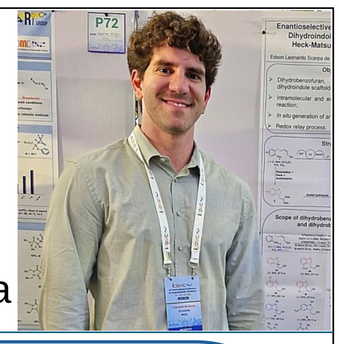
Enantioselective Synthesis of Dihydrobenzofurans derivatives by Merging Intramolecular Heck-Matsuda Reactions from Anilines with Redox-Relay Process



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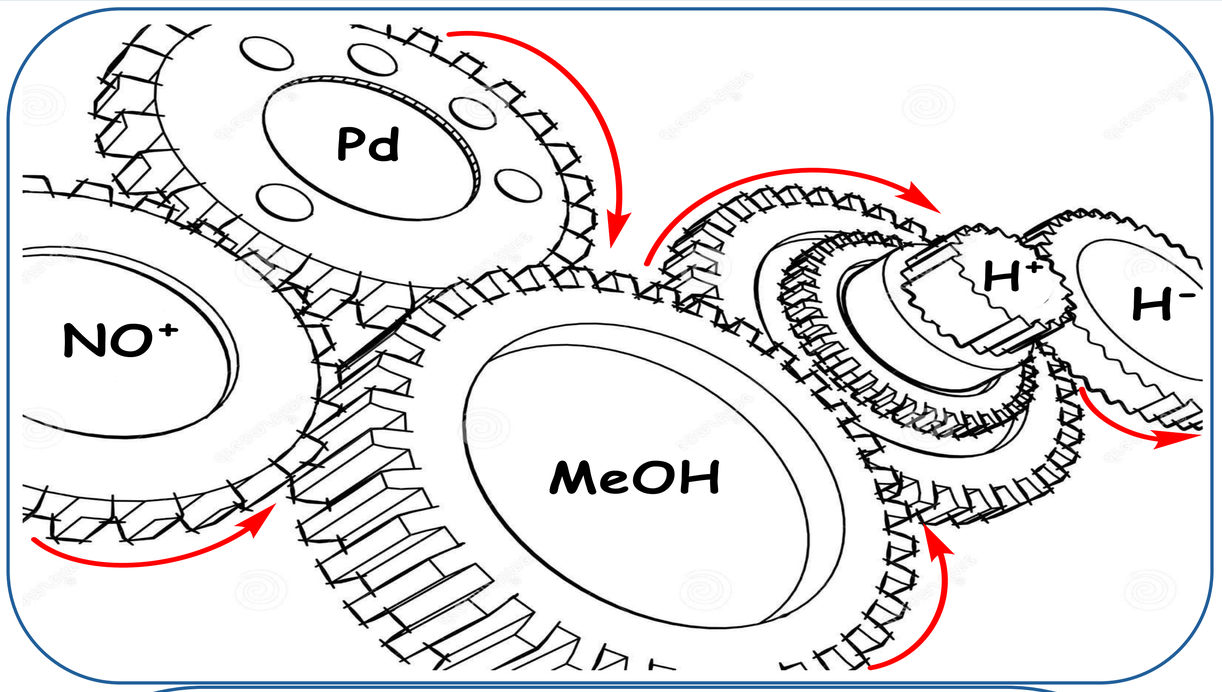
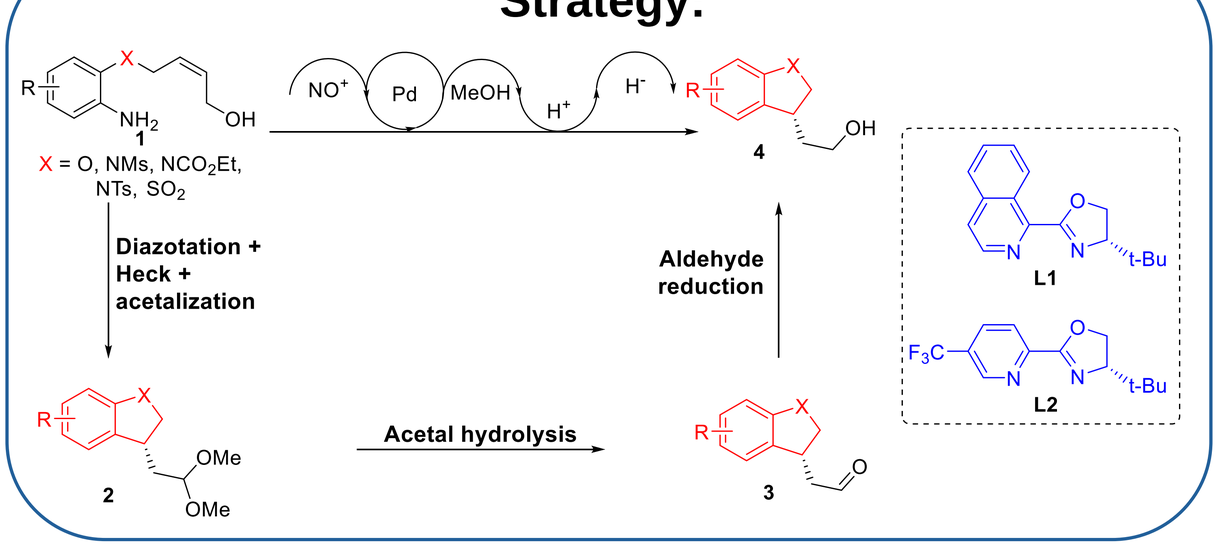
Objectives:

