

## Table of Contents

### 2.1 Metal/Organocatalyst Dual Catalysis

---

#### 2.1.1 General Principles of Metal/Organocatalyst Dual Catalysis

Z. Shao and Y.-H. Deng

---

<b>2.1.1</b>	<b>General Principles of Metal/Organocatalyst Dual Catalysis</b> .....	1
<b>2.1.1.1</b>	Classification of Metal/Organocatalyst Dual Catalysis .....	1
<b>2.1.1.2</b>	The Initial Development and Advent of Metal/Organocatalyst Dual Catalysis ..	3
<b>2.1.1.3</b>	General Metal Catalysis and Activation Models in Dual Catalysis .....	12
<b>2.1.1.4</b>	General Organocatalysis and Activation in Dual Catalysis .....	14
<b>2.1.1.4.1</b>	Aminocatalysis .....	14
<b>2.1.1.4.2</b>	Brønsted Acid Catalysis .....	17
<b>2.1.1.4.3</b>	Lewis Base Catalysis .....	21
<b>2.1.1.4.4</b>	N-Heterocyclic Carbene Catalysis .....	24
<b>2.1.1.4.5</b>	Brønsted Base Catalysis .....	28
<b>2.1.1.4.6</b>	Phase-Transfer Catalysis .....	31
<b>2.1.1.4.7</b>	Lewis Acid Catalysis .....	33
<b>2.1.1.4.8</b>	Direct C—H/C—C Bond Activation .....	38
<b>2.1.1.4.9</b>	Bifunctional Organocatalysts in Dual Catalysis .....	43
<b>2.1.1.5</b>	Asymmetric Metal/Organocatalyst Dual Catalysis .....	48
<b>2.1.1.6</b>	Advantages and Challenges of Metal/Organocatalyst Dual Catalysis .....	49
<b>2.1.1.7</b>	Future Perspectives .....	50

#### 2.1.2 Palladium/Organocatalyst Dual Catalysis

M. R. Vitale

---

<b>2.1.2</b>	<b>Palladium/Organocatalyst Dual Catalysis</b> .....	59
<b>2.1.2.1</b>	Allylic Alkylation Reactions .....	59
<b>2.1.2.1.1</b>	Allylation of Aldehydes .....	59
<b>2.1.2.1.1.1</b>	Allylation of Linear Aldehydes .....	60
<b>2.1.2.1.1.2</b>	Allylation of $\alpha$ -Branched Aldehydes .....	61
<b>2.1.2.1.1.3</b>	Allylation of $\alpha,\beta$ -Unsaturated Aldehydes .....	64
<b>2.1.2.1.2</b>	Allylation of Ketones .....	65
<b>2.1.2.1.3</b>	Allylation of Esters and Derivatives .....	66
<b>2.1.2.1.3.1</b>	Allylation of $\beta$ -Oxo Esters .....	66

