

# Polymeric Materials in Organic Synthesis and Catalysis

*Edited by Michael R. Buchmeiser*

*Foreword by Rolf Mülhaupt*



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**Prof. Dr. Michael R. Buchmeiser**  
Institut für Analytische Chemie und Radiochemie  
Universität Innsbruck  
Innrain 52a  
6020 Innsbruck  
Austria

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**To Andrea**





## Foreword

At the beginning of the 21st century the remarkable progress achieved in the synthetic chemistry of both small molecules and polymers is stimulating the renaissance of the development of polymer-bound reagents and catalysts. The scope of modern polymer supports is expanding well-beyond that of the traditional Merrifield resins. Advanced polymer supports are offering new opportunities for the development of the modern automated high-throughput screening methods as well as of the advanced manufacturing processes with simplified product recovery. Applications include the production of fine chemicals and new intermediates for the chemical and life sciences industries. An increasing number of academic and industrial labs are employing modern polymer supports to facilitate product purification. Novel reagents are being designed to combine the advantages typical for homogeneous and heterogeneous reactions. This strict borderline between heterogeneous and homogeneous reactions is gradually fading away with continuing progress in the development of polymer-mediated reactions. Precise control of polymerization processes using modern living polymerization methods affords an unprecedented control of three-dimensional polymer architectures and allows selective placement of functional groups and linker molecules. Prominent examples of new polymer carrier generations are highly functional nanometer-sized dendritic and hyperbranched polymers with core/shell topology and the high loading of functional groups on the surface. Polymer self-assembly is being exploited to prepare confined environments which can serve as nanoreactors for a variety of chemical reactions. Design and application of polymer supports is attracting attention in combinatorial chemistry, drug discovery research, catalysis, and biosynthesis. Progress in this field is closely related to interdisciplinary research in the various fields of science and reaction engineering. This book meets very successfully the important challenge to bring together leading experts and pioneers from all these relevant fields in order to highlight the outstanding advances and the future potential of the emerging new strategies for the rational development of modern synthetic reactions based upon innovative polymer supports.

The individual chapters address important contributions relevant to the ongoing progress and future success of polymer-mediated reactions in organic synthesis, catalysis, and biosynthesis. All facets of the modern development are presented in this book. Most authors give their complementary views from different

angles on the novel strategies exploiting new methods introduced in polymer synthesis, polymer characterization, and application of functional polymer supports. This includes synthesis of structured polymer supports using living polymerizations and advanced graft copolymerization, the preparation of novel dendritic and hyperbranched carriers with very high loadings, as well as the formation of structured particles, films, membranes, and monolithic systems. Reaction engineering topics cover monitoring and optimization of reactions on solid supports and liquid-phase systems, the development of polymer membrane reactors, the design of combinatorial libraries, and the use of polymer-bound reagents and scavengers in organic multistep syntheses. Several comprehensive overviews focus on the different aspects and the practical applications of such modern polymeric supports in organic syntheses and the emerging new opportunities of nanoreactor design by means of micellar catalysis and novel molecular nanoparticles. Without any doubt this book represents a very valuable asset to everybody who is interested in getting a close-up view on the current state of the art and the exciting new opportunities relating to the use of novel functional polymer systems being applied in catalysis, modern organic synthesis, combinatorial chemistry, and biosynthesis.

May 2003  
Albert-Ludwigs-Universität Freiburg

ROLF MÜLHAUPT

## Contents

**Foreword** VII

**Preface** XIX

**List of Contributors** XXI

<b>1</b>	<b>Structure, Morphology, Physical Formats and Characterization of Polymer Supports</b>	<b>1</b>
	<i>Yolanda de Miguel, Thomas Rohr and David C. Sherrington</i>	
1.1	Synthesis and Molecular Structure of Polymer Supports	1
1.2	Suspension Polymerized Particulate Resin Supports – Structural and Morphological Variants	2
1.2.1	Suspension Polymerization	2
1.2.2	Resin Morphology	3
1.2.3	Novel Morphologies	7
1.2.3.1	Solvent Expanded Gel-type Resins	7
1.2.3.2	Collapsible Macroporous Resins	8
1.2.3.3	Davankov Hypercross-linked Resins	8
1.2.4	Resins with Branched Molecular Architecture	9
1.3	Polymer Supports in Film and Monolithic Format	11
1.3.1	Thin Film Supports	11
1.3.2	Self-supporting Rods, Discs and Plugs	12
1.3.3	PolyHIPE-based Supports	13
1.3.4	Supported Monolithic Structures	15
1.4	Morphological Characterization of Polymer Supports	15
1.4.1	Solvent Imbibition	16
1.4.2	N <sub>2</sub> Sorption Porosimetry Involving Dry Supports	18
1.4.2.1	Adsorption/Desorption Mechanisms Isotherm Hysteresis Loops	20
1.4.2.2	Models for Calculation of Surface Area and Pore Sizes	20
1.4.2.3	Network and Pore Connectivity Effects	23
1.4.3	Hg Intrusion Porosimetry Involving Dry Supports	24
1.4.3.1	Theory	24
1.4.3.2	Comparison between Nitrogen Sorption and Mercury Intrusion	27

