

# Chemical Synthesis Using Supercritical Fluids

Edited by  
Philip G. Jessop and  
Walter Leitner



Weinheim · New York · Chichester  
Brisbane · Singapore · Toronto

# Contents

<b>Preface . . . . .</b>	<b>V</b>
<b>Contents . . . . .</b>	<b>IX</b>
<b>List of Contributors . . . . .</b>	<b>XVII</b>
<b>1      Introduction . . . . .</b>	<b>1</b>
1.1     Supercritical Fluids as Media for Chemical Reactions . . . . .	1
1.1.1    What is a Supercritical Fluid (SCF)? . . . . .	1
1.1.2    Practical Aspects of Reactions in Supercritical Fluids (SFRs) .	6
1.1.3    Motivation for Use of SCFs in Modern Chemical Synthesis .	9
1.1.4    A Brief History of Chemical Synthesis in SCFs . . . . .	13
1.1.4.1   Discovery of SCFs and their Use as Solvents . . . . .	13
1.1.4.2   Early Examples of Chemical Reactions in SCFs . . . . .	20
1.1.4.3   Industrial Use of SCFs as Reaction Media . . . . .	25
References . . . . .	30
1.2     Phase Behavior and Solubility . . . . .	37
1.2.1    Basic Physical Properties of Supercritical Fluids . . . . .	37
1.2.2    Phase Behavior in High Pressure Systems . . . . .	41
1.2.2.1   Types of Binary Phase Diagrams . . . . .	41
1.2.2.2   Asymmetric Binary Mixtures . . . . .	43
1.2.3    Factors Affecting Solubility in Supercritical Fluids . . . . .	47
1.2.3.1   SCF Solvent . . . . .	48
1.2.3.2   Chemical Functionality of the Solute . . . . .	49
1.2.3.3   Temperature and Pressure Effects . . . . .	51
References . . . . .	53

1.3	Physical Properties as Related to Chemical Reactions . . . . .	54
1.3.1	Behavior of Diffusion Coefficients . . . . .	55
1.3.2	Diffusional Effects on Reactions . . . . .	56
1.3.3	Transition-state Theory Applied to SCFs . . . . .	58
1.3.4	Density Dependence of Two Competing Reactions . . . . .	62
1.3.5	Solvation Effects on Reactions . . . . .	63
1.3.6	Conclusions . . . . .	65
	References . . . . .	65
<b>2</b>	<b>Experimental Techniques . . . . .</b>	<b>67</b>
2.1	High-Pressure Reaction Equipment Design . . . . .	67
2.1.1	Introduction . . . . .	67
2.1.2	Basic Equipment and Components . . . . .	69
2.1.2.1	Design of Thick-Walled Vessels . . . . .	69
2.1.2.2	Closures and Connectors . . . . .	71
2.1.2.3	Tubing and Fittings . . . . .	73
2.1.2.4	Valves . . . . .	74
2.1.2.5	Compressors and Pumps . . . . .	76
2.1.2.6	Stirring and Mixing . . . . .	78
2.1.2.7	Optical Windows . . . . .	78
2.1.3	High Pressure Systems . . . . .	78
2.1.3.1	Single-batch High-pressure Reactors . . . . .	80
2.1.3.2	View Cells . . . . .	83
2.1.3.3	Systems for Continuous Processing . . . . .	84
2.1.4	Summary . . . . .	86
	References . . . . .	86
2.2	Extraction and Related Separation Techniques . . . . .	88
2.2.1	General Aspects of Supercritical Fluids as Mass Separating Agents . . . . .	88
2.2.2	Extraction from Solids . . . . .	90
2.2.2.1	Basic Process Design . . . . .	91
2.2.2.2	Process Parameters . . . . .	92
2.2.2.3	Modeling the Extraction . . . . .	93
2.2.2.4	Solids in Multiple Stages and Countercurrent Operation in SFE	95
2.2.2.5	Continuous Extraction of Contaminated Soil with Supercritical Water . . . . .	95
2.2.3	Countercurrent Multistage Extraction . . . . .	97
2.2.3.1	Basic Process Design . . . . .	98
2.2.3.2	Phase Equilibria . . . . .	99
2.2.3.3	Separation Analysis with Respect to Theoretical Stages . . . . .	101
2.2.3.4	Multicomponent Process Simulation . . . . .	102
2.2.3.5	Determination of the Height (Length) of a Theoretical Stage .	102
2.2.3.6	Determination of Column Diameter . . . . .	103
2.2.4	Chromatographic Separation with Supercritical Fluids . . . . .	104

