Rhenium-Catalyzed Didehydroxylation of Vicinal Diols to Alkenes Using a Simple Alcohol as a Reducing Agent

Elena Arceo, Jonathan A. Ellman, Robert G. Bergman
J. Am. Chem. Soc. 2010, 132, ASAP

On the Absolute Configurational Stability of Bromonium and Chloronium Ions

Scott E. Denmark, Matthew T. Burk, Andrew J. Hoover

Antoinette Nibbs
Short Literature Presentation
23 August 2010
development of new methods for production of reduced oxygen-content from renewable biomass resources
development of new methods for production of reduced oxygen-content from renewable biomass resources
**Deoxygenation of Biomass Polyols**

development of new methods for production of reduced oxygen-content from renewable biomass resources

sustainable production of transportation fuels from biomass in an integrated biomass production-conversion system


single-flask, solvent-free deoxygenation procedure to convert glycerol into allyl alcohol (polymer, 3-hydroxyproionic acid)

Arceo, E; Marsden, P.; Bergman, R. G.; Ellman, J. A. Chem. Commun. 2009, 3357
Prior Art


Preliminary Experiments

reaction characteristics

• aliquots at intermediate conversion contained the vicinal diketone

• at the early stages, as amount of olefin increased the amount of diketone increased

• upon complete conversion of olefin, depletion and eventual disappearance of diketone

disproportionation reaction?
Disproportionation Reaction

species simultaneously oxidized and reduced to form two different products

• Cannizzaro reaction

• Tishchenko reaction

![Chemical structures showing the disproportionation reaction](image-url)
**Preliminary Experiments, Part 2**

1,2-tetradenanediol

\[
\text{HO-CH}_{2}\text{CH}-(\text{CH}_2)_{11}\text{CH}_3 \xrightarrow{\text{Re}_2(\text{CO})_{10} (2.5 \text{ mol} \%)} \text{180 °C, air} \xrightarrow{3.5 \text{ h}} \text{(CH}_2)_{11}\text{CH}_3 + \text{H}_2\text{O} \quad 49\%
\]

\[
\text{HO-CH}-(\text{CH}_2)_{11}\text{CH}_3 \xrightarrow{\text{Re}_2(\text{CO})_{10} (2.5 \text{ mol} \%)} \text{<170 °C, air} \quad \text{recovered diol}
\]

\[
\text{HO-CH}-(\text{CH}_2)_{11}\text{CH}_3 \xrightarrow{\text{Re}_2(\text{CO})_{10} (2.5 \text{ mol} \%)} \text{180 °C, N}_2 \quad \text{recovered diol}
\]

**add external alcohol to avoid competing diol oxidation**
Reducing Competing Diol Oxidation

\[
\text{HO-CH}_{2}-\text{CH}_{2}\ldots\text{CH}_{2}-\text{CH}_3
\rightarrow
\text{OH} \quad \text{OH}
\]

\[
\text{Re}_2(\text{CO})_{10} \text{ or BrRe(CO)}_5 (2.5 \text{ mol %}) \quad \text{temp, air}
\]

\[
\rightarrow \quad \text{(CH}_2)_{11}\text{CH}_3 + \text{H}_2\text{O}
\]

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst</th>
<th>reductant (mL)</th>
<th>temp (°C)</th>
<th>time (h)</th>
<th>yield (%)</th>
</tr>
</thead>
</table>

- 5-nonanol
- 3-octanol
- 2-octanol

Use of 9-13 equiv of alcohol afforded complete product in 3.5-4 h. Alcohols generated 1-1.5 equiv of ketone. \(\text{Cp}^{*}\text{Re(CO)}_3\) did not show any activity; \(\text{BrRe(CO)}_5\) exhibited similar activity.
Prior Art


**Internal Diols**

(3R*,4R*)-decane-3,4-diol

\[ \text{Me} - \text{CH}_2 - \text{CH} = \text{(CH}_2)_4 \text{CH}_3 \]

\[ \text{OH} \]

\[ \text{OH} \]