1.4.4	Inverse Size Exclusion Chromatographic (ISEC) Analysis of Solvent Wetted Polymer Supports	29
1.4.5	Other Methods for Characterizing Porous Polymer Morphology	30
1.5	Analytical Techniques for Monitoring Polymer-supported Chemistry	31
1.5.1	Off-bead Analysis	32
1.5.1.1	Cleave-and-Characterize	32
1.5.1.2	Mass Spectrometry	33
1.5.1.3	Analytical Constructs	33
1.5.2	Destructive On-bead Analysis	34
1.5.2.1	Elemental Microanalysis	34
1.5.2.2	Color tests	34
1.5.3	Nondestructive On-bead Analysis	35
1.5.3.1	Mass Balance	35
1.5.3.2	Other Nondestructive Quantitation Methods	35
1.5.3.3	Infrared and Raman Spectroscopy	35
1.5.3.4	Nuclear Magnetic Resonance (NMR) Spectroscopy	41
1.5.4	Spatial Analysis of Resins	44
1.6	Challenges for the Future	46
1.7	References	46
<b>2</b>	<b>Supported Reagents and Scavengers in Multi-Step Organic Synthesis</b>	<b>53</b>
	<i>Ian R. Baxendale, R. Ian Storer and Steven V. Ley</i>	
2.1	Introduction	53
2.1.1	Solid-supported Synthesis and Solution – Solution Manipulation	53
2.1.2	Solid-supported Reagents and Catalysts	54
2.1.2.1	Supporting Materials	55
2.1.2.2	Facilitation of Work-up and Purification	56
2.1.2.3	Immobilization of Toxic and Malodorous Reagents	57
2.1.2.4	Microwaves as a Reliable Heating Method for Polymers	58
2.1.2.5	Effects of Site Isolation	59
2.1.2.6	Mutually Incompatible Reagents in the Same Reaction Compartment	60
2.1.3	Solid-supported Purification Processes	61
2.1.3.1	Supported Scavengers	61
2.1.3.2	Catch and Release	62
2.2	Multi-step Organic Transformations	63
2.2.1	The Early Developments of Polymer-supported Processes in Organic Synthesis	63
2.2.1.1	One Pot Multi-reagent Combinations	63
2.2.1.2	Sequential Multi-step Transformations	69
2.2.2	The Further Development of Scavenging Protocols	72
2.2.3	Immobilized Reagents and Scavenging Techniques in Library Synthesis	76

2.2.3.1	Incorporation of Solid-supported Scavengers into Library Synthesis	76
2.2.3.2	The Application of Immobilized Reagents and Scavengers to Library Synthesis	89
2.2.4	Natural Product Synthesis	116
2.3	Conclusion	131
2.4	References	132
<b>3</b>	<b>Organic Synthesis on Polymeric Supports</b>	<b>137</b>
	<i>Carmen Gil, Kerstin Knepper and Stefan Bräse</i>	
3.1	Introduction	137
3.2	Linkers for Organic Synthesis on Polymeric Supports	138
3.2.1	Linker Families	139
3.2.1.1	Benzyl-Type Linkers including Trityl and Benzhydryl Linkers	139
3.2.1.2	Allyl-Based Linkers	141
3.2.1.3	Ketal/Acetal-Based Linkers	141
3.2.1.4	Ester-, Amide- and Carbamate-Based Linkers	143
3.2.1.5	Silyl Linkers	144
3.2.1.6	Boronate Linkers	144
3.2.1.7	Sulfur-, Stannane- and Selenium-Based Linkers	144
3.2.1.8	Triazene-Based Linkers	149
3.2.1.9	Photocleavable Linkers	151
3.2.2	Linker Strategies	152
3.2.2.1	Safety Catch Linkers	152
3.2.2.2	Cyclative Cleavage (Cyclorelease Strategy)	155
3.2.2.3	Cleavage-Cyclization Cases	156
3.2.2.4	Fragmentation Strategies	156
3.2.2.5	Traceless Linkers	157
3.2.2.6	Multifunctional Cleavage	157
3.2.2.7	Linkers for Asymmetric Synthesis	159
3.2.3	Linkers for Functional Groups	162
3.3	Organic Transformations on Polymeric Supports	164
3.3.1	Oxidation and Reduction Reactions	164
3.3.2	C-C Bond Formation Reactions	165
3.3.2.1	Palladium-Catalyzed Reactions	166
3.3.2.2	Grignard and Similar Reactions	168
3.3.2.3	Michael Reactions and 1,2-Addition Reactions	168
3.3.2.4	Wittig and Horner – Wadsworth – Emmons Reactions	169
3.3.2.5	Alkene Metathesis	169
3.3.3	Cycloaddition Reactions	170
3.3.3.1	Diels-Alder Reactions	170
3.3.3.2	1,3-Dipolar Cycloaddition Reactions	171
3.3.4	Organometallic Chemistry on Polymeric Supports	171
3.3.5	Multicomponent Reactions	172
3.3.5.1	Grieco Reactions	172

