

Green Preparative-Scale Oxidations with Enzymatically-Produced Peracetic Acid



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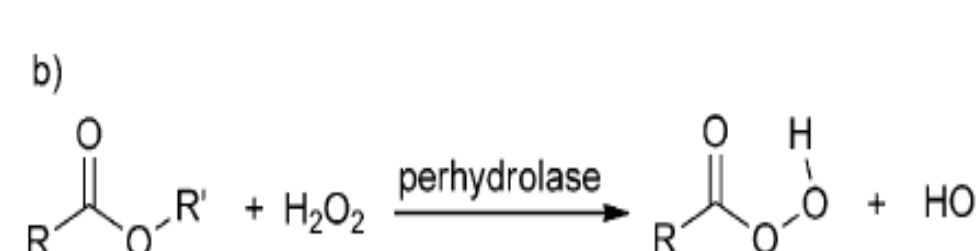
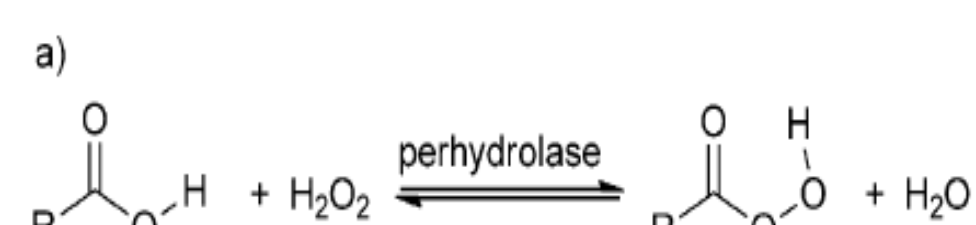
Perhydrolytic Genetically-Engineered Enzymes

Promiscuous Enzymes:

- Catalyze several similar but distinct reactions
- Wild-type does hydrolysis and some perhydrolysis
- Can be modified to give more efficient variants than wild-type, such as F162L optimized for perhydrolysis

Perhydrolysis:

- Yields a peracid
- Not typical in nature
- Irreversible with ester (b)



Modified from: Yin, Delu T et al. (2011)

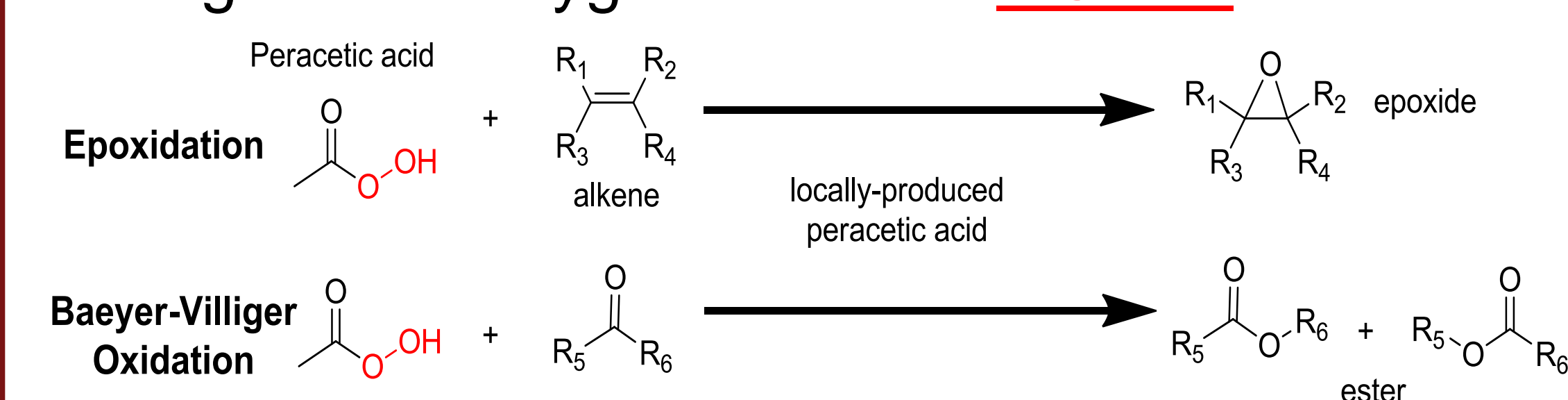
Epoxidation and Baeyer-Villiger Oxidation

Epoxidation:

- Completed with cyclohexene and 1-octene
- Existing methods: environmentally-friendly peroxide and catalyst, perhydrolytic enzymes, and *m*-chloroperbenzoic acid (**mCPBA**)

Baeyer-Villiger (BV) Oxidation:

- Completed with cyclohexanone
- Existing methods: mesoporous materials, Baeyer-Villiger monooxygenases, and **mCPBA**

