Christian Reichardt

Solvents and Solvent Effects in Organic Chemistry

Third, Updated and Enlarged Edition

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To Maria
and in memory of my parents

Preface to the Third Edition

Meeting the demand for the second edition of this book, which is – despite a reprint in 1990 – no longer available, and considering the progress that has been made during the last decade in the study of solvent effects in experimental and theoretical organic chemistry, this improved third edition is presented to the interested reader.

Following the same layout as in the second edition, all topics retained have been brought up to date, with smaller and larger changes and additions on nearly every page. Two Sections (4.4.7 and 5.5.13) are completely new, dealing with solvent effects on host/guest complexation equilibria and reactions in biphasic solvent systems and neoteric solvents, respectively. More than 900 new references have been added, giving preference to review articles, and many older ones have been deleted. New references either replace older ones or are added to the end of the respective reference list of each chapter. The references cover the literature up to the end of 2001.

From the vast number of published papers dealing with solvent effects in all areas of organic chemistry, only some illustrative examples from the didactic and systematic point of view could be selected. This book is not a monograph covering *all* relevant literature in this field of research. The author, responsible for this subjective selection, apologizes in advance to all chemists whose valuable work on solvent effects is not mentioned in this book. However, using the reviews cited, the reader will find easy access to the full range of papers published in a certain field of research on solvent effects.

Great progress has been made during the last decade in theoretical treatments of solvent effects by various quantum-chemical methods and computational strategies. When indicated, relevant references are given to the respective solution reactions or absorptions. However, a critical evaluation of all the theoretical models and methods used to calculate the differential solvation of educts, activated complexes, products, ground and excited states, is outside the expertise of the present author. Thus, a book on all kinds of theoretical calculations of solvent influences on chemical reactions and physical absorptions has still to be written by someone else.

Consistent use of the nomenclature,[a)] symbols,[b)] terms,[c)] and SI units[d)] recommended by the IUPAC commissions has also been made in this third edition.

For comments and valuable suggestions I have to thank many colleagues, in particular Prof. E. M. Kosower, Tel Aviv/Israel, Prof. R. G. Makitra, Lviv/Ukraine, Prof. N. O. Mchedlov-Petrossyan, Kharkiv/Ukraine, and Prof. K. Möckel, Mühlhausen/Germany. For their assistance in drawing formulae, preparing the indices, and providing me with difficult to obtain literature, I thank Mr. G. Schäfer (technician), Mrs. S. Schellenberg (secretary), and Mrs. B. Becht-Schröder (librarian), all at the Department

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[a)] G. J. Leigh, H. A. Favre, and W. V. Metanomski: *Principles of Chemical Nomenclature – A Guide to IUPAC Recommendations*, Blackwell Science Publications, London, 1998.

[b)] I. Mills, T. Cvitas, K. Homann, N. Kallay, and K. Kuchitsu: *Quantities, Units and Symbols in Physical Chemistry*, 2nd ed., Blackwell Science Publications, London, 1993.

[c)] P. Müller: *Glossary of Terms used in Physical Organic Chemistry – IUPAC Recommendations 1994*, Pure Appl. Chem. *66*, 1077 (1994).

[d)] G. H. Aylward and T. J. V. Tristan: *SI Chemical Data*, 4th ed., Wiley, Chichester, 1999; *Datensammlung Chemie in SI-Einheiten*, 3rd ed., Wiley-VCH, Weinheim/Germany, 1999.

of Chemistry, Philipps University, Marburg/Germany. Special thanks are due to the staff of Wiley-VCH Verlag GmbH, Weinheim/Germany, particularly to Dr. Elke Westermann, for their fine work in turning the manuscript into the final book. Lastly, my biggest debt is to my wife Maria, not only for her assistance in the preparation of the manuscript, but also for her constant encouragement and support during the writing of this book.

Marburg (Lahn), Spring 2002 Christian Reichardt

Preface to the Second Edition

The response to the first English edition of this book, published in 1979, has been both gratifying and encouraging. Its mixed character, lying between that of a monograph and a textbook, has obviously made it attractive to both the industrial and academic chemist as well as the advanced student of chemistry.

During the last eight years the study of solvent effects on both chemical reactions and absorption spectra has made much progress, and numerous interesting and fascinating examples have been described in the literature. In particular, the study of ionic reactions in the gas phase – now possible due to new experimental techniques – has allowed direct comparisons between gas-phase and solution reactions. This has led to a greater understanding of solution reactions. Consequently, Chapters 4 and 5 have been enlarged to include a description of ionic gas-phase reactions compared to their solution counterparts.

The number of well-studied solvent-dependent processes, *i.e.* reactions and absorptions in solution, has increased greatly since 1979. Only a representative selection of the more instructive, recently studied examples could be included in this second edition.

The search for empirical parameters of solvent polarity and their applications in multiparameter equations has recently been intensified, thus making it necessary to rewrite large parts of Chapter 7.

