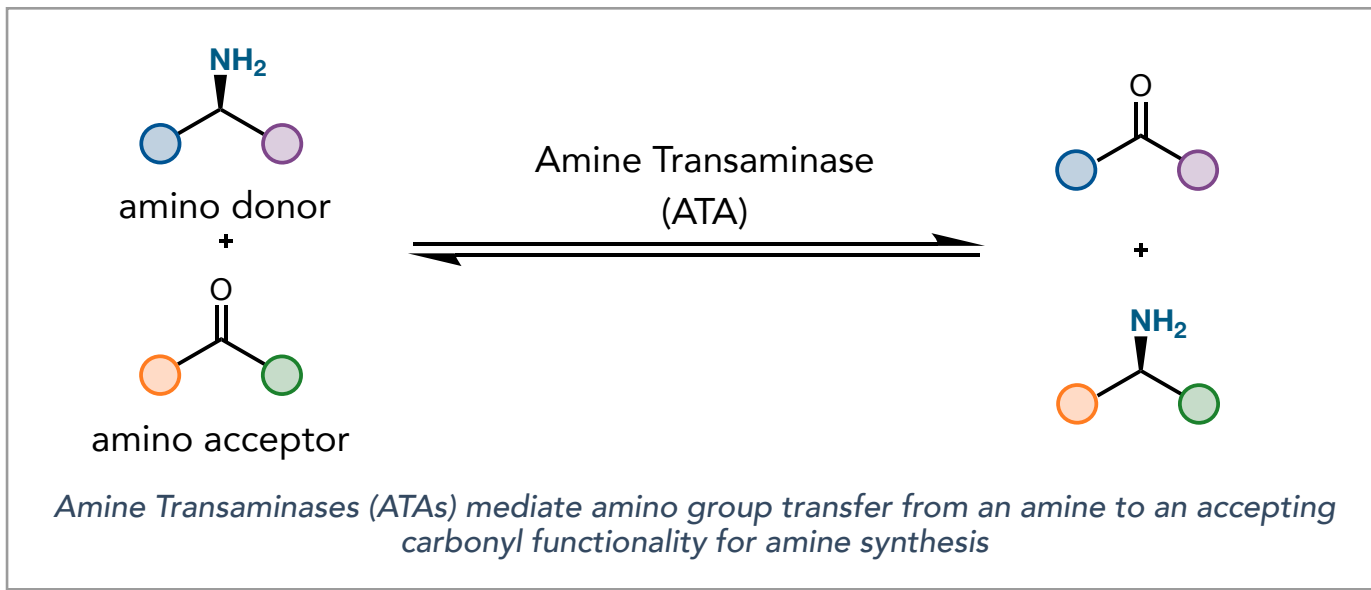
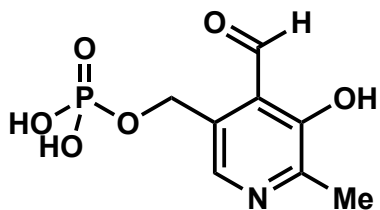


Amine Transaminase (ATA) Overview



organic cofactor

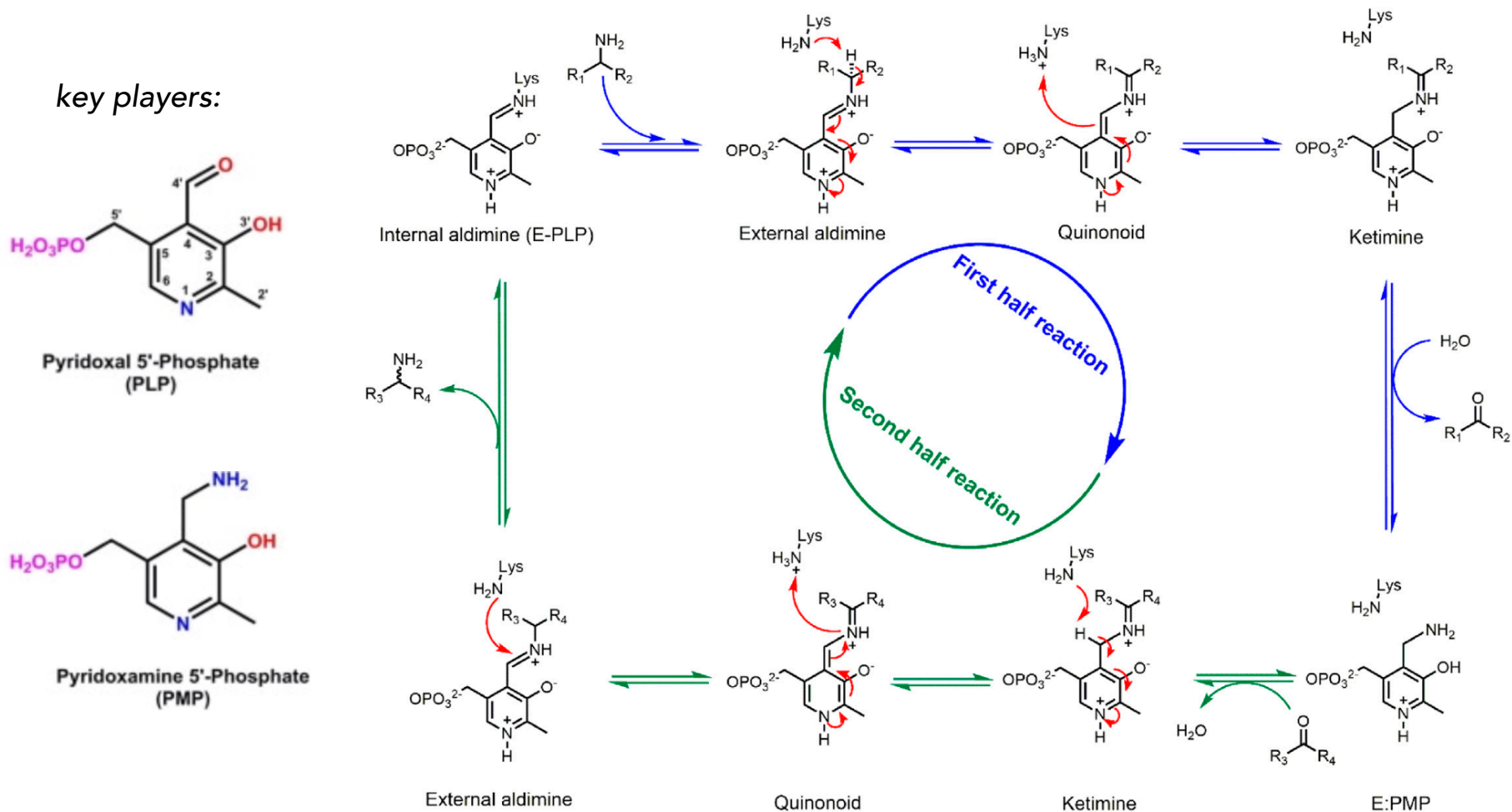


Pyridoxal 5'-Phosphate (PLP)

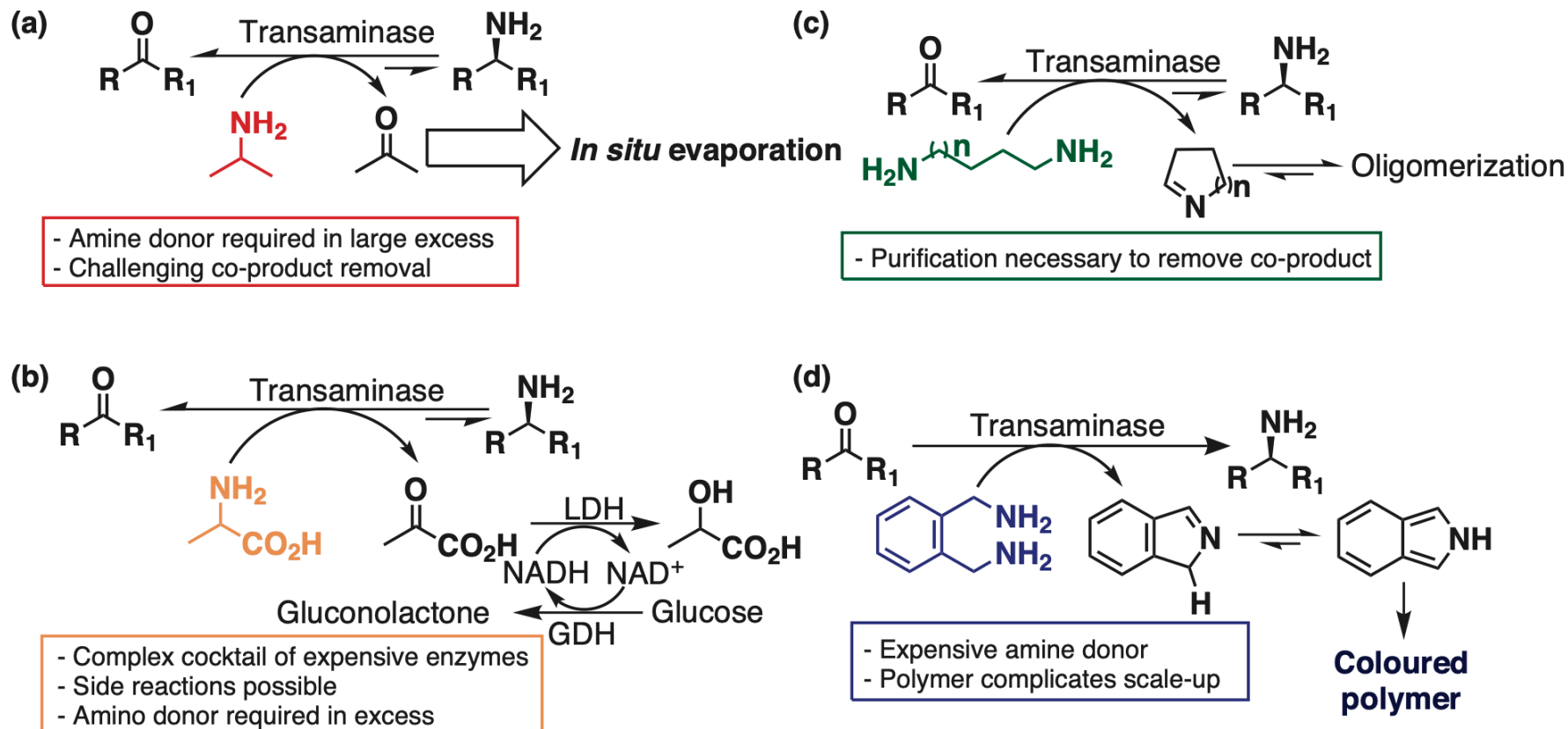
- Dependent on a Pyridoxal 5'-Phosphate (PLP) cofactor
 - a vitamin B6 variant, is the cofactor bound in the active site of TAs by a conserved lysine residue
- Grouped into either α -TAs or ω -TAs
 - α -TAs - catalyze the transfer of amino group at α -carbon of an amino acid thus *only* α -carbon to a *carboxylic group*
 - ω -TAs - catalyze amine transfer *farther away* from carbonyl moiety
- ω -TAs tend to be more functional group permissive in terms of carbonyl moieties, accepting aldehydes and ketones as well, without necessitating a carboxylic acid group
- ω -TAs provide the most synthetic utility of TAs and Amine Transaminases (ATAs) are of particular interest for their versatility