3.3.5.2	Ugi Reactions	172
3.3.6	Mannich Reactions	173
3.3.6.1	Hantzsch Reactions	173
3.3.6.2	Biginelli Reactions	173
3.4	Targets for Synthesis on Polymeric Supports	174
3.4.1	Natural Products	174
3.4.1.1	Solid-phase Target-Oriented Total Synthesis of Natural Products	175
3.4.1.2	Combinatorial Derivatization for Immobilized Natural Product Skeletons and Combinatorial Semi-synthesis	176
3.4.1.3	Construction of Natural Product-Like Libraries	176
3.4.2	Adaptation of New Synthetic Methods for the Solid-phase Synthesis of Combinatorial Libraries	178
3.4.2.1	Heterocycles	178
3.5	Conclusion, Summary and Outlook	187
3.6	List of Abbreviations	187
3.7	References	189
<b>4</b>	<b>Solid-Phase Bound Catalysts: Properties and Applications</b>	<b>201</b>
	<i>Thomas Frenzel, Wladimir Solodenko and Andreas Kirschning</i>	
4.1	Introduction	201
4.2	The Solid Support	203
4.2.1	Polymer Supports	203
4.2.2	Inorganic Supports	207
4.2.3	Selected Examples for Attachment of Ligands to Solid Supports	208
4.3	Applications in Catalysis	211
4.3.1	Polymer Supported Oxidations	211
4.3.1.1	Oxidation of Alcohols	212
4.3.1.2	Epoxidation of Alkenes	213
4.3.1.3	Dihydroxylation and Aminohydroxylation of Alkenes	216
4.3.2	Lewis Acid-mediated Reactions	219
4.3.2.1	Addition Reactions to Carbonyl Compounds	219
4.3.2.2	Addition Reactions to Imines	221
4.3.2.3	Addition Reactions to Carbon–Carbon Double Bonds	222
4.3.2.4	Cycloaddition Reactions	223
4.3.2.5	Miscellaneous Applications	225
4.3.3	Transition Metal Catalysts	226
4.3.3.1	Palladium-catalyzed Coupling Reactions	227
4.3.3.2	Olefin Metathesis	229
4.3.3.3	Transition Metal-catalyzed Hydrogenation and Hydroformylation	229
4.3.4	Miscellaneous	232
4.4	Outlook	234
4.5	Acknowledgments	234
4.6	References	234

<b>5</b>	<b>Soluble Polymers as Catalyst and Reagent Platforms: Liquid-Phase Methodologies</b>	<b>241</b>
	<i>Tobin J. Dickerson, Neal N. Reed and Kim D. Janda</i>	
5.1	Introduction	241
5.2	Overview of Soluble Polymers in Organic Synthesis	242
5.2.1	Properties of Soluble Polymeric Supports	242
5.2.2	Methods for Separating Polymers from Reaction Mixtures	243
5.2.3	Analytical Methods in Liquid-phase Synthesis	244
5.2.4	Listing of Polymers	245
5.2.4.1	Polyethylene Glycol (PEG)	245
5.2.4.2	Non-cross-linked Polystyrene	247
5.3	PEG-supported Catalysts	248
5.3.1	Hydrogenation Catalysts	248
5.3.2	Chinchona Alkaloid Ligands for the Sharpless AD Reaction	249
5.3.3	Phase-transfer Catalysts	251
5.3.4	Epoxidation Catalysts	253
5.3.5	Carbon – Carbon Bond-forming Catalysts	253
5.4	Soluble Polymer-supported Reagents	256
5.4.1	Phosphine Reagents	256
5.4.2	Oxidants	261
5.4.3	Reducing Agents	263
5.4.4	Microgel-supported Reagents	265
5.4.5	Miscellaneous Reagents	266
5.5	Conclusions	272
5.6	Acknowledgements	272
5.7	References	273
<b>6</b>	<b>Polymers for Micellar Catalysis</b>	<b>277</b>
	<i>Oskar Nuyken, Ralf Weberskirch, Thomas Kotre, Daniel Schönfelder and Alexander Wörndle</i>	
6.1	Introduction	277
6.2	Amphiphilic Block Copolymers for Micelle Formation	281
6.2.1	Transition Metal Catalysts Solubilized in Micellar Aggregates	281
6.2.2	Metal Colloids Stabilized in Micellar Aggregates	283
6.2.3	Catalysts Covalently Bound to the Amphiphilic Block Copolymer	286
6.2.3.1	Phosphine-Functionalized Amphiphiles for Rhodium-Catalyzed Hydrogenation	286
6.2.3.2	Triphenylphosphine-Functionalized Amphiphiles for Rhodium-Catalyzed Hydroformylation and Palladium-Catalyzed Heck Coupling Reaction	287
6.2.3.3	ATRP of Methyl Methacrylate in the Presence of an Amphiphilic, Polymeric Macroligand	291
6.3	Amphiphilic Polymers Forming Micelle Analogous Structures	294
6.3.1	Amphiphilic Star Polymers with a Hyperbranched Core	295
6.3.2	Polysoaps	298