Special attention has been given to the chemical and physical properties of organic solvents commonly used in daily laboratory work. Therefore, all Appendix Tables have been improved; some have been completely replaced by new ones. A new well-referenced table on solvent-drying has been added (Table A-3). Chapter 3 has been enlarged, in particular by the inclusion of solvent classifications using multivariate statistical methods (Section 3.5). All these amendments justify the change in the title of the book to *Solvents and Solvent Effects in Organic Chemistry*.

The references have been up-dated to cover literature appearing up to the first part of 1987. New references were added to the end of the respective reference list of each chapter from the first edition.

Consistent use of the nomenclature, symbols, terms, and SI units recommended by the IUPAC commissions has also been made in the second edition.*)

I am very indebted to many colleagues for corrections, comments, and valuable suggestions. Especially helpful suggestions came from Professors H.-D. Försterling, Marburg, J. Shorter, Hull/England, and R. I. Zalewski, Poznań/Poland, to whom I am very grateful. For critical reading of the whole manuscript and the improvement of my English I again thank Dr. Edeline Wentrup-Byrne, now living in Brisbane/Australia. Dr. P.-V. Rinze, Marburg, and his son Lars helped me with the author index. Finally, I would like to thank my wife Maria for her sympathetic assistance during the preparation of this edition and for her help with the indices.

Marburg (Lahn), Spring 1988 Christian Reichardt

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* *Cf.* Pure Appl. Chem. *51*, 1 (1979); ibid. *53*, 753 (1981); ibid. *55*, 1281 (1983); ibid. *57*, 105 (1985).

Preface to the First Edition

The organic chemist usually works with compounds which possess labile covalent bonds and are relatively involatile, thereby often rendering the gas-phase unsuitable as a reaction medium. Of the thousands of reactions known to occur in solution only few have been studied in the gas-phase, even though a description of reaction mechanisms is much simpler for the gas-phase. The frequent necessity of carrying out reactions in the presence of a more or less inert solvent results in two main obstacles: The reaction depends on a larger number of parameters than in the gas-phase. Consequently, the experimental results can often be only qualitatively interpreted because the state of aggregation in the liquid phase has so far been insufficiently studied. On the other hand, the fact that the interaction forces in solution are much stronger and more varied than in the gas-phase, permits to affect the properties and reactivities of the solute in manifold modes.

Thus, whenever a chemist wishes to carry out a chemical reaction he not only has to take into consideration the right reaction partners, the proper reaction vessels, and the appropriate reaction temperature. One of the most important features for the success of the planned reaction is the selection of a suitable solvent. Since solvent effects on chemical reactivity have been known for more than a century, most chemists are now familiar with the fact that solvents may have a strong influence on reaction rates and equilibria. Today, there are about three hundred common solvents available, nothing to say of the infinite number of solvent mixtures. Hence the chemist needs, in addition to his intuition, some general rules and guiding-principles for this often difficult choice.

The present book is based on an earlier paperback "Lösungsmitteleffekte in der organischen Chemie" [1], which, though following the same layout, has been completely rewritten, greatly expanded, and brought up to date. The book is directed both toward the industrial and academic chemist and particularly the advanced student of chemistry, who on the one hand needs objective criteria for the proper choice of solvent but on the other hand wishes to draw conclusions about reaction mechanisms from the observed solvent effects.

A knowledge of the physico-chemical principles of solvent effects is required for proper bench-work. Therefore, a description of the intermolecular interactions between dissolved molecules and solvent is presented first, followed by a classification of solvents derived therefrom. Then follows a detailed description of the influence of solvents on chemical equilibria, reaction rates, and spectral properties of solutes. Finally, empirical parameters of solvent polarity are given, and in an appendix guidelines to the everyday choice of solvents are given in a series of Tables and Figures.

The number of solvent systems and their associated solvent effects examined is so enormous that a complete description of all aspects would fill several volumes. For example, in Chemical Abstracts, volume 85 (1976), approximately eleven articles per week were quoted in which the words "Solvent effects on ..." appeared in the title. In the present book only a few important and relatively well-defined areas of general importance have been selected. The book has been written from the point of view of practical use for the organic chemist rather than from a completely theoretical one.

In the selection of the literature more recent reviews were taken into account mainly. Original papers were cited in particular from the didactic point of view rather than priority, importance or completeness. This book, therefore, does not only have the character of a monograph but also to some extent that of a textbook. In order to help the reader in his use of the literature cited, complete titles of the review articles quoted are given. The literature up until December 1977 has been considered together with a few papers from 1978. The use of symbols follows the recommendations of the Symbols Committee of the Royal Society, London, 1971 [2].

I am very grateful to Professor Karl Dimroth, Marburg, who first stimulated my interest in solvent effects in organic chemistry. I am indebted to Professors W. H. Pirkle, Urbana/Illinois, D. Seebach, Zürich/Switzerland, J. Shorter, Hull/England, and numerous other colleagues for helpful advice and information. Thanks are also due to the authors and publishers of copyrighted materials reproduced with their permission (cf. Figure and Table credits on page 495). For the careful translation and improvement of the English manuscript I thank Dr. Edeline Wentrup-Byrne, Marburg. Without the assistance and patience of my wife Maria, this book would not have been written.

