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Nota di contenuto	Chemistry for the 21st Century; Contents; 1 Some Reflections on Chemistry - Molecular, Supramolecular and Beyond; 1.1 From Structure to Information. The Challenge of Instructed Chemistry; 1.2 Steps Towards Complexity; 1.3 Chemistry and Biology, Creativity and Art; 2 Chemical Synthesis and Biological Studies of the Epothilones - Microtubule Stabilizing Agents with Enhanced Activity Against Multidrug Resistant Cell Lines and Tumors; 2.1 Introduction; 2.2 Total Synthesis of Epothilones; 2.3 First Generation Syntheses of Epothilones A and B; 2.4 First Generation Synthesis of the Acyl Domain 2.5 Investigation of C9-C10 Bond Construction Through Ring Closing Metathesis 2.6 B-Alkyl Suzuki Strategy; 2.7 Macrolactonization and Macroaldolization Approaches; 2.8 A New and More Efficient Synthesis of Epothilone B; 2.9 Dianion Equivalents Corresponding to the Polypropionate Domain of Epothilone B; 2.10 B-Alkyl Suzuki Merger; 2.11 Stereoselective Noyori Reduction; 2.12 Discovery of a Remarkable Long-Range Effect on the Double Diastereoface Selectivity in an Aldol Condensation; 2.13 Preparation of Other Epothilone Analogs; 2.14

## Biological Evaluation of Epothilones

2.15 SAR Analysis of Epothilones: The Zone Approach; 2.16 In Vitro Analysis Comparison to Paclitaxel and Related Agents; 2.17 In Vivo Analysis: Comparisons to Paclitaxel; 2.18 Conclusions; 2.19

Acknowledgements; 3 The Spirotetrahydrofuran Motif: its Role in Enhancing Ligation in Belted Ionophores, Biasing Cyclohexane Conformation, and Restricting Nucleoside/Nucleotide Conformation; 3.1 Introduction; 3.2 syn-1,3,5-Orientation on a Cyclohexane Core; 3.3 Maximally Substituted Hexa(spirotetrahydrofuranyl)-cyclohexanes; 3.4 Spirocyclic Restriction of Nucleosides/Nucleotides; 3.5

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Understanding; 4.1 Introduction; 4.2 A Case Study Ammonia Synthesis; 4.3 The Surface Science Approach; 4.4 The Atomic Mechanism of a Catalytic Reaction: Oxidation of Carbon Monoxide; 4.5 Further Aspects;

5 Drugs for a New Millennium; 5.1 Introduction; 5.2 Cell Death; 5.3 Stroke and Myocardial Infarct; 5.4 Schizophrenia; 5.4.1 Neuroleptic Drug Development; 5.4.2 Drug Psychoses; 5.5 Drugs of Abuse; 5.5.1 Definitions and Varieties; 5.5.2 Approaches to Treatment: Focus on Cocaine; 5.6 Conclusions and New Directions; 5.7 Acknowledgements

6 Protein Folding and Beyond; 6.1 Introduction; 6.1.1 Computational Protein Folding; 6.1.2 All-atom Simulations of Protein Unfolding and Short Peptide Folding; 6.2 All-Atom Simulations of Folding of Small Proteins; 6.2.1 Concomitant Hydrophobic Collapse and Partial Helix Formation; 6.2.2 A Marginally Stable Intermediate State; 6.3 A Perspective View; 7 The Enzymology of Biological Nitrogen Fixation; 7.1

Early History; 7.2 Practical Applications; 7.3 Biochemistry of N<sub>2</sub> Fixation; 7.4 First Product of N<sub>2</sub> Fixation; 7.5 Studies with <sup>15</sup>N as a Tracer; 7.6 N<sub>2</sub> Fixation with Cell-Free Preparations

7.7 Nitrogenase Consists of Two Proteins

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### Sommario/riassunto

Here, numerous winners of the Wolf prize from all chemical disciplines provide an overview of the new ideas and approaches that will shape this dynamic science over the forthcoming decades and so will have a decisive influence on our living conditions. This glimpse of the future is naturally based on the findings granted us by the rapid increase in chemical research during the 20th century. It may be said that a silent "revolution" took place, the positive results of which are still not fully predicted. For example, chemists in research laboratories nowadays are able to develop drugs

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