



Adventures in Green Chemistry

A Greener Synthesis of
 α -Trimethylsilyl Phenyl Vinyl Ketone

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Outline

-
- ✦ What is Green Chemistry?
 - ✦ Baylis-Hillman Reaction
 - ✦ Preparation of α -Trimethylsilyl Phenyl Vinyl Ketone (TMS-PVK)
 - ✦ My Research

What is Green Chemistry?



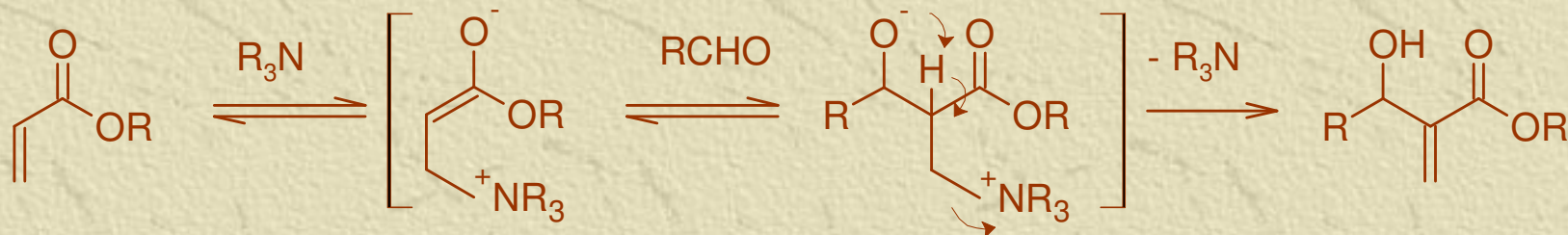
“The utilization of a set of principles that reduces or eliminates the use or generation of hazardous substance in the design, manufacture and application of chemical products.”

- Doxsee, K.M. and Hutchison, J.E. *Green Chemistry: Strategies, Tools, and Laboratory Experiments*. Thomson, Brookes, and Cole. **2003**.

Green Chemistry is:

- ✦ An emerging field within organic chemistry
- ✦ Pollution prevention at the most fundamental level, atoms and molecules
- ✦ Focuses on reducing intrinsic hazards of reactions and making them more efficient

Baylis-Hillman Reaction



Utility of Baylis-Hillman Adduct

- Densely functionalized
- Broad use as substrate in other reactions

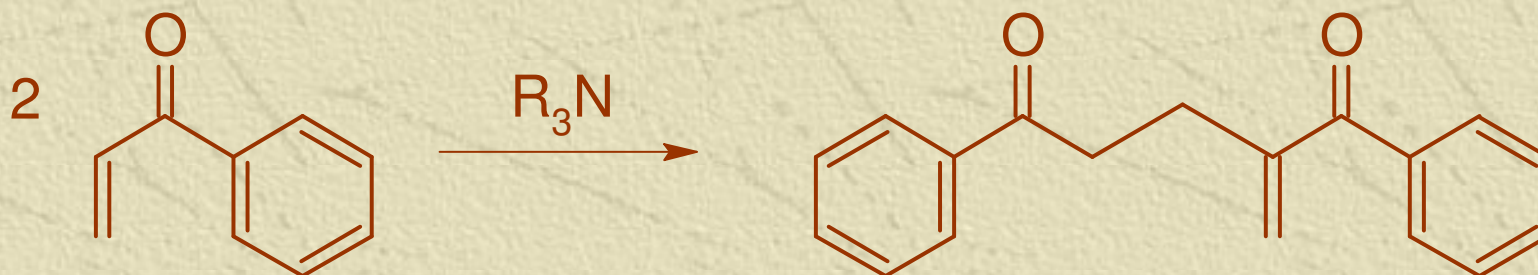
“Greenness” of Baylis-Hillman Reaction

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- ✦ Mild reaction conditions
 - ✦ Very little waste formed
 - ✦ Atom efficient
 - ✦ No need for solvent
 - ✦ No aqueous quench
 - ✦ Easily recovered catalysts
 - ✦ Reagents and products low in toxicity

