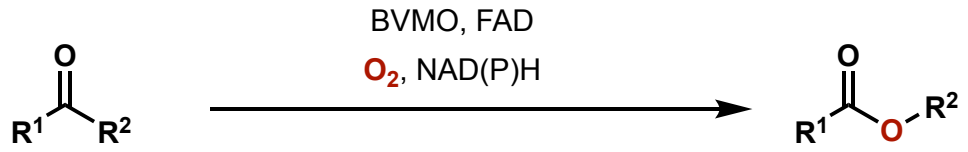
Introduction to Baeyer-Villager Monooxygenases (BVMOs)



Baeyer-Villiger Monooxygenases (BVMOs) are FAD-dependent enzymes that catalyze oxygen insertion into cyclic and acyclic carbonyl compounds

- Also a premier biocatalyst system for heteroatom-oxygen bond formation

sulfur-oxygen
(typically stereoselective)

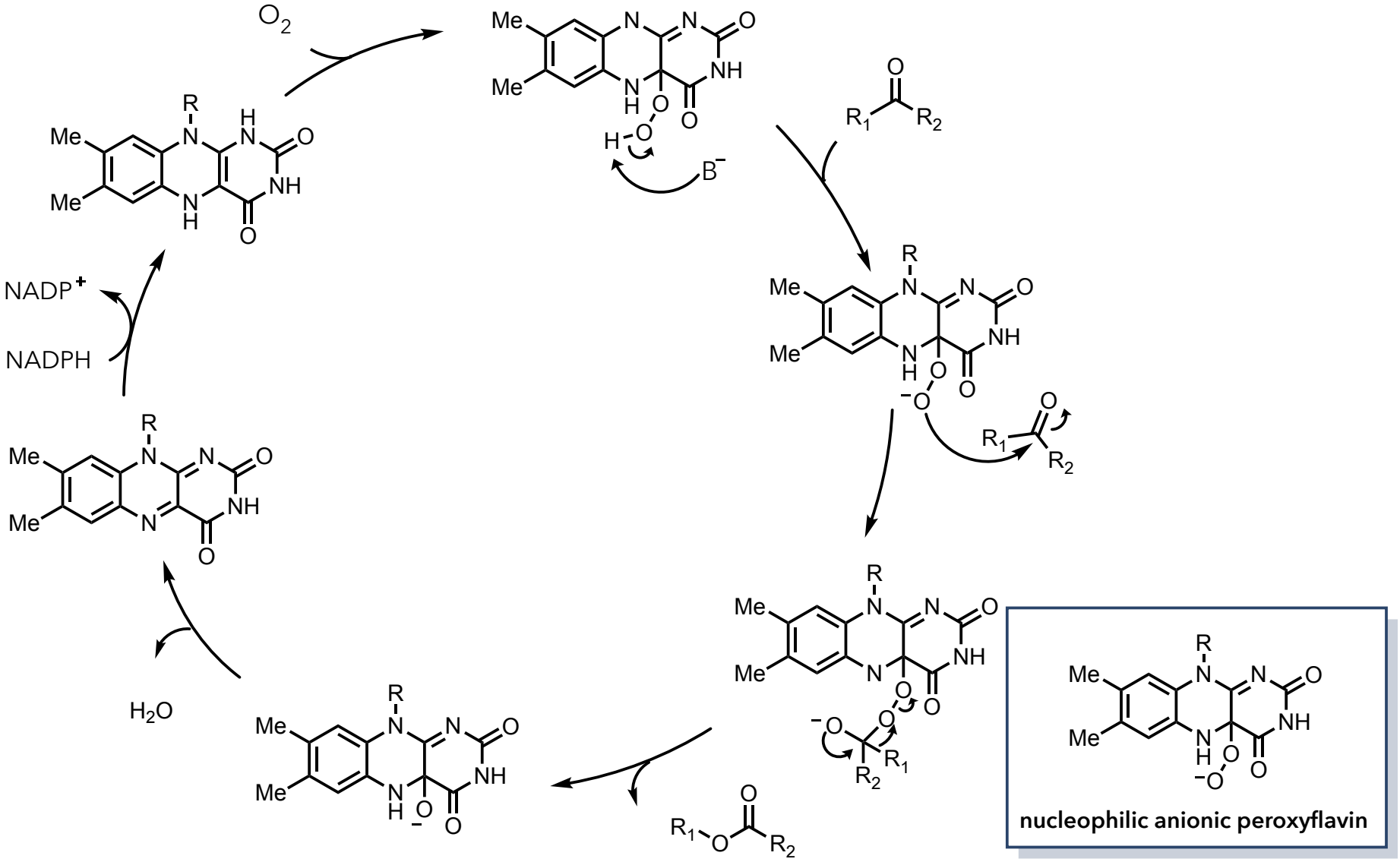
nitrogen-oxygen

phosphorus-oxygen

boron-oxygen

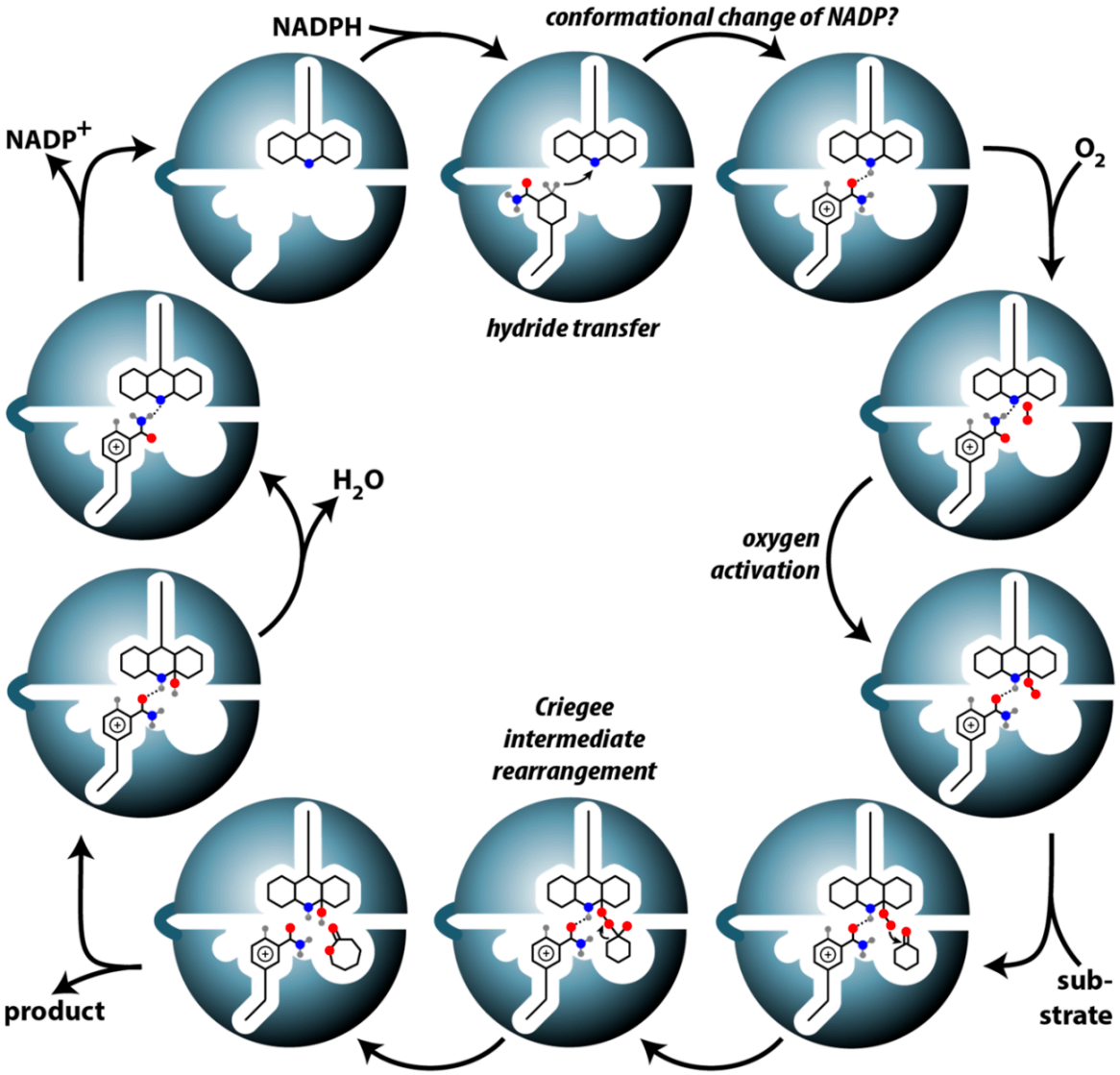
Chem. Rev. 2011, 111, 7, 4165-4222

Introduction to Baeyer-Villager Monooxygenases (BVMOs): Mechanism



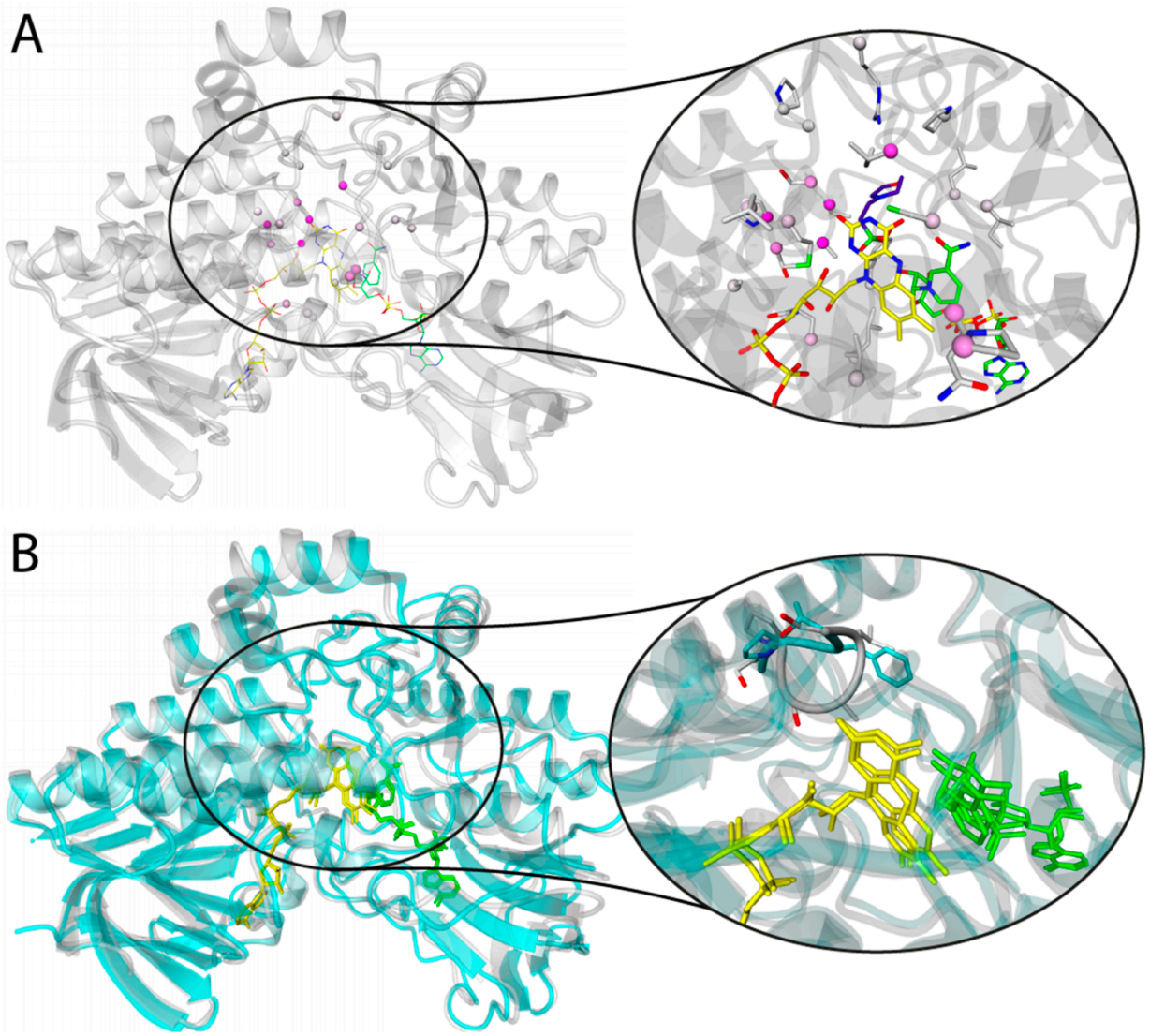
Nat. Prod. Rep.. 2013, 30, 175.