2.2.4.1	Design of SFC Apparatus . . . . .	105
2.2.4.2	Methods for Scale-up of Chromatography . . . . .	106
2.2.5	Conclusion . . . . .	106
	References . . . . .	106
2.3	Precipitation and Crystallization Techniques . . . . .	108
2.3.1	Introduction . . . . .	108
2.3.2	Thermodynamics and Phase Equilibria . . . . .	109
2.3.2.1	CSS, PGSS and RESS . . . . .	109
2.3.2.2	GASP . . . . .	112
2.3.3	Process Basics and Reference Schemes . . . . .	115
2.3.3.1	Crystallization from a Supercritical Solution (CSS) . . . . .	115
2.3.3.2	Formation of Particles from Gas Saturated Solution (PGSS) . . . . .	115
2.3.3.3	Rapid Expansion of a Supercritical Solution (RESS) . . . . .	117
2.3.3.4	Precipitation by a Gas or a Supercritical Antisolvent (GASP) . . . . .	120
2.3.4	Example . . . . .	123
2.3.5	Concluding Remarks . . . . .	125
	References . . . . .	125
2.4	Microemulsions, Emulsions and Latexes . . . . .	127
2.4.1	Introduction . . . . .	127
2.4.2	Interfacial Tension . . . . .	128
2.4.3	Microemulsions . . . . .	130
2.4.3.1	Phase Behavior . . . . .	131
2.4.3.2	UV-Vis Indicators . . . . .	132
2.4.3.3	Electron Paramagnetic Resonance Techniques . . . . .	133
2.4.3.4	Neutron Scattering . . . . .	134
2.4.3.5	Enzymes . . . . .	134
2.4.3.6	Organic–CO <sub>2</sub> Microemulsions . . . . .	135
2.4.4	Emulsions . . . . .	135
2.4.4.1	Organic–CO <sub>2</sub> Emulsions . . . . .	135
2.4.4.2	Water–CO <sub>2</sub> Emulsions and CO <sub>2</sub> –Water Emulsions . . . . .	137
2.4.5	Reactions in SCF Emulsions, Microemulsions and Latexes . . . . .	140
2.4.5.1	Phase-Transfer Reactions Between Water and CO <sub>2</sub> . . . . .	140
2.4.5.2	<i>In Situ</i> Studies of Dispersion Polymerization . . . . .	142
2.4.6	Conclusions . . . . .	143
2.4.7	Acknowledgments . . . . .	144
	References . . . . .	144
<b>3</b>	<b>Spectroscopy of SCF Solutions . . . . .</b>	<b>147</b>
3.1	Vibrational Spectroscopy . . . . .	147
3.1.1	Introduction . . . . .	147
3.1.2	Dilute Solutions . . . . .	148
3.1.2.1	Infrared Spectroscopy . . . . .	148
3.1.2.2	Raman Spectroscopy . . . . .	150

