

Dynamic Kinetic Resolution (DKR) and Dynamic Kinetic Asymmetric Transformations (DYKAT)

	Preface	V
	Abstracts	IX
	Table of Contents	XIX
1	Introduction J.-E. Bäckvall	1
2	Dynamic Kinetic Resolution and Dynamic Kinetic Asymmetric Transformation: Concepts, Classification, and Computing Tools C. K. Winkler, K. Faber, and W. Kroutil	3
3	Organocatalytic Dynamic Kinetic Resolution X. Wu, Y. Liu, and Z. Jin	49
4	Organocatalytic Dynamic Kinetic Asymmetric Transformations A. Córdova, K. Zhang, and L. Deiana	103
5	Chemoenzymatic Dynamic Kinetic Resolution of Amines K. Adriaensen and D. De Vos	143
6	Chemoenzymatic Dynamic Kinetic Resolution of Alcohols K. Kanomata and S. Akai	181
7	Applications of Chemoenzymatic Dynamic Kinetic Resolution for the Synthesis of Biologically Active Compounds and Natural Products S. González-Granda and V. Gotor-Fernández	219
8	Chemoenzymatic Dynamic Kinetic Asymmetric Transformation O. Pàmies	263
9	Transition-Metal-Catalyzed Dynamic Kinetic Asymmetric Transformations (DYKATs) and Stereoablative Transformations N. J. Hafeman, S. R. Sardini, Jr., V. Bhat, and B. M. Stoltz	295
10	Applications of Metal-Catalyzed Dynamic Kinetic Resolutions and Dynamic Kinetic Asymmetric Transformations for the Synthesis of Complex Molecules F. W. Goetzke, F. Modicom, and S. P. Fletcher	331

11	Dynamic Kinetic Resolution in Asymmetric Hydrogenation and Transfer Hydrogenation J.-H. Xie and Q.-L. Zhou	371
12	Dynamic Kinetic Resolution and Dynamic Kinetic Asymmetric Transformation of Atropisomers J. Berreur, B. S. L. Collins, and J. Clayden	441
	Author Index	485
	Abbreviations	507

Table of Contents

1	Introduction J.-E. Bäckvall	
1	Introduction	1
2	Dynamic Kinetic Resolution and Dynamic Kinetic Asymmetric Transformation: Concepts, Classification, and Computing Tools C. K. Winkler, K. Faber, and W. Kroutil	
2	Dynamic Kinetic Resolution and Dynamic Kinetic Asymmetric Transformation: Concepts, Classification, and Computing Tools	3
2.1	Desymmetrization: Prochiral and <i>meso</i> -Substrates	5
2.2	Starting from Racemates	9
2.2.1	Kinetic Resolution	9
2.2.2	Parallel Kinetic Resolution and Divergent Reactions of a Racemic Mixture	13
2.2.3	Sequential Kinetic Resolution	15
2.2.3.1	SEKIRE I	16
2.2.3.2	SEKIRE II	18
2.3	Deracemization Processes	21
2.3.1	Stereoinversion	22
2.3.2	Cyclic Deracemization	24
2.3.3	Enantioconvergent Parallel Kinetic Resolution	28
2.3.4	Dynamic Kinetic Resolution	30
2.3.5	Dynamic Kinetic Asymmetric Transformations	36
2.3.5.1	Deracemization of Enantiomers via Diastereomers Involving a Chiral Catalyst (DYKAT Types I and II)	36
2.3.5.2	De-epimerization of Diastereomers via Diastereomers (DYKAT Types III and IV)	40
2.4	Conclusions	43
3	Organocatalytic Dynamic Kinetic Resolution X. Wu, Y. Liu, and Z. Jin	
3	Organocatalytic Dynamic Kinetic Resolution	49
3.1	Dynamic Kinetic Resolution with Amine Catalysts	49
3.1.1	Proline-Derived Secondary Amine Catalysts	50
3.1.2	Imidazole Catalysts	54
3.1.3	4-(Dimethylamino)pyridine-Derived Catalysts	55
3.1.4	Brønsted Base Catalysts	60

