New Chiral Porphyrin Designs Utilising Cinchona Alkaloids

1. Introduction

- Metalloporphyrins are the most employed asymmetric ligand for group transfer reactions such as C-H functionalisation.
  - Fine-tune the reactivity – metal, π- & meso-substituents on porphyrin ring(s).
- Various of metals are tolerated, for example: Fe, Mn, Ru, Rh, Zn, Sn, Ni, Cu etc.
- Challenges in render catalysis asymmetric with porphyrin ligands – distance of peripheral substituents to metal centre.
- Existing strategies feature steric hindrances and non-covalent interactions approaches:

2. Prior work & Project Aims

- Total synthesis of (±)-L-DHQ-3.
- Total synthesis of diastereomer of (±)-L-DHQ-3.
- Total synthesis of racemic L-DHQ-3.

3. Method A: Ion-Paired Porphyrins & Application to Asymmetric Epoxidation

A) Synthesis of ion-paired porphyrin:
- Based on C*-symmetric ABA ion-pair scaffold.
- Ion-induced variation of different parameters – chiral cation, sulfate position.

B) Application to Asymmetric Epoxidation of Simple Aliphatic Donor Substrates:
- Focus on asymmetric oxidation and C-H functionalisation reactions, whereby inducing chirality with TM complexes are challenging.

4. Method B: Covalent Attachment of Cinchona Alkaloid to Porphyrin

A) Proposal of Covalent Linked Porphyrin:
- Covalent linkage between alkaloid and porphyrin unit – ensure chirality is present on transition.

B) Selected Covalent Catalysts Synthesised:
- Catalyst synthesised from 1-alkylcinchonidines and 1,3-bisphosphonates.

C) Application to Asymmetric Epoxidation:
- Results show moderate selectivity but poor enantioselectivity in investigated reactions.
- Alkaloid scaffold – not able to induce asymmetry in epoxidation reactions.

5. Method B: Tetrasubstituted Covalent Linked Porphyrin

A) Structure of Groups and Heterocyclic catalysts: Two approaches synthesized:
- Top schematic illustrates the alkaloid backbone.

B) Heterocyclic catalysts: Synthesis route:
- Via 1,3-bisphosphonates.

C) Application of Catalysts:
- Use of different catalysts to both enantiomers.
- Use of alkaloid containing a spatially hindered lactone (larger size).
- Use of alkaloid containing an aminocarbonyl (smaller size).
- Use of alkaloid containing a branched lactone (larger size).

D) Conclusion:
- Catalyst design and synthesis is effective.

6. Future Work

- Tetrasubstituted catalysts: incorporating cage life structures.
- Investigation of different architectures – may add substituents in advantageous positions during transition state.

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References:
- B. A. Adams, J. R. Phipps, unpublished results.