ATA Mechanism

- TAs follow a ping-pong reaction mechanism
- Pyridoxal 5'-Phosphate (PLP) cofactor - transient custodian of the amino group

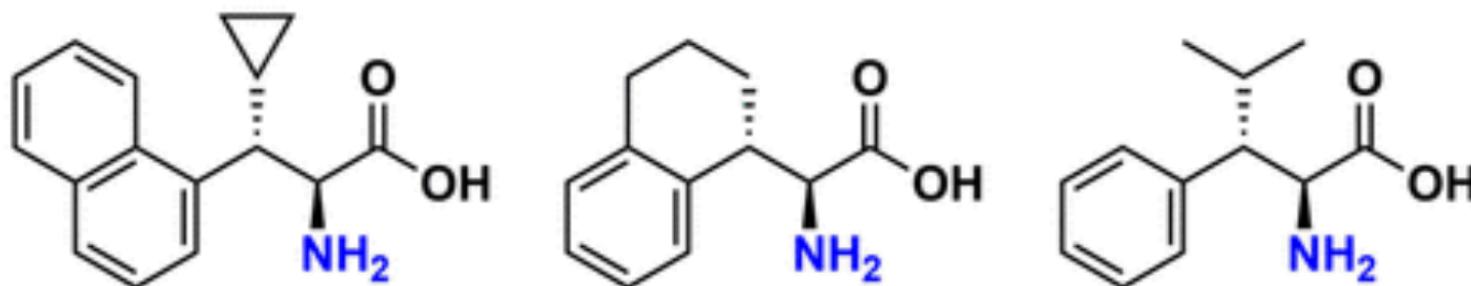
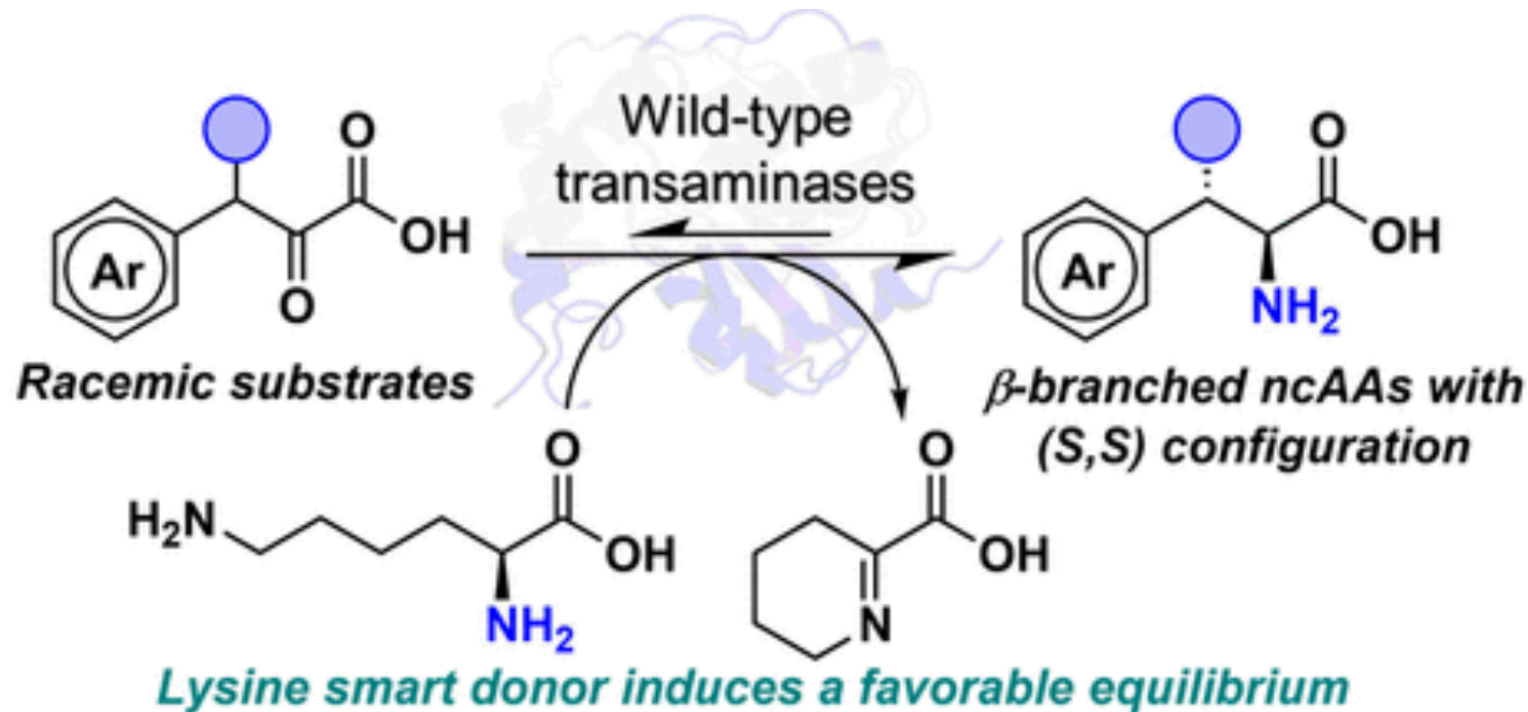


