Introduction

Honors Organic Chemistry Lab Presentation
HAPPY BIRTHDAY DR. PINHAS
Past Research

3 Key Components

- Cyclic Carbonate Formation
- Catalysts
- High Speed Ball Mill
Cyclic Carbonate Formation

Reaction Needs:
- Oxirane
- Carbon Dioxide
- Catalytic Component

Conversion of oxiranes and CO$_2$ to organic cyclic carbonates using a recyclable, bifunctional polystyrene-supported organocatalyst. Christopher J. Whiteoak, Andrea H. Henseler, Carles Ayats, Arjan W. Kleij, Miquel A. Pericàs
Catalytic Component

- Salt Catalysts
- Iron Catalysts
- Lewis Acid Catalysts

All catalysts form complexes with the oxirane and lower activation energies.
High Speed Ball Milling

- Relatively new in the realm of organic synthesis
- Adapting methodology from recent years
- Increases reaction rate by effecting collision rate of molecules in a system
Different monosubstituted cyclic carbonates have different functionalities:

- ethylene carbonate and propylene carbonate utilized as industrial solvents
- used in various topical medications
- large dipole moments allow it to be used as electrolytes in lithium ion batteries

Main Research Question

Which combination of salt catalyst and CO$_2$ concentration will lead to ideal cyclic carbonate yield?
Mechanism
Areas of Research Addressed

- Variation in the concentration of CO$_2$
- The effectiveness of different epoxides as starting material
- Variation in the reaction time
- Changes in the chiral configuration between starting material and product
- Addressing the effectiveness of different catalysts
  - Cations v.s. Anions
  - Size - single atom vs. complex molecule
  - Hard/Soft Acid Base Theory - mixing of catalysts
Examination of various substituted oxiranes on cyclic carbonate synthesis
Initial Approach to Experiment

- Lithium Iodide salt catalyst suggested
- Styrene Oxide as oxirane reacting with dry ice
Experimental Design

1. Obtain oxirane, LiI, CO$_2$ (Note: oxirane and catalyst in 1:1 equivalence).

1. Place components in vial with O-ring and ball, seal tightly with parafilm, run in mill for 16.99 hours.
Initial Results
1,2-epoxy-2-methylpropane with Lil
trans-2,3-epoxybutane with LiI oxide with LiI

Bromo styrene
1,2-epoxyhexane

Weak carbonyl stretch at 1785.9 cm⁻¹
In search of better results...

- Refer to the literature, a mixture of previous works
  1. **Tetrabutylammonium** halide salts (at 120°C)
  2. **Tributylammonium** cation coupled with Br⁻

--- Use of catalytic amount (0.2 equivalence) ---

1. Conversion of oxiranes and CO₂ to organic cyclic carbonates using a recyclable, bifunctional polystyrene-supported organocatalyst† Christopher J. Whiteoak,a Andrea H. Henseler,a Carles Ayats,a Arjan W. Kleij*a,b and Miquel A. Pericàs*a,c T
2. Bifunctional Porphyrin Catalysts for the Synthesis of Cyclic Carbonates from Epoxides and CO₂: Structural Optimization and Mechanistic Study Tadashi Ema,*,† Yuki Miyazaki,† Junta Shimonishi,† Chihiro Maeda,† and Jun-ya Hasegawa*,‡
Tetraethyl vs. Tetrabutyl Ammonium Bromide with Bromo styrene oxide

Lacking carbonyl stretch present at 1812 cm\(^{-1}\)

Carbonyl stretch
- Molar weight of product is 243.04 g/mol
Comparison of Tetrabutyl Salts

1,2 Epoxyhexane with Tetrabutylammonium Iodide
Carbonyl stretch at 1794 cm\(^{-1}\)

1,2 Epoxyhexane with Tetrabutylammonium Bromide
Carbonyl stretch at 1795 cm\(^{-1}\)
Tetrabutylammonium bromide reactions

Styrene Oxide with Tetrabutylammonium Bromide

Carbonyl stretch at 1795 cm\(^{-1}\)