6.4	Summary and Outlook	301
6.5	References	302
<b>7</b>	<b>Dendritic Polymers as High-Loading Supports for Organic Synthesis and Catalysis</b>	<b>305</b>
	<i>Rainer Haag and Sebastian Roller</i>	
7.1	Introduction	305
7.2	General Aspects of Dendritic Polymers and Solid-phase Hybrid Polymers	305
7.2.1	Special Properties of Soluble Dendritic Polymeric Supports	307
7.2.2	Methods for Separating Dendritic Polymer Supports from Reaction Mixtures	307
7.2.3	Dendritic Hybrid Polymers as High-Loading Solid-phase Supports	310
7.3	Dendritic Polymer-supported Organic Synthesis	312
7.3.1	Perfect Dendrimers as Supports in Organic Synthesis	312
7.3.2	Hyperbranched Polymeric Supports in Organic Synthesis	316
7.3.3	Other Soluble Multivalent Supports in Organic Synthesis	319
7.3.4	Dendronized Solid-phase Supports for Organic Synthesis	322
7.4	Dendritic Polymer-supported Reagents and Scavengers	328
7.5	Dendritic Polymers as High-Loading Supports for Catalysts	331
7.5.1	Dendritic Polymeric Supports in Homogeneous Catalysis	331
7.5.1.1	Selected Examples for Dendritic Polymer-supported Catalysis	332
7.5.2	Dendritic Polymeric Supports in Heterogeneous Catalysis	338
7.6	Conclusions	339
7.7	Acknowledgements	340
7.8	Abbreviations	341
7.9	References	342
<b>8</b>	<b>Metathesis-Based Polymers for Organic Synthesis and Catalysis</b>	<b>345</b>
	<i>Michael R. Buchmeiser</i>	
8.1	Introduction	345
8.2	Polymeric Catalytic Supports Prepared by ROMP	345
8.2.1	Precipitation Polymerization-based Techniques	345
8.2.2	Grafting Techniques	347
8.2.2.1	Grafted Supports for Heck Reactions	347
8.2.2.2	Grafted Supports for ATRP	349
8.2.2.3	Grafted Supports for Ring-closing Metathesis (RCM) and Related Reactions	350
8.2.2.4	Other Grafted Supports	351
8.2.3	Coating Techniques	351
8.2.3.1	Heck Supports Based on Coated Silica	351
8.2.3.2	ATRP Supports Based on Coated Silica	353
8.2.3.3	RCM Supports Based on Coated Silica	353
8.3	ROMP gels and Other Functional Metathesis-based Polymers	354
8.4	Monolithic Catalytic Supports	358



8.4.1	Basics and Concepts	358
8.4.2	Manufacture of Metathesis-based Monolithic Supports	359
8.4.3	Microstructure of Metathesis-based Rigid Rods	360
8.4.4	Functionalization, Metal Removal and Metal Content	361
8.4.5	Applications of Functionalized Metathesis-based Monoliths in Catalysis	364
8.4.5.1	Grafted Supports for Ring-closing Metathesis (RCM) and Related Reactions	364
8.4.5.2	Poly-(N,N-dipyrid-2-yl-7-oxanorborn-2-en-5-ylcarbamido·PdCl <sub>2</sub> )-grafted Monolithic Supports for Heck Reactions	366
8.4.5.3	Poly-(N,N-dipyrid-2-yl-7-oxanorborn-2-en-5-ylcarbamido·PdCl <sub>2</sub> )-coated Monolithic Supports for Heck Reactions	367
8.5	Conclusion, Summary and Outlook	367
8.6	Acknowledgement	368
8.7	References	368
<b>9</b>	<b>New Strategies in the Synthesis of Grafted Supports</b>	<b>371</b>
	<i>R. Jordan</i>	
9.1	Introduction and Scope	371
9.2	Self-assembled Monolayers	372
9.2.1	Two Dimensional Self-assembly	372
9.2.2	Self-assembled Monolayers of Alkanethiols	374
9.2.3	Self-assembled Monolayers of Silanes	376
9.2.4	Self-assembled Monolayers for Surface Engineering	378
9.2.5	Surface Reconstruction: A Dynamic View of Self-assembled Monolayer Systems	381
9.2.6	Self-assembled Monolayers of Rigid Mercaptobiphenyls	382
9.2.6.1	Self-Assembly of Dipoles	386
9.2.7	Patterned Self-assembled Monolayers	388
9.2.8	Self-assembled Monolayers as Tailored Functional Surfaces in Two and Three Dimensions	393
9.3	Polymers on Surfaces	397
9.3.1	Polymer Brushes by Surface-initiated Polymerizations	400
9.3.2	Surface-initiated Polymerization Using Free Radical Polymerization	406
9.3.3	Surface-initiated Polymerization Using Living Ionic Polymerization	413
9.3.3.1	Surface-initiated Polymerization Using Living Anionic Polymerization	414
9.3.3.2	Surface-initiated Polymerization Using Living Carbocationic Polymerization (LCSIP)	417
9.3.4	Surface-initiated Polymerization Using Controlled Radical Polymerization	423
9.3.5	Surface-initiated Polymerization by Miscellaneous Techniques	430
9.4	Summary and Outlook	433
9.5	References	434