3.1.5	Bifunctional (Thio)Urea Catalysts	62
3.1.6	Peptide-Derived Small-Molecule Catalysts	66
3.2	Dynamic Kinetic Resolution with Brønsted Acid Catalysts	68
3.2.1	Enantioselective Synthesis of Compounds with Chiral Centers	68
3.2.2	Enantioselective Synthesis of Axially Chiral Compounds	70
3.3	Dynamic Kinetic Resolution with N-Heterocyclic Carbene Catalysts	73
3.3.1	N-Heterocyclic Carbene Catalyzed Intramolecular Dynamic Kinetic Resolution	74
3.3.1.1	Aldehyde Activation	74
3.3.1.2	Carboxylic Acid Activation	79
3.3.2	N-Heterocyclic Carbene Catalyzed Intermolecular Dynamic Kinetic Resolution	80
3.3.2.1	Benzoin Reactions	80
3.3.2.2	[3 + 2] Annulation	81
3.3.2.3	[4 + 2] Annulation	82
3.3.2.4	Transesterification	84
3.3.2.5	Asymmetric Acylation	86
3.4	Dynamic Kinetic Resolution through Miscellaneous Organocatalytic Methods	92
3.4.1	Phosphine-Catalyzed Dynamic Kinetic Resolution Transformations	92
3.4.1.1	Michael Addition to α,β -Unsaturated Alkenes	92
3.4.1.2	Electrophilic γ -Addition of Allenates	93
3.4.2	Guanidine-Catalyzed Dynamic Kinetic Resolution Transformations	95
3.4.3	Isothiourea-Catalyzed Dynamic Kinetic Resolution Transformations	96
3.4.3.1	Isothiourea-Catalyzed Dynamic Kinetic Resolution of Azlactones	97
3.4.3.2	Isothiourea-Catalyzed Dynamic Kinetic Resolution of Carboxylic Acids	97
3.5	Conclusions	99

4 Organocatalytic Dynamic Kinetic Asymmetric Transformations

A. Córdova, K. Zhang, and L. Deiana

4	Organocatalytic Dynamic Kinetic Asymmetric Transformations	103
4.1	DYKAT with Chiral Secondary and Primary Amine Catalysts	106
4.2	DYKAT Catalyzed by Brønsted Bases	115
4.3	DYKAT Catalyzed by N-Heterocyclic Carbenes	118
4.4	DYKAT Catalyzed by Chiral Amino Squaramides	120
4.5	DYKAT by Enantioselective Acyl-Transfer Catalysis	122
4.6	DYKAT by Combining Organocatalysis with Metal Catalysis	127
4.7	Conclusions	138

5	Chemoenzymatic Dynamic Kinetic Resolution of Amines K. Adriaensen and D. De Vos	
5	Chemoenzymatic Dynamic Kinetic Resolution of Amines	143
5.1	DKR of Primary Amines	144
5.1.1	DKR of Primary Benzylic Amines	144
5.1.1.1	Homogeneous Metal-Based Racemization Catalysts	144
5.1.1.2	Heterogeneous Metal-Based Racemization Catalysts	150
5.1.2	DKR of Primary Aliphatic Amines	162
5.1.2.1	Homogeneous Racemization Catalysts	162
5.1.2.2	Heterogeneous Racemization Catalysts	163
5.1.2.3	Radical-Mediated Racemization in DKR	167
5.2	DKR of Secondary Amines	172
5.3	Applications of DKR of Amines in Organic Synthesis	173
5.4	Conclusions	177
6	Chemoenzymatic Dynamic Kinetic Resolution of Alcohols K. Kanomata and S. Akai	
6	Chemoenzymatic Dynamic Kinetic Resolution of Alcohols	181
6.1	Ruthenium Complex/Lipase Co-catalysis	182
6.1.1	Simple Secondary Alcohols	182
6.1.2	Functionalized Secondary Alcohols	188
6.1.3	Bulky Secondary Alcohols	190
6.1.4	Alcohols with Two Stereogenic Centers	191
6.1.5	Axially Chiral Biaryls	193
6.2	Oxovanadium/Lipase Co-catalysis	196
6.2.1	1-Phenylethanol Derivatives	196
6.2.2	Allylic Alcohols	197
6.2.2.1	Homogeneous Oxovanadium Catalysts	197
6.2.2.2	Heterogeneous Oxovanadium Catalysts	198
6.2.3	Propargylic Alcohols	202
6.2.4	Tertiary Alcohols	203
6.3	Miscellaneous Racemization Catalysts for DKR in Combination with Lipases	203
6.3.1	Iron Catalysts	203
6.3.2	Palladium Catalysts	204
6.3.3	Iridium Catalysts	205
6.3.4	Lewis and Brønsted Acid Catalysts	206

