**In Vivo Olefin Metathesis – challenges, approaches and applications**

Summarized enough

Summarized moderately

Lot of missing info

No info at all

Introduction

1. Olefin metathesis overview

In this chapter I'll present very briefly the history of olefin metathesis, general reaction mechanism, metals used to catalyze it, phosphine ligands and carbenes, including Schrock's and Fischer's. Some non-biological industry use-cases might be interesting as well.

1. Principles of bioorthogonal chemistry

As my work attempts to describe OM as a bioorthogonal process, some detail on existing bioorthogonal reactions is needed – definition, short history, two-three examples of the following:

* native chemical ligation
* Staudinger ligation
* copper-catalysed azide-alkyne cycloaddition
* strain-promoted [3 + 2] reactions
* tetrazine ligation
* metal-catalysed coupling reactions
* oxime and hydrazone ligations
* photoinducible bioorthogonal reactions

I can use [this](https://pubmed.ncbi.nlm.nih.gov/34585143) article.

Body:

1. Reasons to attempt in-vivo metathesis and examples of specific reactions

Not sure if this section should be in the end (more inspiring) or the beginning (makes more sense in introducing the challenges). Here I'd present in detail both the existing and proposed usages:

* "Living factories" inside organisms
* Drug synthesis, transport and uncaging/deprotection
* Protein modification
* DNA modification
* Further examples
* Replacement of different bioorthogonal reactions (not OM)

1. Challenges and requirements

The things that currently prevent us from achieving in-vivo metathesis in industry scale.

* 1. General (limitations of every OM)

There must be alkenes…

Side reactions must be avoided…

Removing ruthenium from the final products…

* 1. Reaction-specific

Two ways I can explain this:

* + the common grouping of OM reactions – RCM, CM, ROMP and ADMET, which is better and which present challenges
  + effect of specific groups in biological reactants, such as OH in sugars, steric hindrance in proteins, side reactions and reactivity of products
  1. Water-related
  2. Biology-related

The reaction must be fast…

Low substrate concentration…

Specificity

That damned GSH

Poisoning the organism - Ru is usually considered toxic and carcinogenic :(

Catalyst poisoning, decomposition, chelation and aggregation

Probably more about it in my summaries

* 1. use-case-specific (e.g. blood/cancer environment)

componentization of the reaction to the correct organ/organelle inside the cell

1. Solutions (can include lessons from other biorthogonal reactions)
   1. Catalysts

Generally, why Ru is the best and the rest suck

* + 1. GHII (and III?) catalysts

Why carbenes are the best and phosphines suck

Short introduction to GHII, GHIII, AquaMet and Grela with comparative studies of their STABILITY, TON, TOF and selectivity in some reactions

* + 1. Charged catalysts

Cationic and anionic and what's good about them, should compare to previous point's catalysts in same/similar table

* + 1. Metalloproteins/metalloenzymes – design, synthesis and usage+examples
    2. Getting rid of the catalyst afterward
  1. Biologically relevant conditions and model reactions – choice of substrate and reaction partners

Pseudo-amino acids and how to make them

The chalcogen effect

Steric optimizations

All the nice things that facilitate reactions

* 1. Modification of the environment/additional reagents

Should be careful that these reagents are chemically and biologically inert

* 1. Choice of the organism

In case we get to – a good place for lessons from other reactions

Discussion

1. Recommended catalyst for each use-case
2. Most- and least-fitting OM reactions
3. Challenges that still aren't answered and if I have any possible solutions
4. More ideas for applications

Conclusion