Marburg (Lahn), Summer 1978 Christian Reichardt

References

[1] C. Reichardt: *Lösungsmitteleffekte in der organischen Chemie*. 2nd edition. Verlag Chemie, Weinheim 1973;
Effets de solvant en chimie organique (translation of the first-mentioned title into French, by I. Tkatchenko), Flammarion, Paris 1971;
Rastvoriteli v organicheskoi khimii (translation of the first-mentioned title into Russian, by E. R. Zakhsa), Izdatel'stvo Khimiya, Leningrad 1973.

[2] *Quantities, Units, and Symbols*, issued by The Symbols Committee of the Royal Society, London, in 1971.

Contents

List of Abbreviations

Abbreviations and Recommended Values of Some Fundamental Constants and Numbers[a,b]

N_A	Avogadro constant	$6.0221 \cdot 10^{23}$ mol^{-1}
c_0	speed of light in vacuum	$2.9979 \cdot 10^{8}$ m $\cdot$ s^{-1}
ε_0	absolute permittivity of vacuum [$= 1/(\mu_0 \cdot c_0{}^2)$; μ_0 = permeability of vacuum]	$8.8542 \cdot 10^{-12}$ C$^2 \cdot$ J$^{-1} \cdot$ m^{-1}
e	elementary charge	$1.6022 \cdot 10^{-19}$ C
h	Planck constant	$6.6261 \cdot 10^{-34}$ J $\cdot$ s
R	gas constant	8.3145 J $\cdot$ K$^{-1} \cdot$ mol^{-1} (or 0.08206 L $\cdot$ atm $\cdot$ K$^{-1} \cdot$ mol^{-1})
k_B	Boltzmann constant ($= R/N_A$)	$1.3807 \cdot 10^{-23}$ J $\cdot$ K^{-1}
V_m	standard molar volume of an ideal gas (at $t = 0$ °C and $p = 100$ kPa)	22.711 L $\cdot$ mol^{-1}
T_0	zero of the Celsius scale	273.15 K
π	ratio of the circumference to the diameter of a circle	3.1416
e	exponential number and base of natural logarithms (ln)	2.7183
ln 10	natural logarithm of ten (ln x = ln 10 $\cdot$ lg x; lg = decadic logarithm)	2.303

Abbreviations and Symbols for Units[a,b]

bar	bar ($= 10^5$ Pa $= 10^5$ N $\cdot$ m^{-2})	pressure
cg/g	centigram/gram	weight percent
cL/L, cl/l	centilitre/litre	volume percent
cmol/mol	centimol/mol	mole percent
cm	centimetre (10^{-2} m)	length
cm^3	cubic centimetre (millilitre mL; 10^{-6} m^3)	volume
C	coulomb	electric charge

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[a] I. Mills, T. Cvitaš, K. Homann, N. Kallay, and K. Kuchitsu: *Quantities, Units and Symbols in Physical Chemistry*. 2nd ed., Blackwell Scientific Publications, London, 1993.

[b] G. H. Aylward and T. J. V. Tristan: *SI Chemical Data*. 4th ed., Wiley, Chichester, 1999; *Datensammlung Chemie in SI-Einheiten*. 3rd ed., Wiley-VCH, Weinheim/Germany, 1999.

°C	degrees centigrade (Celsius)	temperature
dm^3	cubic decimetre (litre L; 10^{-3} m^3)	volume
J	joule	energy
kJ	kilojoule (10^3 J)	energy
K	kelvin	temperature
L, l	litre (1 dm^3; 10^{-3} m^3)	volume
m	metre	length
min	minute	time
mol	mole	amount of substance
MPa	megapascal (10^6 Pa)	pressure
mT	millitesla (10^{-3} T)	magnetic flux density (magnetic field)
nm	nanometre (10^{-9} m)	length
Pa	pascal ($1\ N \cdot m^{-2} = 10^{-5}$ bar)	pressure
percent (%)	part per hundred (10^{-2})	dimensionless fraction
ppm	part per million (10^{-6})	dimensionless fraction
s	second	time

Abbreviations and Symbols for Properties[c)]

a_i	activity of solute i	
$a(^1H)$	ESR hyperfine coupling constant (coupling with ^1H)	mT ($= 10^{-3}$ T)
A_j	the solvent's anion-solvating tendency or 'acity' (Swain)	
AN	solvent acceptor number, based on ^{31}P NMR chemical shift of Et_3PO (Gutmann and Meyer)	
α	electric polarizability of a molecule, polarizability volume	$C^2 \cdot m^2 \cdot J^{-1}$ or $4\pi\varepsilon_0 \cdot cm^3$
α	empirical parameter of solvent hydrogen-bond donor acidity (Taft and Kamlet)	
B	empirical parameter of solvent Lewis basicity (Palm and Koppel)	
B_{MeOD}	IR based empirical parameter of solvent Lewis basicity (Palm and Koppel)	

[c)] P. Müller: *Glossary of Terms used in Physical Organic Chemistry – IUPAC Recommendations 1994*. Pure Appl. Chem. *66*, 1077 (1994).