Driving the Equilibrium in ATA Reactions

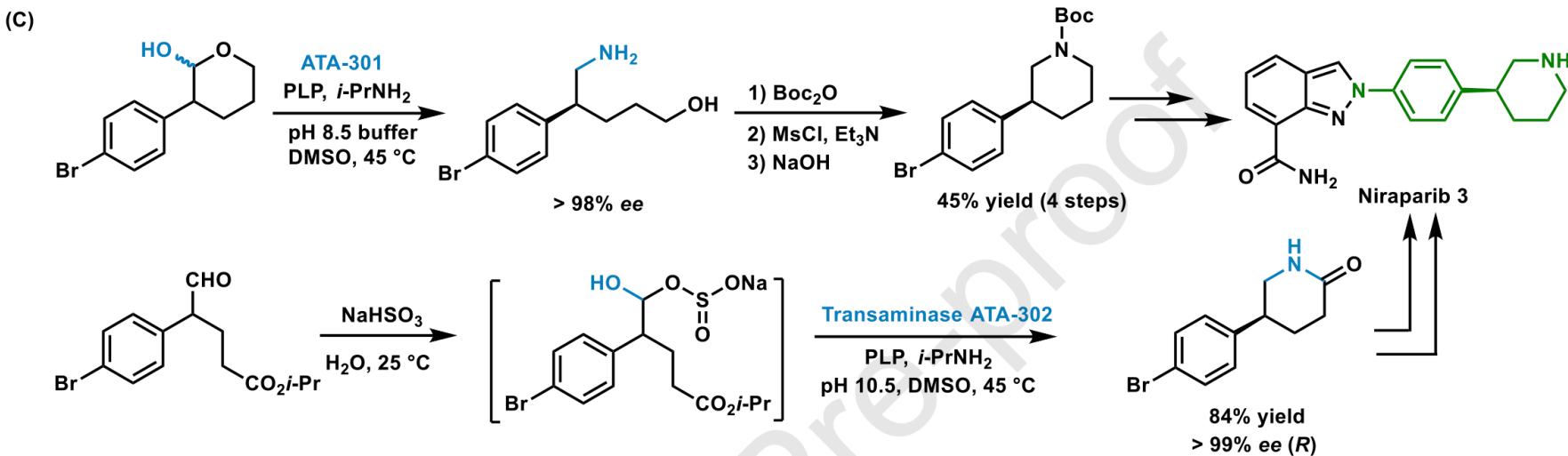
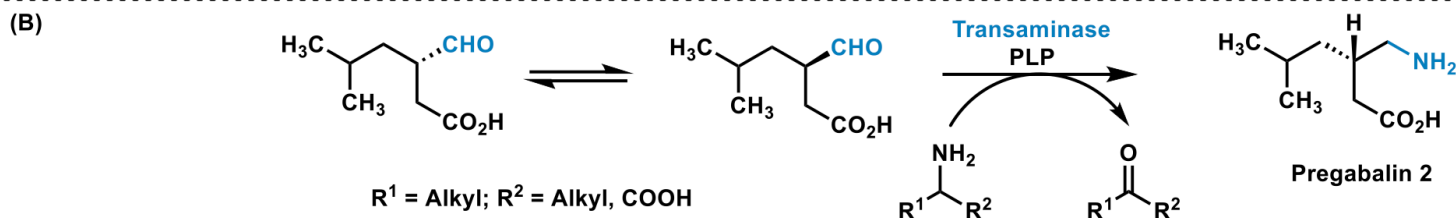
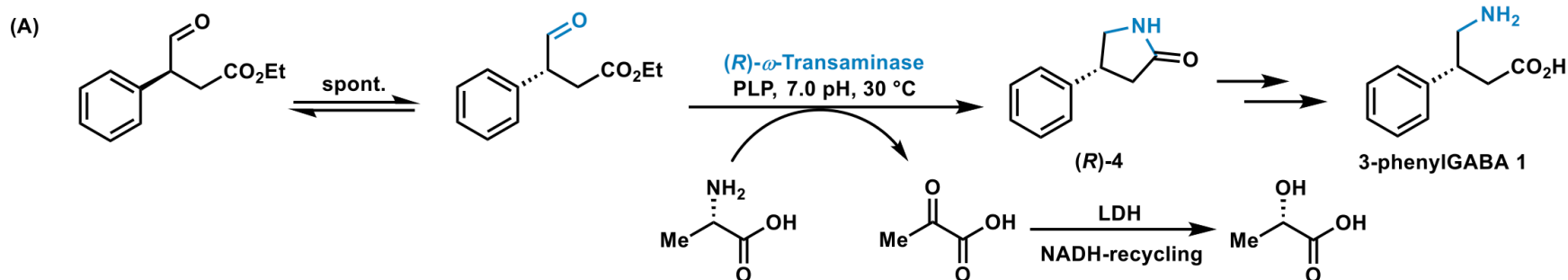


Current Opinion in Chemical Biology

Example: Lysine as a Smart Donor

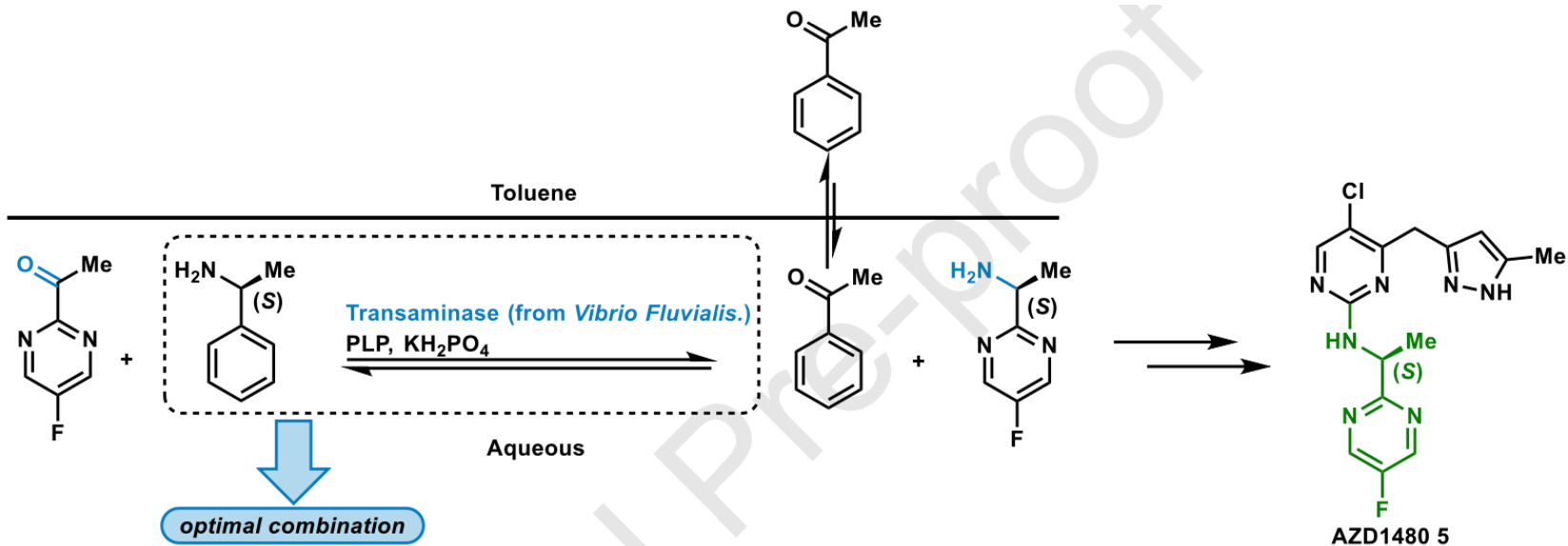


ATA Uses in Pharmaceutical Preparation: Aldehydes

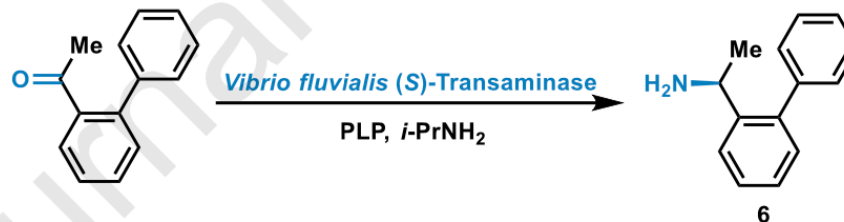


ATA Uses in Pharmaceutical Preparation: Acetophenone-Type Substrates

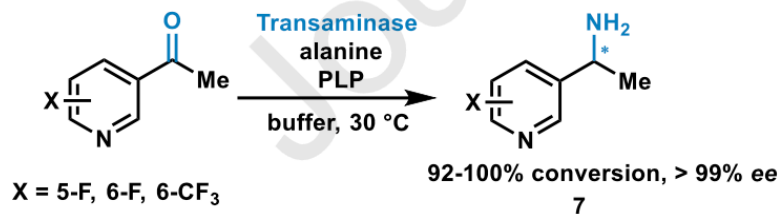
(A)



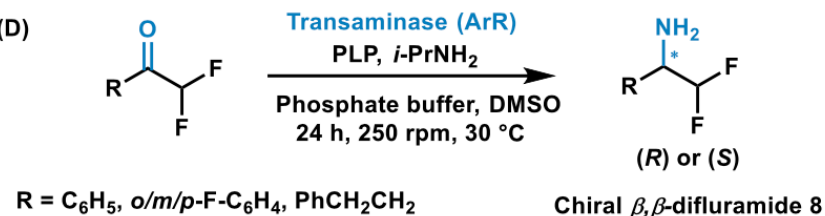
(B)



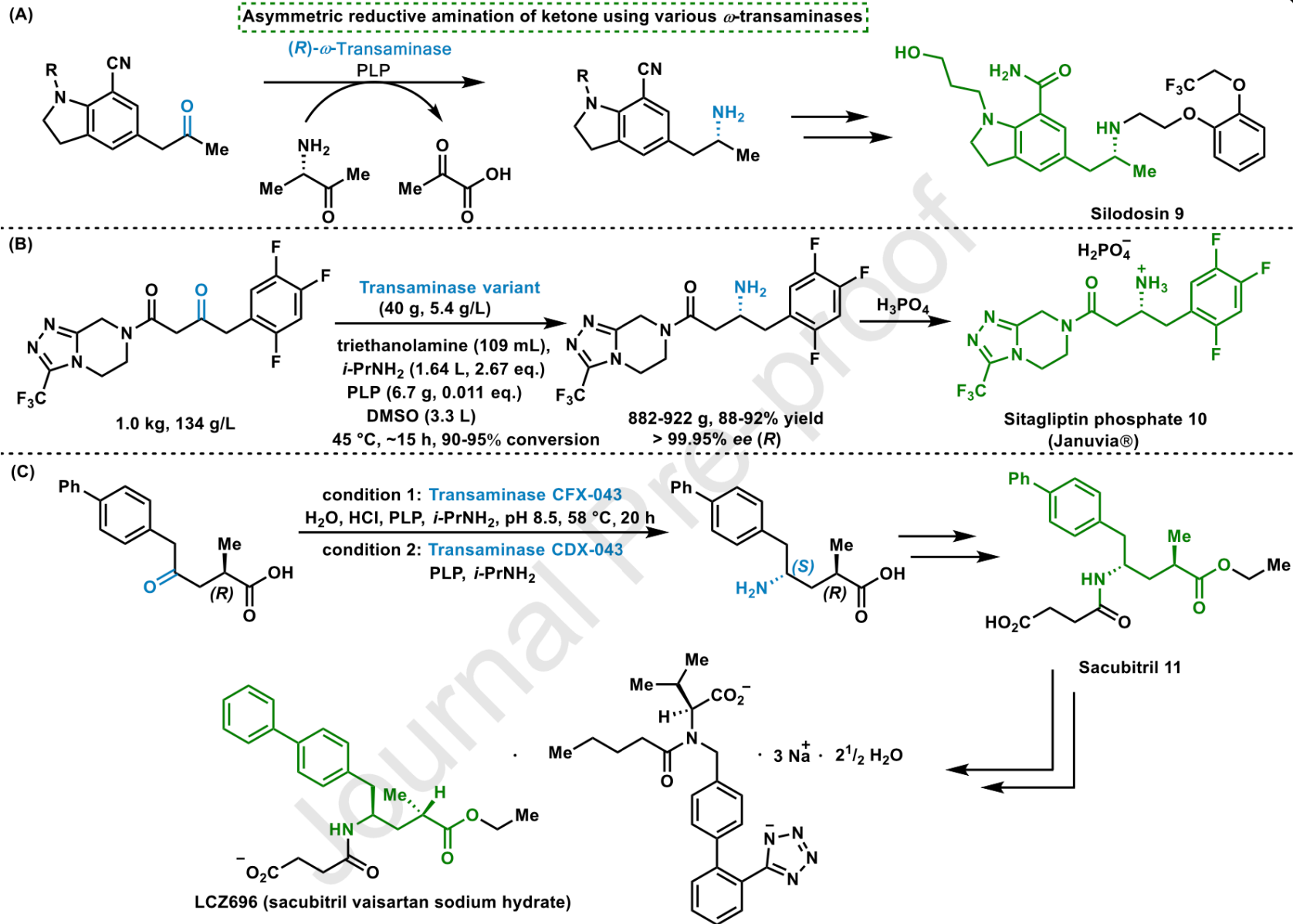
(C)