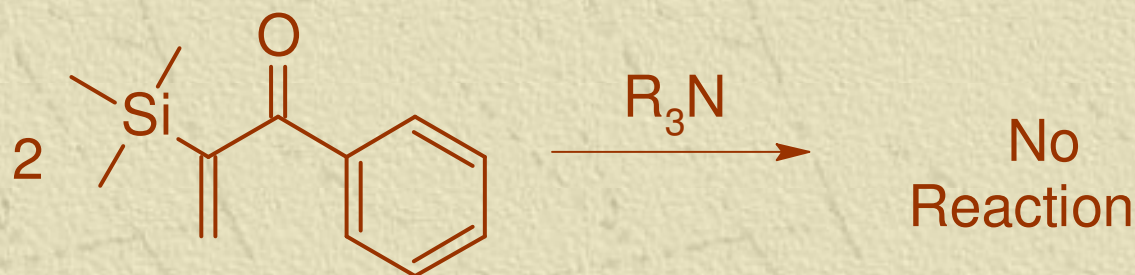
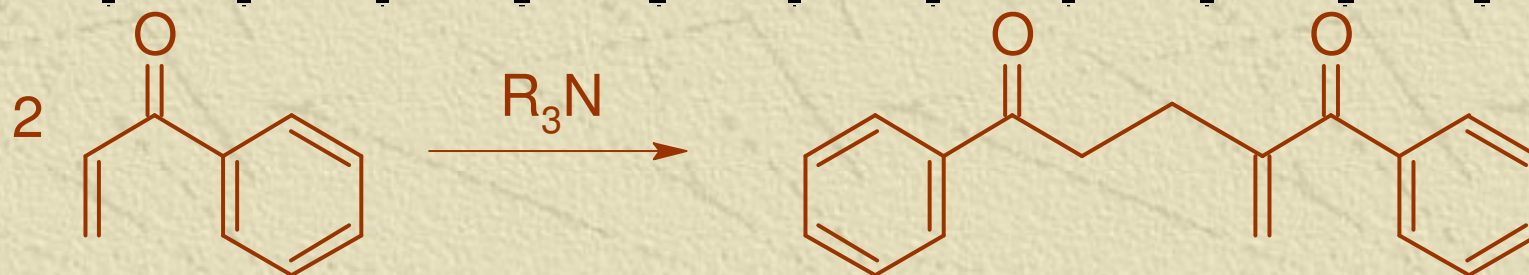
Limitations of the Baylis-Hillman Reaction

- ✦ Limited number of activated olefins suitable for the reaction due to competitive dimerization.
- ✦ Phenyl vinyl ketone (PVK), which dimerizes rapidly under Baylis-Hillman conditions, is essentially unsuitable as a substrate.

