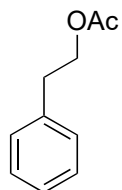
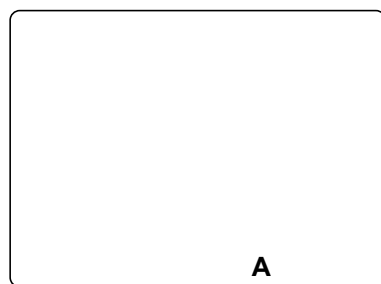


## Chemoenzymatic Total Synthesis of *ent*-Oxycodone: Fourth generation

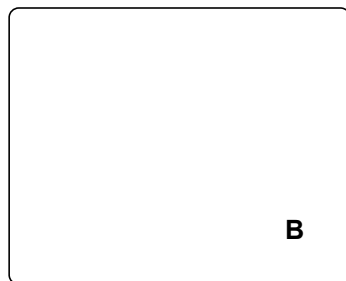
Mariia Makarova, Mary Ann A. Endoma-Arias, Helen E. Dela Paz, Razvan Simionescu, Tomas Hudlicky\*  
*J. Am. Chem. Soc.*, 2019, 10.1021/jacs.9b05033



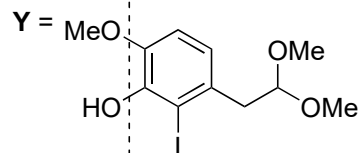
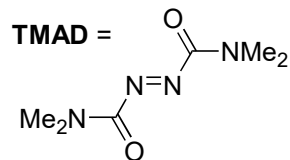
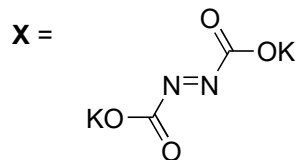
1-4



5-11



- 1) toluene dioxygenase, *E. coli* JM 109
- 2) **X**, MeOH, AcOH
- 3) TBSCl, imH
- 4) **Y**, TMAD, *n*-Bu<sub>3</sub>P



How would you synthesize **Y**?

- 5) Pd(OAc)<sub>2</sub>, dppp, Ag<sub>2</sub>CO<sub>3</sub>
- 6) OsO<sub>4</sub>, NMO
- 7) MsCl, NEt<sub>3</sub>
- 8) DBU,  $\Delta$
- 9) NaOH, MeOH
- 10) TPAP, NMO, H<sub>2</sub>O
- 11) EDCI • HCl, DMAP, MeOH

Step 5: It's a name reaction! Which one?

Step 6: It's a name reaction! Which one?

Step 10: It's a name reaction! Which one?

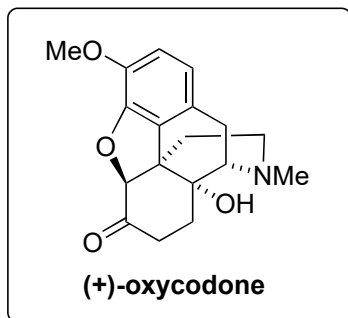
12-14

- 12) TFA, H<sub>2</sub>O
- 13) MeNHOH • HCl, NaOAc
- 14) SmI<sub>2</sub>



15-18

- 15) Raney-Ni, H<sub>2</sub>
- 16) BH<sub>3</sub>
- 17) TBAF
- 18) DMP



Step 14: Propose a reasonable mechanism!