B_{PhOH}	IR based empirical parameter of solvent Lewis basicity (Koppel and Paju; Makitra)	
B_{j}	the solvent's cation-solvating tendency or 'basity' (Swain)	
β	empirical parameter of solvent hydrogen-bond acceptor basicity (Taft and Kamlet)	
c	cohesive pressure (cohesive energy density) of a solvent	MPa (= 10^6 Pa)
$c_{\mathrm{i}}, c(\mathrm{i})$	molar concentration of solute i	$\mathrm{mol \cdot L^{-1}}$
$C_{\mathrm{A}}, C_{\mathrm{B}}$	Lewis acidity and Lewis basicity parameter (Drago)	
cmc	critical micelle concentration	$\mathrm{mol \cdot L^{-1}}$
D_{HA}	molar bond-dissociation energy of the bond between H and A	$\mathrm{kJ \cdot mol^{-1}}$
D_{π}	empirical parameter of solvent Lewis basicity, based on a 1,3-dipolar cycloaddition reaction (Nagai *et al.*)	
DN	solvent donor number (Gutmann) [$= -\Delta H(\mathrm{D{-}SbCl_5})$]	$\mathrm{kcal \cdot mol^{-1}}$
DN^{N}	normalized solvent donor number (Marcus)	
$\delta, \delta_{\mathrm{H}}$	Hildebrand's solubility parameter	$\mathrm{MPa^{1/2}}$
δ	chemical shift of NMR signals	ppm
δ	solvent polarizability correction term (Taft and Kamlet)	
E	energy, molar energy	$\mathrm{kJ \cdot mol^{-1}}$
E	electric field strength	$\mathrm{V \cdot m^{-1}}$
E	enol constant (K. H. Meyer)	
E	empirical parameter of solvent Lewis acidity (Palm and Koppel)	
$E_{\mathrm{A}}, E_{\mathrm{a}}$	Arrhenius activation energy	$\mathrm{kJ \cdot mol^{-1}}$
$E_{\mathrm{A}}, E_{\mathrm{B}}$	Lewis acidity and Lewis basicity parameter (Drago)	
EA	electron affinity	$\mathrm{kJ \cdot mol^{-1}}$
$E_{\mathrm{B}}^{\mathrm{N}}$	empirical solvent Lewis basicity parameter, based on the $n \rightarrow \pi^*$ absorption of an aminyloxide radical (Mukerjee; Wrona)	
E_{K}	empirical solvent polarity parameter, based on the $d \rightarrow \pi^*$ absorption of a molybdenum complex (Walther)	$\mathrm{kcal \cdot mol^{-1}}$

E^*_{MLCT}	empirical solvent polarity parameter, based on the $d \rightarrow \pi^*$ absorption of a tungsten complex (Lees)	
E_{T}	molar electronic *t*ransition *e*nergy, molar electronic excitation energy	$\mathrm{kJ \cdot mol^{-1}}$ or $\mathrm{kcal \cdot mol^{-1}}$
$E_{\mathrm{T}}(30)$	empirical solvent polarity parameter, based on the intramolecular CT absorption of a pyridinium-*N*-phenolate betaine dye (Dimroth and Reichardt)	$\mathrm{kcal \cdot mol^{-1}}$
$E_{\mathrm{T}}^{\mathrm{N}}$	normalized $E_{\mathrm{T}}(30)$ solvent polarity parameter (Reichardt)	
$E_{\mathrm{T}}^{\mathrm{SO}}$	empirical solvent polarity parameter, based on the $n \rightarrow \pi^*$ absorption of an *S*-oxide (Walter)	$\mathrm{kcal \cdot mol^{-1}}$
EPA	electron-pair acceptor	
EPD	electron-pair donor	
ε_{r}	relative permittivity ($=\varepsilon/\varepsilon_0$) ("dielectric constant")	
Φ	empirical solvent polarity parameter, based on the $n \rightarrow \pi^*$ absorption of ketones (Dubois)	
G	IR based empirical solvent polarity parameter (Schleyer and Allerhand)	
ΔG°	standard molar Gibbs energy change	$\mathrm{kJ \cdot mol^{-1}}$
$\Delta G^{\neq}$	standard molar Gibbs energy of activation	$\mathrm{kJ \cdot mol^{-1}}$
$\Delta G^\circ_{\mathrm{solv}}$	standard molar Gibbs energy of solvation	$\mathrm{kJ \cdot mol^{-1}}$
$\Delta G^\circ_{\mathrm{hydr}}$	standard molar Gibbs energy of hydration	$\mathrm{kJ \cdot mol^{-1}}$
$\Delta G^\circ_{\mathrm{t}}(\mathrm{X, O \rightarrow S})$, $\Delta G^\circ_{\mathrm{t}}(\mathrm{X, W \rightarrow S})$	standard molar Gibbs energy of transfer of solute X from a reference solvent (O) or water (W) to another solvent (S)	$\mathrm{kJ \cdot mol^{-1}}$
γ_{i}	activity coefficient of solute i	
ΔH°	standard molar enthalpy change	$\mathrm{kJ \cdot mol^{-1}}$
$\Delta H^{\neq}$	standard molar enthalpy of activation	$\mathrm{kJ \cdot mol^{-1}}$
ΔH_{v}	molar enthalpy (heat) of vapourization	$\mathrm{kJ \cdot mol^{-1}}$
H_0	acidity function (Hammett)	
HBA	hydrogen-bond acceptor	

