

Modern Solvents in Organic Synthesis

Volume Editor: Paul Knochel

With contributions by

J. Augé, B. Betzemeier, B. Cornils, D. P. Curran,
P. Knochel, W. Leitner, B. Linclau, A. Loupy,
A. Lubineau, J. J. Maul, P. J. Ostrowski, D. Sinou,
G. A. Ublacker



Springer

This series presents critical reviews of the present position and future trends in modern chemical research. It is addressed to all research and industrial chemists who wish to keep abreast of advances in the topics covered.

As a rule, contributions are specially commissioned. The editors and publishers will, however, always be pleased to receive suggestions and supplementary information. Papers are accepted for "Topics in Current Chemistry" in English.

In references Topics in Current Chemistry is abbreviated Top. Curr. Chem. and is cited as a journal.

Springer WWW home page: <http://www.springer.de>

Visit the TCC home page at <http://www.springer.de/>

ISSN 0340-1022

ISBN 3-540-66213-8

Springer-Verlag Berlin Heidelberg New York

Library of Congress Catalog Card Number 74-644622

This work is subject to copyright. All rights are reserved, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other ways, and storage in data banks. Duplication of this publication or parts thereof is only permitted under the provisions of the German Copyright Law of September 9, 1965, in its current version, and permission for use must always be obtained from Springer-Verlag. Violations are liable for prosecution under the German Copyright Law.

© Springer-Verlag Berlin Heidelberg 1999

Printed in Germany

The use of general descriptive names, registered names, trademarks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

Cover design: Friedhelm Steinen-Broo, Barcelona; MEDIO, Berlin

Typesetting: Fotosatz-Service Köhler GmbH, 97084 Würzburg

SPIN: 10669000 02/3020 – 5 4 3 2 1 0 – Printed on acid-free paper

206

Topics in Current Chemistry

Editorial Board:

A. de Meijere · K.N. Houk · H. Kessler

J.-M. Lehn · S.V. Ley · S.L. Schreiber · J. Thiem

B.M. Trost · F. Vögtle · H. Yamamoto

Springer

Berlin

Heidelberg

New York

Barcelona

Hong Kong

London

Milan

Paris

Singapore

Tokyo

Volume Editor

Prof. Paul Knochel

Ludwig Maximilians-Universität München
Institut für Organische Chemie
Butenanderstr. 5 – 13
D-81377 München, Germany
E-mail: Paul.Knochel@cup.uni-muenchen.de

Editorial Board

Prof. Dr. Armin de Meijere

Institut für Organische Chemie
der Georg-August-Universität
Tammannstraße 2
D-37077 Göttingen, Germany
E-mail: ameijer1@uni-goettingen.de

Prof. Dr. Horst Kessler

Institut für Organische Chemie
TU München
Lichtenbergstraße 4
D-85747 Garching, Germany
E-mail: kessler@ch.tum.de

Prof. Steven V. Ley

University Chemical Laboratory
Lensfield Road
Cambridge CB2 1EW, Great Britain
E-mail: svl1000@cus.cam.ac.uk

Prof. Dr. Joachim Thiem

Institut für Organische Chemie
Universität Hamburg
Martin-Luther-King-Platz 6
D-20146 Hamburg, Germany
E-mail: thiem@chemie.uni-hamburg.de

Prof. Dr. Fritz Voegtle

Kekulé-Institut für Organische Chemie
und Biochemie der Universität Bonn
Gerhard-Domagk-Straße 1
D-53121 Bonn, Germany
E-mail: voegtle@uni-bonn.de

Prof. K.N. Houk

Department of Chemistry and Biochemistry
University of California
405 Hgard Avenue
Los Angeles, CA 90024-1589, USA
E-mail: houk@chem.ucla.edu

Prof. Jean-Marie Lehn

Institut de Chimie
Université de Strasbourg
1 rue Blaise Pascal, B.P.Z 296/R8
F-67008 Strasbourg Cedex, France
E-mail: lehn@chimie.u-strasbg.fr

Prof. Stuart L. Schreiber

Chemical Laboratories
Harvard University
12 Oxford Street
Cambridge, MA 02138-2902, USA
E-mail: sls@slsiris.harvard.edu

Prof. Barry M. Trost

Department of Chemistry
Stanford University
Stanford, CA 94305-5080, USA
E-mail: bmtrost@leland.stanford.edu