Schematic for Redox State Control



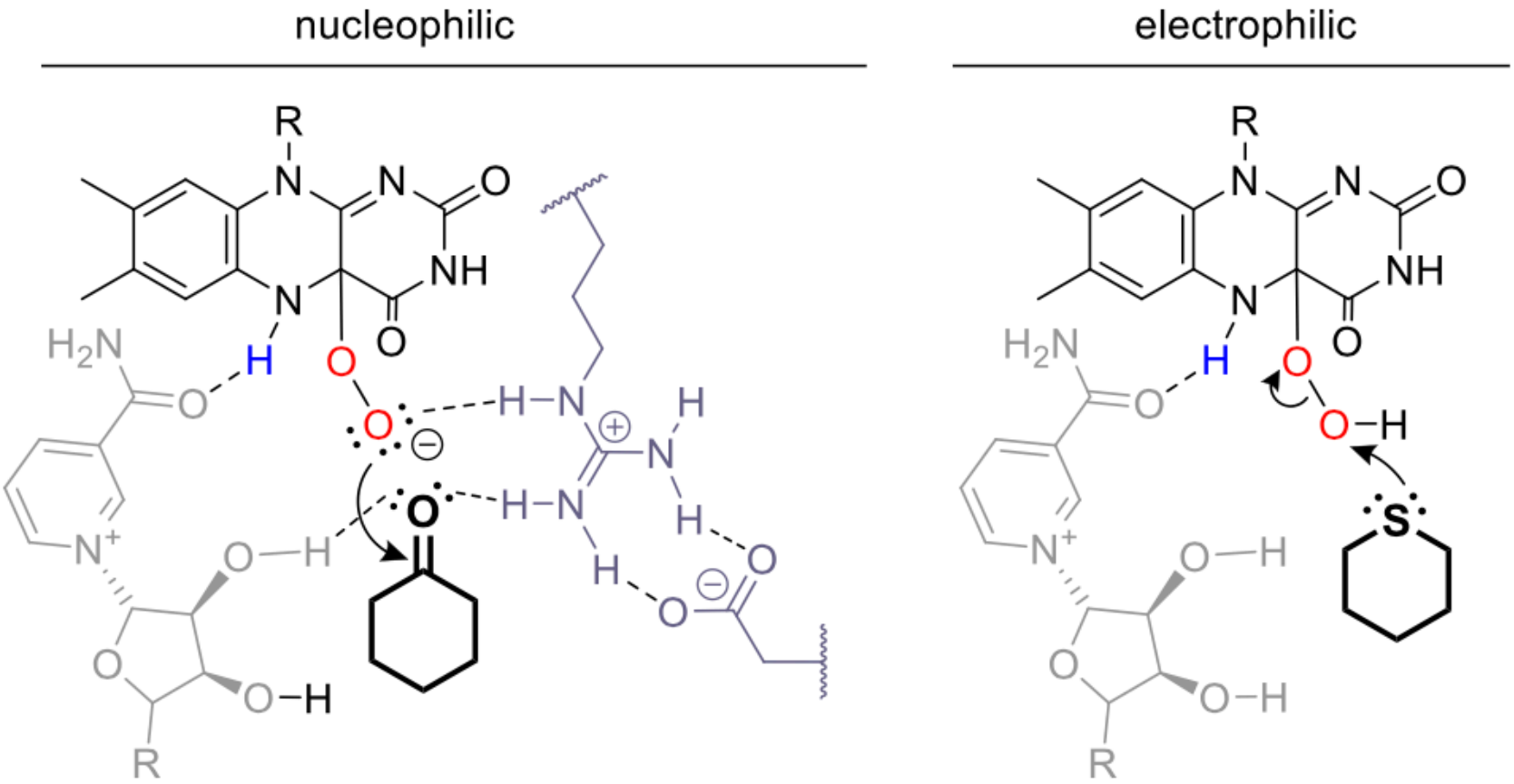
ACS Catal. **2019**, *9*, 11207-11241.

BVMOs: A Peak Into the (Conserved) Enzyme Active Site



ACS Catal. **2019**, *9*, 11207-11241.

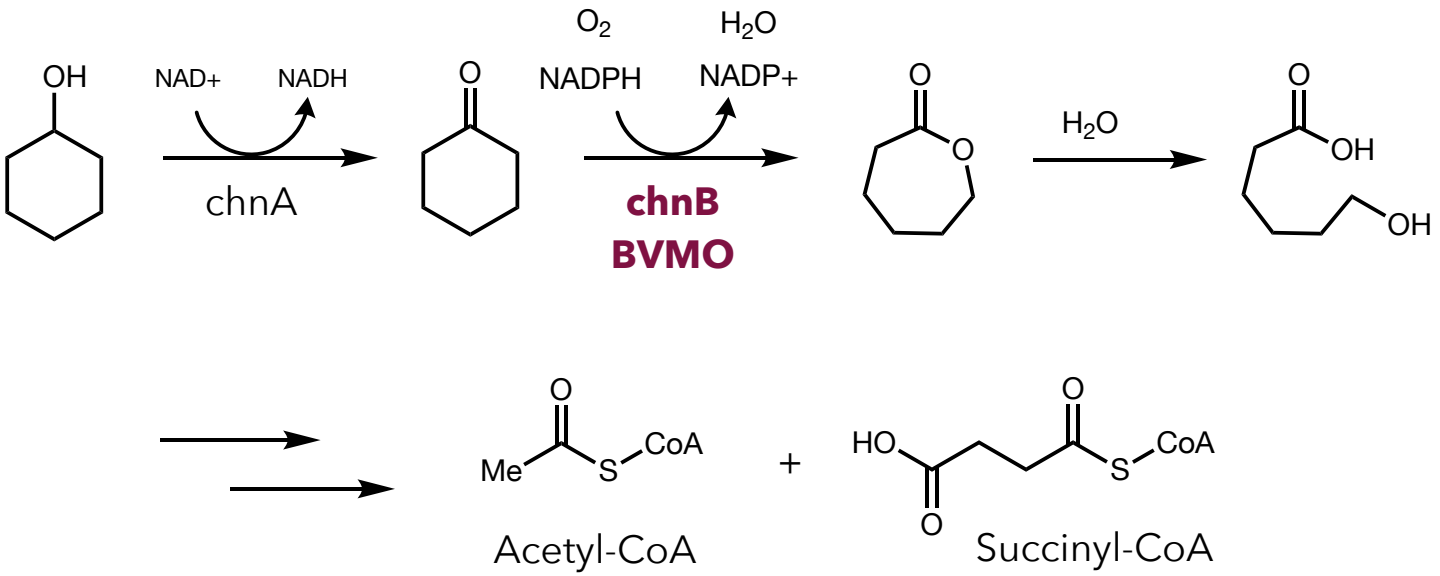
Nucleophilic vs Electrophilic Mechanisms



ACS Catal. **2019**, *9*, 11207-11241.