6.4	S-Selective Dynamic Kinetic Resolution	207
6.4.1	Dynamic Kinetic Resolution Using Subtilisin	207
6.4.2	Dynamic Kinetic Resolution Using an Engineered Lipase	208
6.5	Synthetic Applications of the Products of Dynamic Kinetic Resolution of Alcohols	210
7	Applications of Chemoenzymatic Dynamic Kinetic Resolution for the Synthesis of Biologically Active Compounds and Natural Products S. González-Granda and V. Gotor-Fernández	
7	Applications of Chemoenzymatic Dynamic Kinetic Resolution for the Synthesis of Biologically Active Compounds and Natural Products ...	219
7.1	Hydrolase-Catalyzed DKR in the Presence of Metal Species	220
7.1.1	DKR of Alcohols	220
7.1.2	DKR of Amines and Amino Acid Derivatives	231
7.1.3	DKR by Derivatization of Functionalities Other than Alcohols or Amines	239
7.2	Hydrolase-Catalyzed DKR in the Absence of Metals	239
7.3	DKR Using Nonhydrolytic Enzymes	248
7.4	Conclusions	259
8	Chemoenzymatic Dynamic Kinetic Asymmetric Transformation O. Pàmies	
8	Chemoenzymatic Dynamic Kinetic Asymmetric Transformation	263
8.1	Basic Requirements for an Efficient Chemoenzymatic DYKAT Process: Mechanistic Considerations	265
8.2	Chemoenzymatic DYKAT of Symmetrical Substrates	266
8.3	Chemoenzymatic DYKAT of Unsymmetrical Substrates	278
8.4	Conclusions	292
9	Transition-Metal-Catalyzed Dynamic Kinetic Asymmetric Transformations (DYKATs) and Stereoablative Transformations N. J. Hafeman, S. R. Sardini, Jr., V. Bhat, and B. M. Stoltz	
9	Transition-Metal-Catalyzed Dynamic Kinetic Asymmetric Transformations (DYKATs) and Stereoablative Transformations	295
9.1	Carbon–Carbon Bond Forming Reactions	295
9.1.1	Asymmetric Allylic Alkylation	295
9.1.2	Cross Coupling	299
9.1.3	Cycloadditions	303

9.1.4	Hydroacylation	306
9.2	Carbon–Heteroatom Bond Forming Reactions	307
9.2.1	C–N Bond Forming Reactions	307
9.2.2	C–O Bond Forming Reactions	308
9.2.3	C–F Bond Forming Reactions	311
9.2.4	C–P Bond Forming Reactions	312
9.2.5	C–S Bond Forming Reactions	313
9.3	Stereoablative Enantioselective Transformations	314
9.3.1	Asymmetric Alkylation	315
9.3.2	Cross Coupling	321
9.4	Conclusions	328
10	Applications of Metal-Catalyzed Dynamic Kinetic Resolutions and Dynamic Kinetic Asymmetric Transformations for the Synthesis of Complex Molecules F. W. Goetzke, F. Modicom, and S. P. Fletcher	
10	Applications of Metal-Catalyzed Dynamic Kinetic Resolutions and Dynamic Kinetic Asymmetric Transformations for the Synthesis of Complex Molecules	331
10.1	Dynamic Kinetic Resolutions (DKRs)	331
10.1.1	DKR Hydrogenations	331
10.1.2	DKR Transfer Hydrogenations	336
10.2	Dynamic Kinetic Asymmetric Transformations (DYKATs)	341
10.2.1	Asymmetric Hydrogenation and Transfer Hydrogenation through DYKAT	341
10.2.2	Asymmetric Allylic Substitution	344
10.2.2.1	Palladium-Catalyzed Allylic Substitution	344
10.2.2.2	Rhodium-Catalyzed Allylic Substitution	351
10.2.2.3	Copper-Catalyzed Allylic Substitution	354
10.2.2.4	Iridium-Catalyzed Allylic Substitution	355
10.2.3	Asymmetric C–P Coupling	359
10.2.4	Redox Isomerization	360
10.2.5	Asymmetric Radical Coupling via DYKAT or DKR	361
10.2.5.1	Copper-Catalyzed Radical Coupling	361
10.2.5.2	Nickel-Catalyzed Radical Coupling	362
10.2.6	Asymmetric C–N Coupling via DYKAT or DKR	364
10.3	Conclusions	367