HBD	hydrogen-bond donor	
HOMO	highest occupied molecular orbital	
E_i, I, IP	ionization energy	$kJ \cdot mol^{-1}$
I	gas-chromatographic retention index (Kováts)	
J	NMR spin-spin coupling constant	Hz
k	rate constant for monomolecular ($n = 1$) and bimolecular ($n = 2$) reactions	$(L \cdot mol^{-1})^{n-1} \cdot s^{-1}$
k_0	rate constant in a reference solvent or in the gas phase for monomolecular ($n = 1$) and bimolecular reactions ($n = 2$)	$(L \cdot mol^{-1})^{n-1} \cdot s^{-1}$
k_0	in Hammett equations the rate constant of unsubstituted substrates	$(L \cdot mol^{-1})^{n-1} \cdot s^{-1}$ with $n = 1$ or 2
K, K_c	equilibrium constant (concentration basis; v = stoichiometric number)	$(mol \cdot L^{-1})^{\Sigma v}$
K_a, K_b	acid and base ionization constants	$(mol \cdot L^{-1})^{\Sigma v}$
K_{auto}	autoionization ion product, autoprotolysis constant	$mol^2 \cdot L^{-2}$
$K_{Assoc}, K_{Dissoc}, K_{ion}, K_T$	equilibrium constants of association, dissociation, ionization, resp. tautomerization reactions	$(mol \cdot L^{-1})^{\Sigma v}$
$K_{o/w}$	1-octanol/water partition constant (Hansch and Leo)	
KB	kauri-butanol number	
L	desmotropic constant (K. H. Meyer)	
LUMO	lowest unoccupied molecular orbital	
λ	wavelength	nm ($= 10^{-9}$ m)
m	mass of a particle	g
M_r	relative molecular mass of a substance ("molecular weight")	
M	miscibility number (Godfrey)	
MH	microscopic hydrophobicity parameter of substituents (Menger)	
μ	empirical solvent softness parameter (Marcus)	
μ	permanent electric dipole moment of a molecule	$C \cdot m$ (or D)
μ_{ind}	induced electric dipole moment of a molecule	$C \cdot m$ (or D)

μ_i°	standard chemical potential of solute i	$kJ \cdot mol^{-1}$
μ_i^∞	standard chemical potential of solute i at infinite dilution	$kJ \cdot mol^{-1}$
n, n_D	refractive index (at sodium D line) $(= c_0/c)$	
N	empirical parameter of solvent nucleophilicity (Winstein and Grunwald)	
N_+	nucleophilicity parameter for (nucleophile + solvent)-systems (Ritchie)	
ν	frequency	Hz, s^{-1}
ν°	frequency in the gas phase or in an inert reference solvent	Hz, s^{-1}
$\tilde{\nu}$	wavenumber $(= 1/\lambda)$	cm^{-1}
Ω	empirical solvent polarity parameter, based on a Diels-Alder reaction (Berson)	
p	pressure	Pa $(= 1 N \cdot m^{-2})$, bar $(= 10^5$ Pa)
P	measure of solvent polarizability (Palm and Koppel)	
P	empirical solvent polarity parameter, based on ^{19}F NMR measurements (Taft)	
PA	proton affinity	$kJ \cdot mol^{-1}$
Py	empirical solvent polarity parameter, based on the $\pi^* \rightarrow \pi$ emission of pyrene (Winnik)	
$P_{o/w}$	1-octanol/water partition coefficient (Hansch and Leo)	
pH	$-\lg[H_3O^+]$, $-\lg c(H_3O^+)$ (abbreviation of *p*otentia *h*ydrogenii or *p*uissance d'*h*ydrogène (Sörensen 1909)	
pK	$-\lg K$	
π	internal pressure of a solvent	MPa $(= 10^6$ Pa)
π^*	empirical solvent dipolarity/polarizability parameter, based on the $\pi \rightarrow \pi^*$ absorption of substituted aromatics (Taft and Kamlet)	

π^*_{azo}	empirical solvent dipolarity/polarizability parameter, based on the $\pi \rightarrow \pi^*$ absorption of azo merocyanine dyes (Buncel)	
π_{X}	hydrophobicity parameter of substituent X in H_5C_6-X (Hansch)	
r	radius of sphere representing an ion or a cavity	cm ($= 10^{-2}$ m)
r	distance between centres of two ions or molecules	cm ($= 10^{-2}$ m)
ρ	density (mass divided by volume)	$\mathrm{g \cdot cm^{-3}}$
ρ, ρ_{A}	Hammett reaction resp. absorption constants	
S	generalized for solvent	
S	empirical solvent polarity parameter, based on the Z-values (Brownstein)	
$\mathscr{S}$	lg k_2 for the Menschutkin reaction of tri-*n*-propylamine with iodomethane (Drougard and Decroocq)	
ΔS°	standard molar entropy change	$\mathrm{J \cdot K^{-1} \cdot mol^{-1}}$
$\Delta S^{\neq}$	standard molar entropy of activation	$\mathrm{J \cdot K^{-1} \cdot mol^{-1}}$
S_{p}	solvophobic power of a solvent (Abraham)	
SA	empirical parameter of solvent hydrogen-bond donor acidity (Catalán)	
SB	empirical parameter of solvent hydrogen-bond acceptor basicity (Catalán)	
SPP	empirical parameter of solvent dipolarity/polarizability, based on the $\pi \rightarrow \pi^*$ absorption of substituted 7-nitrofluorenes (Catalán)	
σ	Hammett substituent constant	
σ	NMR screening constant	
t	Celsius temperature	°C
T	thermodynamic temperature	K
t_{mp}	melting point	°C
t_{bp}	boiling point	°C
U	internal energy	kJ
ΔU_{v}	molar energy of vapourization	$\mathrm{kJ \cdot mol^{-1}}$