<b>10</b>	<b>Biocatalyzed Reactions on Polymeric Supports: Enzyme-Labile Linker Groups</b> 445
	<i>Reinhard Reents, Duraiswamy Jeyaraj and Herbert Waldmann</i>
10.1	Introduction 445
10.2	Endo-linkers 446
10.3	Exo-linkers 458
10.4	References 465
<b>11</b>	<b>Polymer-Supported Olefin Metathesis Catalysts for Organic and Combinatorial Synthesis</b> 467
	<i>Jason S. Kingsbury and Amir H. Hoveyda</i>
11.1	Introduction 467
11.2	The First Polymer-supported Ru Catalyst for Olefin Metathesis 468
11.3	Homogeneous Catalysis through Heterogeneous Ru Carbenes 469
11.3.1	Recyclable Monomers Act through a 'Release/Return' Mechanism 469
11.3.2	The First Carbene-tethered Polymeric Catalyst 470
11.3.3	A Poly(ethylene glycol)-based Catalyst with Solvent-dependent Solubility 472
11.4	Dendrimers as Recyclable Metathesis Catalysts 475
11.4.1	Synthesis and Metathesis Activity of Ru-based Carbosilane Dendrimers 475
11.4.2	Evidence for Ru Release and Return During Olefin Metathesis 477
11.4.3	Dendrimer Microfiltration: A New but Underdeveloped Strategy for Catalyst Recovery 479
11.5	A Recent Approach to Permanent Immobilization of a Ru-based Catalyst 480
11.6	A PS-supported Ru Catalyst with Unsaturated <i>N</i> -Heterocyclic Carbene Ligation 482
11.7	A New Recyclable Catalyst Based on the Bidentate Styrene Ether 484
11.8	Alternative Solid Supports Expand the Scope of Existing Catalyst Systems 486
11.8.1	A Comparative Study of Three Poly-DVB-supported Ru Carbenes 486
11.8.2	A Wang-supported Styrene Ether Catalyst for Stereoselective Cross Metathesis 487
11.9	Easily Recyclable Ru Catalysts for Combinatorial Synthesis 489
11.10	The First Supported Chiral Metathesis Catalyst 493
11.11	Conclusions and Future Outlook 499
11.12	References 499

<b>12</b>	<b>Monitoring and Optimizing Organic Reactions Carried Out on Solid Support</b>	<b>503</b>
	<i>Bing Yan</i>	
12.1	Introduction	503
12.1.1	Quality of Combinatorial Libraries	503
12.1.2	Purification and the Chemical Yield of Synthesis	504
12.1.3	Methods for Monitoring the Reaction Completion	505
12.2	Non-chemical Factors Affecting the Completion of Solid-phase Reactions	507
12.2.1	Esterification Reaction Using Resin Beads of Various Sizes	507
12.2.2	Bromination Reaction on Resin Beads of Various Sizes	510
12.3	Monitoring the Reaction Completion	510
12.3.1	Reaction Completion Monitored by Single Bead FTIR	510
12.3.2	Reaction Completion Monitored by Combination of Methods	511
12.3.3	Pitfalls to Avoid in Reaction Monitoring	511
12.4	Monitoring the Cleavage Completion	516
12.4.1	Cleavage from Acid-labile Linker	516
12.4.1.1	TFA Cleavage of Resin-Bound Products	517
12.4.1.2	Comparison of TFA Cleavage Reactions	518
12.4.2	Cleavage from Marshall Linker	520
12.4.2.1	Cleavage of Resin-Bound Thiophenol Esters with <i>n</i> -Butylamine	520
12.4.2.2	Cleavage with 3,4-Dimethoxyphenethylamine	523
12.4.2.3	Cleavage with 1-Piperonylpiperazine	524
12.4.2.4	Effect of Temperature on Cleavage Reaction	524
12.4.2.5	Cleavage Rate after Linker Oxidation	524
12.5	Concluding Remarks	524
12.6	Acknowledgements	525
12.7	References	526
<b>13</b>	<b>Polymeric Membranes for Integrated Reaction and Separation</b>	<b>527</b>
	<i>J.T.F. Keurentjes</i>	
13.1	Introduction	527
13.2	Membrane Systems for Improved Chemical Synthesis	528
13.2.1	Efficient Catalyst Recycle	528
13.2.2	Pervaporation Membranes for Shifting Chemical Equilibrium	530
13.3	Membrane Bioreactors	536
13.3.1	Lactic Acid Production	537
13.3.2	Bioreactors for Environmental Applications	538
13.3.3	Enzyme Reactors	540
13.4	Concluding Remarks	544
13.5	References	545
<b>Index</b>		<b>549</b>



## Preface

It was in December 2001, when Dr. Peter Göllitz called me and “encouraged” me to edit a book on recent relevant aspects of polymer chemistry in organic synthesis and catalysis. Facing the bitter cup of sorrow I accepted for four reasons.

First, I could not turn down Peter Göllitz’ suggestion. Second, the area of polymer science is a rapidly developing field that certainly deserved another book. Third, hardly any other discipline has had such a strong influence on almost all other areas of chemistry. And finally, though already introduced to both organic synthesis and catalysis in the 1960s, the most substantial improvements in these areas have been made during the last ten years. Therefore, I soon found myself contacting colleagues asking for contributions, tables of contents and manuscripts. Quite surprising, I received hardly any negative replies. This and the professional attitude of all contributors in terms of deadlines and quality of their manuscripts soon sweetened the cup.