2-methyl-1,2-Epoxypropane with Tetrabutylammonium Bromide

Carbonyl stretch at 1793 cm\(^{-1}\)
## Summary of Reactions

<table>
<thead>
<tr>
<th>Epoxide</th>
<th>Salt Catalyst</th>
<th>Carbonyl Stretch?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Styrene Oxide</td>
<td>LiI</td>
<td>No</td>
</tr>
<tr>
<td>1,2-epoxy-2-methylpropane</td>
<td>LiI</td>
<td>No</td>
</tr>
<tr>
<td>1,2-epoxyhexane</td>
<td>LiI</td>
<td>No</td>
</tr>
<tr>
<td>Bromo Styrene Oxide</td>
<td>LiI</td>
<td>No</td>
</tr>
<tr>
<td>Trans-1,2-epoxybutane</td>
<td>LiI</td>
<td>No</td>
</tr>
<tr>
<td>Styrene Oxide</td>
<td>LiCl</td>
<td>No</td>
</tr>
<tr>
<td>Bromo Styrene Oxide</td>
<td>Tetrabutylammonium bromide</td>
<td>Yes; at 1820 cm⁻¹</td>
</tr>
<tr>
<td>Bromo Styrene Oxide</td>
<td>Tetrabutylammonium iodide</td>
<td>Yes; at 1820 cm⁻¹</td>
</tr>
<tr>
<td>Bromo Styrene Oxide</td>
<td>Tetraethylammonium bromide</td>
<td>No</td>
</tr>
<tr>
<td>1,2-epoxyhexane</td>
<td>Tetrabutylammonium bromide</td>
<td>Yes; at 1786 cm⁻¹</td>
</tr>
<tr>
<td>1,2-epoxyhexane</td>
<td>Tetrabutylammonium iodide</td>
<td>Yes; at 1794 cm⁻¹</td>
</tr>
</tbody>
</table>
Conclusions:

- 1,2-epoxyhexane provides strongest carbonyl stretch in the presence of any catalyst studied.

- Tetrabutylammonium Bromide is a promising catalyst in cyclic carbonate synthesis.
  More organic character (dissolved in styrene oxide more efficiently)
  Larger R groups (more induction?, bulkier, sterics?)

- Lithium Iodide results in presence of alcohol (Iodide opens cyclic molecule allowing -OH to form).
Moving Forward:

- Search literature for improved catalysts.

- Examine various oxiranes and determine which produced desired product and why.

- Determine optimal catalytic amount (i.e. 0.1 eq, 0.2 eq, 0.3 eq, etc.)
Acknowledgements

Special thank you to Dr. Lieberman and Dr. Pinhas!
Thank you Heather!
Thank you peers!

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Highly efficient and quantitative synthesis of a cyclic carbonate by iron complex catalysts Xingfeng Sheng, Lijun Qiao, Yusheng Qin, Xianhong Wang, Fosong Wang

Ball milling in organic synthesis: solutions and challenges Achim Stolle, * Tony Szuppa, Silke E. S. Leonhardt and Bernd Ondruschka
Comparison of LiI and NH$_4$I as catalysts in the conversion of an epoxide to a cyclic carbonate

Sam Perry and Chantal Woodson
Reaction

Exact Mass: 120.06

Exact Mass: 164.05
Research Process

**Initial**
Determine optimal amounts of CO₂

**Trial 1**
LiI as catalyst

**Comparison**
Similarity to aziridine and oxazolidinone

**Trial 2**
NH₄I as catalyst

**Side Trial**
No catalyst for cyclic carbonate formation
Experimental Design

- 2 vials
  - beginning: control vial and HSBM vial
  - end: 2 HSBM vials with differing catalyst

- Trial without catalyst, at least 2 HSBM runs
  - No product formation

- Comparison Study
  - 2, 1, 0.5 equivalents of LiI and NH₄I
  - Catalytic amounts of LiI and NH₄I
  - Controls and methods
Results

- Commonly see 222 and 248 m/z species
  - Major products at about 13.03 min (248 m/z) and 17.50 min (222 m/z)
  - 248 species—loss of I
  - 17.50 min not present in catalytic trial
  - Similar patterns across all gas chromatographs
- Consistent -OH peaks on IR
  - No distinguishable carbonyl peaks
Results

Chemical structures:

1. Exact Mass: 120.06
2. Exact Mass: 247.97
3. Exact Mass: 122.07

Sam and Chantal 5
Results

- Major species is typically styrene oxide
  - Still have 13.04 peak (248 m/z); loss of I (121)
  - More product in catalytic trial than starting material
  - Generally “cleaner” reaction

- Consistently see split carbonyl peak
  - ex. 1816 cm\(^{-1}\) to 1795 cm\(^{-1}\)
  - Generally no -OH peak (error in catalytic trial)
Conclusions

- Conclusions
  - LiI opens the epoxide and shows up on a large alcohol peak on the IR
  - Possibly formation of a styrene oxide dimer
  - at .5 and catalytic equivalent small amount of product formed
  - Iodine may represent affect shape of graph

- Further Study
  - More trials of NH$_4$I to confirm results
  - Other I salts to explore pattern
The Effect of Reaction Time on the Cycloaddition of Carbon Dioxide to Styrene Oxide

by Connor Schroeder and Trevor Plunkett
Initial Aim/Research Background

- Initial aim to identify best anion to produce the cyclic carbonate
- Spun off to try and produce product with KBr, and KI
- Research Involving Metalloporphyrin catalysts gave reactivity order of I<Cl<Br

Bifunctional Porphyrin Catalysts for the Synthesis of Cyclic Carbonates from Epoxides and CO2: Structural Optimization and Mechanistic Study Tadashi Ema,, Yuki Miyazaki, Junta Shimonishi, Chihiro Maeda, and Jun-ya Hasegawa

Connor Schroeder and Trevor Plunkett
Initial Trials

Trials of KI and KBr for one 16.67 hour run

Connor Schroeder and Trevor Plunkett IV 2
Methods

- Millimole equivalents of salt and styrene oxide
- Run time of 33.3 hours.
- Packed vials with Dry Ice
- Did not uncap vials between runs

Connor Schroeder and Trevor Plunkett IV
Results KBr

Peak at 164

Carbonyl: 1808.5, 1793.4.
Results KI

Peak at 164

Carbonyl: 1814
Conclusions

We are unable to conclude which is the more effective anion between Iodine and Bromine at this time. This is due to both experiments with iodine and bromine producing variable amounts of cyclocarbonate. Also several erroneous trials occurred over the semester which included experiments that didn’t hold CO$_2$ pressure or produce the expected product. More trials are required to get a clear picture of the most effective anion. After increasing the time of reactions in the ball mill we did see an increase in the amount of cyclocarbonates being formed. More trials are required to test how time of the reaction affects the amount of product formation. We would recommend for future test to perform this cyclo addition of CO$_2$ with the same catalyst and run for different time variables (1, 2, and 3 full runs in the ball mill).
Experimentation regarding Active Properties of Complex Organic Catalysts in Cyclic Carbonate Production
Figure 2. Hard-soft trends for acids on left, with hard-soft trends for bases on right. The arrows denote an increase in the soft character of element.

Methods

Each Reaction was run under controlled conditions:
- 1 mol drops of styrene oxide
- excess CO$_2$
- 1/1 ratio of styrene oxide and catalyst
- 17 hours in the ball mill + 3 hours at rest
Utilizing HSAB Theory: Will the formation of MgBr$_2$ increase efficiency of product formation?

**Trial 1**: 1.0 mol LiBr  
- 0% product formation

**Trial 2**: 1.0 mol MgCl$_2$  
- 0% product formation

**Trial 3**: 0.5 mol LiBr + 0.5 mol MgCl$_2$  
- 5% product, without ring closure, Bromine still bound; MW: 245 m/z

Figure 3. IR of Trial 3: mixing catalysts LiBr and MgCl$_2$
Change in Direction: Lithium vs. Ammonium as Cation within Catalyst

Figure 4. 1.0 mol LiI
- 8.7% product formation, MW: 164 m/z
- 6.9% unknown product formation, MW: 222 m/z

Figure 5. 1.0 mol NH4I
- 3.9% product formation, MW: 164 m/z
- No -OH peak; relevant in comparison to all trials run with Lithium, which display -OH peaks
Final Test: Small Magnesium vs. Large Ammonium as Cation within Catalyst

Figure 6. 1.0 mol MgBr₂
- 22.5% ring opening with Bromine remaining bound; MW: 204 m/z
- 21.0% unknown product formation, MW: 182-185 m/z

Figure 7. 1.0 mol Tetra-butyl NH₄Br
- 44.1% product formation, MW: 164 m/z

#BekBoone2016
Conclusions

- The mixing of salts using HSAB theory to provide a target catalyst did not prove effective.

