

# Dendrimers

Towards Catalytic, Material and  
Biomedical Uses

ANNE-MARIE CAMINADE, CÉDRIC-OLIVIER TURRIN,  
RÉGIS LAURENT, ARMELLE OUALI and BÉATRICE  
DELAVAUX-NICOT

*Laboratoire de Chimie de Coordination du CNRS  
Toulouse, France*



A John Wiley & Sons, Ltd., Publication

# Contents

<i>Preface</i>	xv
<b>Part 1 Generalities, Syntheses, Characterizations, and Physicochemical Properties</b>	<b>1</b>
<b>1 Syntheses of Dendrimers and Dendrons</b>	<b>3</b>
<i>Anne-Marie Caminade</i>	
1.1 Introduction: What Are Dendrimers and Dendrons?	3
1.2 Syntheses of Poly(propyleneimine) Dendrimers (PPI)	5
1.3 Synthesis of Poly(amidoamine) Dendrimers (PAMAM)	5
1.4 Syntheses of Poly(ether) Dendrimers	7
1.5 Syntheses of Poly(ester) Dendrimers	10
1.6 Synthesis of Poly(lysine) Dendrimers	14
1.7 Syntheses of Silicon-Containing Dendrimers	15
1.8 Syntheses of Phosphorus-Containing Dendrimers	16
1.9 Syntheses of Carbon-Based Dendrimers	17
1.10 Syntheses of Dendrimers Constituted of Nitrogen Heterocycles	19
1.11 Syntheses by Self-Assembly	21
1.12 Accelerated Syntheses	26
1.13 Conclusion	30
References	30
<b>2 Methods of Characterization of Dendrimers</b>	<b>35</b>
<i>Anne-Marie Caminade</i>	
2.1 Introduction	35
2.2 Spectroscopy and Spectrometry	36
2.2.1 Nuclear Magnetic Resonance (NMR)	36
2.2.2 Mass Spectrometry	40
2.2.3 X-ray Diffraction	41
2.2.4 Infrared (IR) and Raman Spectroscopy	42
2.2.5 Ultraviolet–Visible (UV–vis) Spectroscopy	43
2.2.6 Fluorescence	44
2.2.7 Chirality, Optical Rotation, and Circular Dichroism (CD)	45

2.2.8	Electron Paramagnetic Resonance (EPR)	45
2.2.9	Electrochemistry	46
2.2.10	Magnetometry	46
2.2.11	Mössbauer Spectroscopy	46
2.2.12	X-ray Spectroscopies	47
2.3	Scattering Techniques	47
2.3.1	Laser Light Scattering (LLS)	47
2.3.2	Small-Angle Neutron Scattering (SANS)	47
2.3.3	Small-Angle X-ray Scattering (SAXS) and Wide-Angle X-ray Scattering (WAXS)	48
2.4	Microscopy	48
2.4.1	Transmission Electron Microscopy (TEM)	49
2.4.2	Atomic Force Microscopy (AFM)	49
2.4.3	Polarizing Optical Microscopy (POM)	50
2.5	Rheology and Physical Characterizations	50
2.5.1	Intrinsic Viscosity	50
2.5.2	Differential Scanning Calorimetry (DSC)	50
2.5.3	Dielectric Spectroscopy (DS)	51
2.5.4	Dipole Moments	51
2.6	Separation Techniques	52
2.6.1	Size Exclusion Chromatography	52
2.6.2	Electrophoresis	53
2.7	Conclusion	53
	References	54
<b>3</b>	<b>Luminescent Dendrimers</b>	<b>67</b>
	<i>Anne-Marie Caminade</i>	
3.1	Introduction	67
3.2	Dendrimers with Fluorescent Terminal Groups	68
3.2.1	Fully Substituted Dendrimers	68
3.2.2	Partially Substituted Dendrimers	69
3.3	Luminescent Group at the Core of Dendrimers and Energy/Light-Harvesting Properties	74
3.3.1	Organic Fluorophores as Cores	74
3.3.2	Porphyryns and Phthalocyanines as Cores	77
3.3.3	Metallic Cores	78
3.4	Fluorescent Groups inside the Structure of Dendrimers	79
3.5	Intrinsically Fluorescent Dendrimers	81
3.5.1	Fluorescent Groups throughout the Dendrimeric Structure	81
3.5.2	Fluorescence of Dendrimers without Known Fluorophores	86
3.6	Two-Photon-Excited Fluorescence of Dendrimers	86
3.7	Conclusion	89
	References	90