As a result, it is now my pleasure to present this book. As can be deduced from its title, it was intended to cover the most relevant achievements of polymer chemistry in the areas of organic synthesis and catalysis. For this purpose, 30 authors have contributed to this venture in 13 chapters. The book commences with some general properties of cross-linked polymers relevant to the above-mentioned applications, then turns to polymer-bound reagents, scavengers, catalysts and reactions (including biocatalyzed reactions) that can be carried out. Special attention has been given to soluble polymers including dendritic polymers and micelles used in organic synthesis and catalysis as well as to the synthetic advancements in the preparation of these materials. Metathesis-based techniques have had an enormous impact, so two chapters covering both heterogeneous metathesis catalysts and metathesis-derived supports have been added. Finally, the on- and off-bead monitoring of reactions as well as technical aspects including those of high-throughput screening and the use of membranes are summarized.

Any edited book strongly depends on the quality of every single contribution. It was both my privilege and honor to win such well-known authors. With their contributions, I am convinced that we have now a book in hand that represents the state of the art and a comprehensive summary on the present status quo. It is designed to attract equally students and advanced readers working in the areas of organic chemistry, organometallic chemistry, catalysis, polymer science, physical

chemistry and technical chemistry by providing both substantial background information and interdisciplinary up-to-date knowledge. Special consideration has been given to the literature sections, which should facilitate further reading. Unfortunately, for economical and practical reasons, every book has to be limited to a certain number of pages. Therefore, few additional, interesting aspects had to be shortened or even neglected. Nevertheless, I am sure Peter Gölitz will find somebody else to write a book on these topics.

Finally, one thing remains to be done, that is to thank all those who have helped me in putting this book together: The contributing authors and Wiley-VCH, in particular Dr. Elke Westermann, for her support, encouraging e-mails and patience.

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MICHAEL R. BUCHMEISER

## List of Contributors

Dr. IAN R. BAXENDALE  
Department of Chemistry  
University of Cambridge  
Lensfield Rd.  
Cambridge, CB2 1EW, UK

Prof. Dr. STEFAN BRÄSE  
Kekulé-Institut für  
Organische Chemie und Biochemie  
Rheinische Friedrich-Wilhelms-  
Universität Bonn  
Gerhard-Domagk-Str. 1  
D-53121 Bonn

Prof. Dr. MICHAEL R. BUCHMEISER  
Institut für Analytische Chemie  
und Radiochemie  
Universität Innsbruck  
Innrain 52a  
A-6020 Innsbruck

TOBIN J. DICKERSON  
Department of Chemistry and  
The Skaggs Institute for Chemical  
Biology  
The Scripps Research Institute  
10550 North Torrey Pines Rd.  
La Jolla, CA 92037

CARMEN GIL  
Kekulé-Institut für  
Organische Chemie und Biochemie  
Rheinische Friedrich-Wilhelms-  
Universität Bonn  
Gerhard-Domagk-Str. 1  
D-53121 Bonn

Dr. RAINER HAAG  
Freiburger Materialforschungszentrum  
und Institut für Makromolekulare  
Chemie  
Albert-Ludwigs-Universität Freiburg  
Stefan-Meier-Str. 21  
D-79104 Freiburg

Prof. Dr. AMIR H. HOVEYDA  
Department of Chemistry  
Merkert Chemistry Center  
Boston College  
Chestnut Hill MA 02467

Prof. Dr. KIM D. JANDA  
Department of Chemistry and  
The Skaggs Institute for Chemical  
Biology  
The Scripps Research Institute  
10550 North Torrey Pines Rd.  
La Jolla, CA 92037

DR. DURAISWAMY JEYARAJ  
MPI für Molekulare Physiologie  
Abteilung Chemische Biologie  
Otto-Hahn Str. 11  
D-44227 Dortmund

DR. RAINER JORDAN  
Lehrstuhl für Makromolekulare Stoffe  
TU München  
Lichtenbergstr. 4  
D-85747 Garching

Prof. Dr. KEURENTJES  
Chemical Engineering and Chemistry  
Process Development  
Eindhoven University of Technology  
NL-5600 MB Eindhoven

DR. JASON S. KINGSBURY  
Department of Chemistry  
Merkert Chemistry Center  
Boston College  
Chestnut Hill MA 02467

Prof. Dr. ANDREAS KIRSCHNING  
Institut für Organische Chemie  
der Universität Hannover  
Schneiderberg 1B  
D-30167 Hannover

KERSTIN KNEPPER  
Kekulé-Institut für  
Organische Chemie und Biochemie  
Rheinische Friedrich-Wilhelms-  
Universität Bonn  
Gerhard-Domagk-Str. 1  
D-53121 Bonn

Prof. Dr. J. T. F. KEURENTJES  
Process Development Group  
Eindhoven University of Technology  
P.O. Box 513  
NL-5600 MB Eindhoven

THOMAS KOTRE  
Lehrstuhl für Makromolekulare Stoffe  
TU München  
Lichtenbergstr. 4  
D-85747 Garching

Prof. Dr. STEVEN V. LEY  
Department of Chemistry  
University of Cambridge  
Lensfield Rd.  
Cambridge, CB2 1EW, UK

Y. DE MIGUEL  
Department of Chemistry  
King's College  
London, UK

Prof. Dr.-Ing. OSKAR NUYKEN  
Lehrstuhl für Makromolekulare Stoffe  
TU München  
Lichtenbergstr. 4  
D-85747 Garching

NEAL N. REED  
Department of Chemistry and  
The Skaggs Institute for Chemical  
Biology  
The Scripps Research Institute  
10550 North Torrey Pines Rd.  
La Jolla, CA 92037