$V_\mathrm{m}, V_\mathrm{m,i}$	molar volume (of i)	$\mathrm{cm}^3 \cdot \mathrm{mol}^{-1}$
$\Delta V^{\neq}$	molar volume of activation	$\mathrm{cm}^3 \cdot \mathrm{mol}^{-1}$
$x_\mathrm{i}, x(\mathrm{i})$	mole fraction of i ($x_\mathrm{i} = n_\mathrm{i}/\sum n$)	
X	empirical solvent polarity parameter, based on an $\mathrm{S_E2}$ reaction (Gielen and Nasielski)	
$\chi_\mathrm{R}, \chi_\mathrm{B}$	empirical solvent polarity parameters, based on the $\pi \rightarrow \pi^*$ absorption of merocyanine dyes (Brooker)	$\mathrm{kcal} \cdot \mathrm{mol}^{-1}$
${}^\mathrm{O}y_\mathrm{X}^\mathrm{S}, {}^\mathrm{W}y_\mathrm{X}^\mathrm{S}$	solvent-transfer activity coefficient of a solute X from a reference solvent (O) or water (W) to another solvent (S)	
Y	empirical parameter of solvent ionizing power, based on *t*-butyl chloride solvolysis (Winstein and Grunwald)	
Y_OTs	empirical parameter of solvent ionizing power, based on 2-adamantyl tosylate solvolysis (Schleyer and Bentley)	
Y	measure of solvent polarization (Palm and Koppel)	
z_i	charge number of an ion i	positive for cations, negative for anions
Z	empirical solvent polarity parameter, based on the intermolecular CT absorption of a substituted pyridinium iodide (Kosower)	$\mathrm{kcal} \cdot \mathrm{mol}^{-1}$

"*Agite, Auditores ornatissimi, transeamus alacres ad aliud negotii! quum enim sic satis excusserimus ea quatuor Instrumenta artis, et naturae, quae modo relinquimus, videamus quintum genus horum, quod ipsi Chemiae fere proprium censetur, cui certe Chemistae principem locum prae omnibus assignant, in quo se jactant, serioque triumphant, cui artis suae, prae aliis omnibus effectus mirificos adscribunt. Atque illud quidem Menstruum vocaverunt.*"*⁾

Hermannus Boerhaave (1668–1738)
De menstruis dictis in chemia, in:
Elementa Chemiae (1733) [1, 2].

1 Introduction

The development of our knowledge of solutions reflects to some extent the development of chemistry itself [3]. Of all known substances, water was the first to be considered as a solvent. As far back as the time of the Greek philosophers there was speculation about the nature of solution and dissolution. The Greek alchemists considered all chemically active liquids under the name "Divine water". In this context the word "water" was used to designate everything liquid or dissolved.

The alchemist's search for a universal solvent, the so-called "Alkahest" or "Menstruum universale", as it was called by Paracelsus (1493–1541), indicates the importance given to solvents and the process of dissolution. Although the eager search of the chemists of the 15th to 18th centuries did not in fact lead to the discovery of any "Alkahest", the numerous experiments performed led to the uncovering of new solvents, new reactions, and new compounds**⁾. From these experiences arose the earliest chemical rule that "like dissolves like" *(similia similibus solvuntur)*. However, at that time, the words solution and dissolution comprised all operations leading to a liquid product and it was still a long way to the conceptual distinction between the physical dissolution of a salt or of sugar in water, and the chemical change of a substrate by dissolution, for example, of a metal in an acid. Thus, in the so-called chemiatry period (iatrochemistry period), it was believed that the nature of a substance was fundamentally lost upon dissolution. Van Helmont (1577–1644) was the first to strongly oppose this contention. He claimed that the dissolved substance had not disappeared, but was present in the solution, although in aqueous form, and could be recovered [4]. Nevertheless, the dissolution

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* "Well then, my dear listeners, let us proceed with fervor to another problem! Having sufficiently analyzed in this manner the four resources of science and nature, which we are about to leave (*i.e.* fire, water, air, and earth) we must consider a fifth element which can almost be considered the most essential part of chemistry itself, which chemists boastfully, no doubt with reason, prefer above all others, and because of which they triumphantly celebrate, and to which they attribute above all others the marvellous effects of their science. And this they call the solvent (menstruum)."