BVMO Uses in Nature

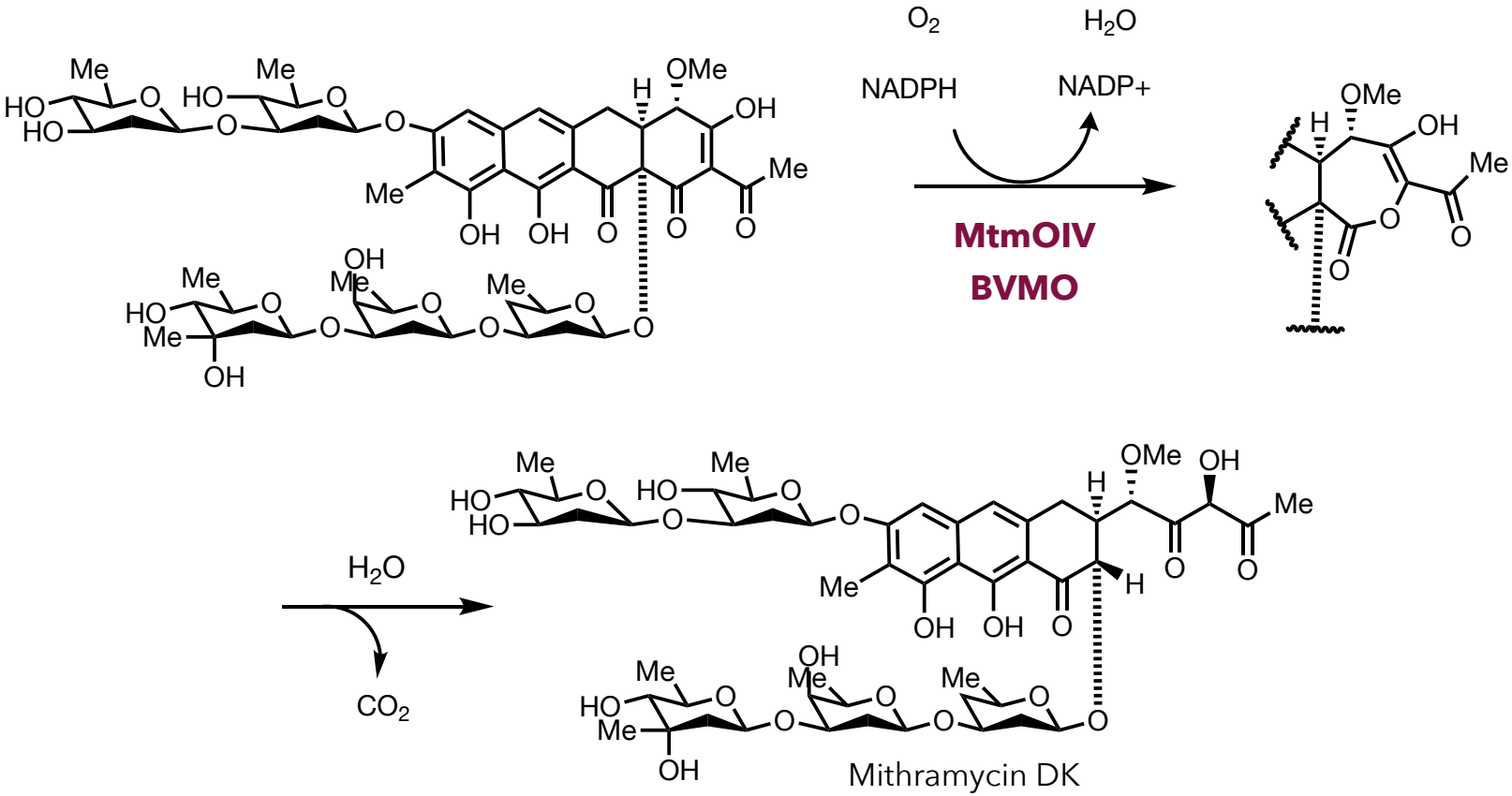
- cyclohexanol metabolism



Nat. Prod. Rep.. 2013, 30, 175.

BVMO Uses in Nature

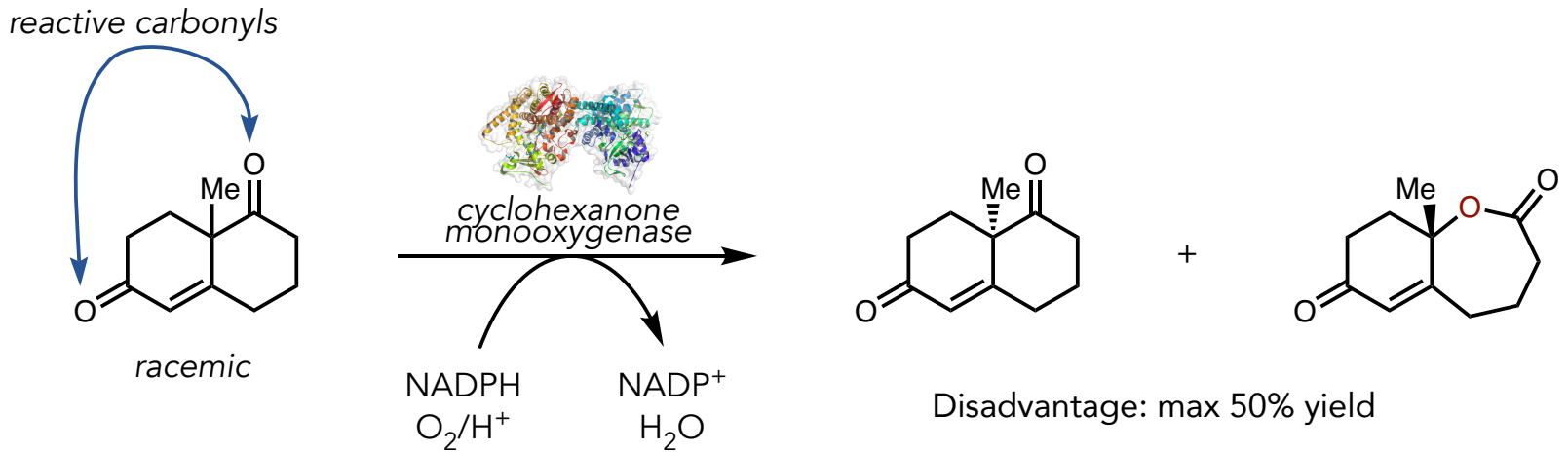
- mithramycin biosynthesis



Chem. Rev.. 2011, 111, 4165.

