

INTRODUCTION

CHRISTIAN REICHARDT

Department of Chemistry, Philipps University, Marburg, Germany

Chemical transformations can be performed in a gas, liquid, or solid phase, but, with good reasons, the majority of such reactions is carried out in the liquid phase in solution. At the macroscopic level, a liquid is the ideal medium to transport heat to and from exo- and endothermic reactions. From the molecular-microscopic point of view, solvents break the crystal lattice of solid reactants, dissolve gaseous or liquid reactants, and they may exert a considerable influence over reaction rates and the positions of chemical equilibria. Because of nonspecific and specific intermolecular forces acting between the ions or molecules of dissolved reactants, activated complexes as well as products and solvent molecules (leading to differential solvation of all solutes), the rates, equilibria, and the selectivity of chemical reactions can be strongly influenced by the solvent. Other than the fact that the liquid medium should dissolve the reactants and should be easily separated from the reaction products afterwards, the solvent can have a decisive influence on the outcome (i.e., yield and product distribution) of the chemical reaction under study. Therefore, whenever a chemist wishes to perform a certain chemical reaction, she/he has to take into account not only suitable reaction partners and their concentrations, the proper reaction vessel, the appropriate reaction temperature, and, if necessary, the selection of the right reaction catalyst but also, if the planned reaction is to be successful, the selection of an appropriate solvent or solvent mixture.

Solvent effects on chemical reactivity have been studied for more than a century, beginning with the pioneering work of Berthelot and Saint Gilles¹ in Paris in 1862 on esterification reactions and with that of Menshutkin² in St. Petersburg in 1880 on the quaternization of tertiary amines by haloalkanes. At this time Menshutkin remarked that “a reaction cannot be separated from the medium in which it is performed... Experience shows that solvents exert considerable influence on reaction rates.” Today, we can suggest a striking example to reinforce his remark, the rate of the unimolecular heterolysis of 2-chloro-2-methylpropane observed in water and benzene increases by a factor of approximately 10^{11} when the nonpolar benzene is replaced by water.^{3,4} The influence of solvents on the position of chemical equilibria was discovered in 1896 by Claisen⁵ in Aachen, Knorr⁶ in Jena, Wislicenus⁷ in Würzburg, and Hantzsch⁸ in Würzburg. They investigated almost simultaneous but independent of one another the keto-enol tautomerism of 1,3-dicarbonyl compounds and the nitro-isonitro tautomerism of primary and secondary

aliphatic nitro compounds. With this example, the enol content of acetylacetone increases from 62 to 95 % when acetonitrile is substituted with n-hexane.^{3,9}

The proper solvent and solvent mixture selection is not only important for chemical but also for physical processes such as recrystallization, all extraction processes, partitioning, chromatographic separations, phase-transfer catalytic reactions, etc. Of particular interest in this context is the influence of solvents on all types of light absorption processes, e.g., on UV/Vis, IR, ESR, and NMR spectra, caused by differential solvation of the ground and excited states of the absorbing species.^{3,12} In 1878, Kundt¹⁰ in Zürich proposed the rule that increasing dispersion interactions between the absorbing solute and the solvent lead in general to a bathochromic shift of an UV/Vis absorption band. Later, in 1922, Hantzsch¹¹ termed the solvent-dependence of UV/Vis absorption spectra “solvatochromism”. UV/Vis absorption of solute molecules can be influenced not only by the surrounding solvent sphere, but also by other entities in the surroundings such as solids, polymers, glasses, and surfaces. In order to emphasize this influence, the use of the more general term “perichromism” (from Greek *peri* = around) has been recommended.^{12,13} A typical, more recent, example of extraordinary solvatochromism is the intramolecular charge-transfer Vis-absorption of 2,6-diphenyl-4-(2,4,6-triphenyl-1-pyridinio)phenolate, a zwitterionic betaine dye: its corresponding absorption band is shifted from $\lambda_{\max} = 810$ nm to $\lambda_{\max} = 453$ nm ($\Delta\lambda = 357$ nm) when diphenyl ether is replaced by water as solvent.^{3,12} Such solvatochromic dyes can be used as empirical solvent polarity indicators.¹²

The number of solvents generally available to chemists working in research and industrial laboratories is between 250 and 300^{3,14} (there is an infinite number of solvent mixtures), and this number is increasing. More recently and for obvious reasons, the search for new solvents has been intensified: peroxide-forming solvents are being substituted by solvents which are more stable against oxidation (e.g., diethyl ether by t-butyl methyl ether or by formaldehyde dialkyl acetals), toxic solvents are being replaced by nontoxic ones (e.g., the cancerogenic hexamethylphosphoric triamide, HMPT, by N,N'-dimethylpropyleneurea, DMPU¹⁵) and environmentally dangerous solvents by benign ones (e.g., tetrachloromethane by perfluorohexane¹⁶). The development of modern solvents for organic syntheses is the subject of much current research.¹⁷ Amongst these modern solvents, also called “neoteric solvents” (neoteric = recent, new, modern) in contrast to the classical ones, are ionic liquids (i.e., room-temperature liquid salts such as 1-ethyl-3-methylimidazolium tetra-chloroaluminates^{18,19}), supercritical-fluid solvents, SCF, (such as SCF carbon dioxide^{20,21}), and perfluorinated solvents (e.g., partially or perfluorinated hydrocarbons as used in so-called “fluorous biphasic catalysis reactions”, making possible mono-phase reactions and a two-phase separation of catalyst and reaction products²²⁻²⁴). Even plain water has found a magnificent renaissance as a solvent for organic reactions.^{25,26} These efforts have also recently strengthened the search for completely solvent-free reactions, thus avoiding the use of expensive, toxic, and environmentally problematic solvents.^{27,28}