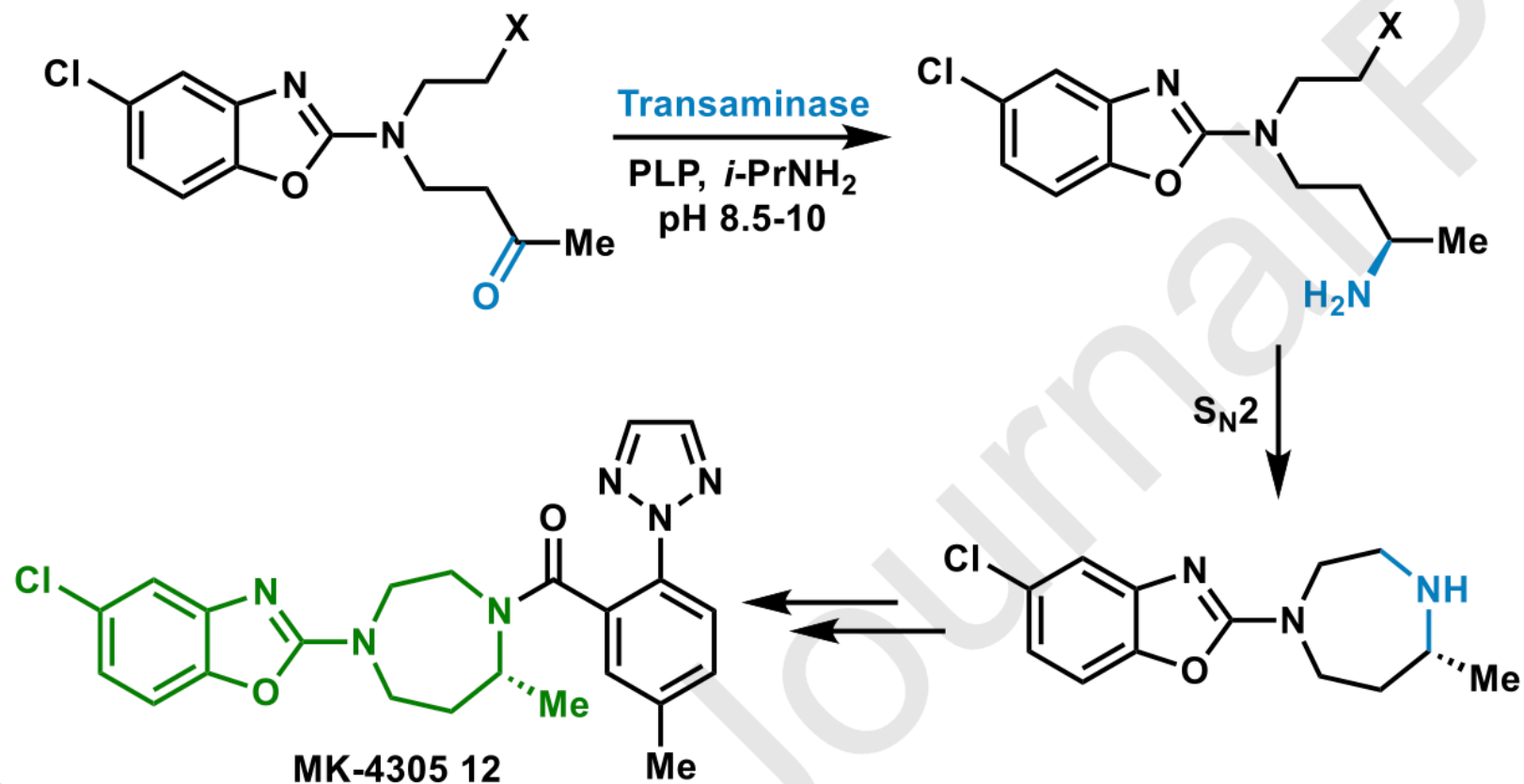
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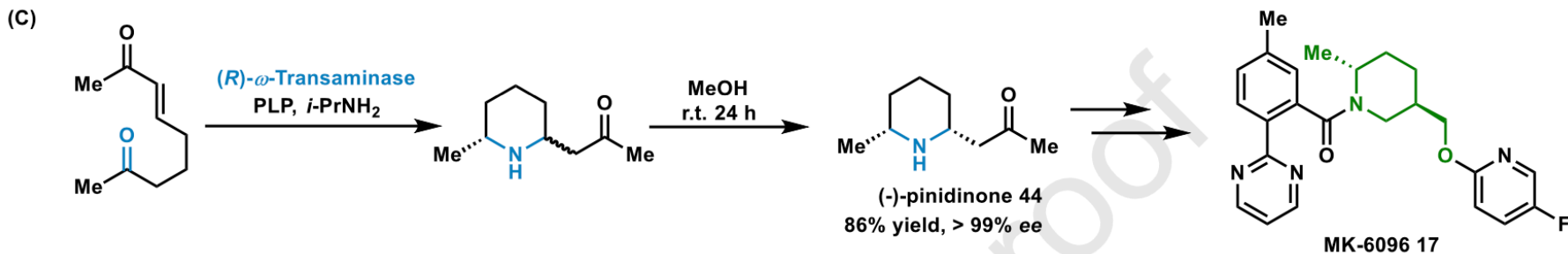
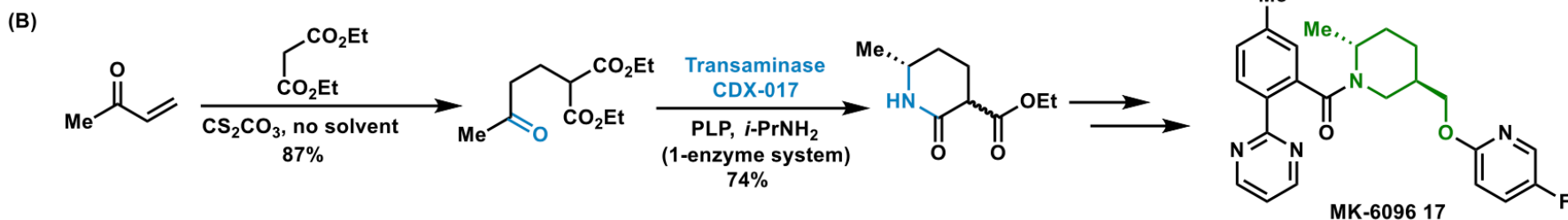
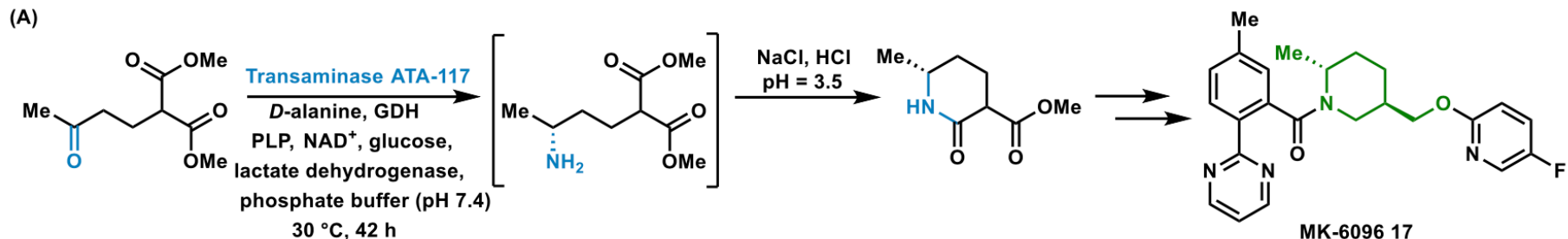
ATA Uses in Pharmaceutical Preparation: Longer-Chain Acyclics