[Re\(_2\)(CO)\(_{10}\)] (2.5 mol %)

3-octanol, 170 °C, air

2 h

\[ \text{Me} - \text{CH} = \text{CH} - \text{(CH}_2)_4 \text{CH}_3 \]

(82%)

trans stereoisomer did not react in the presence of alcohol or solvent-free conditions
Let’s Make It Better

- Decrease the reaction temperature by use of an additive

Sugar polyols (or sugar alcohol)
- Glycerol
- Erythritol
- Arabinol
- Xylitol
- Mannitol
- Sorbitol

Bases
- Longer reaction times
- Total obstruction of activity

Acids
- TsOH or H$_2$SO$_4$ shortened the reaction times
- Lower reaction temperature
- Lower catalyst loading
Optimized Results

1,2-tetradenanediol

\[ \text{Re}_2(\text{CO})_{10} \text{ (2.5 mol \%)} \]
\[ \text{TsOH (T) or H}_2\text{SO}_4 (S) \]

\[ \rightarrow \text{ (CH}_2\text{)}_{11}\text{CH}_3 \]

3-octanol, temp

1 : 0.025 : 10 ratio of diol, catalyst, and 3-octanol

<table>
<thead>
<tr>
<th>entry</th>
<th>cat (mol %)</th>
<th>alcohol (mL)</th>
<th>acid (mol %)</th>
<th>temp (°C)</th>
<th>time (h)</th>
<th>yield (%)</th>
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<tbody>
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<td>1</td>
<td>2.5</td>
<td>4</td>
<td>-</td>
<td>155</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>2.5</td>
<td>4</td>
<td>T (5)</td>
<td>155</td>
<td>2.5</td>
<td>74 (76)</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>3</td>
<td>-</td>
<td>170</td>
<td>16</td>
<td>46</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>3</td>
<td>T (2)</td>
<td>155</td>
<td>1.5</td>
<td>77</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>5</td>
<td>T (2)</td>
<td>155</td>
<td>1.8</td>
<td>87 (83)</td>
</tr>
<tr>
<td>6</td>
<td>2.5</td>
<td>5</td>
<td>S (2)</td>
<td>155</td>
<td>2</td>
<td>82 (85)</td>
</tr>
<tr>
<td>7</td>
<td>1.25</td>
<td>5</td>
<td>S (2)</td>
<td>155</td>
<td>2</td>
<td>79</td>
</tr>
</tbody>
</table>

reaction did not proceed in the presence of acid and absence of catalyst
Applications


\[
\begin{align*}
\text{Re}_2(\text{CO})_{10} \; (1.5 \text{ mol} \%) \\
\text{TsOH} \; (1.7 \text{ mol} \%)
\end{align*}
\]

\[
\begin{align*}
\text{meso-erythritol} & \xrightarrow{160 \degree C, 12 \text{ h}} \text{3-octanol, air} & \text{cyclopentanol} \\
& \text{(62\% NMR yield)} \\
& \text{55\% isolated yield} \\
& \text{>94 mol \% pure}
\end{align*}
\]
"In contrast to the simplicity of the reaction methodology, the mechanism of the reaction is still unknown."

temperature and oxygen dependence suggests an **oxidized rhenium species** as the active catalyst and...
diol has to be capable of achieving **cis stereochemistry** so...

**rhenium diolate species**

some metal diolates extrude corresponding alkene on thermolysis

affect of acid on catalyst related to assisted olefin extrusion by protonation of a rhenium diolate intermediate
Conclusions

new catalytic system rhenium-mediated didehydroxylation of vicinal diols (internal or external) using external alcohol as an environmentally friendly reducing agent