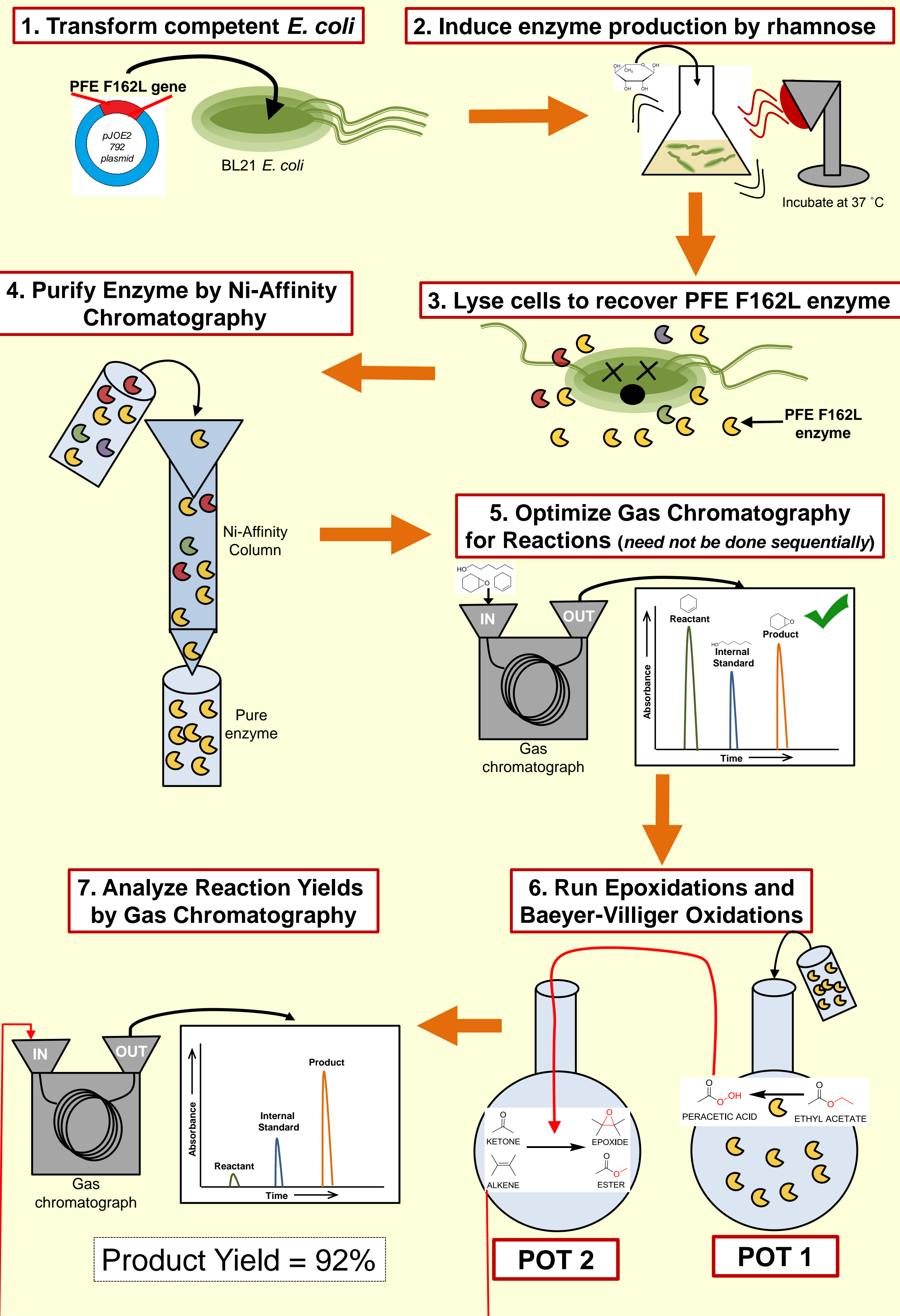


Replacing mCPBA

- Most preparative-scale epoxidations and BV oxidations use mCPBA ✔ Improvement ✘ Similar

| mCPBA Oxidations | PAA Oxidations |
|---|---|
| 1. Atom inefficient – high molecular weight oxidant | ✔ Atom efficient – lower molecular weight oxidant |
| 2. Requires halogenated solvents | ✔ May not require halogenated solvents |
| 3. Degradation product (<i>m</i> -chlorobenzoic acid) is harmful | ✔ Degradation product (acetic acid) is nearly benign in low concentrations |
| 4. Stored as "wet", dangerous compound | ✔ Does not require storage when produced onsite |
| 5. ~70 wt.% – complicates quantitative use | ✘ Contains ~60 vol.% acetic acid and water impurities |
| 6. Requires stoichiometric quantities | ✘ Also requires stoichiometric quantities |