Prof. Hisashi Yamamoto

School of Engineering
Nagoya University
Chikusa, Nagoya 464-01, Japan
E-mail: j45988a@nucc.cc.nagoya-u.ac.jp

Topics in Current Chemistry

Now Also Available Electronically

For all customers with a standing order for Topics in Current Chemistry we offer the electronic form via LINK free of charge. You will receive a password for free access to the full articles. Please register at:

http://link.springer.de/series/tcc/reg_form.htm

If you do not have a standing order you can nevertheless browse through the table of contents of the volumes and the abstracts of each article at:

<http://link.springer.de/series/tcc>

There you will also find information about the

- Editorial Board
- Aims and Scope
- Instructions for Authors

Preface

In recent years the choice of a given solvent for performing a reaction has become increasingly important. More and more, selective reagents are used for chemical transformations and the choice of the solvent may be determining for reaching high reaction rates and high selectivities. The toxicity and recycling considerations have also greatly influenced the nature of the solvents used for industrial reactions. Thus, the development of reactions in water is not only important on the laboratory scale but also for industrial applications. The performance of metal-catalyzed reactions in water for example has led to several new hydrogenation or hydroformylation procedures with important industrial applications. The various aspects of organic chemistry in water will be presented in this book. Recently, novel reaction media such as perfluorinated solvents or supercritical carbon dioxide has proven to have unique advantages leading to more practical and more efficient reactions. Especially with perfluorinated solvents, new biphasic catalyses and novel approaches to perform organic reactions have been developed. These aspects will be examined in detail in this volume.

Finally, the performance of reactions in the absence of solvents will show practical alternatives for many reactions.

More than ever before, the choice of the solvent or the solvent system is essential for realizing many chemical transformations with the highest efficiency. This book tries to cover the more recent and important new solvents or solvent systems for both academic and industrial applications.

Munich, June 1999

Paul Knochel

Contents of Volume 192

Organofluorine Chemistry Fluorinated Alkenes and Reactive Intermediates

Volume Editor: R. D. Chambers

ISBN 3-540-63171-2

Nucleophilic Reactions of Fluorinated Alkenes

R. D. Chambers and J. F. S. Vaughan

Reactions of Electrophiles with Polyfluorinated Olefins

U. A. Petrov and V. V. Bardin

Fluorinated Free Radicals

W. R. Dolbier, Jr.

Telomerisation Reactions of Fluorinated Alkenes

B. Améduri and B. Boutevin

Contents of Volume 193

Organofluorine Chemistry Techniques and Synthons

Volume Editor: R. D. Chambers

ISBN 3-540-63170-4

Elemental Fluorine in Organic Chemistry

J. Hutchinson and G. Sandford

Fluorinated Organometallic Compounds

D. J. Burton and L. Lu

Enzymatically Controlled Reactions of Organofluorine Compounds

T. Kitazume and T. Yamazaki

Building Block Approaches to Aliphatic Organofluorine Compounds

J. M. Percy

Electrofluorination of Organic Compounds

F. G. Drakesmith

Contents

Water as Solvent in Organic Synthesis	
A. Lubineau, J. Augé	1
Metal Catalysis in Water	
D. Sinou	41
Perfluorinated Solvents – a Novel Reaction Medium in Organic Chemistry	
B. Betzemeier, P. Knochel	61
Benzotrifluoride and Derivatives: Useful Solvents for Organic Synthesis and Fluorous Synthesis	
J. J. Maul, P. J. Ostrowski, G. A. Ublacker, B. Linclau, D. P. Curran	79
Reactions in Supercritical Carbon Dioxide (scCO₂)	
W. Leitner	107
Modern Solvent Systems in Industrial Homogeneous Catalysis	
B. Cornils	133
Solvent-free Reactions	
A. Loupy	153
Author Index Volumes 201 – 206	209

Water as Solvent in Organic Synthesis

André Lubineau¹ · Jacques Augé²

¹ Laboratoire de Chimie Organique Multifonctionnelle, bat 420, Université de Paris-Sud, F-91405 Orsay, France. E-mail: lubin@icmo.u-psud.fr

² Université de Cergy-Pontoise, 5 mail Gay-Lussac, Neuville-sur-Oise, F-95031 Cergy-Pontoise, France. E-mail: auge@u-cergy.fr

Organic reactions using water as solvent are reviewed with a focus on pericyclic reactions, carbonyl additions, stoichiometric organometallic reactions, oxidations and reductions which show an unusual outcome in terms of reactivity and selectivity compared with those performed in organic solvent. The advantages of using water as a solvent are discussed and related to the hydrophobic effects and the hydrogen-bonding ability of water with a special emphasis on its very high cohesive energy density which strongly favors organic reactions having a negative activation volume.