\[
\begin{align*}
\text{Me} & \quad \text{OH} & \text{(CH}_2\text{)}_4\text{CH}_3 \\
\text{OH} & \quad \text{Re}_2(\text{CO})_{10} (2.5 \text{ mol } \%) & \quad \text{Me} & \quad \text{OH} & \text{(CH}_2\text{)}_4\text{CH}_3 \\
(3R^*, 4R^*)\text{-decane-3,4-diol} & \quad \text{3-octanol, 170 } ^\circ\text{C, air} & \quad 2 \text{ h} & \quad (82\%)
\end{align*}
\]

addition of acid allows for milder reaction conditions (155 °C, up to 2 h reaction time)

method can be applied to producing unsaturated compounds from other biomass-derived polyols

\[
\begin{align*}
\text{HO} & \quad \text{OH} & \quad \text{OH} & \quad \text{OH} \\
\text{HO} & \quad \text{Re}_2(\text{CO})_{10} (1.5 \text{ mol } \%) & \quad \text{TsOH} (1.7 \text{ mol } \%) & \quad \text{160 } ^\circ\text{C, 12 h} \\
\text{meso-erythritol} & \quad \text{3-octanol, air} & \quad \text{ (62\% NMR yield)} & \quad \text{55\% isolated yield} \\
& & & \quad >94 \text{ mol } \% \text{ pure}
\end{align*}
\]
**Electrophilic Halofunctionalization of Olefins**

only a few enantioselective variants

few of those variants require substoichiometric amounts of chiral promoter

![Chemical reaction](image)


![Chemical structure](image)


(−)-napyradiomycin A1
Electrophilic Halofunctionalization of Olefins

only a few enantioselective variants

ever of those variants require substoichiometric amounts of chiral promoter

\[ (-)-napyradiomycin \text{ A1} \]


\[ \text{chlorosulpholipid cytotoxin} \]


What Do We Know About Them?

The paucity of such methods can be ascribed in part to a lack of understanding of the factors that influence the configurational stability of the intermediate halonium ions.

bromine exchange between bromonium ions and olefins can be rapid

\[
\text{1-Br}^+ + \text{Ad}=\text{Ad} \rightleftharpoons \text{1-I}^+ + \text{X}^-\text{Ad} + \text{OTf}^-
\]


similar to processes for thiiranium and seleniranium ions

\[
\text{SbF}_6^- \rightleftharpoons \text{R}^+ + \text{R}^2 \rightleftharpoons \text{R}^1 \text{R}^2\text{H}_n \rightleftharpoons \text{R}^1 \text{R}^2\text{E}^+ + \text{SbF}_6^-
\]

RE = PhSe, n-BuSe

Denmark, S. E.; Collins, W. R.; Cullen, M. D. J. Am. Chem. Soc. 2009, 131, 3490-3492
Absolute Configurational Stability of Bromonium Ions

Enantiopure bromonium ions have been demonstrated to be stable in the absence of olefins.

*Chem. Commun.* **2009**, *1082-1084*

No studies for olefin-to-olefin transfer observation.
Chloronium Ions In Days of Old

**absolute** configurational stability of chloronium ions has never been demonstrated under any conditions. **relative** configurational stability established in classic studies by Lucas and Weinstein.

**JOURNAL OF THE AMERICAN CHEMICAL SOCIETY**

Volume 83, October 6, 1941

[Contribution from the Gates and Crellin Laboratories of Chemistry, California Institute of Technology, No. 885]

The Conversion of the 3-Chloro-2-butanol to the 2,3-Dichlorobutanes; Evidence for a Cyclic Chloronium Intermediate

By H. J. Lucas and C. W. Gould, Jr.