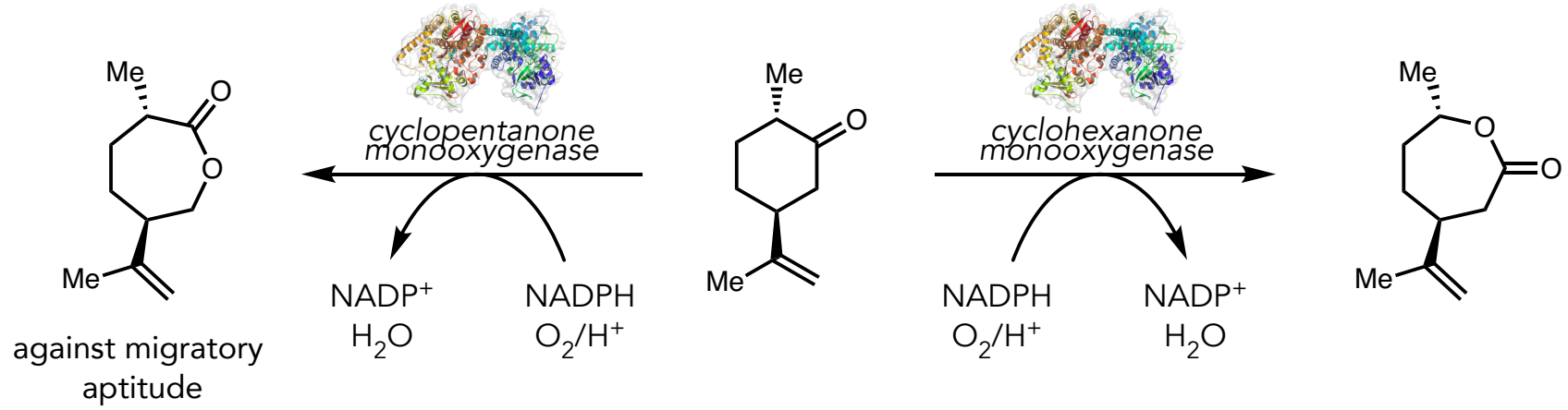
Standard Uses for BVMOs in Biocatalysis

High Chemoselectivity

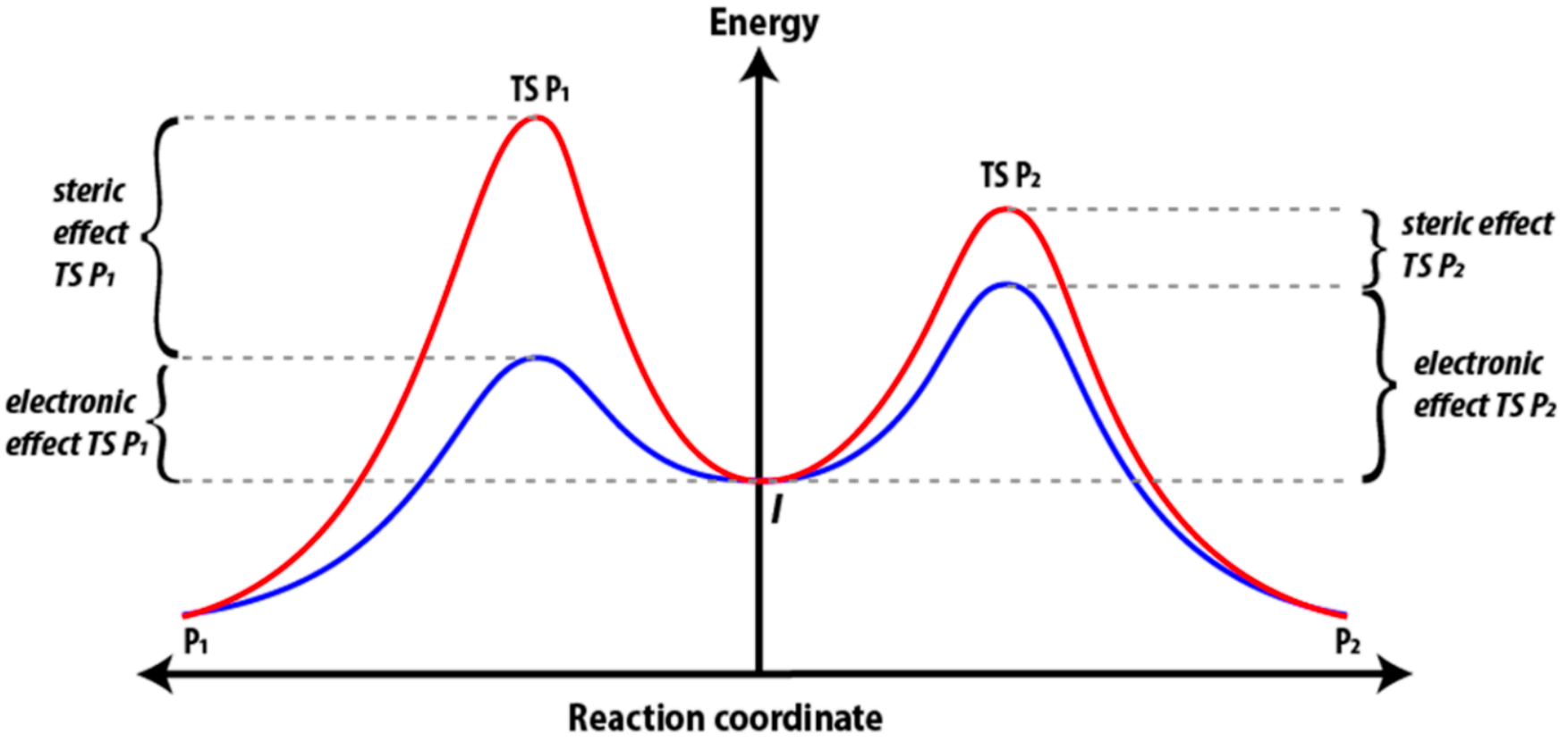


Disadvantage: max 50% yield

Divergent Reactivity ("the OG of Skeletal Editing")