XII      *Contents*

3.1.2.3	Polymer Modification . . . . .	151
3.1.2.4	Vibrational Spectroscopic Studies of Aqueous Microemulsions in SCFs. . . . .	153
3.1.3	Concentrated Solutions. . . . .	154
3.1.4	Monitoring of Fast Reactions in SCFs using Time-resolved Vibrational Spectroscopy. . . . .	156
3.1.5	Conclusions . . . . .	161
3.1.6	Acknowledgments . . . . .	161
	References . . . . .	161
3.2	NMR Spectroscopy . . . . .	165
3.2.1	Background. . . . .	165
3.2.2	Some Toroid Probe Designs . . . . .	167
3.2.3	General Properties of Supercritical Media. . . . .	172
3.2.4	Measurement of Dynamic and Equilibrium Processes in CO <sub>2</sub> . . . . .	177
3.2.5	Rate and Selectivity Measurements Associated with Propylene Hydroformylation in CO <sub>2</sub> . . . . .	184
3.2.6	Diffusion and Relaxation Time Measurements . . . . .	187
3.2.7	NMR of Quadrupolar Nuclei in Supercritical CO <sub>2</sub> . . . . .	188
3.2.8	Future Research . . . . .	191
3.2.9	Acknowledgments . . . . .	192
	References . . . . .	193
3.3	UV, EPR, X-ray and Related Spectroscopic Techniques . . . . .	195
3.3.1	UV-Vis . . . . .	195
3.3.2	Fluorescence . . . . .	198
3.3.3	Electron Paramagnetic Resonance . . . . .	199
3.3.4	X-ray Absorption Fine Structure. . . . .	200
3.3.5	X-ray and Neutron Scattering and Diffraction . . . . .	206
3.3.5.1	Small Angle Scattering . . . . .	207
3.3.5.2	Wide Angle Scattering. . . . .	208
3.3.6	Conclusions . . . . .	209
3.3.7	Acknowledgment. . . . .	209
	References . . . . .	209
<b>4</b>	<b>Reactions in SCF . . . . .</b>	<b>213</b>
4.1	Synthesis of Inorganic Solids . . . . .	213
4.1.1	Historical Summary . . . . .	214
4.1.2	Experimental Techniques. . . . .	216
4.1.3	Hydrothermal Chemistry . . . . .	226
4.1.3.1	Metal Oxides. . . . .	226
4.1.3.2	Phosphates and Silicates . . . . .	229
4.1.3.3	Metal Sulfides . . . . .	232
4.1.3.4	Other Hydrothermal Syntheses. . . . .	233
4.1.4	Supercritical Amines . . . . .	234

4.1.5 Other Solvents . . . . .	237
4.1.6 Conclusions . . . . .	238
References . . . . .	239
4.2 Synthesis of Coordination Compounds . . . . .	243
4.2.1 Introduction . . . . .	243
4.2.2 Strategy . . . . .	244
4.2.3 Chemistry . . . . .	245
4.2.4 Equipment . . . . .	248
4.2.5 Detailed Syntheses . . . . .	252
4.2.5.1 Preparation of Cr(CO) <sub>5</sub> (C <sub>2</sub> H <sub>4</sub> ) . . . . .	253
4.2.5.2 Preparation of CpMn(CO) <sub>2</sub> ( $\eta^2$ -H <sub>2</sub> ) . . . . .	255
4.2.5.3 Preparation of Cp*Mn(CO) <sub>2</sub> ( $\eta^2$ -H <sub>2</sub> ) from Cp*Mn(CO) <sub>2</sub> ( $\eta^2$ -HSiEt <sub>3</sub> ) . . . . .	256
4.2.6 Conclusions . . . . .	257
4.2.7 Acknowledgments . . . . .	257
References . . . . .	257
4.3 Stoichiometric Organic Reactions . . . . .	259
4.3.1 Experimental Methods . . . . .	260
4.3.2 Supercritical Carbon Dioxide . . . . .	260
4.3.2.1 Diels–Alder Reactions . . . . .	262
4.3.2.2 Reduction and Coupling . . . . .	265
4.3.2.3 Esterification . . . . .	266
4.3.2.4 Cracking and Rearrangements . . . . .	266
4.3.3 Superheated and Supercritical Water . . . . .	267
4.3.3.1 Oxidation of Methane . . . . .	267
4.3.3.2 Cleavage/Hydrolysis . . . . .	268
4.3.3.3 Elimination Reactions . . . . .	271
4.3.3.4 Diels–Alder Reactions . . . . .	272
4.3.3.5 Rearrangement . . . . .	273
4.3.4 Other Fluids . . . . .	275
References . . . . .	276
4.4 Photochemical and Photo-induced Reactions . . . . .	280
4.4.1 Introduction . . . . .	280
4.4.1.1 Definition of a Supercritical Fluid . . . . .	280
4.4.1.2 Solvent Properties of SCFs . . . . .	280
4.4.1.3 Scope of this Chapter . . . . .	281
4.4.1.4 Experimental Considerations . . . . .	282
4.4.2 Photochemical Reactions in Supercritical Fluid Solvents . . . . .	285
4.4.2.1 Geometric Isomerization . . . . .	285
4.4.2.2 Photodimerization . . . . .	285
4.4.2.3 Carbonyl Photochemistry . . . . .	287
4.4.3 Photo-induced Reactions in Supercritical Fluid Solvents . . . . .	289
4.4.3.1 Free Radical Brominations of Alkyl Aromatics in Supercritical Carbon Dioxide . . . . .	289