Establish configurational stability of bromonium and chloronium ions under conditions where racemization could be competitive with intermolecular trapping by nucleophiles.
**Preliminary Experiments**

establish configurational stability of bromonium and chloronium ions under conditions where racemization could be competitive with intermolecular trapping by nucleophiles

generated by anchimERICally assisted ionization of enantiomerically enriched, C2 symmetric B-halo sulfonates in strongly ionizing media

demonstrate bromonium ion formation and trapping in the presence of subsolvent quantities of nucleophiles

\[
\text{HFIP as solvent}
\]

\[
\begin{align*}
\text{er} &= 97:3 \\
\text{er:} &= 97:3 \\
\text{100\% enantiospecificity}
\end{align*}
\]

\[
\begin{align*}
\text{enantiospecificity} &= \frac{\text{ee}_{\text{prod}}}{\text{ee}_{\text{sm}}} \times 100\%
\end{align*}
\]

**what’s the next step?**

- demonstrate bromonium ion formation and trapping in the presence of subsolvent quantities of nucleophiles
- provide for degenerate bromine exchange
- HFIP as solvent
HFIP
strong ionizing solvent, low nucleophilicity
dissolve both nucleophilic salts and significant quantities of the olefin

Solvolysis of Enantiomerically Enriched Bromide

HFIP, 23 °C

NaOAc (2 equiv) 79% yield 97:3 er 100% es

MeOH (10 equiv) 80% yield 97:3 er 100% es

n-Bu₄NN₃ (2 equiv) 80% yield 95:5 er 96% es

minor racemization pathway - nucleophilic attack at bromine to generate BrN₃
Solvolysis of EnantiomERICALLY Enriched Bromide

\[
\begin{align*}
\text{n-Pr} & \quad \text{OTs} & \quad \text{n-Pr} \\
\text{Br} & \quad \quad \quad & \quad \quad \quad \\
\text{MOAc} & \quad \text{HFIP, 23 °C} \\
\end{align*}
\]

introduction of olefin leads to lower specificity
Solvolysis of Enantiomerically Enriched Bromide

**Increased trapping rate due to less coordinated and more nucleophillic anion**

**Introduction of olefin leads to lower specificity**

![Chemical reaction diagram](image)
Modulating Olefin-to-Olefin Transfer Rate

assuming you can generate and trap chloronium ions enantiospecifically, even in the absence of olefin-to-olefin transfer

Denmark, S. E.; Collins, W. R.; Cullen, M. D. J. Am. Chem. Soc. 2009, 131, 3490-3492

RE = PhSe, n-BuSe
**Solvolyis of Enantiomerically Enriched Chloride**

\[
\begin{align*}
\text{OTf} & \quad \text{HCO}_2\text{Na} \text{ (13 equiv)} \\
n-\text{Pr} & \quad \text{HCO}_2\text{H}, 23 \, ^\circ\text{C} \\
& \quad \text{(76\%)} \\
\text{Cl} & \quad \text{OCHO} \\
n-\text{Pr} & \\
\end{align*}
\]

- er = 98:2
- dr > 99:1

100\% enantiospecificity

\[
\begin{align*}
\text{BnO} & \quad \text{HCO}_2\text{Na}, \text{HCO}_2\text{H}, 23 \, ^\circ\text{C} \\
& \quad \text{(63\%)} \\
\text{OBn} & \\
\end{align*}
\]

\[
\begin{align*}
\text{OTf} & \quad \text{HCO}_2\text{Na} \text{ (13 equiv)} \\
n-\text{Pr} & \quad \text{HCO}_2\text{H}, 23 \, ^\circ\text{C} \\
& \quad \text{(58\%)} \\
\text{Cl} & \quad \text{OCHO} \\
n-\text{Pr} & \\
\end{align*}
\]

- dr = 99:1

\[
\begin{align*}
\text{OTf} & \quad \text{HCO}_2\text{Na} \text{ (13 equiv)} \\
n-\text{Pr} & \quad \text{HCO}_2\text{H}, 23 \, ^\circ\text{C} \\
& \quad \text{(58\%)} \\
\text{Cl} & \quad \text{OCHO} \\
n-\text{Pr} & \\
\end{align*}
\]

- dr = 97:3
**Solvolysis of Enantiomerically Enriched Chloride**

\[
\begin{array}{c}
\text{OTf} \\
n-\text{Pr} \\
\tilde{\text{Cl}}
\end{array}
\quad + \quad
\begin{array}{c}
n-\text{Pr} \\
\text{Nu}
\end{array}
\quad \xrightarrow{\text{HFIP/CH}_2\text{Cl}_2, 1:1, 23 \degree \text{C}}
\begin{array}{c}
n-\text{Pr} \\
\text{OR} \\
\tilde{\text{Cl}}
\end{array}
\]

