td>
<td>7:1</td>
<td>66</td>
</tr>
<tr>
<td>7</td>
<td>4</td>
<td>t-Bul</td>
<td>Mg(ClO$_4$)$_2$</td>
<td>85</td>
<td>19:1</td>
<td>92</td>
</tr>
<tr>
<td>8</td>
<td>4</td>
<td>t-Bul</td>
<td>Cu(OTf)$_2$</td>
<td>66</td>
<td>50:1</td>
<td>-83</td>
</tr>
</tbody>
</table>

Control of $\alpha$ and $\beta$ Carbon Selectivity

Following addition, trapping occurs in an anti manner
- $R^1$ blocks syn trapping
- Results suggest the stereochemistry at the $\beta$-carbon is primary determinant of $\alpha$-stereochemistry

Outline

• Introduction to Radical Reactions
• Atom Transfers
• Reductive Alkylations
• Fragmentations
• Tandem Addition-Trapping Reactions
• Oxidations
• Summary
Enantioselective Radical Oxidations

- Examples shown to this point involved reductive generation of radical species

- Oxidative generation of cationic radical species is also possible
  - Can undergo coupling reactions
  - Oxidation of activated C-H bonds
  - Oxidation of alcohols and amines
Cross-Coupling Reactions

\[
\begin{align*}
\text{OTMS} & \quad \text{VO(OEt)Cl}_2, \text{1} & \quad \text{R} \\
\text{-e}^- & \quad -\text{TMS}^+ & \quad \text{O} \quad \text{-e}^- & \quad -\text{TMS}^+ \\
\end{align*}
\]

58% yield, 85% ee


\[
\begin{align*}
\text{O} \quad \text{N} & \quad \text{O} \quad \text{Ph} \\
\text{N} & \quad \text{O} \quad \text{Ph} \\
\text{Ph} & \quad \text{O} \quad \text{Ph} \\
\text{Ph} & \quad \text{O} \quad \text{Ph} \\
\text{Ph} & \quad \text{O} \quad \text{Ph} \\
\end{align*}
\]

91%

dl : meso = 25:75
76% ee


\[
\begin{align*}
\text{Ph} & \quad \text{O} \quad \text{Ph} \\
\text{O} & \quad \text{Ph} \\
\text{O} & \quad \text{Ph} \\
\text{O} & \quad \text{Ph} \\
\text{O} & \quad \text{Ph} \\
\end{align*}
\]

Yield (%) ee (%)
89 17
81 93

Activated C-H Bond Oxidation

- Benzylic hydrogens are activated towards oxidation
- Several groups have used porphyrin complexes to effect this transformation enantioselectively

\[ \begin{align*}
X - \text{phenyl} & \quad \text{(catalytic)} \\
1 (\text{catalytic}) & \quad \text{Cl}_2\text{PyNO} \\
Yields: 28-72\% & \quad \text{ee's: 62-76\%} \\
(\text{Ketone accounts for remainder of yield})
\end{align*} \]

\[ \begin{align*}
\text{1} & \quad \text{2a} \quad 25\% \text{ yield, 90\% ee} \\
\text{2b} & \quad 17\% \text{ yield, 81\% ee}
\end{align*} \]

\[ \begin{align*}
\text{Ph} & \quad \text{2 mol\% CuOTf/3} \\
\text{MeCN, -18 °C} & \quad \text{12 d} \\
\text{70\% yield, 4\% ee}
\end{align*} \]

Insight into Mechanism

- Known to proceed by radical mechanism

\[ \text{Path a: H-atom abstraction} \]

\[ \begin{align*}
\text{Path b: SET} & \\
\end{align*} \]

- Kinetic isotope effect result supports path a

\[ \frac{k_H}{k_D} = 4.6 \]

Oxidation of Alcohols: Kinetic Resolution

\[
\text{R} \text{Me} \text{OH} \quad \text{1 (catalytic)} \quad \text{solvent} \quad \text{R} \text{Me} \text{O} \text{R} \text{Me} \text{OH} + \quad \text{1}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>( R_1 )</th>
<th>solvent</th>
<th>Conversion (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph-CH=CH-</td>
<td>( \text{C}_6\text{H}_6 )</td>
<td>76</td>
<td>97</td>
</tr>
<tr>
<td>2</td>
<td>Ph-</td>
<td>( \text{C}_6\text{H}_5\text{Cl} )</td>
<td>65</td>
<td>95</td>
</tr>
<tr>
<td>3</td>
<td>Ph-C=C-</td>
<td>( \text{C}_6\text{H}_5\text{Cl} )</td>
<td>65</td>
<td>&gt;99</td>
</tr>
<tr>
<td>4</td>
<td>PhCH(_2)-</td>
<td>( \text{C}_6\text{H}_5\text{CH}_3 )</td>
<td>58</td>
<td>82</td>
</tr>
</tbody>
</table>

Conclusion

• Much development concerning enantioselective radical reactions has occurred over the last ten years
  – Formation of C-H, C-X, and C-C bonds is possible
  – Asymmetric catalysis is now possible in many systems
  – Reactions proceed under mild conditions and are tolerant of functional groups

• Many areas left to explore
  – Enantioselective group transfer has not been developed
  – Use of alternate reaction conditions (aqueous media, polymer support)
  – Introduction of more functional groups
  – Use in a total synthesis
Acknowledgements

Advisor:
Jeff Johnson

Johnson Group:
Cory Bausch
Ashley Berman
Roy Bowman
Jody Karol
Xin Linghu
Mary Robert Nahm
David Nicewicz
Patrick Pohlhaus
Application of Tandem Radical Reaction

\[
\text{NO}R^1 + \text{I}R^2 \xrightarrow{\text{Ln(OTf)}_2 (0.3-1.0 \text{ eq.})} \text{CH}_2\text{Cl}_2/\text{THF} 2:1, \text{Et}_3\text{B}/\text{O}_2, -78^\circ\text{C}} \rightarrow \text{RCM}
\]

- Example is not enantioselective
- Possibility for enantioselective reaction exists and is current focus

Up to 88%