Methods



Results

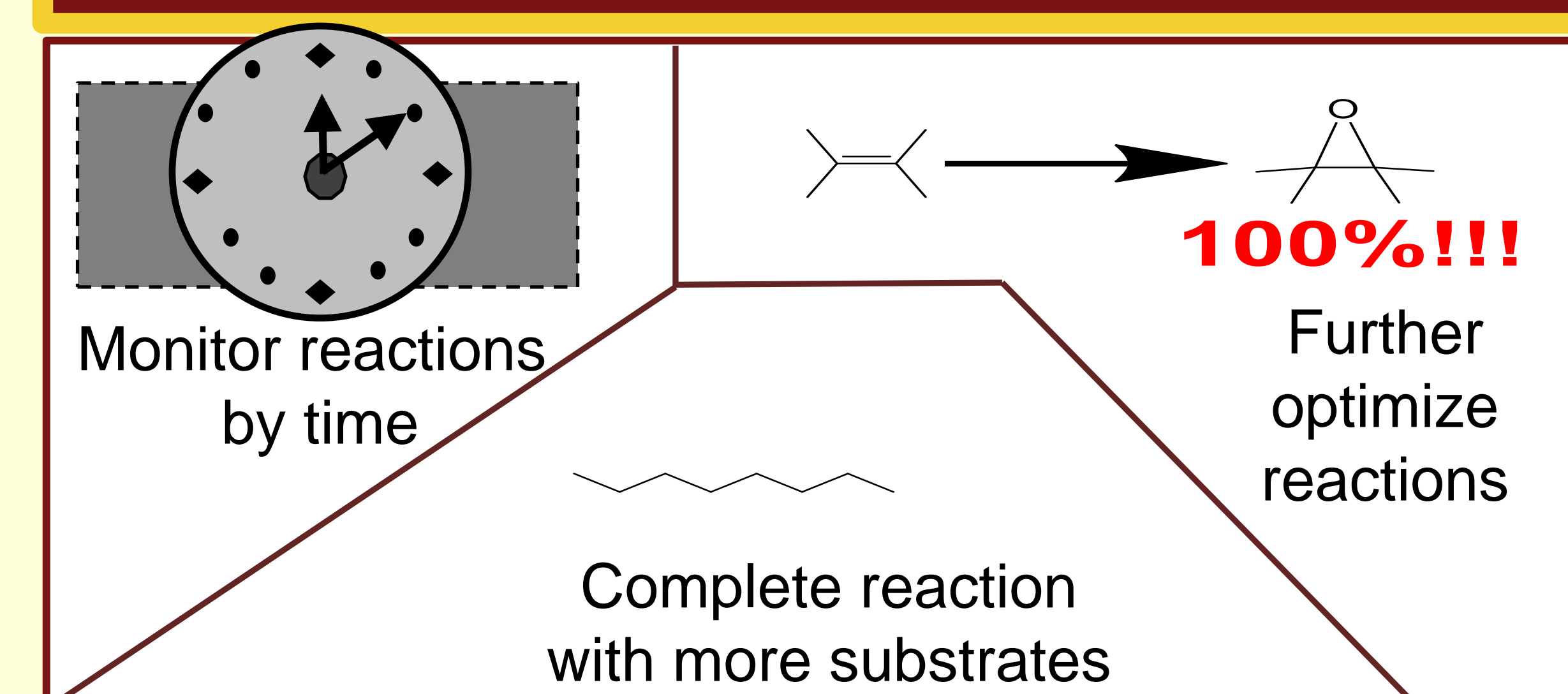
| Product | Onsite-produced PAA Yield | mCPBA Yield | Industrially-produced PAA Yield | Literature-Reported Yields |
|--------------------------|---------------------------|-------------|---------------------------------|---|
| 1,2-epoxyoctane | 6.2 & 7.0% | 100% | 10 & 17% | 50% [1] <10% [2] 85% [3] |
| cyclohexene oxide | 54 & 79% | 100% | 41 & 61% | 95% [4] 2% [5] 10% [6] 57% [7] |
| ϵ -caprolactone | 29 & 24% | 100% | 9.4 & 9.0% | 47% [8] 40% [9] 90% [10] |

Conclusions

mCPBA is Still Preferred:

- Permits 100% conversion of substrate
 - Is a simple method with minimal substrate handling
- ### Cyclohexene Epoxidation Potentially Practical:
- A higher conversion than with 1-octene
 - Is competitive with currently available methods
- ### Baeyer-Villiger Oxidation Needs Optimization:
- Some conversion achieved, however not practical
 - Formation of side products (6-hydroxyhexanoic acid, adipic acid, and 6-oxohexanoic acid) potentially