DR. REINHARD REENTS  
MPI für Molekulare Physiologie  
Abteilung Chemische Biologie  
Otto-Hahn Str. 11  
D-44227 Dortmund

SEBASTIAN ROLLER  
Freiburger Materialforschungszentrum  
und Institut für Makromolekulare  
Chemie  
Albert-Ludwigs-Universität Freiburg  
Stefan-Meier-Str. 21  
D-79104 Freiburg



Prof. Dr. DAVID C. SHERRINGTON  
Department of Pure and Applied  
Chemistry  
University of Strathclyde  
Cathedral Street  
Glasgow UK

Dr. THOMAS ROHR  
Chemical Technology of Organic  
Materials  
Vienna University of Technology  
A-1010 Vienna

DANIEL SCHÖNFELDER  
Lehrstuhl für Makromolekulare Stoffe  
TU München  
Lichtenbergstr. 4  
D-85747 Garching

R. IAN STORER  
Department of Chemistry  
University of Cambridge  
Lensfield Rd.  
Cambridge, CB2 1EW, UK

Dr. RALF WEBERSKIRCH  
Lehrstuhl für Makromolekulare Stoffe  
TU München  
Lichtenbergstr. 4  
D-85747 Garching

Prof. Dr. HERBERT WALDMANN  
MPI für Molekulare Physiologie  
Abteilung Chemische Biologie  
Otto-Hahn Str. 11  
D-44227 Dortmund

ALEXANDER WÖRNDLE  
Lehrstuhl für Makromolekulare Stoffe  
TU München  
Lichtenbergstr. 4  
D-85747 Garching

Dr. BING YAN  
ChemRx Division  
Discovery Partners International Inc.  
385 Oyster Point Blvd.  
South San Francisco, CA 94080



## 1

## Structure, Morphology, Physical Formats and Characterization of Polymer Supports

YOLANDA DE MIGUEL, THOMAS ROHR and DAVID C. SHERRINGTON

## 1.1

### Synthesis and Molecular Structure of Polymer Supports

The overwhelming majority of synthetic macromolecules used as supports are vinyl addition polymers. Styrene-based species are by far the most important of these, with methacrylate- and acrylamide-based systems finding more limited application. Styrene-based polymer supports have the major advantage of being relatively chemically inert and yet readily functionalized by powerful electrophiles. The ester and amide functions in methacrylate- and acrylamide-based polymer supports make these more susceptible to chemical degradation, and so more care is required in exploiting these species. Though these monomer types can be polymerized via a variety of mechanisms involving free radical [1, 2], cationic, anionic [3] and dipolar [4] reactive intermediates, in practice most polymers destined for use as supports are produced by a free radical polymerization process.

Vinyl polymers can be synthesized as linear macromolecules (Fig. 1.1 a) which will dissolve to form isotropic solutions in a suitable solvent. They can also be produced in a highly branched form (Fig. 1.1 b) and again these macromolecules are completely soluble in appropriate solvents. Linear polymers and branched or dendritic polymers can be used as supports and these species form the subject of other chapters in this book. If however a vinyl monomer is copolymerized with a divinyl monomer then an infinite cross-linked network (Fig. 1.1 c) results, and though these macromolecular species will swell in a thermodynamically compatible solvent, their molecular weight is effectively infinite and this prevents their dissolution to form isotropic solutions. Instead the solvent swollen material appears as a highly flexible gel when low levels of cross-linking comonomer are used or indeed a relatively rigid one when high levels of cross-linker are employed. However, if the individual particles of the cross-linked species are small enough they will disperse in a suitable solvent and may superficially appear to dissolve, while in practice they will be present as microgel.

This chapter will focus exclusively on cross-linked vinyl polymer supports either in a spherical bead or resin form, or in some other macroscopic format. These essentially insoluble materials lead to considerably simplified reaction work-up and product isolation procedures when used e.g. in solid phase synthesis or as catalyst or

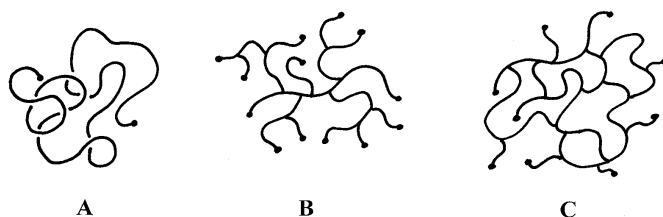


Fig. 1.1 Synthetic macromolecular architectures A) linear B) branched C) cross-linked.

scavenger supports. They are also readily adaptable to continuous flow technologies and robotic instrumentation, and not surprisingly have become the work-horse of many combinatorial and parallel synthetic and screening procedures. Further details are available in extensive reviews [5, 6] and in a number of textbooks [7–12].

## 1.2

### Suspension Polymerized Particulate Resin Supports – Structural and Morphological Variants

#### 1.2.1

##### Suspension Polymerization

Since cross-linked polymers cannot be re-formed or re-shaped it is necessary to synthesize them in the final physical form appropriate for each particular application. Particles in the size range  $\sim 50\text{--}1000\ \mu\text{m}$  are suitable for laboratory scale chemistry, while larger particles have advantages in large scale continuous processes. Irregularly shaped particles are susceptible to mechanical attrition and breakdown to ‘fines’, whereas the process of suspension polymerization [13] yields uniform spherical cross-linked polymer particles often referred to as beads, pearls or resins. These are much more mechanically robust and are widely exploited on both a small and large scale e.g. as the basis of ion exchange resins [14].