PVK Dimer Formation

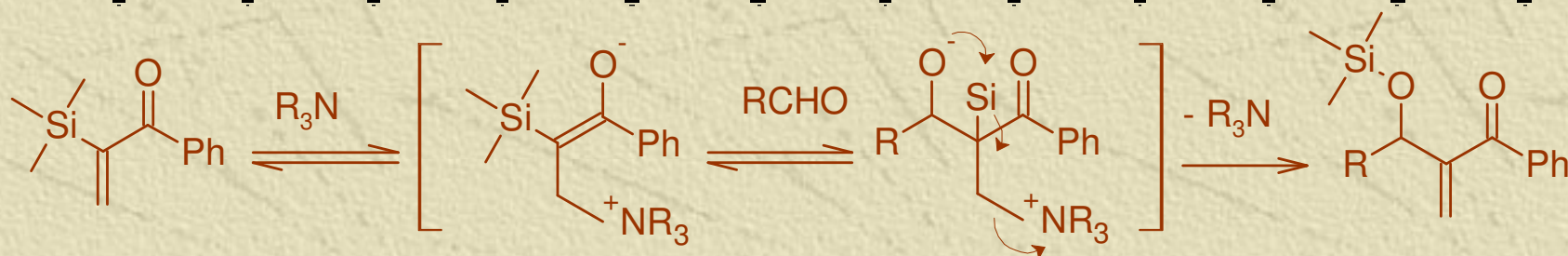


Dimer Prevention



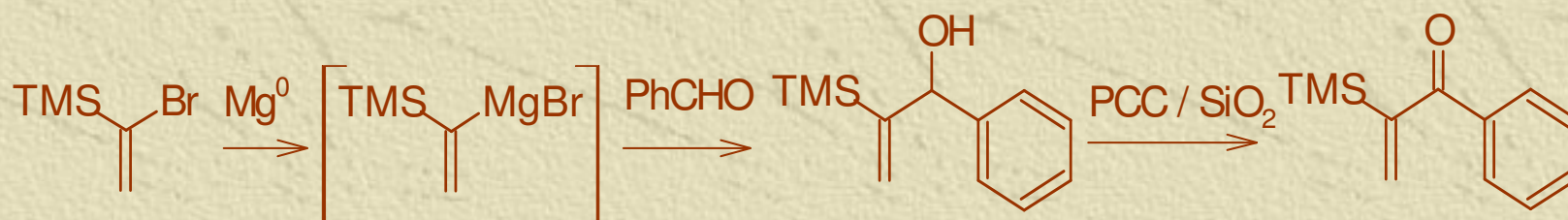
✦ Essentially eliminates head-to-tail dimerization of PVK under reaction conditions

Silicon-Mediated Baylis-Hillman Reaction



✚ This methodology is allowing new applications of the Baylis-Hillman reaction to be developed

Original Synthetic Route for Preparation of TMS-PVK

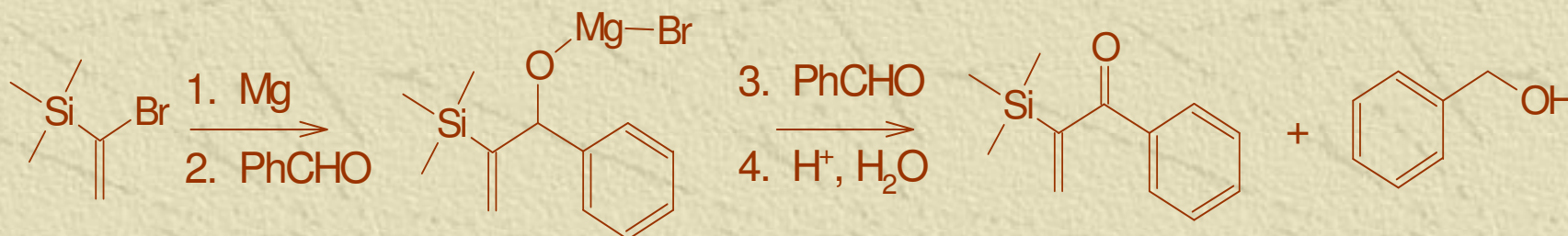


✦ Substrate preparation assessed

Problems with Synthesis of TMS-PVK

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- ✦ Pyridinium chlorochromate (PCC) is used to make Trimethylsilyl Phenyl Vinyl Ketone
 - PCC is a known carcinogen
 - Chromium waste products are formed
 - ✦ Oxidation reactions are generally non-green due to their use of heavy metals and toxic reagents.