<b>4</b>	<b>Stimuli-Responsive Dendrimers</b>	<b>99</b>
	<i>Anne-Marie Caminade</i>	
4.1	Introduction	99
4.2	Photoreponsive Dendrimeric Structures	100
	4.2.1 Azobenzene-Containing Dendrimers and Dendrons	101
	4.2.2 Other Types of Photoreponsive Dendrimers	108
4.3	Thermoresponsive Dendrimeric Structures	110
	4.3.1 Thermoresponsive Properties of Dendrimers	110
	4.3.2 Thermoresponsive Properties of Dendrons and Dendronized Polymers	112
4.4	Dendrimers Responsive to Solution Media Changes	114
	4.4.1 pH-Responsive Dendrimers	114
	4.4.2 Dendrimers Disassembly	115
4.5	Conclusion	117
	References	118
<b>5</b>	<b>Liquid Crystalline Dendrimers</b>	<b>125</b>
	<i>Anne-Marie Caminade</i>	
5.1	Introduction	125
5.2	Mesogenic Groups as Terminal Functions of Dendrons	126
5.3	Mesogenic Groups as Terminal Functions of Dendrimers	131
5.4	Mesogenic Groups as Branches of Dendrimers	134
5.5	Conclusion	135
	References	136
<b>6</b>	<b>Dendrimers and Nanoparticles</b>	<b>141</b>
	<i>Cédric-Olivier Turrin and Anne-Marie Caminade</i>	
6.1	Introduction	141
6.2	Dendrimers or Dendrons for Coating Nanoparticles	142
	6.2.1 Dendronization of Nanoparticles by Ligand Exchange	142
	6.2.2 Direct Synthesis of Dendronized Nanoparticles	147
	6.2.3 Dendrimer Coated Nanoparticles	149
	6.2.4 Nanocomposites with Interdendrimer Nanoparticles	151
6.3	Dendrimers as Templates for the Synthesis of Dendrimer-Encapsulated Nanoparticles (DENs)	152
	6.3.1 Catalysis with Dendrimer-Encapsulated Nanoparticles	153
	6.3.2 Other Uses of Dendrimer-Encapsulated Nanoparticles	154
6.4	Conclusion and Perspectives	154
	References	155
<b>Part 2</b>	<b>Applications in Catalysis</b>	<b>163</b>
<b>7</b>	<b>Terminal Groups of Dendrimers as Catalysts for Homogeneous Catalysis</b>	<b>165</b>
	<i>Armelle Ouali and Anne-Marie Caminade</i>	

7.1	General Introduction	165
7.1.1	The “Dendrimer Effect”	165
7.1.2	Recycling the Catalysts	166
7.2	Catalytic Organometallic Sites as Catalysts for Homogeneous Catalysis	167
7.2.1	Formation of C–X Bonds (X = C, N, O)	167
7.2.2	Addition Reactions on a C=X Double Bond (X = C, O)	175
7.2.3	Oxidation Reactions	177
7.3	Organocatalysis with Dendrimers	178
7.4	Conclusion	178
	References	179
<b>8</b>	<b>Catalytic Sites inside the Dendrimeric Structure for Homogeneous Catalysis</b>	<b>183</b>
	<i>Armelle Ouali and Anne-Marie Caminade</i>	
8.1	Introduction	183
8.2	Catalytic Sites as the Core of Dendrimers	184
8.2.1	Dendrimers Bearing a Transition-Metal-Based Complex at the Core	184
8.2.2	Dendrimers Bearing an Organocatalyst at the Core	188
8.3	Catalytic Sites inside the Branches of Dendrimers	191
8.3.1	Formation of C–X Bonds (X = C, N, O)	191
8.3.2	Addition Reactions on a C=C Double Bond: Olefin Hydrogenation	192
8.4	Conclusion	192
	References	193
<b>9</b>	<b>Dendrimers as Homogeneous Enantioselective Catalysts</b>	<b>197</b>
	<i>Armelle Ouali and Anne-Marie Caminade</i>	
9.1	Introduction	197
9.2	Catalytic Organometallic Sites as Catalysts for Homogeneous Catalysis	198
9.2.1	Formation of C–X Bonds (X = C, N, O)	198
9.2.2	Addition Reactions on a C=X Double Bond (X = C, O)	204
9.3	Organocatalysis with Dendrimers	209
9.3.1	Aldolizations	209
9.3.2	Aza–Morita–Baylis–Hillmann Reactions	209
9.3.3	Transaminations	210
9.4	Conclusion	210
	References	210
<b>10</b>	<b>Catalysis with Dendrimers in Particular Media</b>	<b>215</b>
	<i>Régis Laurent and Anne-Marie Caminade</i>	
10.1	Introduction	215
10.2	Two-Phase (Liquid–Liquid) Media	216