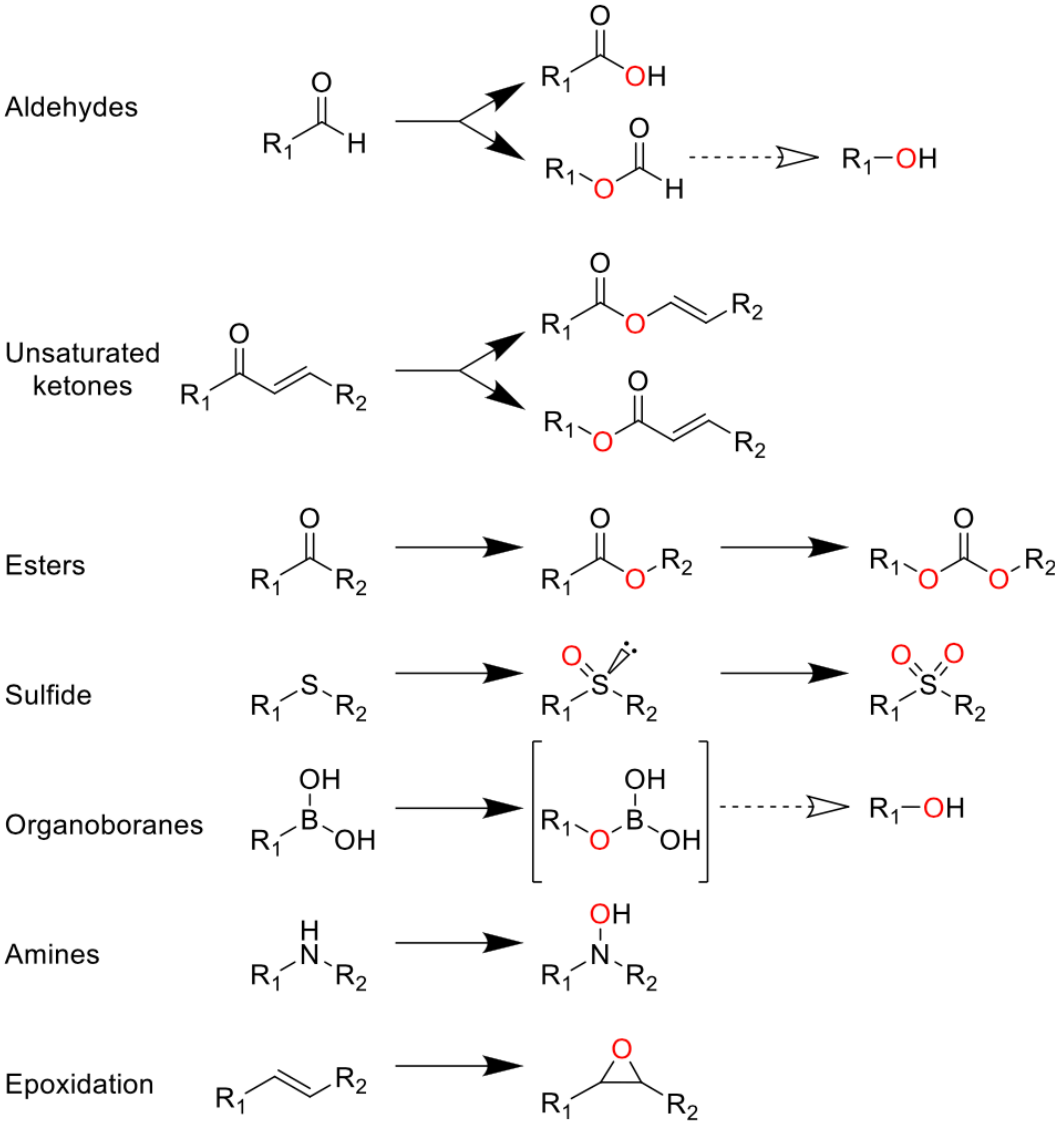


BVMOs: The Only Evolvable Platform for Tuning BV Product Distribution



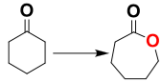
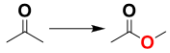
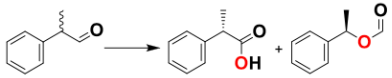
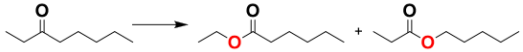
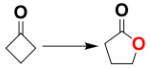
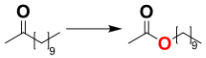
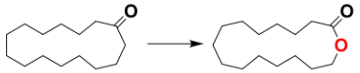
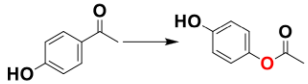
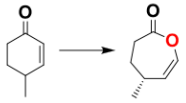
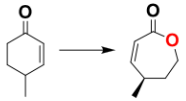
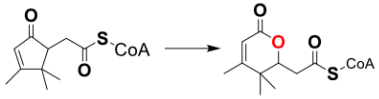
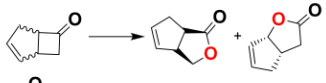
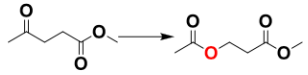
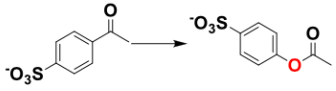
ACS Catal. **2019**, *9*, 11207-11241.

Non-Canonical Oxidations by BVMOs



ACS Catal. **2019**, *9*, 11207-11241.

Prototypical Reactions of BVMOs

Name	Substrate	Prototype reaction	k_{cat} [s^{-1}]	K_m [μM]	Ref
AcCHMO	cyclohexanone		6.0-39	3-9	46, 182-183
GoACMO	acetone		1.4	170	184
BVMO4	2-phenyl-propionaldehyde		n.d.	n.d.	185
BVMOAfl838	3-octanone		6.6	170	51
CAMO	cyclobutanone		6.8	7	186
CmBVMO	2-dodecanone		0.4	4	187
CPDMO	cyclopentadecanone		4.2	6.0	155
HAPMO	4-hydroxy-acetophenone		10-12	9-40	103, 188
ObBVMO	4-methylcyclohex-2-en-1-one		n.d.	n.d.	106
PlBVMO	4-methylcyclohex-2-en-1-one		n.d.	n.d.	106
OTEMO	2-oxo-Δ^3-4,5,5-trimethyl-cyclo pentenylacetyl-CoA		4.8	18	57
PockeMO	bicyclo[3.2.0] hept-2-en-6-one		3.3	400	47
RpBVMO	methyl levulinate		1.5	350	189
SAPMO	4-sulfoacetophenone		2.9	60	190

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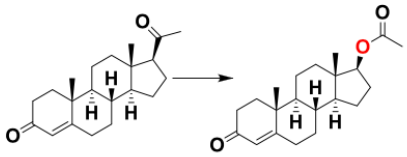
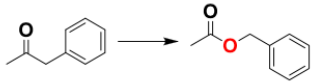
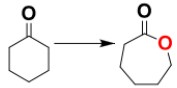
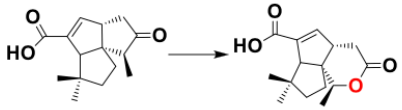
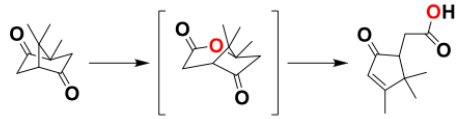
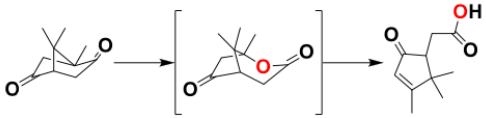
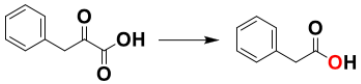
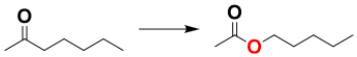
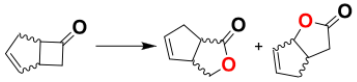
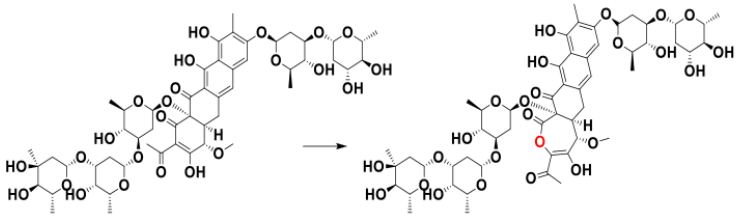
Prototypical Reactions of BVMOs

STMO	progesterone		0.7	85	191-192
TfPAMO	phenylacetone		1.9-3	60-80	169, 193
TmCHMO	cyclohexanone		2.0	<1	46
PtlE	1-deoxy-11-oxopentalenate		n.d.	n.d.	153
2,5-DKCMO	2,5-diketocamphane		n.d.	n.d.	164
3,6-DKCMO	3,6-diketocamphane		n.d.	n.d.	164
AtYUC6	phenylpyruvate		0.31	43	158
HsFMO5	2-heptanone		n.d.	n.d.	194
RjFMO-E	bicyclo[3.2.0] hept-2-en-6-one		2.0-4.3	3	161-162
MtmOIV	premithramycin B		0.7	70	195