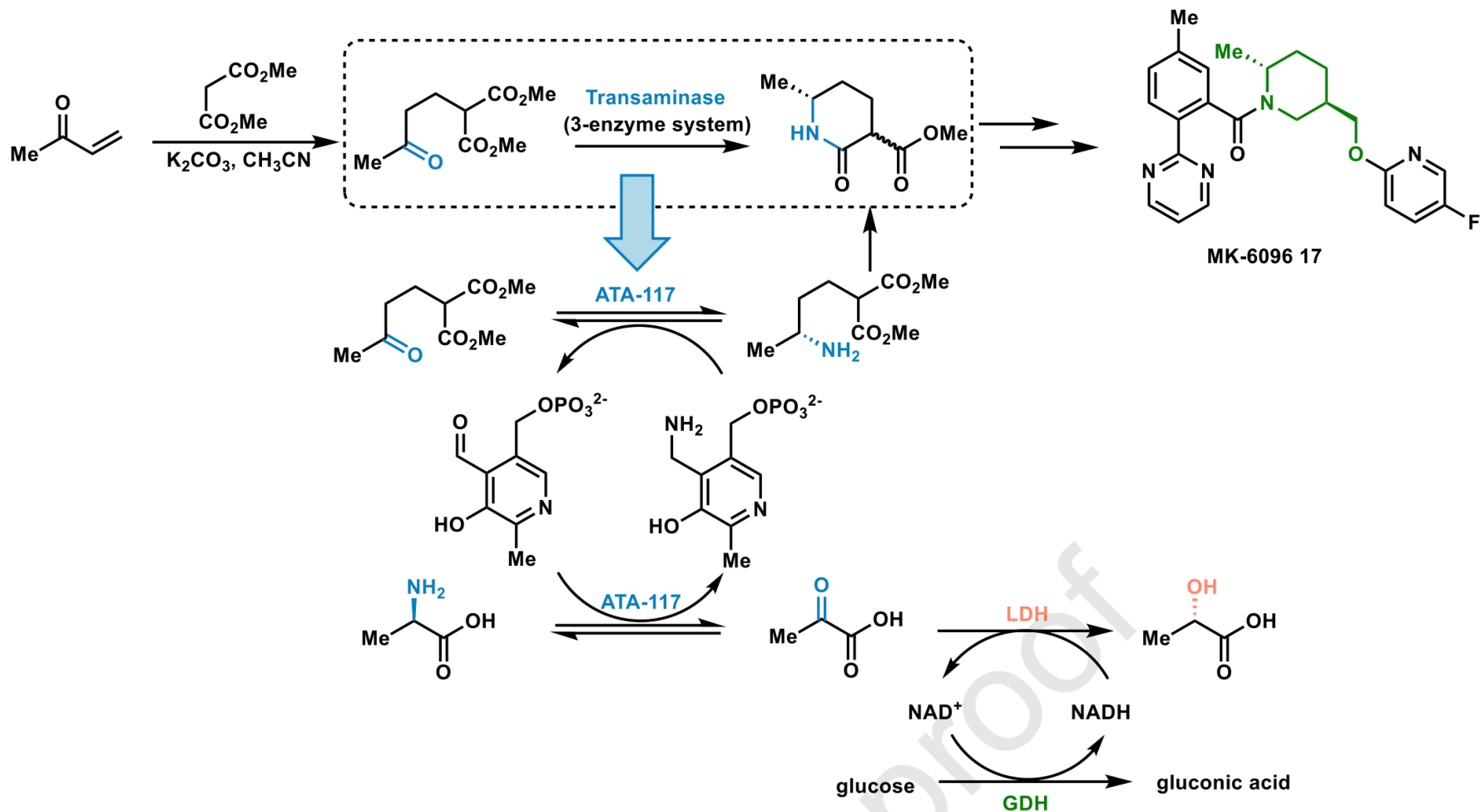
ATA Uses in Pharmaceutical Preparation: ATA-Triggered Cyclization Toward MK-4305 12



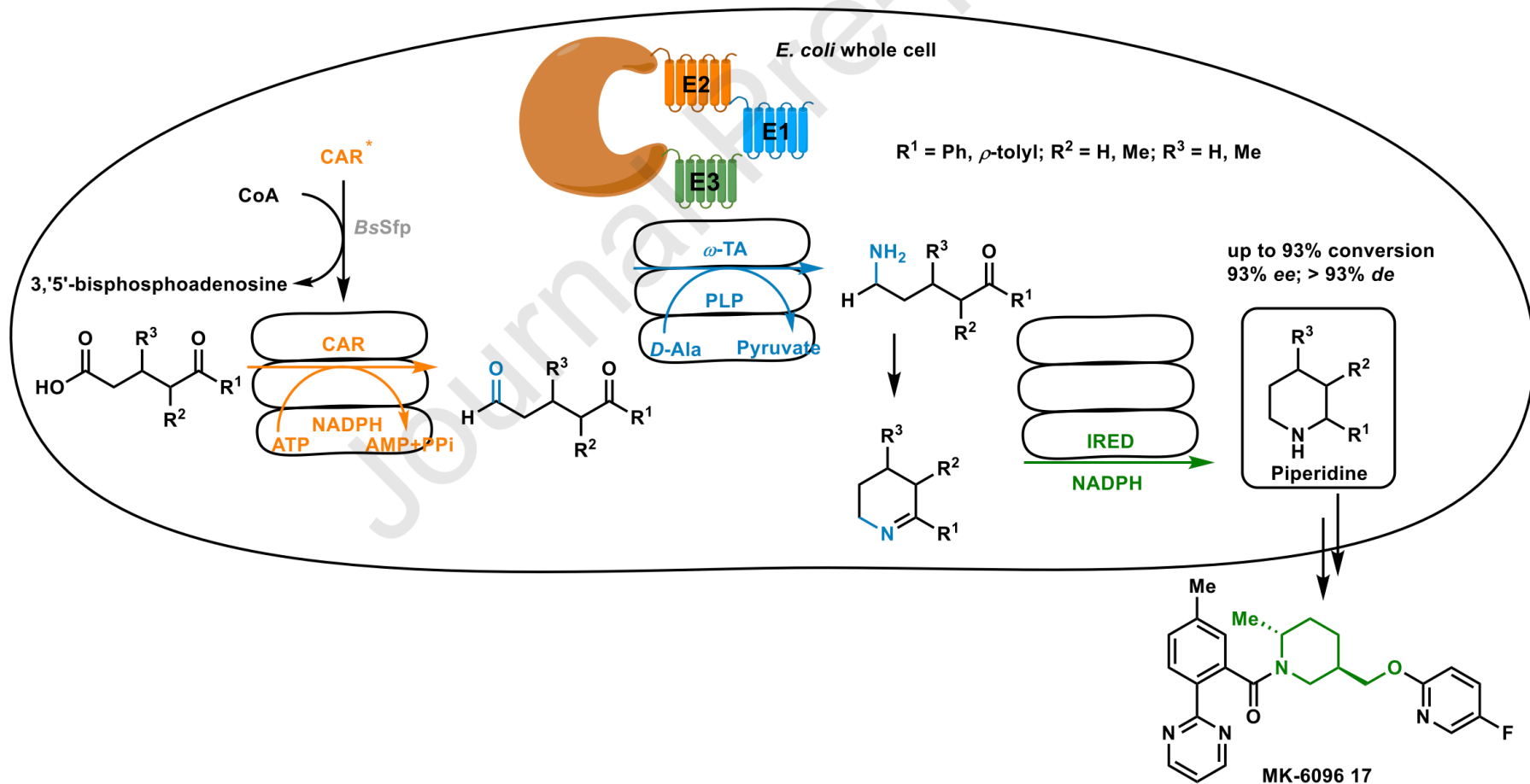
ATA Uses in Pharmaceutical Preparation: Chemoenzymatic Routes to MK-6096