2.1.2.1.3.2	Allylation of Glycine Imino Esters	68
2.1.2.1.3.3	Allylation of Arylacetic Esters	69
2.1.2.1.3.4	Miscellaneous Allylations	71
2.1.2.2	Arylation Reactions	72
2.1.2.2.1	Arylation of Aldehydes	72
2.1.2.2.2	Arylation of Ketones	73
2.1.2.2.3	Arylation of Alkenes	74
2.1.2.3	Cycloaddition Reactions	76
2.1.2.3.1	Iminium–Enamine Organocatalysis	76
2.1.2.3.1.1	Palladium as a $\pi$ -Lewis Acid	76
2.1.2.3.1.2	Palladium in Cascade Allylic Alkylation Processes	78
2.1.2.3.2	N-Heterocyclic Carbene Organocatalysis	81
2.1.2.4	Conclusions	82
2.1.3	<b>Gold/Organocatalyst Dual Catalysis</b> X. Shi and J. Wang	
2.1.3	<b>Gold/Organocatalyst Dual Catalysis</b>	87
2.1.3.1	Merging Gold Catalysis with Aminocatalysis	87
2.1.3.1.1	Gold/Aminocatalysis with Alkynes	87
2.1.3.1.1.1	Reactions Involving Enamine Catalysis	87
2.1.3.1.1.2	Reactions Involving Iminium Catalysis	90
2.1.3.1.1.3	Reactions Involving Iminium/Enamine Catalysis	92
2.1.3.1.1.4	Reactions Involving Enamine/Enamine Catalysis	94
2.1.3.1.2	Gold/Aminocatalysis with Allenes	95
2.1.3.1.3	Gold/Aminocatalysis with Alkenes	97
2.1.3.2	Merging Gold Catalysis with Brønsted Acid Catalysis	98
2.1.3.2.1	Reactions Initiated by Intramolecular Nucleophilic Addition to Alkynes or Allenes	98
2.1.3.2.2	Reactions Initiated by Intermolecular Nucleophilic Addition to Alkynes	107
2.1.3.2.3	Reactions Initiated by Imine Formation	109
2.1.3.2.4	Reactions Initiated by both Nucleophilic Addition and Imine Formation	112
2.1.3.3	Merging Gold Catalysis with Hydrogen-Bonding Catalysis	115
2.1.3.3.1	Reactions Involving Imines as Electrophiles	116
2.1.3.3.2	Reactions with Nitroalkenes as Electrophiles	118
2.1.3.3.3	Reactions Involving Diazo Compounds as Electrophiles	119
2.1.3.4	Miscellaneous Dual Gold/Organocatalysis	121
2.1.3.5	Conclusions	121

<b>2.1.4</b>	<b>Rhodium/Organocatalyst Dual Catalysis</b> F. A. Cruz and V. M. Dong	
<hr/>		
<b>2.1.4</b>	<b>Rhodium/Organocatalyst Dual Catalysis</b> .....	125
<b>2.1.4.1</b>	Brønsted Acid Catalysis .....	125
<b>2.1.4.1.1</b>	Asymmetric Aldol-Type Reactions with Rhodium(II) .....	125
<b>2.1.4.1.2</b>	Enantioselective Mannich-Type Reaction with Rhodium(II) .....	127
<b>2.1.4.1.3</b>	Enantioselective Carbonyl Ylide Reduction with Rhodium(II) .....	136
<b>2.1.4.1.4</b>	Enantioselective NH Insertion with Rhodium(II) .....	137
<b>2.1.4.1.5</b>	Enantioselective Addition of Oxonium Ylides to <i>ortho</i> -Quinomethanes with Rhodium(II) .....	138
<b>2.1.4.2</b>	Hydrogen-Bonding Catalysis .....	140
<b>2.1.4.2.1</b>	Enantioselective Semipinacol Rearrangement/Michael Addition Cascade .....	140
<b>2.1.4.3</b>	Imine Catalysis .....	141
<b>2.1.4.3.1</b>	Imine-Directed <i>ortho</i> CH Functionalization with Rhodium(III) .....	141
<b>2.1.4.3.2</b>	C—C Bond Activation with Rhodium(I) To Make Ketones .....	142
<b>2.1.4.3.3</b>	C—H Activation with Rhodium(I) .....	146
<b>2.1.4.4</b>	Enamine Catalysis .....	147
<b>2.1.4.4.1</b>	Domino Rhodium-Catalyzed Hydroformylation/Enantioselective Cross-Aldol Reaction .....	147
<b>2.1.4.4.2</b>	Sequential Hydroformylation/Enantioselective Mannich Reaction .....	149
<b>2.1.4.4.3</b>	Hydroformylation/S <sub>N</sub> 1 Alkylation Sequence .....	150
<b>2.1.4.4.4</b>	Michael Addition with Rhodium(III) Lewis Acids .....	151
<b>2.1.4.4.5</b>	Rhodium(I)-Catalyzed C—H Activation: Ketone Alkylation/Alkenylation .....	152
<b>2.1.4.4.6</b>	Rhodium(I) Hydride Catalyzed Alkyne Isomerization: Aldehyde Allylation .....	156
<b>2.1.4.5</b>	Lewis Base Catalysis .....	157
<b>2.1.4.5.1</b>	Rhodium(I)-Catalyzed C—H Arylation Using Amides as an Arylation Source ..	157
<b>2.2</b>	<b>Metal/Biocatalyst Dual Catalysis</b> M. Diéguez, J.-E. Bäckvall, and O. Pàmies	
<hr/>		
<b>2.2</b>	<b>Metal/Biocatalyst Dual Catalysis</b> .....	161
<b>2.2.1</b>	Dynamic Kinetic Resolution and Dynamic Kinetic Asymmetric Transformation of Alcohols .....	162
<b>2.2.1.1</b>	Dynamic Kinetic Resolution of Unfunctionalized Secondary Alcohols .....	162
<b>2.2.1.2</b>	Dynamic Kinetic Resolution of 1-Hetarylethanol .....	169
<b>2.2.1.3</b>	Dynamic Kinetic Resolution of Halo Alcohols .....	172
<b>2.2.1.4</b>	Dynamic Kinetic Resolution of β-Hydroxynitriles .....	174
<b>2.2.1.5</b>	Dynamic Kinetic Resolution of β-Azido Alcohols .....	175