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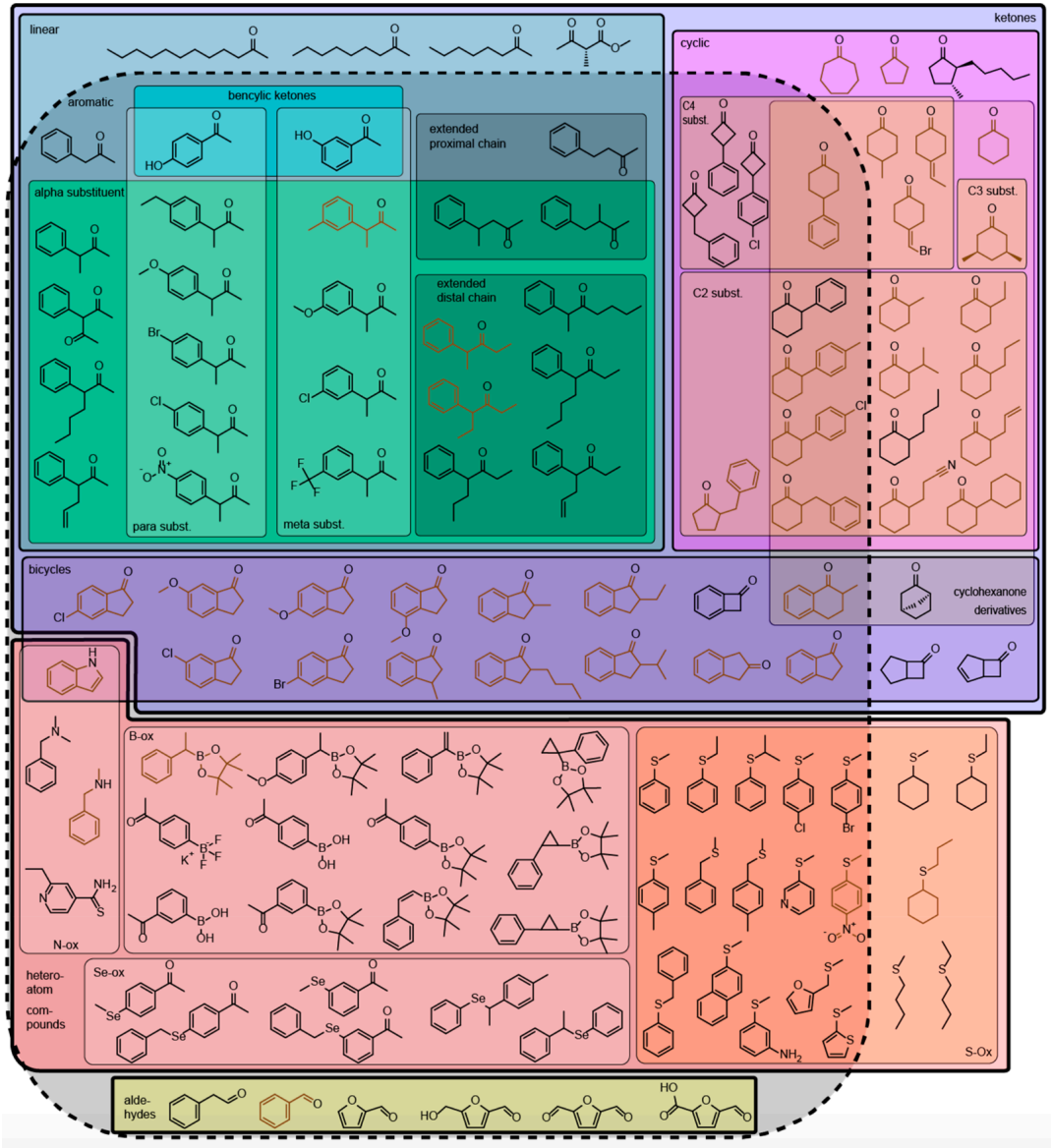
Phenylacetone Monooxygenase (PAMO): A Broadly Substrate Permissive Biocatalyst



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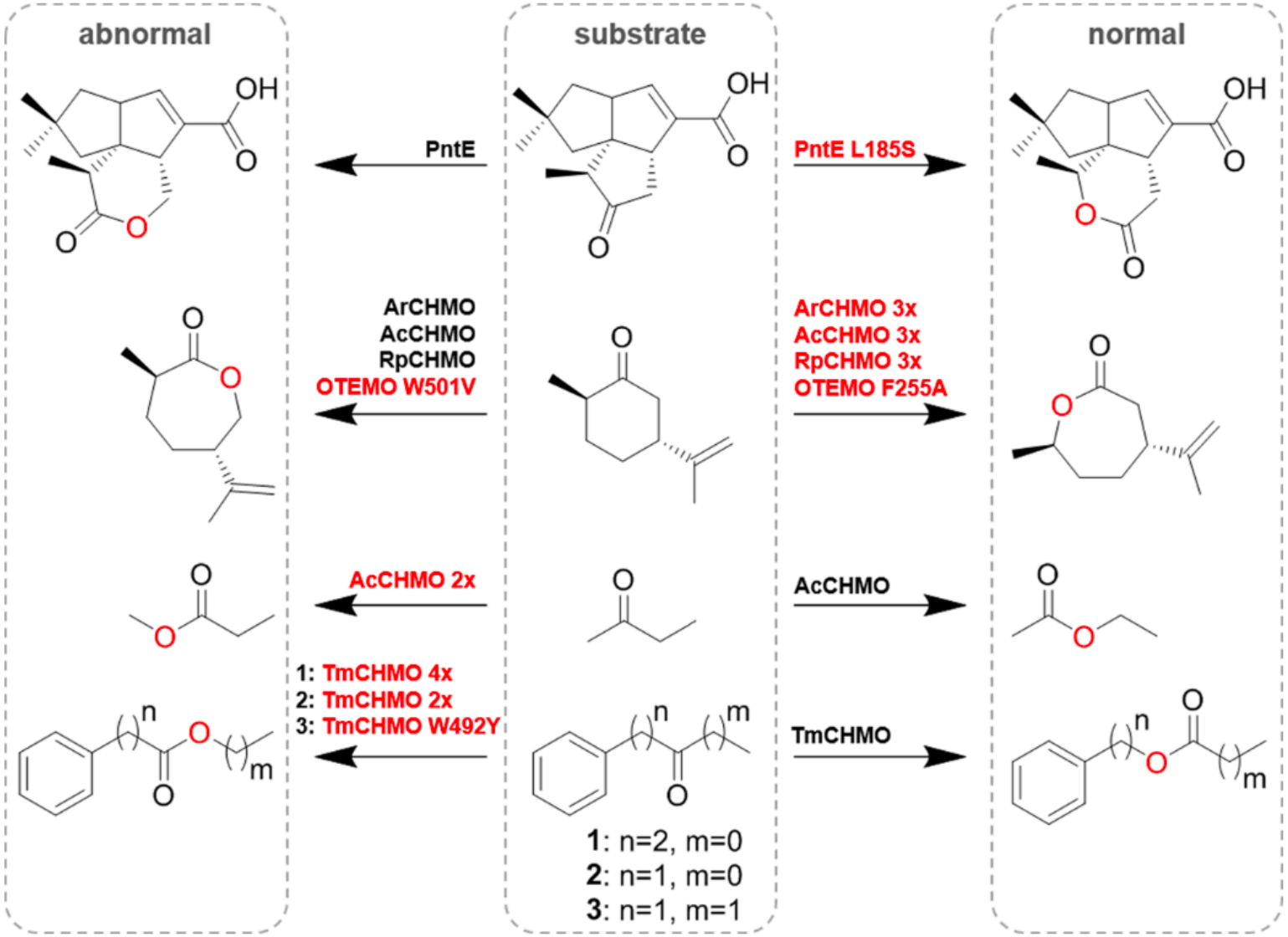
Engineering BVMOs to Change Regioselectivity