- Lithium may be inhibitory to the efficiency of the reaction - it bonds too tightly to the oxygen, which might lower the final yield of product.
  - It is the cause of significant -OH peaks in the IR spectra.
  - It causes sizable formation of an unknown product with the MW: 222 m/z

- The larger the cation within the salt, the more efficient the reaction.
  - Large cations are also soft acids, which ties into the HSAB theory initially explored.
Continuing Research

- Flesh out the research on MgBr$_2$
  - Run more tests in an attempt to create the cyclocarbonate.

- Investigate anions in relation to Tetra-Butyl NH$_4^+$
  - Bromine was the focus of this research, but Iodine is a softer base, and therefore might be more effective.

- Investigate the size of the cation.
  - At what size do we get peak efficiency? Are the large, complex catalysts we attempted to simplify necessary?
Introduction

Research Background: LiI was found to be the most effective catalyst in the synthesis of oxazolidinone from aziridine.
- determine if the same applies to synthesis of cyclic carbonates

Initial Objective:
- Determine which cation (Li\(^+\), Na\(^+\), K\(^+\), t-butyl ammonium) works best with iodine as a catalyst.

General Reaction:
- styrene oxide + CO\(_2\) + [X]I → phenyl cyclic carbonate
- use 1.0 mmol of styrene oxide, stoichiometric amount of catalyst, excess CO\(_2\) in HSBM for ~ 17 hours.

Rone & Woodward
Reaction #1: LiI Catalyst

Purpose: determine how effective LiI is as a catalyst

Results: 222.1 g/mol species predominantly produced (H₂O presence reason?)
Reaction #2: Effect of H₂O

Purpose: determine if the presence of H₂O is responsible for the production of the 222 g/mol species.

Results:

IR: 1684.7 cm⁻¹ stretch indicates a different carbonyl produced.

GC/MS: 222 g/mol species solely produced

H₂O reason for side-product; dry catalyst
Reaction #3: NaI Catalyst

Purpose: determine how effective NaI is as a catalyst.

Results: 1811.53 stretch and 164 g/mol = product formation; 230 g/mol species present
Reaction #4: LiI and St. Oxide

Purpose: determine if the 222 g/mol species is formed without H$_2$O as a proton source from the reaction of LiI and styrene oxide (add H$_2$O as work-up)

Results: IR & GC/MS shown for the analysis w/o H$_2$O workup

IR: big OH stretch, carbonyl stretch at 1677 cm$^{-1}$

GC/MS: 222 g/mol species still formed.

*LiI does not work with styrene oxide
New Direction

- LiI reacts with styrene oxide to form a 222 g/mol species instead of catalyze the formation of cyclic carbonate.

  - Proposed reasoning: I\textsuperscript{-} breaks open epoxide, forming an alcohol that can tautomerize.

- Moving forward, begin testing each catalyst without CO\textsubscript{2} to see if any interference occurs.
Reaction #5: St. Oxide and NaI
No CO$_2$, no H$_2$O work up

Purpose: determine if NaI reacts with styrene oxide without CO$_2$ or a proton source like LiI does.

Results: only styrene oxide present; GC/MS peak at 120 g/mol & no notable IR peaks (H$_2$O workup same)
*Nal does not form a side product unless CO$_2$ is present.
Reaction #6: KI Catalyst

Purpose: determine if KI is an effective catalyst & if a side product is formed without CO$_2$ and with/without H$_2$O as a proton source.

Results: only styrene oxide present; GC/MS peak at 120 g/mol.
*KI does not effectively function as a catalyst
Reaction #6 (con’t): St. Oxide & KI, No CO₂ or H₂O work up

Results: GC/MS peak at 120 g/mol in both this and H₂O workup; only styrene oxide present.
- shows KI does not interact with styrene oxide at all

Rone & Woodward
Purpose: determine if t-butylammonium iodide is an effective catalyst & if a side product is formed without CO$_2$ and with/without H$_2$O as a proton source.