** Even if the once famous scholar J. B. Van Helmont (1577–1644) claimed to have prepared this "Alkahest" in a phial, together with the adherents of the alkahest theory he was ridiculed by his contemporaries who asked in which vessel he has stored this universal solvent.

of a substance in a solvent remained a rather mysterious process. The famous Russian polymath Lomonosov (1711–1765) wrote in 1747: "Talking about the process of dissolution, it is generally said that all solvents penetrate into the pores of the body to be dissolved and gradually remove its particles. However, concerning the question of what forces cause this process of removal, there does not exist any somehow reasonable explanation, unless one arbitrarily attributes to the solvents sharp wedges, hooks or, who knows, any other kind of tools" [27].

The further development of modern solution theory is connected with three persons, namely the French researcher Raoult (1830–1901) [28], the Dutch physical chemist van't Hoff (1852–1911) [5], and the Swedish scientist Arrhenius (1859–1927) [6]. Raoult systematically studied the effects of dissolved nonionic substances on the freezing and boiling point of liquids and noticed in 1886 that changing the solute/solvent ratio produces precise proportional changes in the physical properties of solutions. The observation that the vapour pressure of solvent above a solution is proportional to the mole fraction of solvent in the solution is today known as Raoult's law [28].

The difficulty in explaining the effects of inorganic solutes on the physical properties of solutions led in 1884 to Arrhenius' theory of incomplete and complete dissociation of ionic solutes (electrolytes, ionophores) into cations and anions in solution, which was only very reluctantly accepted by his contemporaries. Arrhenius derived his dissociation theory from comparison of the results obtained by measurements of electroconductivity and osmotic pressure of dilute electrolyte solutions [6].

The application of laws holding for gases to solutions by replacing pressure by osmotic pressure was extensively studied by van't Hoff, who made osmotic pressure measurements another important physicochemical method in studies of solutions [5].

The integration of these three basic developments established the foundations of modern solution theory and the first Nobel prizes in chemistry were awarded to van't Hoff (in 1901) and Arrhenius (in 1903) for their work on osmotic pressure and electrolytic dissociation, respectively.

The further development of solution chemistry is connected with the pioneering work of Ostwald (1853–1932), Nernst (1864–1941), Lewis (1875–1946), Debye (1884–1966), E. Hückel (1896–1980), and Bjerrum (1879–1958). More detailed reviews on the development of modern solution chemistry can be found in references [29, 30].

The influence of solvents on the rates of chemical reactions [7, 8] was first noted by Berthelot and Péan de Saint-Gilles in 1862 in connection with their studies on the esterification of acetic acid with ethanol: "… l'éthérification est entravée et ralentie par l'emploi des dissolvants neutres étrangers à la réaction" [9][*]. After thorough studies on the reaction of trialkylamines with haloalkanes, Menschutkin in 1890 concluded that a reaction cannot be separated from the medium in which it is performed [10]. In a letter to Prof. Louis Henry he wrote in 1890: "Or, l'expérience montre que ces dissolvants exercent sur la vitesse de combinaison une influence considérable. Si nous représentons par 1 la constante de vitesse de la réaction précitée dans l'hexane C_6H_{14}, cette constante pour la même combinaison dans $CH_3—CO—C_6H_5$, toutes choses égales d'ailleurs sera 847.7. La différence est énorme, mais, dans ce cas, elle n'atteint pas encore le maxi-

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[*] "… the esterification is disturbed and decelerated on addition of neutral solvents not belonging to the reaction" [9].

mum.... Vous voyez que les dissolvants, soi-disant indifférents ne sont pas inertes; ils modifient profondément l'acte de la combinaison chimique. Cet énoncé est riche en conséquences pour la théorie chimique des dissolutions" [26]*). Menschutkin also discovered that, in reactions between liquids, one of the reaction partners may constitute an unfavourable solvent. Thus, in the preparation of acetanilide, it is not without importance whether aniline is added to an excess of acetic acid, or *vice versa*, since aniline in this case is an unfavorable reaction medium. Menschutkin related the influence of solvents primarily to their chemical, not their physical properties.

The influence of solvents on chemical equilibria was discovered in 1896, simultaneously with the discovery of keto-enol tautomerism**) in 1,3-dicarbonyl compounds (Claisen [14]: acetyldibenzoylmethane and tribenzoylmethane; Wislicenus [15]: methyl and ethyl formylphenylacetate; Knorr [16]: ethyl dibenzoylsuccinate and ethyl diacetylsuccinate) and the nitro-isonitro tautomerism of primary and secondary nitro compounds (Hantzsch [17]: phenylnitromethane). Thus, Claisen wrote: "Es gibt Verbindungen, welche sowohl in der Form $\text{—C(OH)=}\overset{|}{\text{C}}\text{—CO—}$ wie in der Form $\text{—CO—}\overset{|}{\text{C}}\text{H—CO—}$ zu bestehen vermögen; von der Natur der angelagerten Reste, von der Temperatur, bei den gelösten Substanzen auch von der Art des Lösungsmittels hängt es ab, welche von den beiden Formen die beständigere ist" [14]***). The study of the keto-enol equilibrium of ethyl formylphenylacetate in eight solvents led Wislicenus to the conclusion that the keto form predominates in alcoholic solution, the enol form in chloroform or benzene. He stated that the final ratio in which the two tautomeric forms coexist must depend on the nature of the solvent and on its dissociating power, whereby he suggested that the dielectric constants were a possible measure of this "power". Stobbe was the first to review these results [18]. He divided the solvents into two groups according to their ability to isomerize tautomeric compounds. His classification reflects, to some extent, the modern division into protic and aprotic solvents. The effect of solvent on constitutional and tautomeric isomerization equilibria was later studied in detail