2.2.1.6	Dynamic Kinetic Resolution of $\alpha$ -Hydroxy Ketones and Aldehydes	176
2.2.1.7	Dynamic Kinetic Resolution of Hydroxy Acid Derivatives	178
2.2.1.8	Dynamic Kinetic Resolution of Hydroxy Phosphonates and Hydroxy Sulfones	180
2.2.1.9	Dynamic Kinetic Resolution of Allylic and Homoallylic Alcohols	182
2.2.1.10	Dynamic Kinetic Asymmetric Transformation and Dynamic Kinetic Resolution of Amino Alcohols	186
2.2.1.11	Dynamic Kinetic Asymmetric Transformation of Secondary Diols	188
2.2.1.12	Dynamic Kinetic Resolution of Primary Alcohols	192
2.2.2	Dynamic Kinetic Resolution of Amines	193
2.2.2.1	Dynamic Kinetic Resolution of Unfunctionalized Amines	194
2.2.2.2	Dynamic Kinetic Resolution of Amino Acid Derivatives	198
2.2.2.3	Hydrogenation/Dynamic Kinetic Resolution of Ketoximes	200
2.2.3	Dynamic Kinetic Resolution of Allenes	201
2.2.4	Dynamic Kinetic Resolution of Unsaturated Carboxylic Acids	202
<b>2.3</b>	<b>Dual Catalysis with Two Organocatalysts</b> H.-Y. Wang and G. Zhao	
<b>2.3</b>	<b>Dual Catalysis with Two Organocatalysts</b>	207
2.3.1	Multicatalysis with Two Organocatalysts	212
2.3.1.1	Enamine Catalysis with Iminium Catalysis	212
2.3.1.2	Enamine Catalysis with Enamine Catalysis	218
2.3.1.3	Enamine Catalysis with Brønsted Base Catalysis	219
2.3.1.4	Iminium Catalysis with Brønsted Base Catalysis	220
2.3.1.5	N-Heterocyclic Carbene Catalysis with Enamine Catalysis	221
2.3.1.6	N-Heterocyclic Carbene Catalysis with Iminium Catalysis	223
2.3.1.7	N-Heterocyclic Carbene Catalysis with Nucleophilic Catalysis	225
2.3.2	Cooperative Catalysis with Two Organocatalysts	227
2.3.2.1	Enamine Catalysis with Hydrogen-Bonding Catalysis	227
2.3.2.2	Enamine Catalysis with Ion-Pair Catalysis	230
2.3.2.3	Iminium Catalysis with Hydrogen-Bonding Catalysis	231
2.3.2.4	Iminium Catalysis with Ion-Pair Catalysis	232
2.3.2.5	Enamine Catalysis with Iminium Catalysis	235
2.3.2.6	Nucleophilic Catalysis with Hydrogen-Bonding Catalysis	236
2.3.2.7	Nucleophilic Catalysis with Ion-Pair Catalysis	241
2.3.2.8	Brønsted Acid Catalysis with Hydrogen-Bonding Catalysis	246
2.3.3	Supramolecular Catalysis with Two Organocatalysts	247
2.3.3.1	Enamine Catalysis with Ion-Pair Catalysis	247