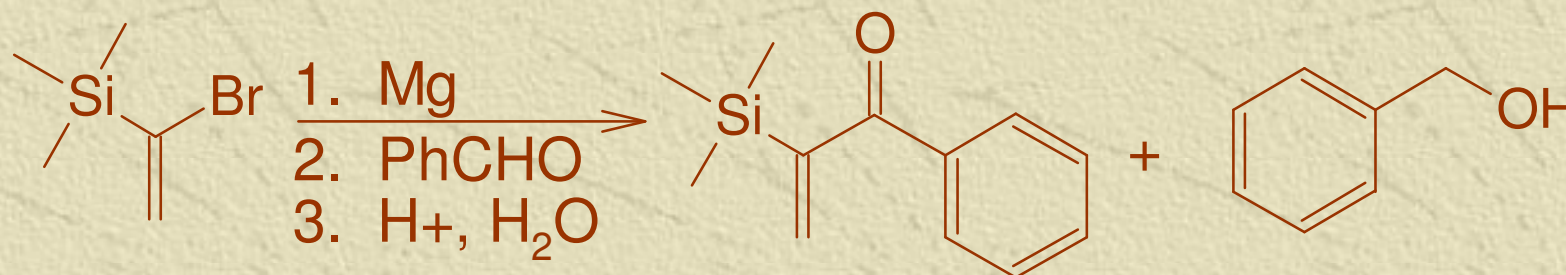
TMS-PVK by the Tandem Grignard-Oppenauer Oxidation



✚ 2 equivalents of benzaldehyde were added to the Grignard reaction

- ✚ 1st equivalent was electrophile for Grignard
- ✚ 2nd equivalent was oxidizing agent for the Oppenauer Oxidation

Results



- ✦ 80% yield of TMS-PVK
- ✦ 100% yield of benzyl alcohol
- ✦ Results demonstrate successful Grignard addition and complete oxidation
- ✦ Benefits
 - ◆ Reduced synthesis by one step and utilizes oxidizing potential of the magnesium alkoxide salt.
 - ◆ Eliminated the use of PCC.

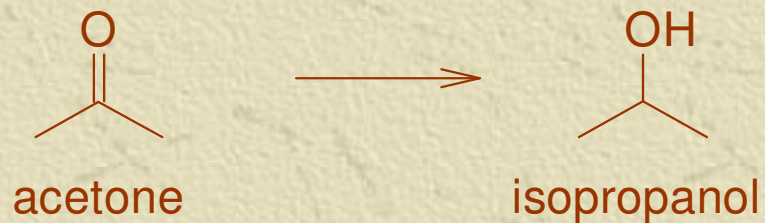
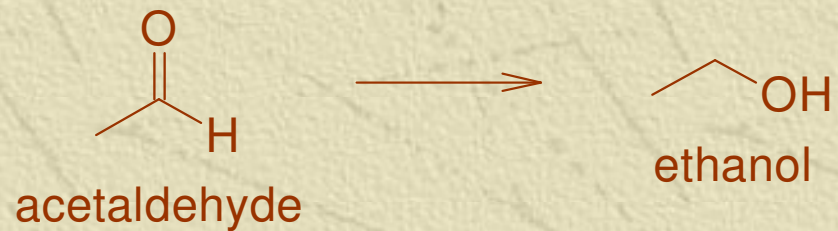
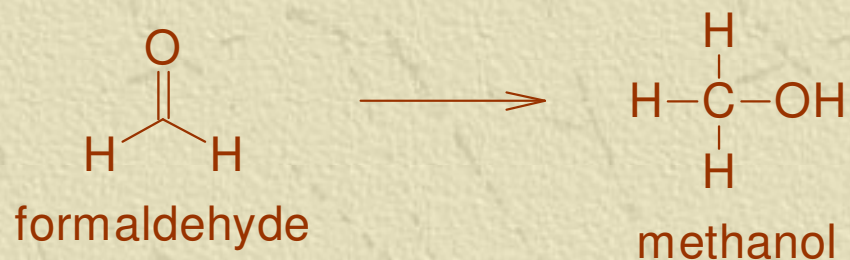
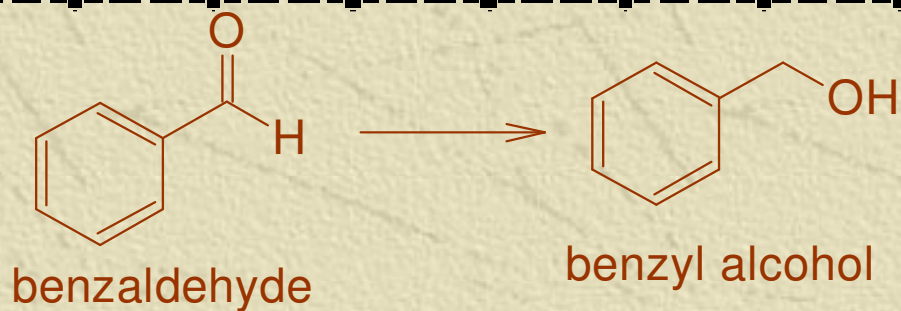
Greenest Route?