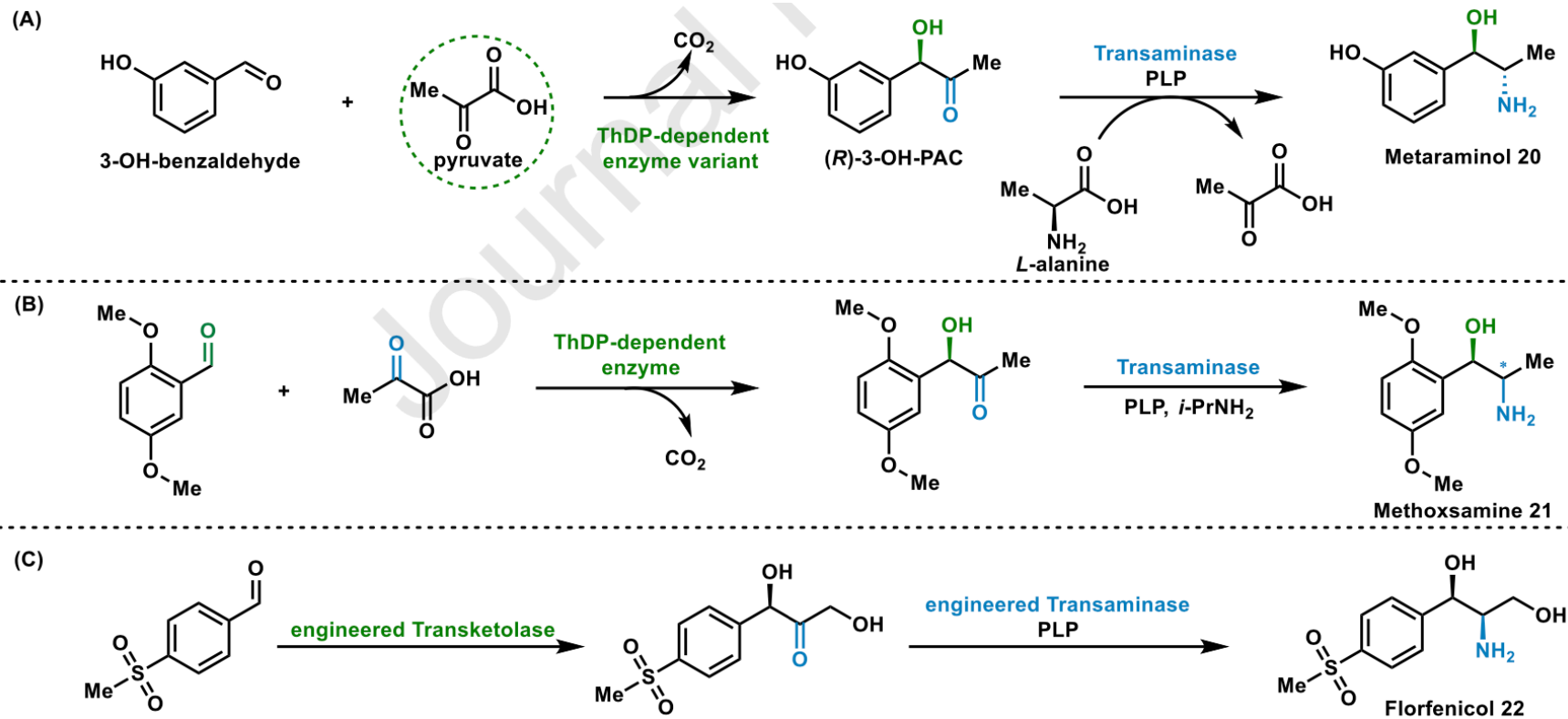
ATA Uses in Pharmaceutical Preparation: Transition to Whole Cell Process



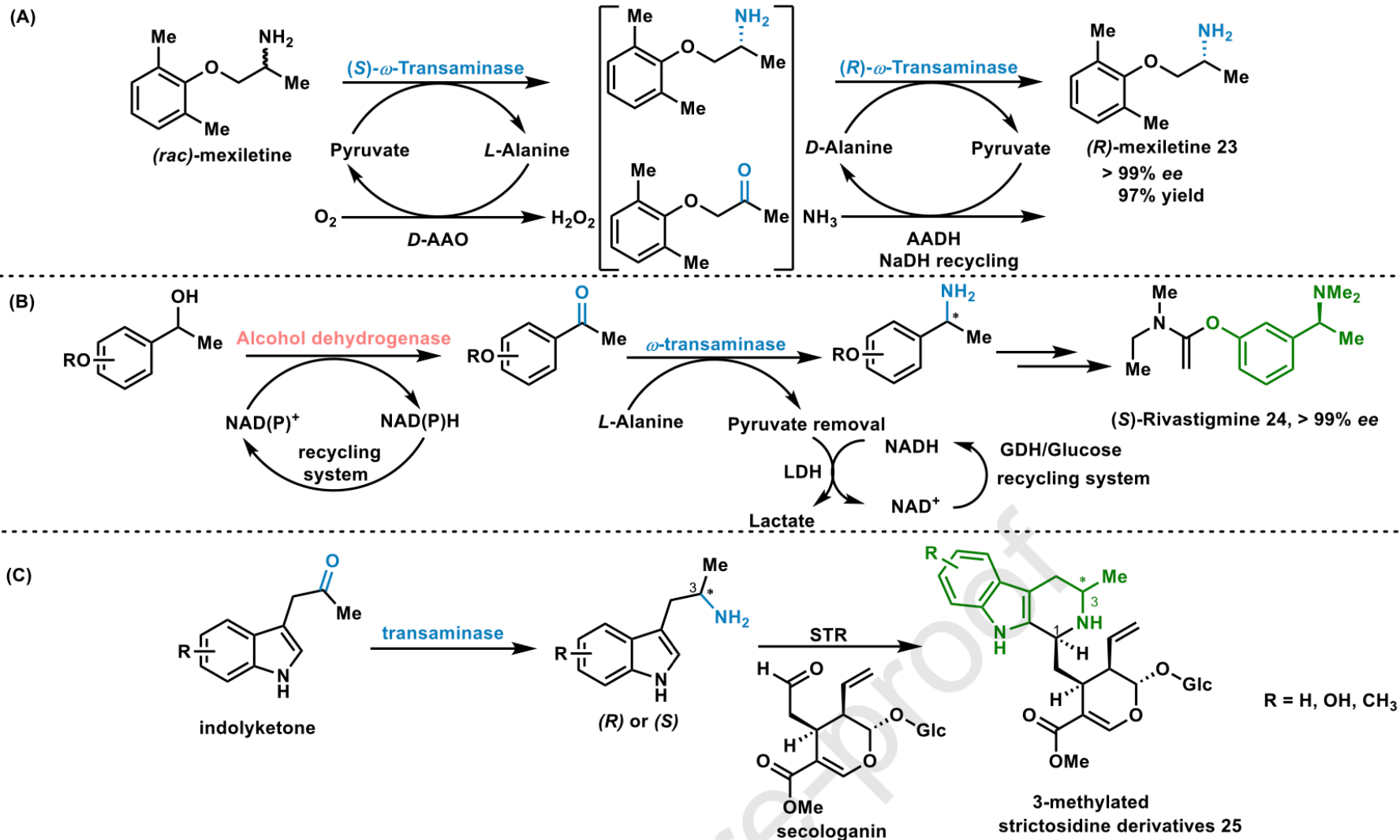
ATA Uses in Pharmaceutical Preparation: Transition to Whole Cell Process



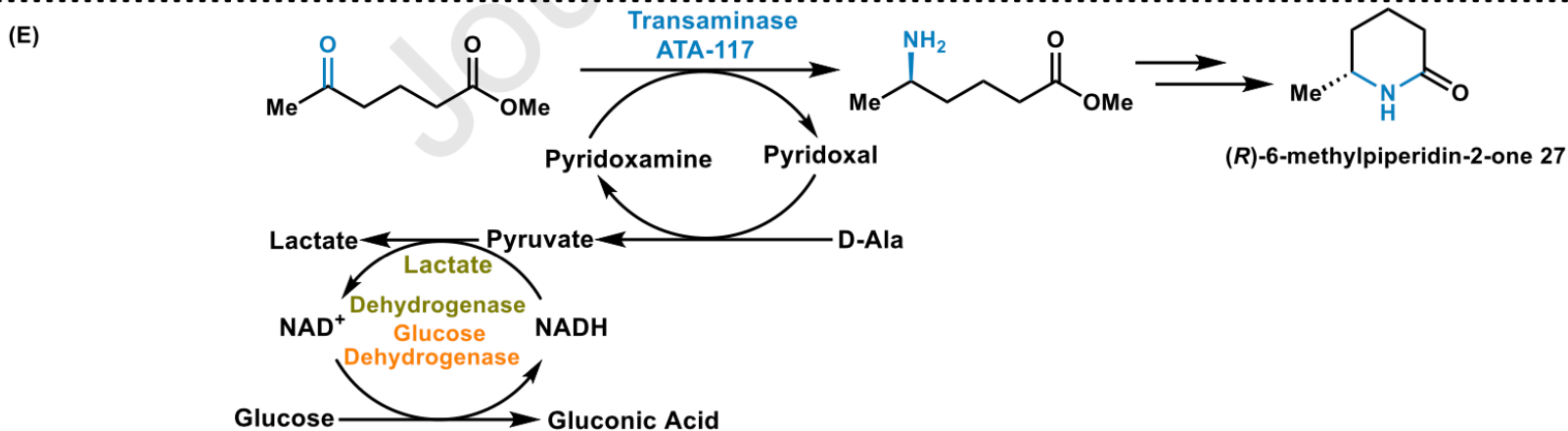
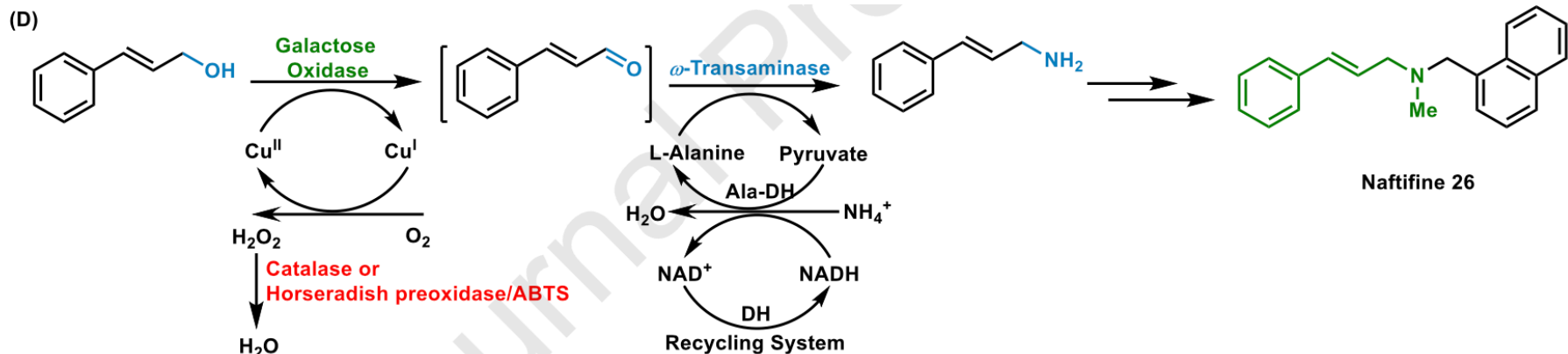
ATA Uses in Pharmaceutical Preparation: Cascades from Aldehydes