<table>
<thead>
<tr>
<th>R</th>
<th>Nu</th>
<th>olefin (equiv)</th>
<th>yield (%)</th>
<th>er</th>
<th>e.s. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ac</td>
<td>( n-\text{Bu}_4\text{NOAc} )</td>
<td>0</td>
<td>32</td>
<td>98:2</td>
<td>100</td>
</tr>
<tr>
<td>Ac</td>
<td>( n-\text{Bu}_4\text{NOAc} )</td>
<td>0.25</td>
<td>39</td>
<td>98:2</td>
<td>100</td>
</tr>
<tr>
<td>Ac</td>
<td>( n-\text{Bu}_4\text{NOAc} )</td>
<td>1.0</td>
<td>43</td>
<td>98:2</td>
<td>100</td>
</tr>
<tr>
<td>Me</td>
<td>MeOH</td>
<td>0</td>
<td>42</td>
<td>98:2</td>
<td>100</td>
</tr>
</tbody>
</table>

NaOAc gave complex mixtures of products

**low chemical stability** of 1,2-dialkylchloronium ions dictates the use of *more reactive* nucleophile to trap them before low energy decomposition pathways can intervene.
Stability of Halonium Ions

inverse relationship

classical stability

stereochemical stability

_inverse relationship_

\[ n-\text{Pr} \rightleftharpoons n-\text{Pr} \]

 chlorine

 greater electronegativity of chlorine
 less positive charge on chlorine
 more positive charge on carbon
 increased propensity toward processes characteristic of carbocations

 bromine

 lesser electronegativity of bromine
 olefin-olefin transfer proceeds via nucleophilic attack by olefin at bromine
 favored by greater positive charge on bromine

\[ n-\text{Pr} \rightleftharpoons n-\text{Pr} \]

\[ n-\text{Pr} \rightleftharpoons n-\text{Pr} \]
Conclusions

Enantiospecific generation and trapping of bromonium ions

\[
\text{OTs} \quad \begin{array}{c}
\text{Br} \\
n-\text{Pr}
\end{array}
\xrightarrow{\text{HCO}_2\text{Na (13 equiv)}}
\text{OCHO} \\
\begin{array}{c}
\text{Br} \\
n-\text{Pr}
\end{array}
\]

\[\text{er} = 97:3\]

Racemization of bromonium ions via olefin-to-olefin transfer is competitive with intermolecular capture by anionic nucleophiles

\[
\text{OTs} \quad \begin{array}{c}
\text{Br} \\
n-\text{Pr}
\end{array}
\xrightarrow{\text{NaOAc}}
\text{OAc} \\
\begin{array}{c}
\text{Br} \\
n-\text{Pr}
\end{array}
\]

\[\text{HFIP, 23 °C} \quad 79\% \text{ yield} \quad 97:3 \text{ er} \quad 100\% \text{ enantioselectivity}\]

Relative rates do not exclude possibility of a catalytic, enantioselective bromination process, but present an obstacle that must be surmounted by any successful catalyst system.

demonstrated first enantioselective generation and trapping of chloronium ions

\[
\text{OTf} \quad \begin{array}{c}
\text{Cl} \\
n-\text{Pr}
\end{array}
\xrightarrow{\text{HCO}_2\text{Na (13 equiv)}}
\text{OCHO} \\
\begin{array}{c}
\text{Cl} \\
n-\text{Pr}
\end{array}
\]

\[\text{er} = 98:2\]

\[\text{dr} > 99:1\]

\[\text{HCO}_2\text{H, 23 °C} \quad 76\% \text{ yield}\]

\[\text{er} = 98:2\]

\[\text{dr} = 98:2\]

\[100\% \text{ enantiospecificity}\]