Vol-3-Abdulaziz-FM.qxd 5/7/2004 10:57 AM Page vii

Contents

Preface **xi**
Series Preface **xiii**

1. Organometallic Compounds in Biomedical Applications **1**
Charles E. Carraher Jr. and Charles U. Pittman Jr.

I. Introduction 2
II. Case for Metal-Containing Bioactive Agents 4
A. Tin-Containing Biocidal Polymers 5
B. Ferrocene: A Therapeutic Role in Polymeric Systems? 6
C. Polymeric Moderation of OsO_4 Toxicity 7
III. Miscellaneous Polymers 7
A. Metal Chelation Polymers 7
B. Condensation Polymers 9
IV. Small-Molecule Analogs 11
V. Summary 16
VI. References 16

2. Metal-Labeled DNA on Surfaces **19**
Heinz-Bernhard Kraatz, Yitao Long, and Todd C. Sutherland

I. Introduction 20
II. Ferrocene Nucleotides 20
III. Ferrocene-DNA Conjugates 22
IV. Other Metal-DNA Conjugates 34
V. Metallated DNA 36
A. Cu-DNA 36
B. M-DNA 37
VI. Summary 43
VII. Acknowledgments 43
VIII. References 43

Vol-3-Abdulaziz-FM.qxd 5/7/2004 10:57 AM Page viii

3. Artificial DNA through Metal-Mediated Base Pairing: Structural Control and Discrete Metal Assembly **45**
Mitsuhiko Shionoya

I. Introduction 46
II. Alternative Hydrogen-Bonding Schemes for DNA Base Pairing 46
III. Non-Hydrogen-Bonding Basepairs in DNA 48
IV. Metal-Mediated Base Pairing in DNA 49
A. Basic Concept 49
B. Artificial Nucleosides Designed for Metal-Mediated Base Pairs 49
C. Incorporation of a Metallo-Base Pair in DNA and Its Effect on Thermal Stability 50
D. Discrete Self-Assembled Metal Arrays in DNA 52
V. Future Prospects for Artificial Metallo-DNA 54
VI. Summary 54
VII. References 55

4. Organotin Macromolecules as Anticancer Drugs **57**
Charles E. Carraher Jr. and Deborah Siegmann-Louda

I. General 58
II. Anticancer Activity of Small Organotin Compounds 59
III. Molecule-Level Studies on Monomeric Organotin Compounds 62
IV. Anticancer Activity of Organotin Polymers 65
V. Future Work 70
VI. References 70

5. Organotin Oligomeric Drugs Containing the Antivirial Agent Acyclovir **75**
Charles E. Carraher Jr. and Robert E. Bleicher

I. Early History of Organotin Compounds 76
II. Mechanisms and Reactions 76
III. General Structures 77
IV. Acyclovir 80
V. Bioactivity of Related Compounds 81
VI. Experimental Work 82
VII. Results and Discussion 83
VIII. References 86

6. Polymeric Ferrocene Conjugates as Antiproliferative Agents **89**
Eberhard W. Neuse

I. Introduction 90
II. The Ferrocene–Ferricenium System in the Biological Environment 92

Vol-3-Abdulaziz-FM.qxd 5/7/2004 10:57 AM Page ix

III. Polymer–Drug Conjugation as a Pharmaceutical Tool for Drug Delivery 98
IV. Polymer–Ferrocene Conjugates: Synthesis and Structure 100
A. The Carrier Component: Structural Considerations 101
B. Conjugates of Amide-Linked Ferrocene 102
C. Conjugates of Ester-Linked Ferrocene 109
V. Bioactivity Screening 110
VI. Summary and Conclusions 113
VII. Acknowledgments 115
VIII. References 115

7. Polymeric Platinum-Containing Drugs in the Treatment of Cancer 119
Deborah W. Siegmann-Louda and Charles E. Carraher Jr.

I. Introduction 120
II. Basic Mechanisms of Pt(II) Complex Formation 121
III. Nomenclature 125
IV. Currently Approved Platinum-Containing Compounds 125
V. Properties of Cisplatin 127
VI. Structure–Activity Relationships 130
VII. Polymer–Drug Conjugation Strategy and Possible Benefits 133
A. Polymers as Carriers 134
B. Polymers as Drugs 135
C. General 136
VIII. Mainchain-Incorporated *cis*-Diamine-Coordinated Platinum 137
A. Simple Amine Derivatives 137
B. Amino Acid Derivatives 141
C. Other Nitrogen–Platinum Products 143
D. Solution Stability 144
E. Thermal Stability 145
F. Antiviral Activity 145
IX. Platinum Carrier-Bound Complexes via Nitrogen Donor Ligands 147
A. Pt-Polyphosphazenes 147
B. Slowly Biofissionable Pt–N Complexes Anchored through Primary and Secondary Amines 149
C. Biofissionable Pt–N Complexes Anchored through Primary and Secondary Amines 154
X. Pt–O-Bound Polymers 161
XI. Mixed Pt–O/Pt–N-Bound Polymers 180
XII. Future Work 182
XIII. Acknowledgments 184
XIV. References 185

Vol-3-Abdulaziz-FM.qxd 5/7/2004 10:57 AM Page x

8. New Organic Polyacid–Inorganic Compounds for Improved Dental Materials **193**
Bill M. Culbertson, Minhhoa H. Dotrong, and Scott R. Schricker

I. Introduction 194
II. Glass Ionomer Technology 194
A. Amino Acid–Modified Glass Ionomers 198
B. *N*-Vinylpyrrolidone (NVP)-Modified Glass Ionomers 201
III. New NVP-Modified Glass Ionomers: Experimental Work 202
A. Materials 202
B. Polymer Synthesis 203
C. Characterization 203
D. Physical Properties 203
IV. Results and Discussion 204
V. Conclusions 205
VI. References 206

Index **209**