2.3.3.2	Iminium Catalysis with Ion-Pair Catalysis	250
2.3.3.3	Enamine Catalysis with Hydrogen-Bonding Catalysis	251
2.3.3.4	Other Modes	254
2.3.3.4.1	Nucleophilic Phosphines with Activated Alkenes	254
2.3.3.4.2	In Situ Assembled Boronates	257
2.3.4	Conclusions and Future Perspectives	259
<b>2.4</b>	<b>Organocatalyst/Photocatalyst Dual Catalysis</b> K. Zeitler	
<b>2.4</b>	<b>Organocatalyst/Photocatalyst Dual Catalysis</b>	263
2.4.1	Combining Photocatalysis with Aminocatalysis	265
2.4.1.1	Enamine Catalysis	267
2.4.1.1.1	$\alpha$ -Functionalization of Aldehydes via Enamine-Mediated Catalysis	267
2.4.1.1.1.1	$\alpha$ -Alkylation of Aldehydes with Alkyl Halides	267
2.4.1.1.1.2	$\alpha$ -Cyanoalkylation of Aldehydes	271
2.4.1.1.1.3	$\alpha$ -Trifluoromethylation and $\alpha$ -Perfluoroalkylation of Aldehydes	273
2.4.1.1.1.4	$\alpha$ -Benzoylation of Aldehydes	274
2.4.1.1.1.5	$\alpha$ -(Thio)Xanthenylation of Aldehydes	275
2.4.1.1.1.6	$\alpha$ -Alkylation of Aldehydes with Alkenes	277
2.4.1.1.2	$\alpha$ -Functionalization of Ketones via Enamine-Mediated Catalysis	279
2.4.1.1.2.1	$\alpha$ -Alkylation of 1,3-Dicarbonyls and Formation of Quaternary Stereocenters	279
2.4.1.1.2.2	$\alpha$ -Functionalization of Ketones via Mannich-Type Transformations	280
2.4.1.1.3	$\beta$ -Functionalization of Unactivated Carbonyl Compounds	282
2.4.1.1.3.1	$\beta$ -Arylation with Cyanoarenes	283
2.4.1.1.3.2	$\beta$ -Functionalization with Aryl Ketones and Imines [Formal Homo( $\beta$ )-aldol and Homo( $\beta$ )-Mannich Reactions]	285
2.4.1.1.3.3	$\beta$ -Alkylation of Aldehydes with Electron-Deficient Alkenes	288
2.4.1.2	Iminium Catalysis	289
2.4.1.2.1	$\beta$ -Alkylation of Cyclic Enones with $\alpha$ -Heteroatom-Substituted Radicals	289
2.4.1.2.2	$\beta$ -Acylation of Cinnamaldehydes (Enals)	292
2.4.1.3	Catalysis with Tertiary Amines/Ammonium Enolate Catalysis	294
2.4.1.3.1	Acroleination of Tetrahydro- $\beta$ -carboline and Tetrahydroisoquinolines	294
2.4.1.3.2	Addition of 4-Nitrophenyl Esters to Tetrahydroquinolines by Sequential Photoredox/Isouthiourea Catalysis	295
2.4.2	Combining Photocatalysis with N-Heterocyclic Carbene (NHC) Catalysis	297
2.4.2.1	Enantioselective $\alpha$ -Acylation of Amines	298
2.4.3	Combining Photocatalysis with Brønsted Acid Catalysis	299