Keywords. Water, Solvents, Organic synthesis, Reactivity, Friendly processes.

1	Introduction	2
2	The Unique Properties of Liquid Water and Aqueous Solutions	3
3	Origin of the Reactivity in Water	5
4	Pericyclic Reactions	7
4.1	Diels-Alder Reactions	7
4.1.1	The Effect of Water and Additives on Chemical Reactivity	7
4.1.2	The Effect of Water and Additives on Selectivity	12
4.2	Hetero-Diels-Alder Reactions	14
4.2.1	Aza-Diels-Alder Reactions	14
4.2.2	Oxa-Diels-Alder Reactions	16
4.3	Miscellaneous Cycloadditions	16
4.4	Claisen Rearrangements	18
5	Carbonyl Additions	20
5.1	Barbier-Type Additions	20
5.1.1	Allylation Mediated by Zinc	20
5.1.2	Allylation Mediated by Tin	22
5.1.3	Allylation Mediated by Indium	24
5.1.4	Miscellaneous Allylations Using Other Metals	27
5.2	Conjugate 1,4-Additions	28

5.2.1	Organometallic Additions	28
5.2.2	Michael Additions	28
5.3	Cross-Aldol and Reformatsky-Type Addition	29
6	Oxidations and Reductions	32
6.1	Oxidations	32
6.2	Reductions	33
7	Outlook	34
8	References	35

1

Introduction

Water as solvent in organic synthesis means first that water must at least partially solubilize the reagents prone to react, and secondly that water cannot be a reactive species in the process. In fact chemical transformations in living systems occur chiefly in an aqueous environment. Nevertheless, in organic synthesis, water was rediscovered as a solvent only in the 1980s [1] and largely popularized in the 1990s [2]. Among the main advantages of using water as the solvent are the following: (i) water is cheap and not toxic, (ii) smooth conditions occur frequently in water-promoted reactions, leading to improvements in terms of yield and selectivity, (iii) the tedious protection-deprotection steps can be avoided in particular cases, such as carbohydrate, nucleoside or peptide chemistry, (iv) water can facilitate ligand exchange in transition-metal catalyzed reactions, and (v) water-soluble catalysts can be reused after filtration, decantation or extraction of the water-insoluble products.

It is certainly illusive to pretend that there is a common explanation for the exact role of water as the solvent but, nevertheless, it is important to have an overview of the unique properties of water to understand at least the outstanding effects of reactions in neat water. More difficult is the understanding of the reactions in mixed solvents, especially when water is used in small amounts. A remarkable feature of water-promoted reactions is that the reactants only need to be sparingly soluble in water and most of the time the effects of water occur under biphasic conditions. If the reactants are not soluble enough, miscible co-solvents can be used as well as surfactants or hydrophilic phase-transfer agents, e.g. carbohydrate [3], carboxylate [4] or sulfonate [5] group, on the hydrophilic reactant or ligand.

This chapter is devoted to reactions using water as the solvent with special emphasis on pericyclic reactions, carbonyl additions, organometallic reactions, oxidations and reductions and is restricted to those which show an unusual outcome when performed in water or in an aqueous medium. Enzymatic reactions are beyond the scope of this review.

2

The Unique Properties of Liquid Water and Aqueous Solutions

It is widely believed that the unique properties of water are responsible for various physicochemical phenomena such as the aggregation of surfactants, the stability of biological membranes, the folding of nucleic acids and proteins, the binding of enzymes to substrates and more generally complex molecular associations in molecular recognition [6].

Among the unique physicochemical properties of liquid water are the following: (i) the small size of the molecule, (ii) a high cohesive pressure (550 cal/ml), (iii) a large heat capacity, (iv) a large surface tension (72 dynes/cm), (v) a low compressibility, (vi) a decrease of viscosity with pressure, and (vii) a strong and anomalous dependence of the thermal expansion coefficient leading to a density maximum at 4°C. Even more surprising are the properties of aqueous solutions of non-polar solutes owing to hydrophobic hydration and hydrophobic interactions [7]. The physical origin of these interactions is still controversial [8]. Several models which emphasize the order and disorder of the hydrogen-bond network have been proposed, i.e. (i) the "iceberg" model [9], (ii) the "flickering clusters" model [10], (iii) the random network model of a dynamic equilibrium between some bonded and non-bonded water molecules [11], (iv) the continuum model based on the concept of strained and bent hydrogen bonds [12], and (v) the percolation model in which liquid water is treated as a large macroscopic space-filling hydrogen-bond network [13].

