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5.3 Ligand Lipophilicity Efficiency Measures5.4 The Combined Influence of Efficiency Metrics and Physical Property Measures; 5.5 The Thermodynamics of Efficient Binding; 6 Conclusions; References; Improving Solubility via Structural Modification; 1 Introduction; 2 Description of Aqueous Solubility; 2.1 Definition of Solubility; 2.2 General Solubility Equation; 2.3 Solvation of Organic Molecules; 2.3.1 Effect of Molecular Size and Shape on Solvation; 2.3.2 Water-Solute Hydrogen Bonding; 2.4 Crystal Lattice Stability and Packing Efficiency; 2.4.1 Effect of Molecular Shape on Packing Efficiency
2.4.2 Intermolecular Interactions in the Solid State2.4.3 The Effect of Molecular Symmetry on Crystal Packing; 3 Tactics for Improving Solubility; 3.1 Reducing LogP; 3.1.1 Introducing a Solubilizing Appendage; Introducing Basic Appendages; Introducing Acidic Appendages; Introduction of Neutral Appendages; 3.1.2 Template and Substituent Modifications; Substituent Modifications; Analysis of Substituent Effects on Solubility; The Dual Nature of Fluorine; Intramolecular Interactions; Examples of Substituent Modifications; Template Modifications; 3.2 Disrupting Crystal Lattice Stability
3.2.1 Disruption of Intermolecular H-Bonding Interactions

Sommario/riassunto

Medicinal chemistry is both science and art. The science of medicinal chemistry offers mankind one of its best hopes for improving the quality of life. The art of medicinal chemistry continues to challenge its practitioners with the need for both intuition and experience to discover new drugs. Hence sharing the experience of drug research is uniquely beneficial to the field of medicinal chemistry. Drug research requires interdisciplinary team-work at the interface between chemistry, biology and medicine. Therefore, the topic-related series Topics in Medicinal Chemistry covers all relevant aspects of drug research, e.g. pathobiochemistry of diseases, identification and validation of (emerging) drug targets, structural biology, drugability of targets, drug design approaches, chemogenomics, synthetic chemistry including combinatorial methods, bioorganic chemistry, natural compounds, high-throughput screening, pharmacological in vitro and in vivo investigations, drug-receptor interactions on the molecular level, structure-activity relationships, drug absorption, distribution, metabolism, elimination, toxicology and pharmacogenomics. In general, special volumes are edited by well known guest editors.