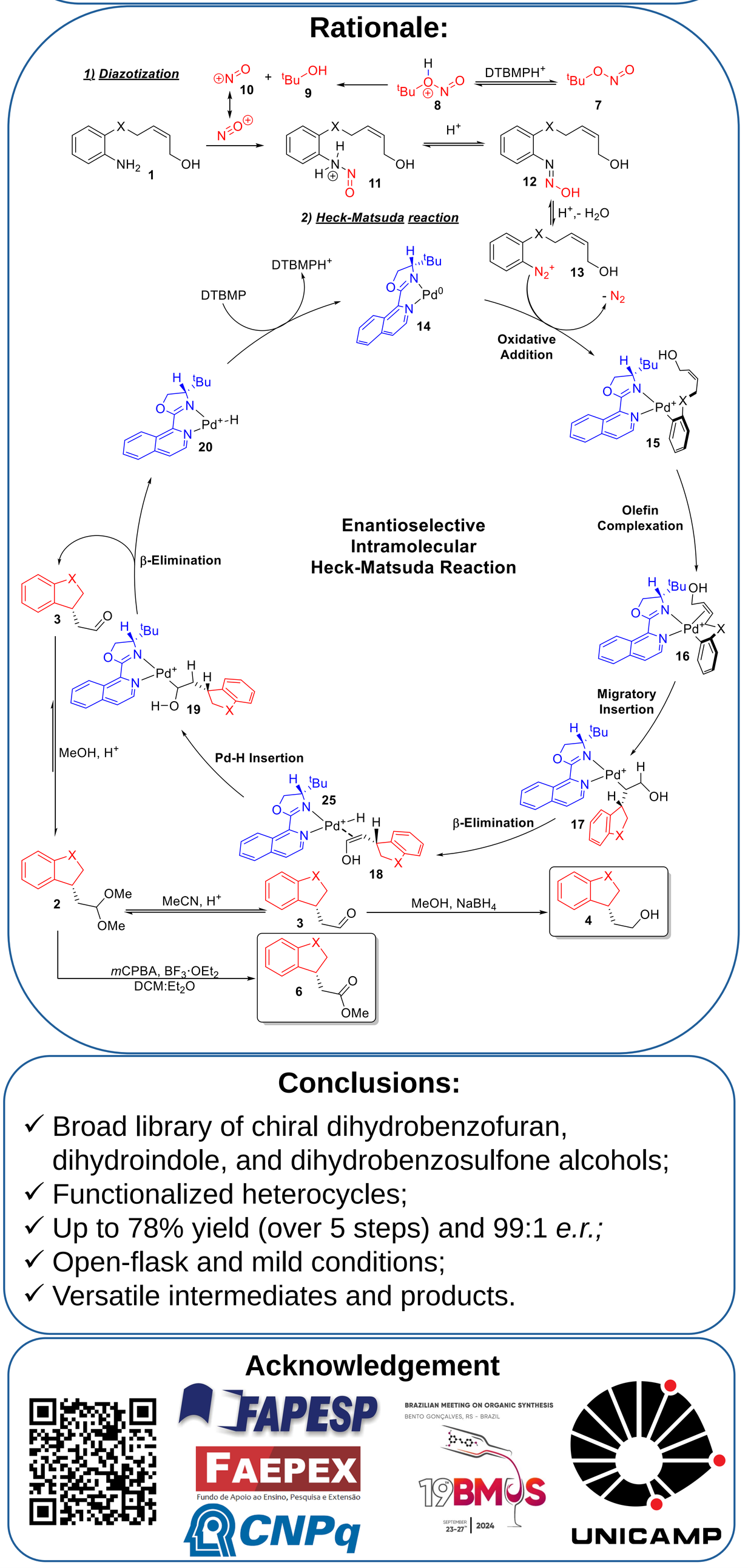
- Dihydrobenzofuran, dihydrobenzosulfone, and dihydroindole scaffolds;
- Intramolecular and enantioselective Heck-Matsuda reaction;
- *In situ* generation of aryldiazonium salts;
- Redox relay process.