In the two-state model liquid, water is represented as an equilibrium between "structured water" constituted by ice-type clusters having low entropy and low density, and "unstructured water" having higher entropy and density in which each molecule has many neighbors. The dissolution of a non-polar solute in water, which is a thermodynamically unfavored process ($\Delta G_{tr} > 0$), brings about an enhancement of the water structure by augmenting the order of water molecules around the solute ($\Delta S_{tr} < 0$) and strengthening the hydrogen-bond pattern ($\Delta H_{tr} < 0$) at low temperatures. This is the well-known enthalpy-entropy compensation effect. X-ray studies on clathrate hydrate crystals of many non-polar compounds provide evidence of such a water reorganization [14]. The local environment around a non-polar solute is favorable for the formation of hydrogen bonds between the neighboring water molecules [15]. This water reorganization originates the positive heat capacity change ($\Delta C_p > 0$) observed when hydrophobic solutes are dissolved in water [16]. Only the water molecules in the first hydration shell are responsible for the heat capacity change which is proportional to the non-polar accessible surface area of the solute, the coefficient averaging $2 \text{ J K}^{-1} \text{ mol}^{-1} \text{ \AA}^{-2}$ approximately [17]. By contrast the perturbation due to polar and small ionic solutes causes a negative heat capacity change ($\Delta C_p < 0$) owing to an increase in the average length and angle of the water-water hydrogen bonds in the first hydration shell [18]. Based on measurements of liquid hydrocarbon-water surface tensions, a macroscopic measure for the hydrophobic Gibbs energy per unit surface area was evaluated [19] to average $310 \text{ J mol}^{-1} \text{ \AA}^{-2}$, which is somehow higher than the microscopic Gibbs energy correlations ranging from 70 to $130 \text{ J mol}^{-1} \text{ \AA}^{-2}$ [8]. The properties of liquid

water strongly change at high temperature or pressure. Unlike the effect of pressure [20], the effect of temperature has been extensively studied. When increasing the temperature, water loses its capacity to maintain hydrogen bonds upon intrusion of a non-polar solute; the solvation enthalpy increases gradually and becomes positive at high temperatures. The breakage of hydrogen bonds thus leads to an increase in solvation entropy which also becomes positive. Dramatic changes in the physicochemical properties of water occur when the temperature increases even more. For example, as the temperature rises from 25 to 300 °C, the density of water decreases from 0.997 to 0.713, its dielectric constant decreases from 78.85 to 19.66, its cohesive pressure decreases from 550 to 210, and its pK_a decreases from 14 to 11.30. This means that water can act as an acid-base bicatalyst, which could have ecological applications in recycle, regeneration, disposal and detoxification of chemicals [21].

Table 1. Cohesive energy density (ced), E_T parameter and dielectric constant ϵ at 25 °C for a range of solvents

	ced (cal cm ⁻³) ^a	E_T (kcal mol ⁻¹) ^b	ϵ^b
Water	550.2	63.1	78.5
Formamide	376.4	56.6	109.5
Ethylene glycol	213.2	56.3	37.7
Methanol	208.8	55.5	32.6
Dimethyl sulfoxide	168.6	45.0	48.9
Ethanol	161.3	51.9	24.3
Nitromethane	158.8	46.3	38.6
1-Propanol	144	50.7	20.1
Acetonitrile	139.2	46.0	37.5
Dimethylformamide	139.2	43.8	36.7
2-Propanol	132.3	48.6	18.3
1-Butanol	114.5	50.2	17.1
<i>tert</i> -Butanol	110.3	43.9	12.2
Dioxane	94.7	36.0	2.2
Acetone	94.3	42.2	20.7
Tetrahydrofuran	86.9	37.4	7.4
Chloroform	85.4	39.1	4.7
Toluene	79.4	33.9	2.4
Diethyl ether	59.9	34.6	4.2
Hexane	52.4	30.9	1.9

^a Ref 24; ^b Ref 23.