10.3	Catalysis in Ionic Liquids	219
10.4	Catalysis in Supercritical Media	220
10.5	Catalysis in Aqueous Media	221
10.6	Conclusion	234
	References	234
<b>11</b>	<b>Heterogeneous Catalysis with Dendrimers</b>	<b>239</b>
	<i>Régis Laurent and Anne-Marie Caminade</i>	
11.1	Introduction	239
11.2	Catalysis with Dendrons Synthesized from a Solid Material	240
	11.2.1 Silica as an Inorganic Support	240
	11.2.2 Polymers and Resins as Organic Supports	248
11.3	Catalysis with Dendrons or Dendrimers Grafted on to a Solid Surface	254
11.4	Catalysis with Insoluble Dendrimers	257
11.5	Conclusion	260
	References	261
<b>Part 3</b>	<b>Applications for the Elaboration or Modification of Materials</b>	<b>267</b>
<b>12</b>	<b>Dendrimers inside Materials</b>	<b>269</b>
	<i>Régis Laurent and Anne-Marie Caminade</i>	
12.1	Introduction	269
12.2	Dendrimers for the Elaboration of Gels	270
	12.2.1 Dendrimers for the Elaboration of Supramolecular Hyrogels	270
	12.2.2 Dendrimers for the Elaboration of Polymer-Type Hyrogels	273
	12.2.3 Dendrimers for the Elaboration of Organogels	276
12.3	Dendrimers inside Silica Gels	280
12.4	Dendrimers inside Other Types of Materials	285
12.5	Dendrimers for the Elaboration of OLEDs	288
	12.5.1 Fluorescent Dendrimers for the Elaboration of OLEDs	290
	12.5.2 Phosphorescent Dendrimers for the Elaboration of OLEDs	295
12.6	Conclusion	298
	References	299
<b>13</b>	<b>Self-Assembly of Dendrimers in Layers</b>	<b>313</b>
	<i>Béatrice Delavaux-Nicot and Anne-Marie Caminade</i>	
13.1	Introduction	313
13.2	Langmuir–Blodgett Films of Dendrons and Dendrimers	314
	13.2.1 Poly(benzyl ether) Derivatives	316
	13.2.2 Poly(amidoamine) and Poly(propyleneimine) Derivatives	319
	13.2.3 Azobenzene Derivatives	320

13.2.4	Poly(carbosilane) Dendrimer Derivatives	321
13.2.5	Fullerene C <sub>60</sub> Derivatives	322
13.2.6	Other Examples	325
13.3	Assemblies of Dendrons and Dendrimers on Solid Surfaces	326
13.3.1	Assembly of Dendrons and Dendrimers on Gold Surfaces	327
13.3.2	Assembly of Dendrons and Dendrimers on Silicon Substrates or Related Substrates	330
13.4	Several Routes for the Formation of Dendron or Dendrimer Multilayers	334
13.5	Nanoimprinting with Dendrons and Dendrimers on Solid Surfaces	342
13.5.1	Dendrimer-Based Self-Assembled Monolayers as Resists for Scanning Probe Lithography	342
13.5.2	Microprinting, Transfer Printing, and Dip-Pen Nanolithography with Dendrimers	344
13.6	Conclusion	350
	References	351
<b>14</b>	<b>Dendrimers as Chemical Sensors</b>	<b>361</b>
	<i>Anne-Marie Caminade</i>	
14.1	Introduction	361
14.2	Dendrimers as Chemical Sensors in Solution	362
14.2.1	Porphyryns and Other Macrocyclic Derivatives as the Core or Branches of Dendrimeric Sensors	362
14.2.2	Terminal Groups of Dendrimers as Sensors in Solution	363
14.3	Dendrimers as Electrochemical Sensors	365
14.4	Dendrimers on Modified Surfaces as Chemical Sensors	367
14.4.1	Dendrimers on Surfaces at the Interface with a Solution	367
14.4.2	Dendrimers on Surfaces at the Interface with a Vapor	368
14.5	Conclusion	370
	References	370
<b>15</b>	<b>Dendrimers as Biological Sensors</b>	<b>375</b>
	<i>Anne-Marie Caminade</i>	
15.1	Introduction	375
15.2	Dendrimers as Sensors in Solutions of Biological Media	375
15.3	Detection by Electrochemical Methods	378
15.4	Dendrimers or Dendrons for DNA Microarrays	380
15.5	Dendrimers for Other Types of Biomicroarrays	383
15.6	Dendrimers on Other Types of Support	384
15.7	Dendrimers as Multiply Labeled Entities Connected to the Target	385
15.8	Conclusion	386
	References	387