11	Dynamic Kinetic Resolution in Asymmetric Hydrogenation and Transfer Hydrogenation J.-H. Xie and Q.-L. Zhou	
11	Dynamic Kinetic Resolution in Asymmetric Hydrogenation and Transfer Hydrogenation	371
11.1	DKR-AH/ATH of Racemic α -Substituted β -Keto Esters and Amides	372
11.1.1	Racemic α -Alkyl-Substituted β -Keto Esters	372
11.1.2	Racemic α -Amido/Amino-Substituted β -Keto Esters	379
11.1.3	Racemic α -Alkoxy- β -keto Esters	387
11.1.4	Racemic α -Halo- β -keto Esters	389
11.1.5	Racemic α -Substituted β -Keto Amides	391
11.2	DKR-AH/ATH of Racemic α -Substituted Ketones	395
11.2.1	Racemic α -Alkyl/Aryl-Substituted Ketones	397
11.2.2	Racemic α -Amino/Amido-Substituted Ketones	404
11.2.3	Racemic α -Alkoxy/Aryloxy-Substituted Ketones	411
11.2.4	Other Racemic α -Substituted Ketones	414
11.3	DKR-AH/ATH of Racemic α -Substituted Aldehydes and Esters/Amides	417
11.3.1	Racemic α -Substituted Aldehydes	417
11.3.2	Racemic α -Substituted Esters and Amides	419
11.4	DKR-AH/ATH of Other Types of Substrates	422
11.4.1	Racemic β -Substituted α -Keto Esters/Amides	422
11.4.2	Racemic α -Substituted 1,3-Diketones	425
11.4.3	Racemic Substituted α - or β -Keto Phosphonates	426
11.4.4	Racemic α -Substituted Imines	429
11.4.5	Racemic β -Substituted Ketones	432
11.4.6	Racemic Allylic Alcohols	434
11.5	Conclusions	435
12	Dynamic Kinetic Resolution and Dynamic Kinetic Asymmetric Transformation of Atropisomers J. Berreur, B. S. L. Collins, and J. Clayden	
12	Dynamic Kinetic Resolution and Dynamic Kinetic Asymmetric Transformation of Atropisomers	441
12.1	Spontaneously Racemizing Biaryls (DKR)	442
12.1.1	Cyclic Starting Materials	442
12.1.1.1	Ring Opening of Biaryls Bridged by a Six-Membered Ring	443
12.1.1.2	Ring Opening of Biaryls Bridged by a Five-Membered-Ring	445

12.1.2	Acyclic Conformationally Labile Compounds	446
12.1.2.1	C—H Atropenantioselective Functionalization at an <i>ortho</i> Position	447
12.1.2.1.1	Via Hetaryl–Metal Coordination	447
12.1.2.1.2	Using a Transient Directing Group	449
12.1.2.1.3	Using Hydrogen-Bond Catalysis	451
12.1.2.2	Conformational Lability Resulting from Secondary Interactions	453
12.2	Chemically Induced Racemization of Unsymmetrical Biaryls (DYKAT)	455
12.2.1	Chiral Metal Catalyst Induced Racemization	455
12.2.2	Chiral Directing Group Strategy	457
12.2.3	Other Modes of Racemization	459
12.3	Non-Biaryl Systems	461
12.3.1	Non-Biaryl C—C Atropisomers	462
12.3.1.1	Benzamides	462
12.3.1.1.1	Diastereoselective Functional-Group Transformation	462
12.3.1.1.2	Enantioselective Functional-Group Transformation	464
12.3.1.1.3	C—H Functionalization of the <i>ortho</i> Position(s)	465
12.3.1.1.4	Dynamic Thermodynamic Resolution (DTR)	467
12.3.1.2	Styrenes	470
12.3.2	C—N Atropisomers	473
12.3.2.1	Via N-Functionalization	473
12.3.2.2	Via Aryl Functionalization	474
12.3.2.3	Other Functionalization Strategies	477
12.3.3	C—O and C—S Atropisomers	478
12.4	Conclusions	480
	Author Index	485
	Abbreviations	507