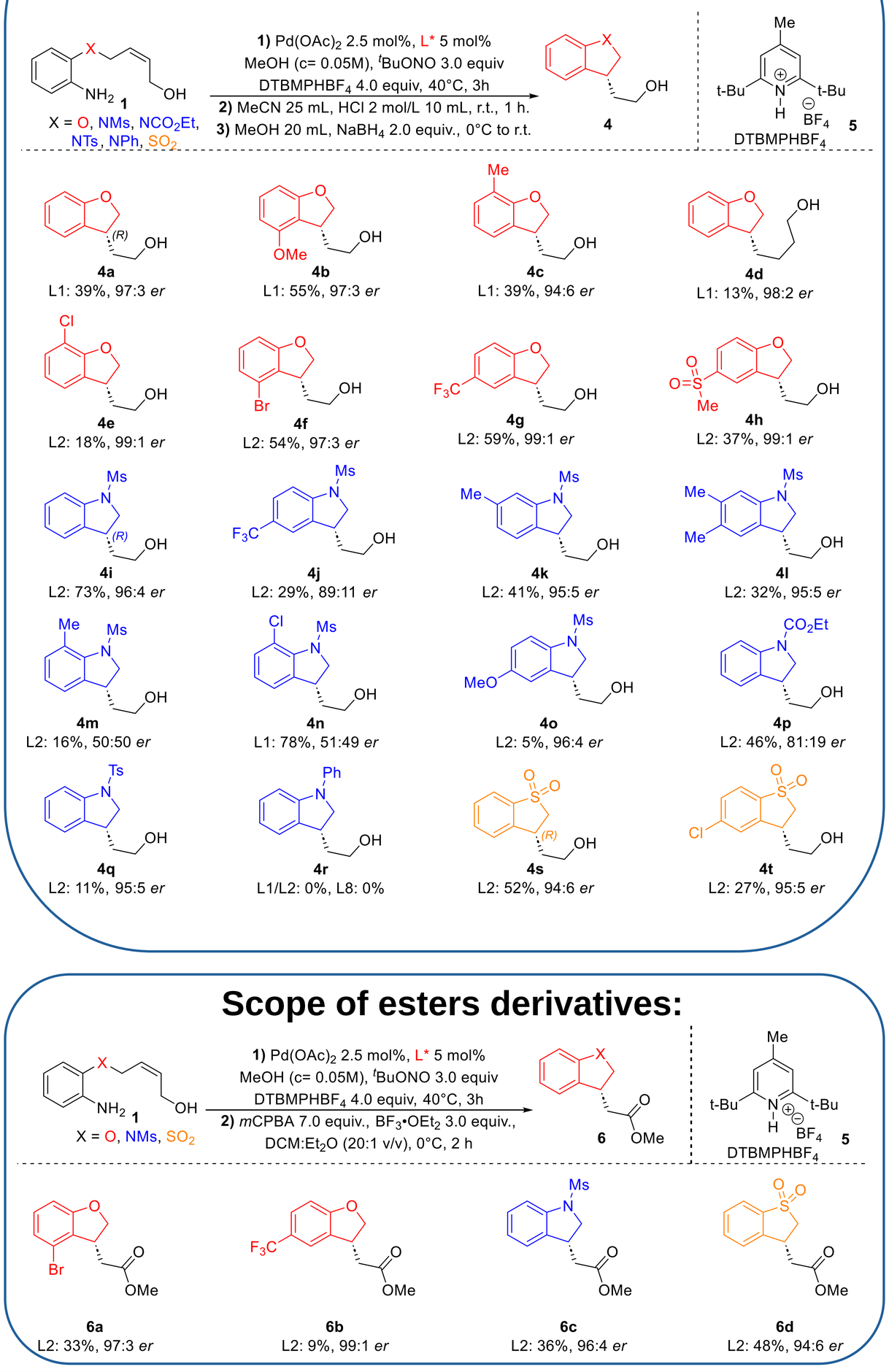
Strategy:



Rationale:



Scope of dihydrobenzofuran, dihydroindole and dihydrobenzosulfone:



4a L1: 39%, 97:3 *er*

4b L1: 55%, 97:3 *er*

4c L1: 39%, 94:6 *er*

4d L1: 13%, 98:2 *er*

4e L2: 18%, 99:1 *er*

4f L2: 54%, 97:3 *er*

4g L2: 59%, 99:1 *er*

4h L2: 37%, 99:1 *er*

4i L2: 73%, 96:4 *er*

4j L2: 29%, 89:11 *er*

4k L2: 41%, 95:5 *er*

4l L2: 32%, 95:5 *er*

4m L2: 16%, 50:50 *er*

4n L1: 78%, 51:49 *er*

4o L2: 5%, 96:4 *er*

4p L2: 46%, 81:19 *er*

4q L2: 11%, 95:5 *er*

4r L1/L2: 0%, L8: 0%

4s L2: 52%, 94:6 *er*

4t L2: 27%, 95:5 *er*

Scope of esters derivatives:

6a L2: 33%, 97:3 *er*

6b L2: 9%, 99:1 *er*

6c L2: 36%, 96:4 *er*

6d L2: 48%, 94:6 *er*

Conclusions:

- ✓ Broad library of chiral dihydrobenzofuran, dihydroindole, and dihydrobenzosulfone alcohols;
- ✓ Functionalized heterocycles;
- ✓ Up to 78% yield (over 5 steps) and 99:1 *e.r.;*
- ✓ Open-flask and mild conditions;
- ✓ Versatile intermediates and products.

Acknowledgement

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