2.4.3.1	Brønsted Acid Catalysis for Ketyl Radical Generation	301
2.4.3.1.1	Reductive Cyclizations	302
2.4.3.1.1.1	Reductive Bis(enone) Cyclization	302
2.4.3.1.1.2	Intramolecular Ketyl–Alkene Cyclization	304
2.4.3.1.1.3	Enantioselective Intramolecular Aza-Pinacol Reaction	305
2.4.3.1.2	Enantioselective Reduction of Activated Carbonyl Derivatives	307
2.4.3.1.2.1	Asymmetric Photoreduction of 1,2-Diketones and $\alpha$ -Oxo Ketimines	307
2.4.3.1.2.2	Enantioselective Dehalogenative Protonation of $\alpha,\alpha$ -Dihalo Substituted Ketones	310
2.4.3.1.2.3	Enantioselective Reduction of Azaarene-Based Ketones	311
2.4.3.1.3	Enantioselective Intermolecular Addition Reactions of Prochiral Carbonyl-Derived Radicals	313
2.4.3.1.3.1	Enantioselective Addition of Prochiral Carbonyl-Derived Radicals to Vinylpyridines	313
2.4.3.1.3.2	Enantioselective Decarboxylative Radical Coupling of <i>N</i> -Arylglycines with Ketyl Radicals	315
2.4.3.1.3.3	Asymmetric Redox-Neutral Radical Coupling of <i>N</i> -Arylaminomethanes with <i>N</i> -Sulfonylaldimine Derived Radicals	317
2.4.3.2	Brønsted Acid Catalysis for Non-Redox Steps	318
2.4.3.2.1	Enantioselective Intermolecular Radical Addition Reactions to Alkenes	318
2.4.3.2.1.1	Conjugate Addition of $\alpha$ -Amino Radicals to 2-Vinylhetarenes	318
2.4.3.2.2	Enantioselective Minisci-Type Radical Addition to Hetarenes	321
2.4.4	Combining Photocatalysis with Hydrogen-Atom Transfer (HAT) Catalysis	325
2.4.4.1	HAT Catalysis for Hydrogen-Atom Donation	326
2.4.4.1.1	Anti-Markovnikov Functionalization of Alkenes by Alkene Oxidation	326
2.4.4.1.1.1	Intermolecular Hydroamination	327
2.4.4.2	HAT Catalysis for Hydrogen-Atom Abstraction	329
2.4.4.2.1	Oxidative Functionalization of Arenes	329
2.4.4.2.2	HAT/Photoredox Dual Catalysis for the Activation of C(sp <sup>3</sup> )–H bonds	331
2.5	<b>Organocatalyst/Biocatalyst Dual Catalysis</b> Y. Yamashita and H. Gröger	
2.5	<b>Organocatalyst/Biocatalyst Dual Catalysis</b>	339
2.5.1	Combination of Organocatalytic Racemization and Biocatalysis	339
2.5.1.1	Racemization Using Achiral Organocatalytic Bases for Deprotonation	339
2.5.1.2	Racemization Using Achiral Organocatalytic Bases for Reversible C–C Bond Formation	342
2.5.1.3	Racemization Using Achiral Acids as Organocatalysts for Migration	343