4.4.3.2	Free Radical Chlorination of Alkanes in Supercritical Fluid Solvents . . . . .	290
4.4.4	Conclusions . . . . .	293
4.4.5	Acknowledgments . . . . .	294
	References . . . . .	294
4.5	Polymerizations in Dense Carbon Dioxide . . . . .	297
4.5.1	Introduction . . . . .	297
4.5.2	Homogeneous Solution Polymerizations . . . . .	300
4.5.2.1	Free-Radical Chain Growth . . . . .	300
4.5.2.2	Cationic Chain Growth . . . . .	303
4.5.3	Heterogeneous Polymerizations . . . . .	305
4.5.3.1	Free-Radical Chain Growth . . . . .	305
4.5.3.2	Cationic Chain Growth . . . . .	317
4.5.4	Metal-catalyzed Polymerizations . . . . .	319
4.5.4.1	Ring-opening Metathesis Polymerization . . . . .	319
4.5.4.2	Epoxide-CO <sub>2</sub> Copolymers . . . . .	319
4.5.4.3	Oxidative Coupling Polymerizations . . . . .	320
4.5.5	Step-growth Polymerizations . . . . .	320
4.5.6	Hybrid Systems . . . . .	321
4.5.7	Conclusions . . . . .	321
4.5.8	Acknowledgments . . . . .	322
	References . . . . .	322
4.6	Free-Radical Polymerization in Reactive Supercritical Fluids . . . . .	326
4.6.1	Introduction . . . . .	326
4.6.2	Experimental Methods and Techniques . . . . .	327
4.6.2.1	On-line Spectroscopy . . . . .	327
4.6.2.2	Kinetic Coefficients from Laser-Assisted Techniques . . . . .	329
4.6.2.3	Continuously Operated High-Pressure Polymerization Reactors . . . . .	331
4.6.3	Ethene Homopolymerization . . . . .	333
4.6.3.1	Propagation and Termination . . . . .	334
4.6.3.2	Chain-Transfer to Monomer . . . . .	336
4.6.3.3	Chain-Transfer to Polymer and β-Scission . . . . .	338
4.6.4	Ethene Copolymerizations . . . . .	341
4.6.4.1	Reactivity Ratios for Copolymerizations of Ethene with Acrylic Acid Esters . . . . .	341
4.6.4.2	Homopropagation and Homotermination Kinetics of the Comonomers . . . . .	345
4.6.4.3	Modeling of High-pressure Ethene Copolymerizations . . . . .	347
4.6.5	Conclusions . . . . .	348
	References . . . . .	348
4.7	Metal-Complex-Catalyzed Reactions . . . . .	351
4.7.1	Introduction . . . . .	351
4.7.1.1	Potential Benefits of Using Supercritical Fluids in Metal-Complex-Catalyzed Reactions . . . . .	351