Results: GC/MS peak at 120 g/mol, indicative of styrene oxide
- all reactions showed only starting material in analysis (suspect due to other results)
Conclusion

Lil reacts with styrene oxide, interfering with cyclic carbonate formation.
- 222 g/mol species forms w/o H₂O

Nal catalyzes the formation of cyclic carbonate with a 230 g/mol side product.
- Side product only formed with CO₂ present

KI does not function as a catalyst of cyclic carbonate formation from styrene oxide.

t-butyl ammonium iodide does not function as a catalyst of cyclic carbonate formation from styrene oxide.
- Suspect, due to other groups’ results
Moving Forward

- determine the 230 g/mol species produced in NaI reactions and find ways to isolate cyclic carbonate from it.
- why didn’t t-butyl ammonium iodide work?
- continue testing different cations for efficiency.
Exploring the chirality of cyclic carbonates

Victoria Hammond and Nada El-Sayed
Reaction

Styrene Oxide \rightarrow \text{CO}_2 \rightarrow \text{Catalyst} \rightarrow 4\text{-phenyl-1,3-Dioxolan-2-one}
<table>
<thead>
<tr>
<th>Salt</th>
<th>Product</th>
<th>OH Peak in IR</th>
</tr>
</thead>
<tbody>
<tr>
<td>CuBr</td>
<td>Yes (once)</td>
<td>Large</td>
</tr>
<tr>
<td>KBr</td>
<td>Some</td>
<td>Large</td>
</tr>
<tr>
<td>LiBr</td>
<td>Some</td>
<td>Large</td>
</tr>
<tr>
<td>Lil</td>
<td>No</td>
<td>Large</td>
</tr>
<tr>
<td>NH₄I</td>
<td>Yes</td>
<td>None</td>
</tr>
<tr>
<td>Tetrabutylammonium Iodide</td>
<td>Yes</td>
<td>None</td>
</tr>
</tbody>
</table>
Cuprous Bromide
IR Spectrum

Vial was left under pressure for five days.
Cuprous Bromide
Mass Spectrum
Bromide Salts

Lithium Bromide
Bromide Salts
Potassium Bromide
Iodide Salts
Lithium Iodide: 1mmol versus 2mmol

Note: The y axis does not start at zero.

Victoria and Nada 7
Salts that Worked

Ammonium Iodide
Salts that Worked
Tetrabutyl Ammonium Iodide

Victoria and Nada 9
We used the (S)-(-)-Styrene Oxide starting material
Chiral Product
Mass Spectrum
Chiral Product
IR Comparison with Literature

source: Bio-Rad Laboratories, Philadelphia, PA

Victoria and Nada 12
Chiral Product
MS Comparison with Literature
We measured the specific rotation of our chiral 4-Phenyl-1,3-dioxolan-2-one:

\[ \alpha_{589} = +7 \]
used DCM

**Literature**
(4R)-4-Phenyl-1,3-dioxolan-2-one

\[ [\alpha]_D^{25} = -26 \]
used CHCl₃

(4S)-4-Phenyl-1,3-dioxolan-2-one

\[ [\alpha]_D^{20} = -44 \]
used CHCl₃
X-Ray Crystallography

Currently Running

Overall Class Results

- 1,2-epoxyhexane is the most effective oxirane tested thus far for yielding desired product, using Tetra-Butyl Ammonium Bromide as a catalyst.

- Soft catalysts, such as Tetra-Butyl Ammonium Iodide, are more efficient at breaking open oxiranes to form cyclic carbonates.

- The anion within the catalyst appears to have a larger influence on the overall efficiency of reaction.

- Many IR spectra displayed double peaks within the carbonyl range; this might represent two different carbonyl species formed.
Doubling of reaction time appears to increase formation of the cyclic carbonate.

Lithium, as a hard acid, binds tightly to the oxygen from the epoxide after the ring opening, preventing the attack on the CO$_2$ from occurring efficiently.

- It also causes a large -OH stretch within the IR spectra.

Lithium Iodide reacts with styrene oxide in the absence of H$_2$O or CO$_2$ to form a 222 g/mol species.

- Lithium Iodide forms the same 222 g/mol product in the presence of CO$_2$.

Sodium Iodide forms a side product of 230 g/mol only when CO$_2$ is present.