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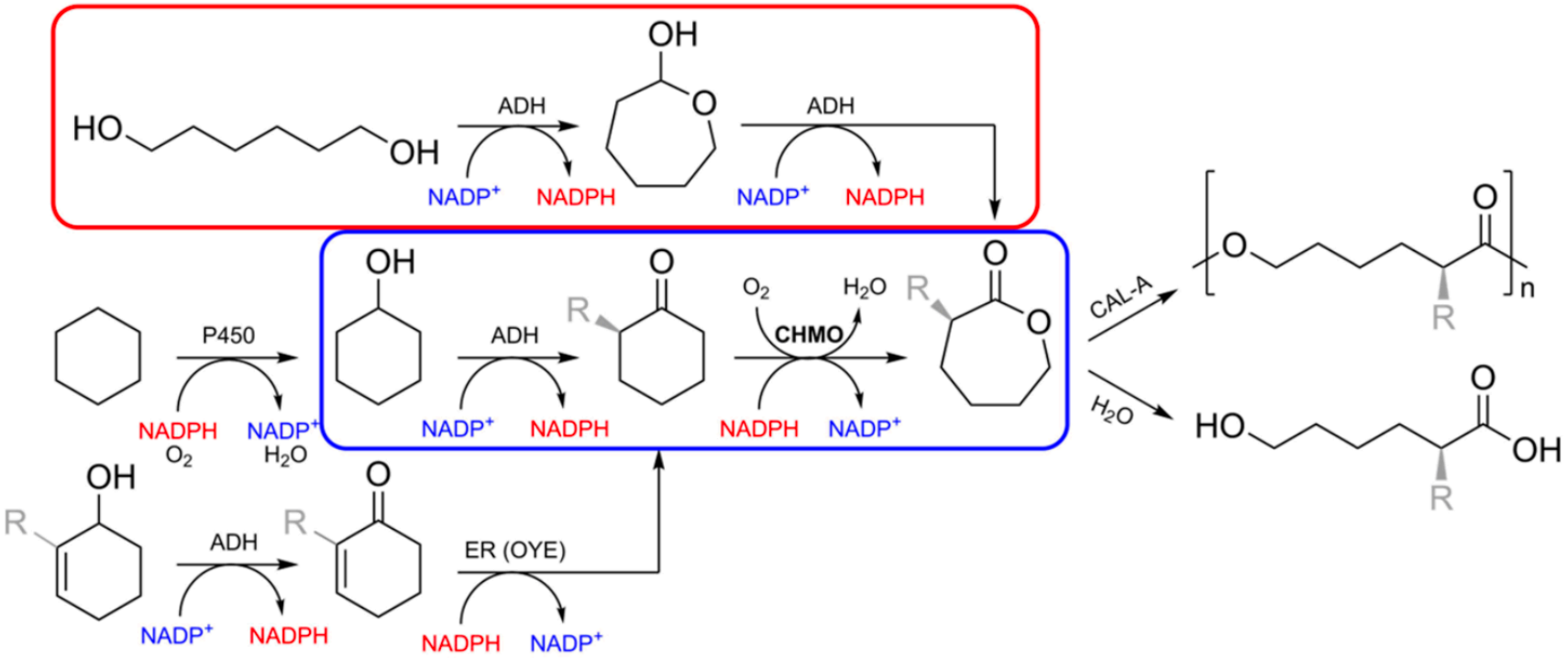
BVMOs in Cascade Biocatalysis



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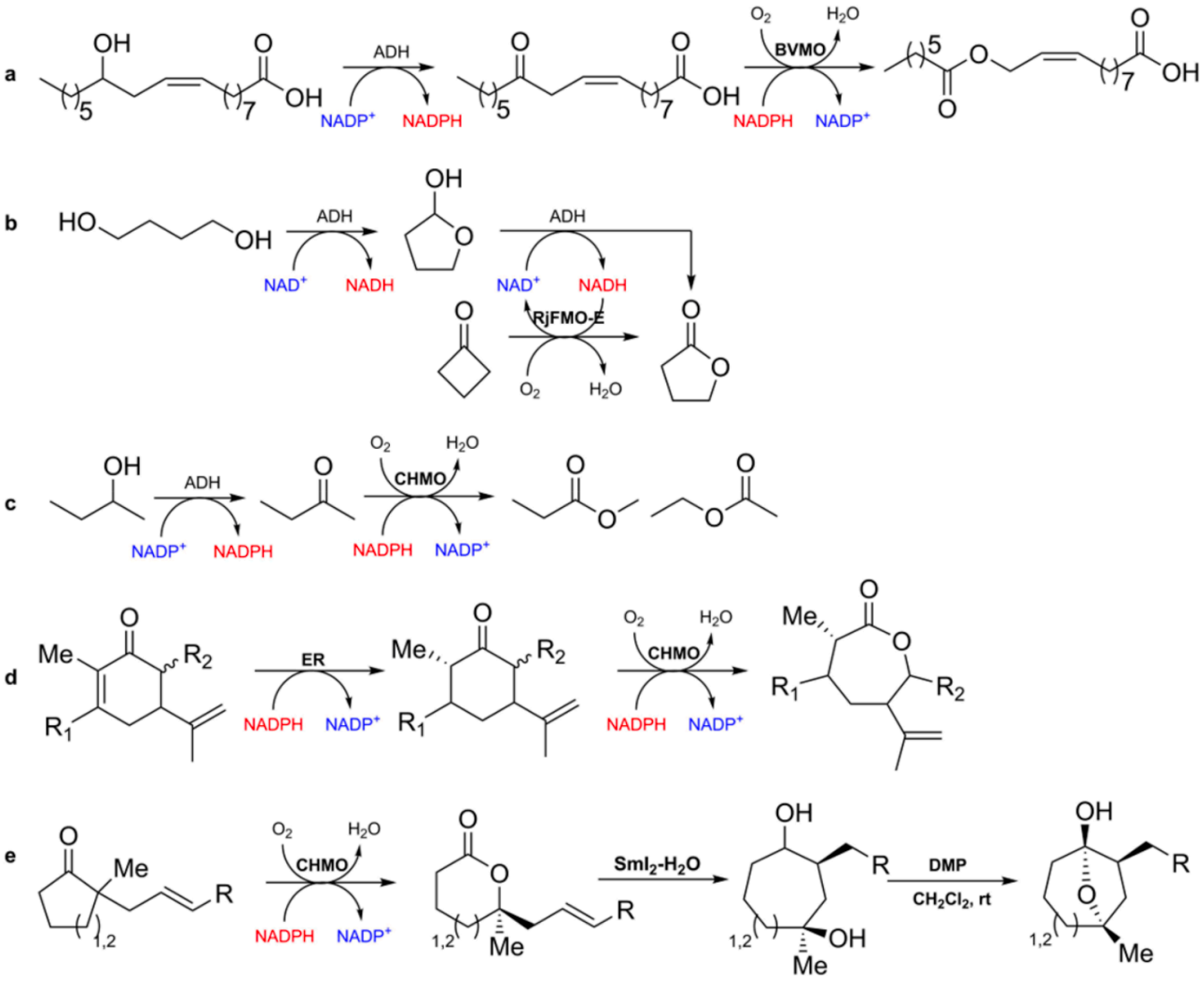
BVMOs in Cascade Biocatalysis



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