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[*] "Now, experience shows that solvents exert considerable influence on reaction rates. If we represent the rate constant of the reaction to be studied in hexane C_6H_{14} by 1, then, all else being equal, this constant for the same reaction in CH_3—CO—C_6H_5 will be 847.7. The increase is enormous, but in this case it has not even reached its maximum.... So you see that solvents, in spite of appearing at first to be indifferent, are by no means inert; they can greatly influence the course of chemical reactions. This statement is full of consequences for the chemical theory of dissolutions" [26].

[**] The first observation of a tautomeric equilibrium was made in 1884 by Zincke at Marburg [11]. He observed that, surprisingly, the reaction of 1,4-naphthoquinone with phenylhydrazine gives the same product as that obtained from the coupling reaction of 1-naphthol with benzenediazonium salts. This phenomenon, that the substrate can react either as phenylhydrazone or as a hydroxyazo compound, depending on the reaction circumstances, was called *Ortsisomerie* by Zincke [11]. Later on, the name *tautomerism*, with a different meaning however from that accepted today, was introduced by Laar [12]. For a description of the development of the concept of tautomerism, see Ingold [13].

[***] "There are compounds capable of existence in the form $\text{—C(OH)=}\overset{|}{\text{C}}\text{—CO—}$ as well as in the form $\text{—CO—}\overset{|}{\text{C}}\text{H—CO—}$; it depends on the nature of the substituents, the temperature, and for dissolved compounds, also on the nature of the solvent, which of the two forms will be the more stable" [14].

by Dimroth [19] (using triazole derivatives, *e.g.* 5-amino-4-methoxycarbonyl-1-phenyl-1,2,3-triazole) and Meyer [20] (using ethyl acetoacetate).

It has long been known that UV/Vis absorption spectra may be influenced by the phase (gas or liquid) and that the solvent can bring about a change in the position, intensity, and shape of the absorption band*). Hantzsch later termed this phenomenon *solvatochromism***) [22]. The search for a relationship between solvent effect and solvent property led Kundt in 1878 to propose the rule, later named after him, that increasing dispersion (*i.e.* increasing index of refraction) is related to a shift of the absorption maximum towards longer wavelength [23]. This he established on the basis of UV/Vis absorption spectra of six dyestuffs, namely chlorophyll, fuchsin, aniline green, cyanine, quinizarin, and egg yolk in twelve different solvents. The – albeit limited – validity of Kundt's rule, *e.g.* found in the cases of 4-hydroxyazobenzene [24] and acetone [25], led to the realization that the effect of solvent on dissolved molecules is a result of electrical fields. These fields in turn originate from the dipolar properties of the molecules in question [25]. The similarities in the relationships between solvent effects on reaction rate, equilibrium position, and absorption spectra has been related to the general solvating ability of the solvent in a fundamental paper by Scheibe *et al.* [25].

More recently, research on solvents and solutions has again become a topic of interest because many of the solvents commonly used in laboratories and in the chemical industry are considered as unsafe for reasons of environmental protection. On the list of damaging chemicals, solvents rank highly because they are often used in huge amounts and because they are volatile liquids that are difficult to contain. Therefore, the introduction of cleaner technologies has become a major concern throughout both academia and industry [31–34]. This includes the development of environmentally benign new solvents, sometimes called *neoteric solvents* (neoteric = recent, new, modern), constituting a class of novel solvents with desirable, less hazardous, new properties [35, 36]. The term *neoteric solvents* covers supercritical fluids, ionic liquids, and also perfluorohydrocarbons (as used in fluorous biphasic systems). Table A-14 in Chapter A.10 (Appendix) collects some recommendations for the substitution of hazardous solvents, together with the relevant literature references.

For the development of a sustainable chemistry based on clean technologies, the best solvent would be no solvent at all. For this reason, considerable efforts have recently been made to design reactions that proceed under solvent-free conditions, using modern techniques such as reactions on solid mineral supports (alumina, silica, clays), solid-state reactions without any solvent, support, or catalyst between neat reactants, solid-liquid phase-transfer catalysed and microwave-activated reactions, as well as gas-phase reactions [37–42]. However, not all organic reactions can be carried out in the absence of a solvent; some organic reactions even proceed explosively in the solid state! Therefore, solvents will still be useful in mediating and moderating chemical reactions and this book on solvent effects will certainly not become superfluous in the foreseeable future.

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* A survey of older works of solvent effects on UV/Vis absorption spectra has been given by Sheppard [21].

** It should be noted that the now generally accepted meaning of the term *solvatochromism* differs from that introduced by Hantzsch (*cf.* Section 6.2).