- ✦ Replacement of 2nd equivalent of benzaldehyde with smaller ketones or aldehydes will improve atom economy.
- ✦ Additionally, use of small ketones or aldehydes would eliminate the need for column chromatography to separate the TMS-PVK from excess benzaldehyde.

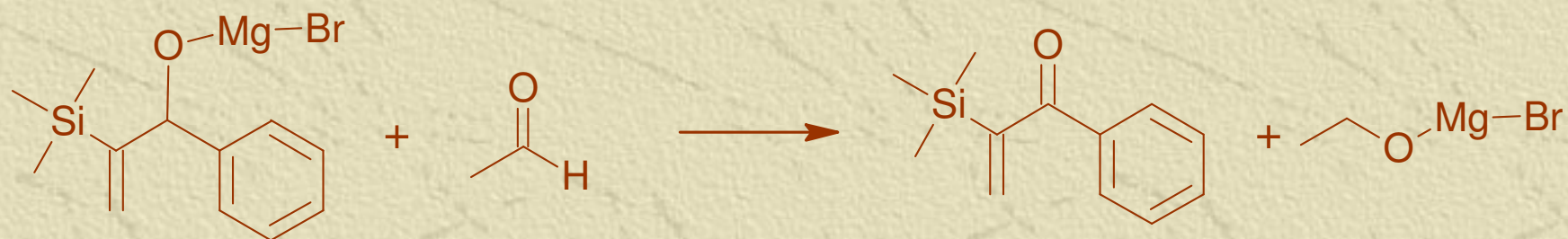
Goal of Research

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- ✦ To find a “greener” oxidizing agent than the benzaldehyde.
 - ✦ Find a reaction that is more atom economic.

Potential Oxidizing Agents

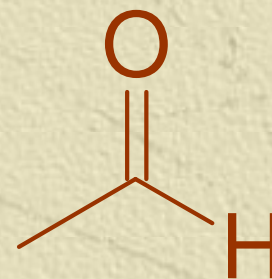


Oppenauer Oxidation with Acetaldehyde



Oxidation with Acetaldehyde

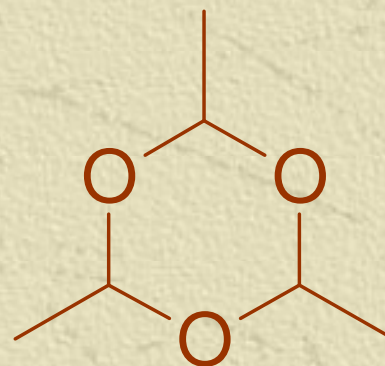
- ✦ Grignard-Oppenauer protocol repeated using acetaldehyde as oxidizing agent
- ✦ Acetaldehyde proved too volatile to use
- ✦ Evaporated immediately when added to the reaction mixture
 - Boiling point = 21°C



Acetaldehyde Alternatives

✦ Trimer of acetaldehyde

➤ Boiling point = 124°C



✦ Less volatile than the acetaldehyde.