With respect to the large and still increasing number of valuable solvents useful for organic syntheses, a chemist needs, in addition to his experience and intuition, to have general rules, objective criteria, and the latest information about the solvents' physical, chemical, and toxicological properties for the selection of the proper solvent or solvent mixture for a planned reaction or a technological process. To make this often cumbersome and time-consuming task easier, this “Handbook of Solvents” with its twenty-five chapters is designed to provide a comprehensive source of information on solvents over a broad range

of applications. It is directed not only to chemists working in research laboratories, but also to all industries using solvents for various purposes. A particular advantage is that the printed handbook is accompanied by a compact-disc (CD-ROM) containing additional solvent databases with hundred ten fields for over eleven hundred solvents. This makes large data sets easily available for quick search and retrieval and frees the book text from bulky tables, thus giving more room for a thorough description of the underlying theoretical and practical fundamental subjects.

Fundamental principles governing the use of solvents (i.e., chemical structure, molecular design as well as physical and chemical properties of solvents) are given in Chapter 2. Solvent classification, methods of solvent manufacture together with properties and typical applications of various solvents are provided in Chapter 3. Chapters 4, 5 and 6 deal with all aspects of the dissolution of materials in solvents as well as with the solubility of selected systems (e.g., polymers and elastomers) and the influence of the solute's molecular structure on its solubility behavior. In particular, the valuable solubility-parameter concept is extensively treated in these chapters. All aspects of solvent transport within polymeric system and the drying of such polymeric systems, including coated films, are described in Chapter 7. The fundamentals of the interaction forces acting between ions or molecules of the solvents themselves and between solutes and solvents in solutions are presented in Chapter 8. Chapter 9 deals with the corresponding properties of solvent mixtures. Specific solute/solvent interactions, particularly Lewis acid/base interactions between electron-pair donors (EPD) and electron-pair acceptors (EPA), are reviewed in Chapter 10, together with the development of empirical scales of solvent polarity and Lewis acidity/basicity, based on suitable solvent-dependent reference processes, and their application for the treatment of solvent effects. The theory for solvent effects on electronic properties is provided in Chapter 11 and extended to solvent-dependent properties of solutes such as fluorescence spectra, ORD and CD spectra. Aggregation, swelling of polymers, their conformations, the viscosity of solutions and other solvent-related properties are treated in Chapter 12. A review concerning solvent effects on various types of chemical reactivity is given in Chapter 13, along with a discussion of the effects of solvent on free-radical polymerization and phase-transfer catalysis reactions.

The second part of this handbook (Chapters 14-25) is devoted more to the industrial use of solvents. Formulating with solvents applied in a broad range of industrial areas such as biotechnology, dry cleaning, electronic industry, food industry, paints and coatings, petroleum refining industry, pharmaceutical industry, textile industry, to mention only a few, is extensively described in Chapter 14. Standard and special methods of solvent detection and solvent analysis as well as the problem of residual solvents in various products, particularly in pharmaceutical ones, are the topics of Chapters 15 and 16.

At present, large-scale chemical manufacturing is facing serious solvent problems with respect to environmental concerns. National and international regulations for the proper use of hazardous solvents are becoming increasingly stringent and this requires the use of environmentally more benign but nevertheless economical liquid reaction media. This has enormously stimulated the search for such new solvent systems within the framework of so-called green chemistry. Supercritical fluids, SCF,^{20,21} and ionic liquids (room temperature liquid salts)^{18,19} have been known and have been the subject of scientific interest for a long time. It is only recently, however, that the potential benefits of these materials in solvent applications have been realized.¹⁷ This handbook includes in Chapters 17-25 all

the knowledge necessary for a safe handling of solvents in research laboratories and in large-scale manufacturing, beginning with the environmental impact of solvents on water, soil, and air in Chapter 17, followed by considerations about safe solvent concentrations and the risks of solvent exposure in various industrial environments in Chapter 18. Chapter 19 summarizes the corresponding legal regulations, valid for North America and Europe, and Chapter 20 describes in detail the toxic effects of solvent exposure to human beings. Authors specializing in different fields of solvent toxicity give the most current information on the effect of solvent exposure from the point of view of neurotoxicity, reproductive and maternal effects, nephrotoxicity, cancerogenicity, hepatotoxicity, chromosomal aberrations, and toxicity to brain, lungs, and heart. This information brings both the results of documented studies and an evaluation of risk in different industrial environments in a comprehensive but easy to understand form to engineers and decision-makers in industry. Chapter 21 is focused on the substitution of harmful solvents by safer ones and on the development of corresponding new technological processes. Chapter 22 describes modern methods of solvent recovery, solvent recycling. When recycling is not possible, then solvents have to be destroyed by incineration or other methods of oxidation, as outlined in Chapter 22. Chapter 23 describes natural attenuation of solvents in groundwater and advanced remediation technologies as well as management strategies for sites impacted by solvent contamination. Protection from contact with solvents and their vapors is discussed in Chapter 24. Finally, new trends in solvent chemistry and applications based on the recent patent literature are discussed in Chapter 25.

In most cases, the intelligent choice of the proper solvent or solvent mixture is essential for the realization of certain chemical transformations and physical processes. This handbook tries to cover all theoretical and practical information necessary for this often difficult task for both academic and industrial applications. It should be used not only by chemists, but also by physicists, chemical engineers, and technologists as well as environmental scientists in academic and industrial institutions. It is to be hoped that the present compilation of all relevant aspects connected with the use of solvents will also stimulate further basic and applied research in the still topical field of the physics and chemistry of liquid media.

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