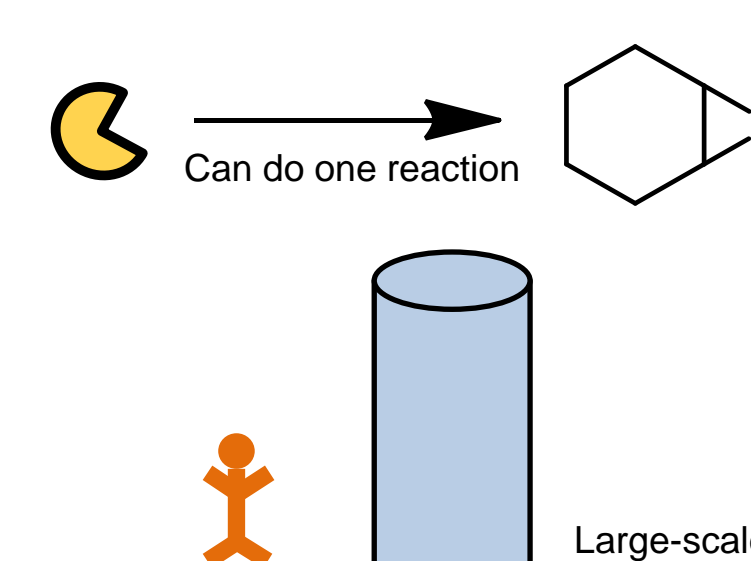
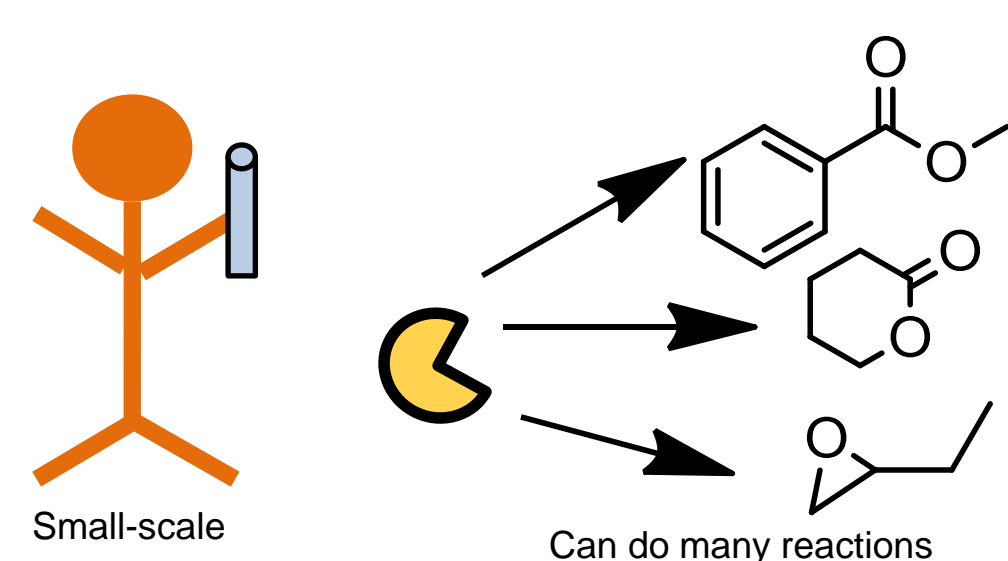
Future Avenues



Oxidation Sizes

Preparative-Scale ✔ Industrial-Scale

- Requires broadly-applicable oxidants and catalysts
- Complicates use of narrowly-applicable enzymes/catalysts
- Can remain practical with narrowly-applicable oxidants and catalysts
- Optimize only once – great for enzymes/catalysts



Acknowledgements/References

I would like to thank both Jan van Langerman and Dr. Romas J. Kazlauskas for their guidance, advice, and support for this project work and revisions.

- Crude product done with PAA in acetic acid solution
- CAL-B-produced peroxyoctanoic acid oxidation done in hexane with gradual addition of H₂O₂
- Achieved after 45 minutes by urea hydrogen peroxide and Novozyme-435
- Achieved after 8.5 h with peracid produced from ϵ -caprolactone and H₂O₂ by Novozyme-435 in organic conditions
- Catalytic oxidation with CAL-B-produced peroxyoctanoic acid, from H₂O₂ and octanoic acid, in hexane
- Chemical oxidation completed with addition of preformed peroxyoctanoic acid in hexane
- Completed with *in situ*-formed PAA by conversion of acetic acid with H₂O₂ non-catalytically (6 h and 50°C), in competition with allylic acetoxylation
- 90% H₂O₂ oxidant and arsenated polystyrene resin catalyst at 80 °C in dioxane solvent
- H₂O₂ oxidant and no catalyst
- With 50% H₂O₂ oxidant and acid catalysis by trifluoroperacetic acid