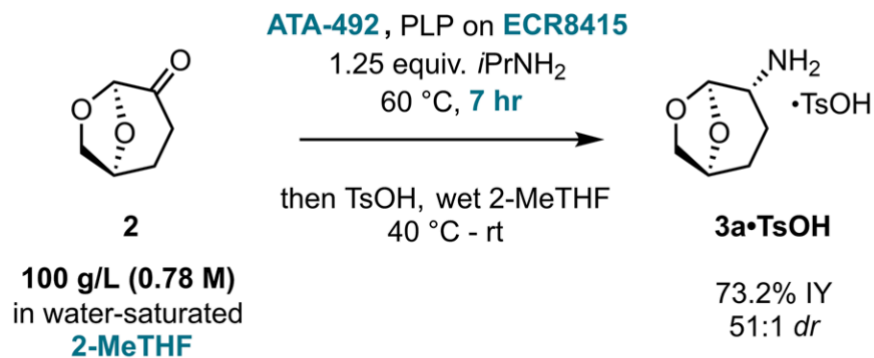
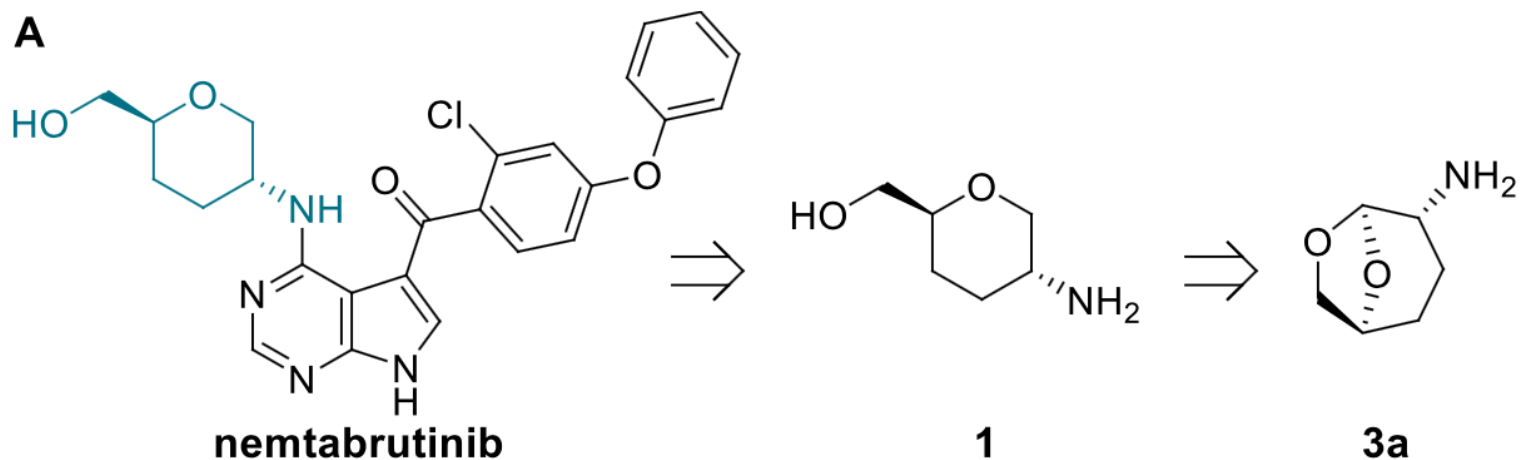
ATA Uses in Pharmaceutical Preparation: Other Notable Examples



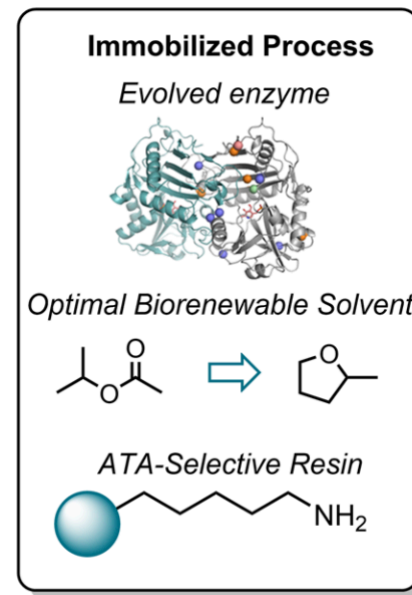
ATA Uses in Pharmaceutical Preparation: Other Notable Examples



From Solvent to Pharmaceutical

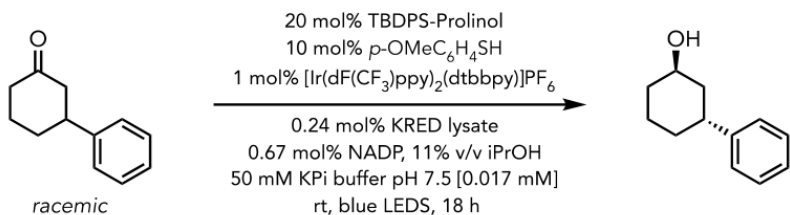


- *Immobilized enzyme enables robust single stream process*
 - *Highly active and selective catalyst*
- *Organic solvent enables direct product crystallization*
 - *Straightforward protein removal*



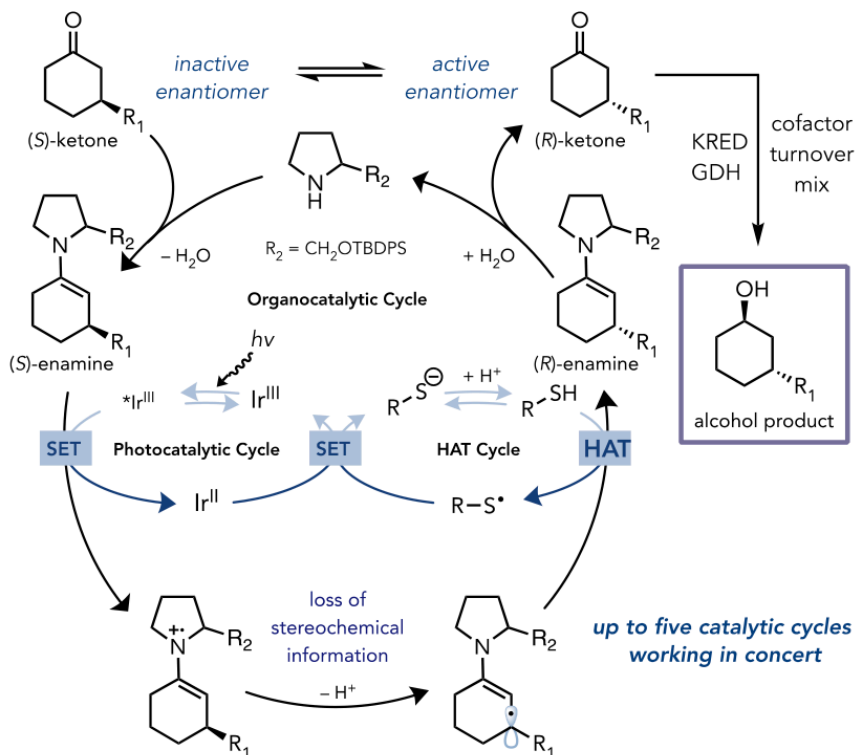
Photoenzymatic Dynamic Kinetic Resolution of β -Stereogenic Ketones