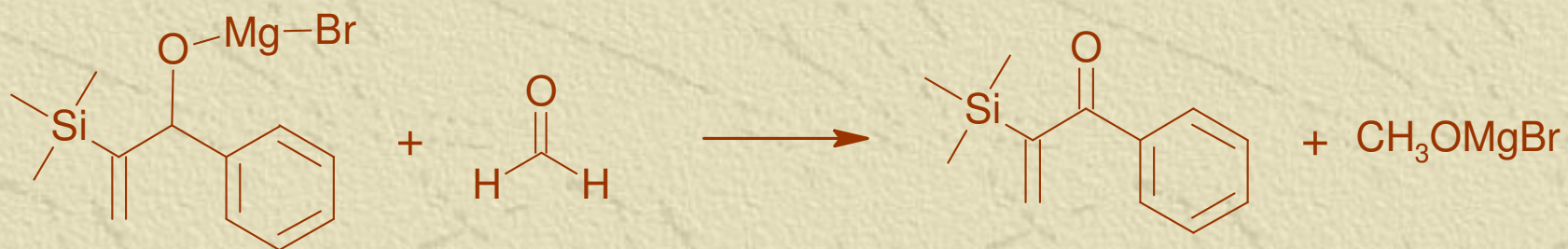
✦ Added an equivalent after the Grignard

● No oxidation occurred

✦ Used it as the solvent replacing THF

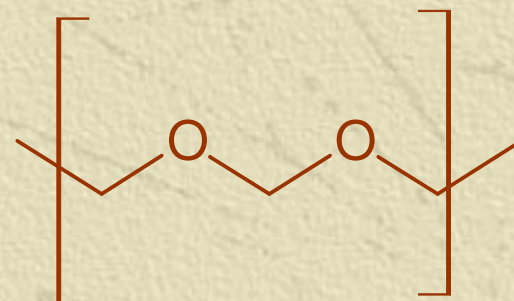
● Still no oxidation occurred

Oppenauer Oxidation with Formaldehyde

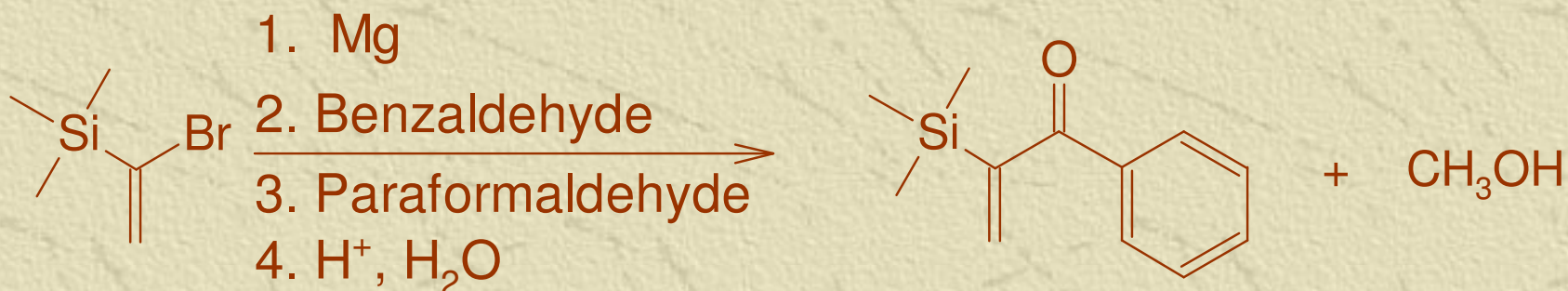


Why Paraformaldehyde?

- ✦ Paraformaldehyde is a polymer of formaldehyde.
- ✦ Formaldehyde is typically found in aqueous solution.
- ✦ The oxidation must be done under anhydrous conditions.



Proposed Tandem Grignard- Oppenauer Oxidation



- Magnesium to generate the Grignard
- Benzaldehyde was used as the electrophile in the Grignard reaction.
- Paraformaldehyde was used as the oxidizing agent for the Oppenauer Oxidation.
- Aqueous workup removes methanol.

Results

- ✦ Preliminary results indicate that TMS-PVK was synthesized, but some alcohol precursor still remained (~2:1 ratio)
- ✦ Results seem inconsistent due to possible experimental error.
- ✦ Needs to be explored further
 - ◆ Additional equivalents of paraformaldehyde
 - ◆ Longer reaction time

Acknowledgements

✦ Thanks to:

- ✦ Maggie Hoyt
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Questions?