4.7.1.2	Practical Considerations . . . . .	352
4.7.1.3	Solubility of Metal Complexes in SCFs. . . . .	356
4.7.2	Hydrogenation and Related Reactions. . . . .	358
4.7.2.1	Hydrogenation of CO <sub>2</sub> under Supercritical Conditions . . . . .	358
4.7.2.2	Hydrogenation of C=C Double Bonds . . . . .	360
4.7.2.3	Hydrogenation of Imines. . . . .	363
4.7.3	Hydroformylation . . . . .	365
4.7.4	C–C Coupling Reactions . . . . .	369
4.7.4.1	Cobalt-catalyzed Cyclization Reactions . . . . .	369
4.7.4.2	Coupling Reactions Involving scCO <sub>2</sub> as Solvent and Substrate	370
4.7.4.3	Olefin Metathesis . . . . .	371
4.7.4.4	Palladium-catalyzed Coupling Reactions of Aryl Halides. . . . .	373
4.7.4.5	Cyclopropanation. . . . .	375
4.7.5	Oxidation. . . . .	377
4.7.5.1	Peroxides as Oxidants . . . . .	377
4.7.5.2	Molecular Oxygen as Oxidant. . . . .	378
4.7.6	Polymerization . . . . .	380
4.7.6.1	Polymerization of Alkenes under Supercritical Conditions . . . . .	380
4.7.6.2	Polymerization Utilizing Compressed CO <sub>2</sub> . . . . .	381
4.7.7	Conclusions . . . . .	384
	References . . . . .	384
4.8	Heterogeneous Catalysis . . . . .	388
4.8.1	Fischer–Tropsch Synthesis . . . . .	389
4.8.1.1	Experimental . . . . .	390
4.8.1.2	Reaction Performance in Three Reaction Phases . . . . .	391
4.8.1.3	Diffusion Behavior of Synthesis Gas . . . . .	393
4.8.1.4	Diffusion and Reaction of the Products. . . . .	393
4.8.1.5	Wax Production: Addition of Heavy Alkene to the Supercritical Phase . . . . .	395
4.8.2	Isomerization Reactions . . . . .	398
4.8.3	<i>t</i> -Butyl Alcohol Synthesis by Air Oxidation of Supercritical Isobutane . . . . .	399
4.8.4	Supercritical Phase Alkylation Reactions over Solid Acid Catalysts	403
4.8.5	Synthesis of Fine Chemicals and Other Products. . . . .	407
4.8.6	Conclusions . . . . .	411
	References . . . . .	411
4.9	Enzymatic Catalysis . . . . .	414
4.9.1	Introduction . . . . .	414
4.9.2	Enzymes . . . . .	415
4.9.3	Enzyme Reactors. . . . .	416
4.9.3.1	Batch Reactors . . . . .	416
4.9.3.2	Recirculating Batch Reactor . . . . .	419
4.9.3.3	Extractive Batch Reactor. . . . .	419
4.9.3.4	Semicontinuous Flow Reactors . . . . .	420
4.9.3.5	Continuous Reactors . . . . .	420

XVI      *Contents*

4.9.4	Experimental Results . . . . .	421
4.9.4.1	A Compilation of Published Experiments . . . . .	421
4.9.4.2	Enzyme Stability in Supercritical Fluids . . . . .	425
4.9.4.3	The Role of Water . . . . .	428
4.9.4.4	Pressure Effects . . . . .	431
4.9.4.5	Mass Transfer Effects . . . . .	434
4.9.4.6	Effects on Selectivity . . . . .	436
4.9.5	Downstream Processing and Costs . . . . .	439
4.9.5.1	Downstream Processing Schemes . . . . .	439
4.9.5.2	Prosessing Cost Estimate . . . . .	441
4.9.6	Summary and Outlook . . . . .	441
	References . . . . .	443
4.10	Phase Transfer and Ammonium Salt Catalyzed Reactions . . . . .	446
4.10.1	Introduction . . . . .	446
4.10.2	Background . . . . .	446
4.10.3	Published Work . . . . .	449
4.10.4	Experimental Procedure . . . . .	451
4.10.5	Related Catalytic Reactions . . . . .	452
4.10.6	Future Directions . . . . .	453
	References . . . . .	453
	<b>Appendices . . . . .</b>	<b>455</b>
	Appendix A: Conversion Factors . . . . .	455
	Appendix B: Abbreviations and Symbols . . . . .	457
	<b>Index . . . . .</b>	<b>465</b>