DKR of β -Stereogenic Ketones Via Synergistic Photoredox Organocatalysis

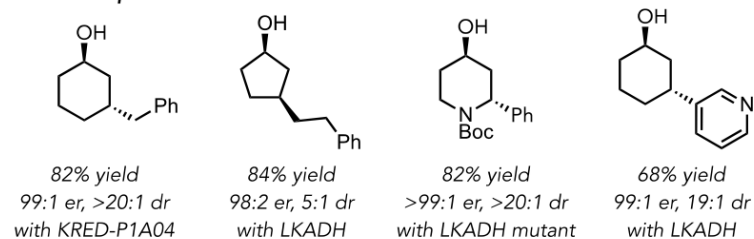


21 examples
 up to 92% yield, >99:1 er, >20:1 dr

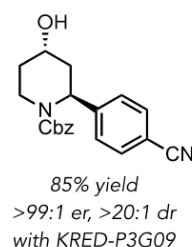
Reaction Mechanism



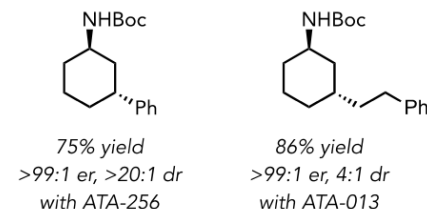
Select Examples



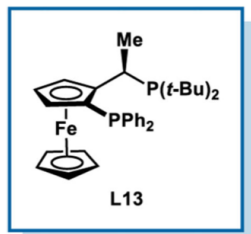
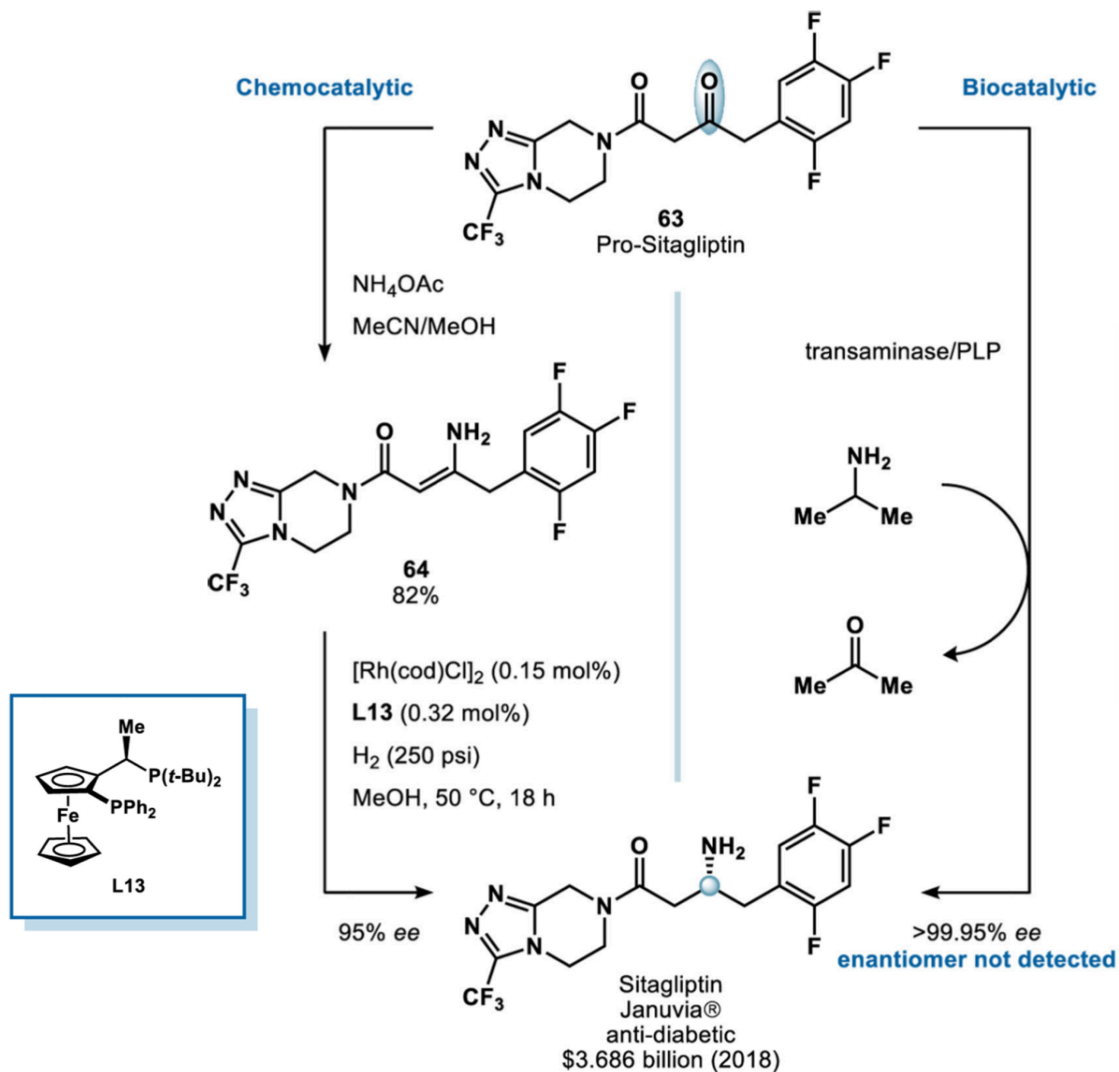
pharmacophore precursor

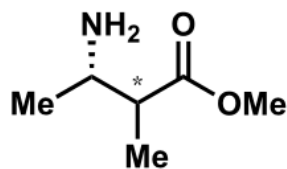
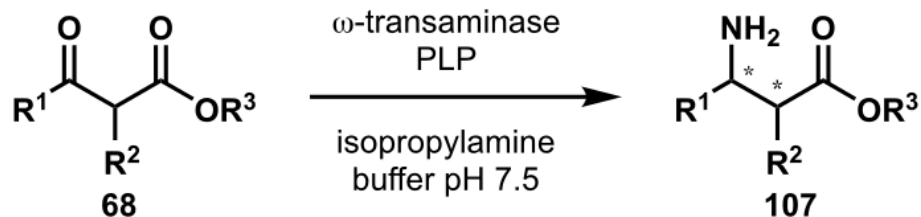


compatibility with aminotransferases (reaction followed up with Boc protection)

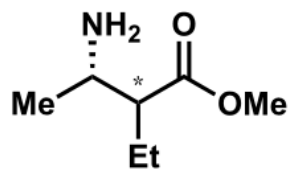


Januvia (Sitagliptin): Landmark Improvement in the Pharmaceutical Industry

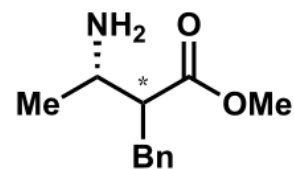




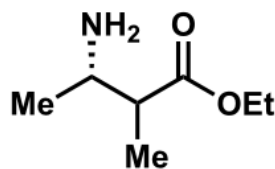
107a
TA-P1-A06,
88% yield, 34/66 dr,
>99% ee, >99% ee



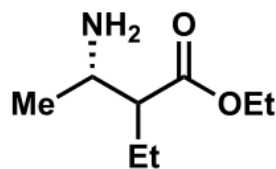
107b
TA-P1-A06,
87% yield, 16/84 dr,
>99% ee, >99% ee



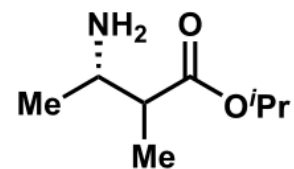
107c
TA-P1-A06,
98% yield, 58/42 dr,
>99% ee, >99% ee



107d
TA-P1-G05,
88% yield, 56/44 dr,
>99% ee, >99% ee

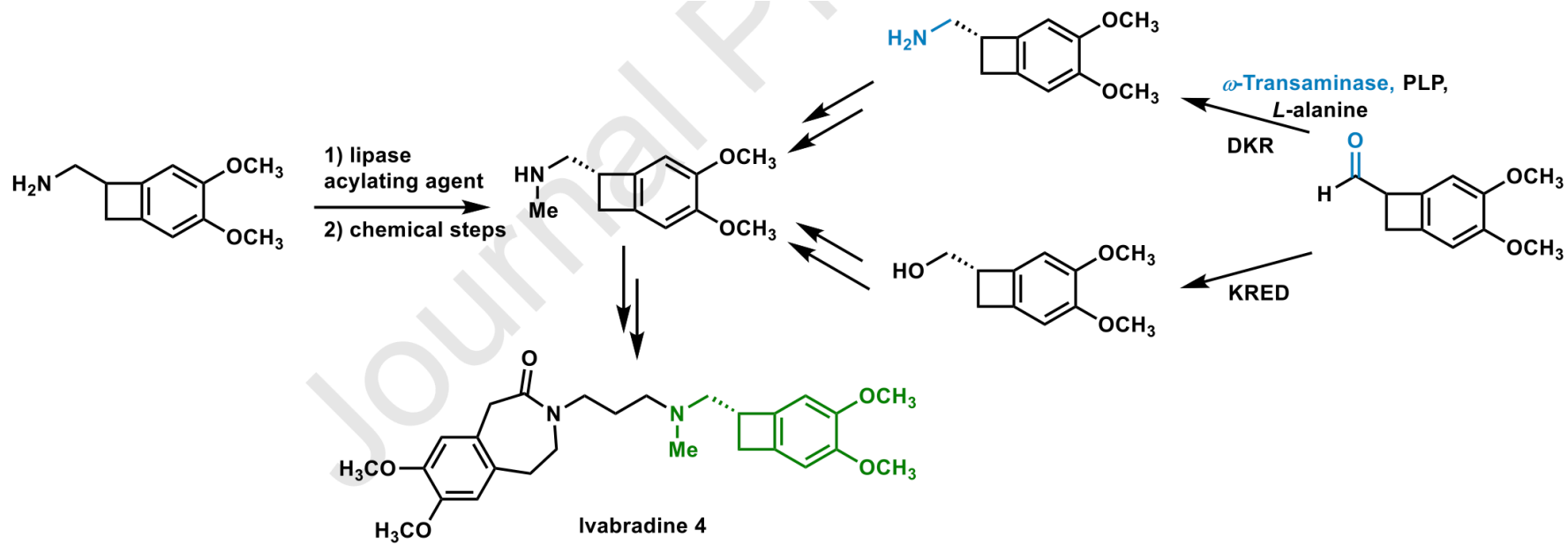


107e
TA-P1-A06,
93% yield, 29/71 dr,
>99% ee, >99% ee



107f
TA-P1-G05,
94% yield, 57/43 dr,
>99% ee, >99% ee

ATA Uses in Pharmaceutical Preparation: Biocatalysis Roadmap to Ivabradine (Pfizer)



Applications of ATAs in Natural Product Synthesis