Table 1 gives a classification of organic solvents based on the decreasing values of the cohesive energy density (ced) at 25 °C. The cohesive energy density is readily obtained from the experimental heats of vaporization ΔH_{vap} via the relationship:

$$ced = \Delta U_{vap}/V = (\Delta H_{vap} - RT)/V$$

The cohesive energy density is expressed in terms of pressure, whence the expression cohesive pressure, but any confusion with the internal pressure of the solvent must be avoided: for example, the internal pressure of water, unlike other solvents, increases with increasing temperature until reaching a maximum at 150 °C, whereas the cohesive pressure decreases regularly with increasing temperature [22]. The cohesive energy density of water, which is much higher than for all organic solvents, reflects the unique organization of water molecules through the hydrogen-bond network.

The E_T parameter, which is usually considered as an appropriate indication of solvent polarity, is an empirical parameter based on energy transitions (E_T) corresponding to a charge transfer bond in ethyl-1-methoxycarbonyl-4-pyridinium iodide. This parameter is incontestably more accurate for evaluating the polarity of the solvent than the dielectric constant [23]. Table 1 shows that water is both the more structured and the more polar solvent and this might have implications on the chemical reactivity. However, it must be kept in mind that water behaves as a fluctuating structure which can be modified by the formation (breakage) of more hydrogen bonds, stronger (slighter) hydrogen bonds, or a reduction (increase) of free OH bonds.

3

Origin of the Reactivity in Water

In the Hughes–Ingold theory, solvent effects are rationalized by studying the Gibbs energy of solvation of the reactants and of the transition states. Solvation effects include the solute–solvent interactions and the reorganization of solvent around the solutes. An enthalpically dominated rate enhancement usually rises from a large decrease in the transition-state enthalpy. Thus the well-known SN_1 solvolysis reactions are accelerated in highly polar solvents, such as water, by strong interactions between the carbonium ions and the solvent in the transition state [23]. With the highest E_T parameter, water is the solvent of choice for reactions which go through a more polar transition state.

Interestingly, Dack considered the volume of activation and predicted that solvents accelerated the rate of a reaction when lowering the value of the volume of the reaction by electrostriction [24]. This is the case when the transition state is more polar than the initial state, but this cannot explain why non-polar reactions such as Diels–Alder reactions are strongly accelerated in water compared to other solvents [1]. What occurs when two hydrophobic molecules, susceptible to reaction, are put together in aqueous solution? Due to hydrophobic interactions, they have a tendency to aggregate but this association is not sufficient to explain the rate enhancement. The hydrophobic hydration, which is unfavorable and proportional to the hydrophobic surface area (*vide supra*), must be lowered by a decrease in the volume of the reactants, which occurs in reaction with a negative volume of activation. In such a reaction, the hydrophobic surface area decreases during the activation process, leading to a less unfavorable hydrophobic Gibbs energy (Fig. 1).

Thus a kinetically controlled reaction between two apolar molecules for which ΔV^\ddagger is negative must be accelerated in water [25]. The origin of such an

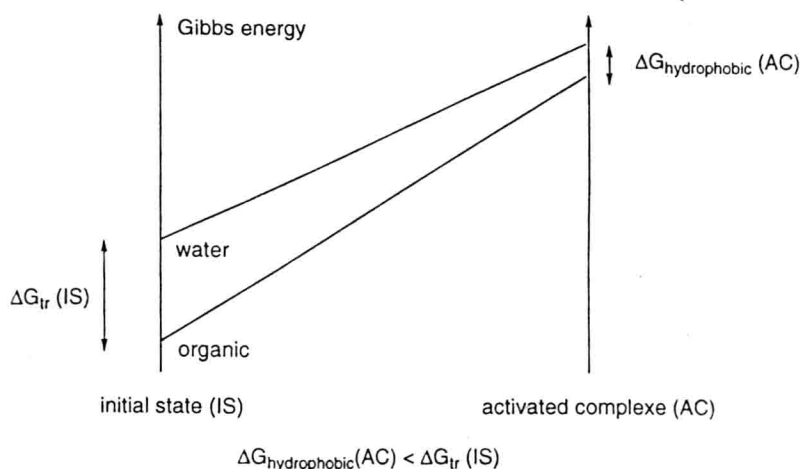


Fig. 1. Hypothetical Gibbs energy of the initial state and the activated complex in organic and water solvent: decreasing the hydrophobic hydration with the decreasing of the hydrophobic surface area

acceleration comes from the hydrophobic effects, which are a consequence of the hydrogen-bond network of water. Cohesive energy density is probably the best parameter to account for this type of acceleration. However, if one of the reactants is a hydrogen donor or acceptor, a charge development in the transition state may occur leading to stabilization of the activated complex versus the initial state. This second factor comes from an enhanced hydrogen-bonding interaction. Both contributions could be active in the same reaction, which means a greater destabilization of the hydrophobic reactants in the initial state than in the transition state, and a greater stabilization of a more polar transition state.

