

Contents

1	Departure from Flask Chemistry	1
1.1	Introduction	1
1.2	Flow Reactors and Batch Reactors	2
1.3	Fluid Dynamics	2
1.4	Residence Time	3
1.5	Relationship Between Residence Time and Reaction Time	4
1.6	How Reaction Proceeds in Batch Reactor	4
1.7	How Reaction Proceeds in Flow Reactor	5
1.8	How to Set Residence Time	6
1.9	Looking Forward	8
	Reference	8
2	Controlling Residence Time	9
2.1	Introduction	9
2.2	Monitoring the Progress of a Reaction in a Flow Reactor: Inline Analysis	10
2.3	Monitoring the Progress of a Reaction in a Flow Reactor: Quench-Flow Method	11
2.4	Generation and Reactions of Oxiranyllthiums: An Example of Quench-Flow Method	11
2.5	General Consideration on Controlling Reactions Involving Unstable Intermediates	15
2.6	Temperature–Residence Time Mapping	18
2.7	Looking Forward	19
	References	19
3	Fast Micromixing for High-Resolution Reaction Time Control . .	21
3.1	Introduction	21
3.2	What Is Mixing?	22
3.3	Mixing by Stirring	23
3.4	Mixing Using Micromixer	25

3.5	Measuring Mixing Efficiency or Speed	29
3.6	Looking Forward	29
	References.	30
4	Use of Short-Lived Reactive Species Achieved by High-Resolution Reaction Time Control	31
4.1	Introduction	31
4.2	Generation of Organometallic Species Containing Alkoxy carbonyl Groups	31
4.3	Decreasing the Reactivity of Organometallic Reagents to Increase Compatibility	32
4.4	Br–Li Exchange Reactions of Alkyl <i>o</i> -Bromobenzoates in a Batch Reactor	34
4.5	Br–Li Exchange Reactions of Alkyl <i>o</i> -Bromobenzoates in a Flow Microreactor	34
4.6	Br–Li Exchange Reactions of Alkyl <i>p</i> -Bromobenzoates in a Flow Microreactor	37
4.7	I–Li Exchange Reactions of Alkyl <i>p</i> -Iodobenzoates in a Flow Microreactor	39
4.8	Looking Forward	41
	References.	41
5	Protecting-Group-Free Synthesis Achieved by High-Resolution Reaction Time Control	43
5.1	Introduction	43
5.2	Protecting Group	43
5.3	Reactions of Organometallic Reagents with Carbonyl Groups	44
5.4	Generation and Reaction of Aryllithium Species Bearing Ketone Carbonyl Groups	46
	References.	50
6	Controlling Isomerization by High-Resolution Reaction Time Control	51
6.1	Introduction	51
6.2	Controlling Positional Isomers	52
6.3	Controlling Diastereomers	52
6.4	Controlling Stereoisomers (Enantiomers)	56
	References.	58
7	Controlling Competitive Consecutive Reactions Using Micromixing	59
7.1	Introduction	59
7.2	Factors Determining Selectivity in Chemical Reactions	60

7.3	Competitive Consecutive Reactions	60
7.4	Disguised Chemical Selectivity	61
7.5	Controlling Selectivity of Friedel–Crafts-Type Reactions Using Micromixing	62
7.6	CFD Simulations	66
7.7	Controlling Other Reactions Using Micromixing	68
	References	70
8	Flash Chemistry	73
8.1	Introduction	73
8.2	What Is Flash Chemistry?	73
8.3	Some Examples of Flash Chemistry	74
8.4	Scientific Merits	75
8.5	High Productivity and Impact on Industry	76
	References	76
9	Space Integration of Reactions	79
9.1	Introduction	79
9.2	Integrating Reactions	79
9.3	Synthesizing <i>o</i> -Disubstituted Benzenes by Space Integration of Two Organolithium Reactions	81
9.4	Synthesizing TAC-101 by Integration of Three Organolithium Reactions	83
9.5	Space Integration of Halogen–Lithium Exchange Reaction and Cross-Coupling Reaction	83
	References	86
10	Polymerization Using Flow Microreactor System	87
10.1	Introduction	87
10.2	Controlling Competitive Consecutive Reactions and Chain-Growth Polymerization	87
10.3	Chemistry of Cationic Polymerization	89
10.4	Flash Cationic Polymerization	91
10.5	Flash Anionic Polymerization	95
10.6	Other Polymerizations Using Flow Microreactor System	98
	References	99
11	Outlook	101
	Appendix	103

Basics of Flow Microreactor Synthesis

Yoshida, J.-i.

2015, IX, 108 p. 102 illus., Softcover

ISBN: 978-4-431-55512-4