Particles of a suitable size and symmetry (Fig. 1.2) are readily prepared by suspension polymerization in which the organic monomer phase containing dissolved free radical initiator is dispersed as droplets in a continuous aqueous phase. The latter usually contains a water-soluble polymer (e.g. polyvinyl alcohol or a polysaccharide) to aid stabilization of the monomer droplets, and the whole system is efficiently stirred. Polymerization is initiated by raising the temperature typically to  $\sim 70^\circ\text{C}$  and maintaining this for  $\sim 6$  hours. The spherical monomer droplets are converted to solid spherical polymer resin beads. In the laboratory the batch reaction can be performed in a round-bottomed flask, but it is better to use a baffled parallel sided reactor with a flattish base typically 0.5–2 liter in volume. More details are available in Ref. [15]. This technology is also practiced widely on an industrial scale where the reactor size is larger and can yield 100s kg of resin in one batch. The major challenge in suspension polymerization is to

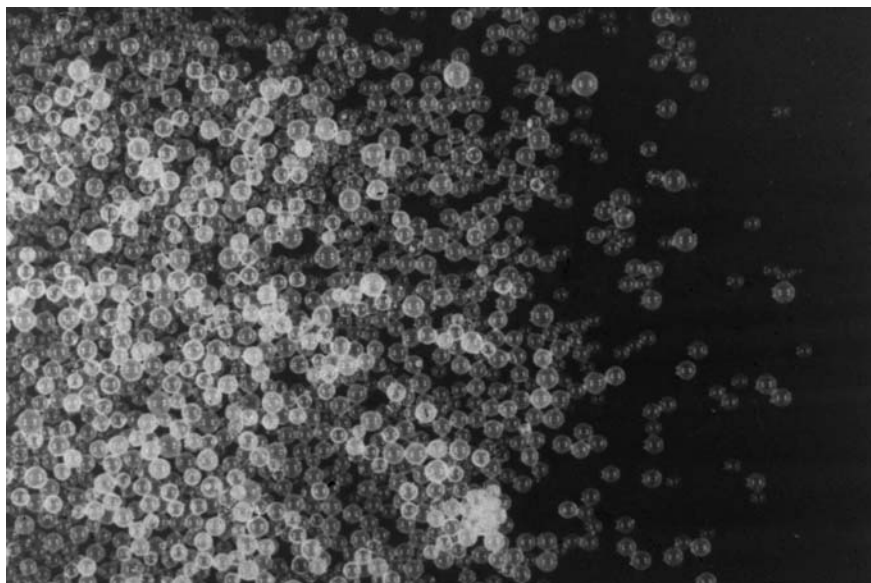


Fig. 1.2 Optical micrograph of suspension polymerized resin beads  $\sim 200 \mu\text{m}$  diameter.

avoid agglomeration of the polymerizing droplets, and since aggregation arises from surface interactions, perhaps somewhat counter-intuitively, small scale suspension reactions are more problematical than large ones. Recently however the use of a small scale oscillatory baffled reactor (Fig. 1.3) has been described allowing efficient suspension polymerization on a gram scale [16].

### 1.2.2

#### Resin Morphology

So-called **gel-type** resins are prepared from a vinyl monomer typically in the presence of a low level ( $\leq 5 \text{ mol}\%$ ) of a divinyl cross-linking comonomer and no other component other than the free radical initiator. Such materials (shown in Fig. 1.4, left) are hard and glassy in the solid state with a surface area  $\leq 5 \text{ m}^2\text{g}^{-1}$  (measured by e.g.  $\text{N}_2$  sorption and application of the BET equation see Section 1.4.2). However, these species can swell readily in a thermodynamically good solvent to provide access to essentially all the segments of the polymer network e.g. to carry out chemical derivatization. The negative aspect of these resins, however, is that they are relatively impenetrable in the dry state and in contact with thermodynamically poor solvents. Their use is therefore restricted to processes involving swelling solvents. Despite this 1–2% cross-linked poly(styrene-divinylbenzene) (PS-DVB) gel-type resins are the supports most used in solid phase synthesis applications.

So-called **macroporous resins** (shown in Fig. 1.4, right) are prepared from a vinyl monomer typically in the presence of higher levels of a divinyl cross-linking



Fig. 1.3 Small scale oscillatory baffled reactor (OBR) for gram scale suspension polymerization.

comonomer (from  $\sim 10$ – $80$  mol%). The term ‘macroporous’ is an old one which in the present context means permanently porous; it is *not* an indication of pore size. The permanently porous morphology of these species is generated by inducing the growing polymer network to phase separate or precipitate during the suspension polymerization. This is achieved by using a porogen in the polymerizing mixture, typically present in an equal volume to that of the comonomers. The porogen is more often than not a simple organic solvent, chosen to form an isotropic solution with the comonomers but to cause precipitation of the copolymer at some desired point in the polymerization. When the network does phase separate, microgel particles typically  $\sim 100$  nm in diameter form and these aggregate within each polymerizing droplet to form a discrete polymer phase, separate from