<b>Part 4 Applications in Biology/Medicine</b>	<b>393</b>
<b>16 Dendrimers for Imaging</b>	<b>395</b>
<i>Cédric-Olivier Turrin and Anne-Marie Caminade</i>	
16.1 Introduction	395
16.2 Magnetic Resonance Imaging with Dendrimers	395
16.2.1 Paramagnetic Dendrimer-Based Contrast Agents	398
16.2.2 PARACEST Dendrimer-Based Contrast Agents	402
16.2.3 Superparamagnetic Dendrimer-Based Contrast Agents	402
16.2.4 Dendrimer-Based <sup>129</sup> Xe HYPER-CEST MRI Contrast Agents	403
16.2.5 <sup>19</sup> F Dendrimer-Based MRI Contrast Agents	403
16.3 Other Types of Imaging with Dendrimers	403
16.3.1 Dendrimers for Optical Imaging	403
16.3.2 Dendrimers for Nuclear Medicine (NM) Imaging and Computed Tomography X-Ray Imaging (CT)	405
16.4 Conclusion and Perspectives	407
References	407
<b>17 Dendrimers as Transfection Agents</b>	<b>413</b>
<i>Cédric-Olivier Turrin and Anne-Marie Caminade</i>	
17.1 Introduction	413
17.2 Gene Transfection with PAMAM Dendrimers	415
17.2.1 Pioneering Results	415
17.2.2 Gene Transfection with Surface-Modified PAMAM	416
17.2.3 Gene Transfection with Core-Modified PAMAM	418
17.2.4 Gene Transfection with PAMAM-Functionalized Nanoparticles	419
17.2.5 Gene Transfection with PAMAM-Like Hyperbranched Polymers	420
17.3 Gene Transfection with Other Dendrimers	421
17.3.1 Gene Transfection with PPI Dendrimers	421
17.3.2 Gene Transfection with Peptide-Based Dendrimers	422
17.3.3 Gene Transfection with Phosphorus-Based Dendrimers	423
17.3.4 Gene Transfection with Silane-Based Dendrimers	424
17.4 Conclusion and Perspective	426
References	426
<b>18 Dendrimer Conjugates for Drug Delivery</b>	<b>437</b>
<i>Cédric-Olivier Turrin and Anne-Marie Caminade</i>	
18.1 Introduction	437
18.2 Improving Bioavailability with Dendrimers	438
18.3 Passive Targeting in Tumors with Dendrimer-Drug Conjugates	440
18.3.1 Dendrimer-Drug Bioconjugates and the EPR Effect	440
18.3.2 PEGylated Dendrimeric Scaffolds	442



18.4	Active Targeting with Site-Specific Dendrimer–Drug Conjugates	446
18.4.1	Addressing with Folic Acid (FA)	446
18.4.2	Addressing with Tumor-Homing Peptides	448
18.4.3	Addressing with Monoclonal Antibodies	449
18.5	Dendrimers for Photodynamic Therapy (PDT)	449
18.6	Dendrimers for Boron Neutron Capture Therapy (BNCT)	451
18.7	Conclusion and Perspectives	452
	References	453
<b>19</b>	<b>Encapsulation of Drugs inside Dendrimers</b>	<b>463</b>
	<i>Cédric-Olivier Turrin and Anne-Marie Caminade</i>	
19.1	Introduction	463
19.2	From Dendritic Boxes to Dendrimer-Based Formulations	464
19.3	Improving Bioavailability with Dendrimers?	464
19.4	Toxicological Issues	465
19.5	Dendrimer-Based Formulations for Drug Delivery	466
19.5.1	Nontargeted Formulations	466
19.5.2	Supramolecular Assemblies Involving Surface Ionic Interactions	473
19.5.3	Targeted Formulations	475
19.6	Conclusion and Perspectives	477
	References	477
<b>20</b>	<b>Unexpected Biological Applications of Dendrimers and Specific Multivalency Activities</b>	<b>485</b>
	<i>Cédric-Olivier Turrin and Anne-Marie Caminade</i>	
20.1	Introduction	485
20.2	Dendrimers and Multivalency	486
20.2.1	Multivalent Effects and Dendrimeric Effects	486
20.2.2	Glycodendrimers	487
20.3	Antimicrobial Dendrimers	488
20.3.1	Polycationic Dendrimers	489
20.3.2	Polyanionic Dendrimers	491
20.4	From Immunomodulation to Regenerative Medicine	494
20.4.1	Immunomodulation and Anti-Inflammation	494
20.4.2	Dendrimers and Regenerative Medicine	498
20.5	Conclusion and Perspectives	501
	References	502
<b>21</b>	<b>General Conclusions and Perspectives</b>	<b>511</b>
	<i>Anne-Marie Caminade</i>	
	<b>Index</b>	<b>515</b>