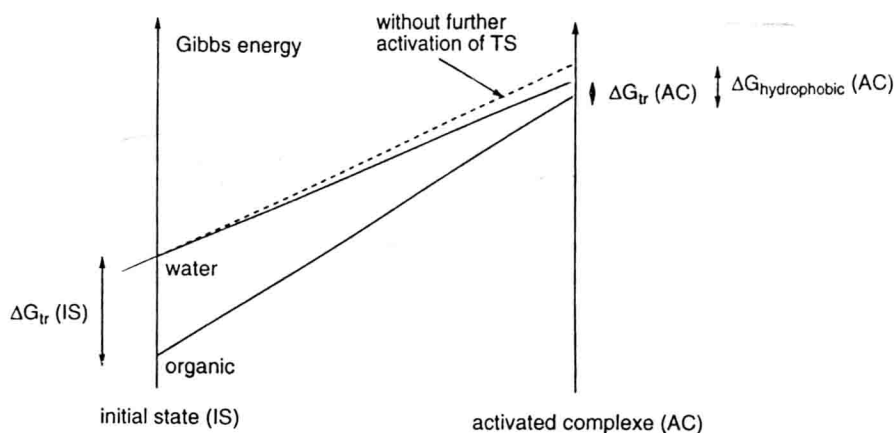


Fig. 2. Gibbs energy of transfer from organic to water solvent for the initial state and the activated complex

The Gibbs energy of transfer for the activated complex from organic or water solvent $\Delta G_{tr}(AC)$ is thus infinitely lower (Fig. 2) and can even be negative in particular cases. The rate acceleration in water is expressed by the negative term $\Delta\Delta G^\ddagger = \Delta G_{tr}(AC) - \Delta G_{tr}(IS)$. The absolute value of this term is all the highest since $\Delta G_{tr}(AC)$ is negative and $\Delta G_{tr}(IS)$ is strongly positive. The respective influence of the hydrophobic effect and hydrogen-bonding contributions was tentatively determined based on Monte Carlo simulations and molecular orbital calculations [26].

Water-tolerant Lewis acids, which can coordinate the reactants, catalyze reactions even in water, but their accelerative effect is less pronounced than in the reactions in organic media, probably by preventing the second factor (hydrogen-bonding enhancement in the transition state) to operate with the same efficiency [27].

4

Pericyclic Reactions

4.1

Diels-Alder Reactions

4.1.1

The Effect of Water and Additives on Chemical Reactivity

The influence of water as solvent on the rate of Diels-Alder reactions is likely the best example of the close relationship between the unique properties of liquid water and its strongly accelerative effect. This is probably due to the large negative value of the activation volume of Diels-Alder reactions; this value (ca. $30 \text{ cm}^3 \text{ mol}^{-1}$) is even somewhat more negative in water versus organic solvents [28].

Although performed in water by Diels and Alder themselves [29] and in aqueous microemulsion [30], the Diels-Alder reaction was known as a reaction insensitive to solvents, until Breslow observed a dramatic accelerating effect in the aqueous reaction of cyclopentadiene with methyl vinyl ketone [1]. He suggested that hydrophobic packing of the reactants is likely to be responsible for the rate enhancement of Diels-Alder reactions [31]. The implication of the hydrophobic effect is supported by effects of additives. A prohydrophobic (salt-ing-out) agent, such as lithium chloride, which increases the energy cost of cavitation by electrostriction, accelerates the reaction even more. Salting-in additives such as guanidinium chloride, which decreases the hydrophobic hydration by acting as a bridge between water molecules and apolar solutes [32], lead to a small decrease in the rate. Moreover, β -cyclodextrin, which promotes a favorable complexation of hydrophobic substrates, accelerates the cycloaddition; by contrast, α -cyclodextrin, with a small size of the hydrophobic cavity preventing both partners being complexed together, slows down the reaction (Scheme 1).

The implication of hydrophobic effects rather than polar effects was further demonstrated by (i) a deviation from linearity when correlating the Gibbs