2.5.1.4	Racemization Using Aldehydes for Organocatalytic Imine Formation	344
2.5.2	Combination of Organocatalytic C—C Bond Formation and Biocatalysis	346
2.5.2.1	Organocatalytic Aldol Reaction	346
2.5.2.2	Organocatalytic Rearrangement	353
2.5.2.3	Organocatalytic Nitroaldol Reaction (Henry Reaction)	354
2.5.2.4	Organocatalytic Mannich Reaction	355
2.5.2.5	Organocatalytic Michael Addition	356
2.5.3	Combination of Organocatalytic Oxidation and Biocatalysis	358
2.5.4	Combination of Organocatalytic C—O Bond Formation and Biocatalysis	360
2.5.5	Combination of Dehydration and Biocatalysis	361
2.5.6	Conclusions and Future Perspectives	362
<b>2.6</b>	<b>Dual Catalysis with Two or More Biocatalysts</b> F. Parmeggiani, J. L. Galman, S. L. Montgomery, and N. J. Turner	
<b>2.6</b>	<b>Dual Catalysis with Two or More Biocatalysts</b>	365
2.6.1	Synthesis of Alkenes	366
2.6.1.1	Vinylation of Unprotected Phenols	366
2.6.1.2	Synthesis of Styrene from Bio-Based L-Phenylalanine	367
2.6.2	Synthesis of Alcohols	367
2.6.2.1	Deracemization of Racemic Secondary Alcohols	367
2.6.2.2	Double Reduction of $\alpha,\beta$ -Unsaturated Carbonyl Compounds	369
2.6.2.3	Synthesis of $\beta$ -Azido Alcohols and $\beta$ -Hydroxynitriles	371
2.6.2.4	Synthesis of 1,2-Diols	373
2.6.3	Synthesis of Amines	375
2.6.3.1	Deracemization of $\alpha$ -Chiral Amines	375
2.6.3.2	Amination of Alcohols	378
2.6.3.3	Synthesis of Amines from $\alpha,\beta$ -Unsaturated Ketones	384
2.6.3.4	Synthesis of Cyclic Secondary Amines via Cyclization Strategies	385
2.6.3.5	Conversion of Alkanes into Amines	389
2.6.3.6	Synthesis of 1,2-Amino Alcohols	391
2.6.4	Synthesis of Ketones	392
2.6.4.1	Oxidation of Methylene Groups to Carbonyl Groups	392
2.6.4.2	Synthesis of Saturated Ketones from Secondary and Tertiary Allylic Alcohols	395
2.6.4.3	Synthesis of $\alpha$ -Hydroxycycloalkanones from Epoxides	396
2.6.4.4	Synthesis of $\alpha$ -Hydroxy Ketones by Carbonylation	397

---

2.6.5	Synthesis of Carboxylic Acids .....	398
2.6.5.1	Oxidation of Primary Alcohols to Carboxylic Acids .....	398
2.6.5.2	Redox-Neutral Conversion of $\alpha,\beta$ -Unsaturated Aldehydes into Saturated Acids .....	400
2.6.5.3	Synthesis of Arylacetic and ( <i>S</i> )-Arylpropanoic Acids from Styrenes .....	402
2.6.6	Synthesis of Hydroxy Acids .....	403
2.6.6.1	Deracemization of Racemic $\alpha$ -Hydroxy Acids .....	403
2.6.6.2	Conversion of L- $\alpha$ -Amino Acids into ( <i>R</i> )- or ( <i>S</i> )- $\alpha$ -Hydroxy Acids .....	404
2.6.6.3	Conversion of Substituted Phenols into ( <i>R</i> )- or ( <i>S</i> )-(4-Hydroxyphenyl)lactic Acids .....	405
2.6.6.4	Synthesis of $\beta$ -Hydroxy Acids from $\alpha$ -Cyano Ketones .....	406
2.6.7	Synthesis of Amino Acids .....	408
2.6.7.1	Approaches to $\alpha$ -Amino Acids Based on Deracemization and Stereoinversion .....	408
2.6.7.2	Synthesis of D-Phenylglycines from Racemic Mandelic Acids .....	412
2.6.7.3	Synthesis of L-Tyrosine Derivatives from Aromatic Hydrocarbons .....	414
2.6.7.4	Synthesis of $\beta$ -Amino Acids .....	415
2.6.8	Synthesis of Esters and Lactones .....	416
2.6.8.1	Reduction and Cyclization of $\alpha,\beta$ -Unsaturated $\gamma$ -Keto Esters .....	416
2.6.8.2	Synthesis of Lactones Based on Baeyer–Villiger Oxidations .....	418
2.6.9	Conclusions .....	420
	<b>Keyword Index</b> .....	425
	<b>Author Index</b> .....	453
	<b>Abbreviations</b> .....	471