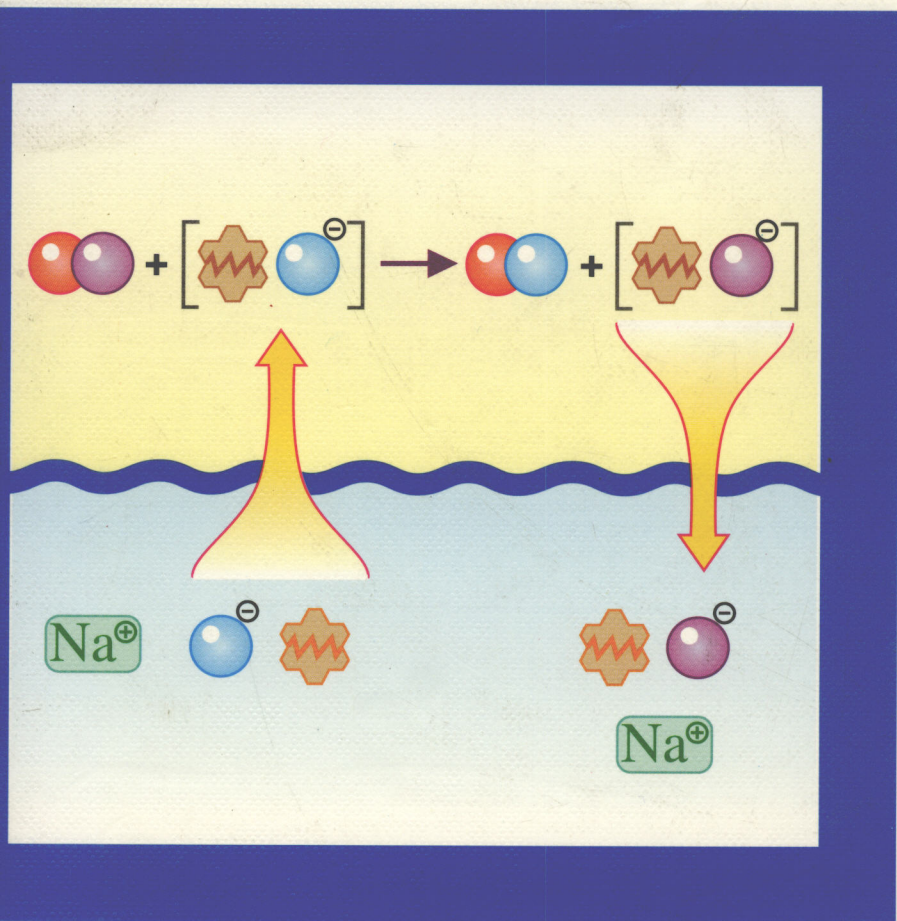


E. V. Dehmlow, S. S. Dehmlow

# Phase Transfer Catalysis

Third, Revised and Enlarged Edition



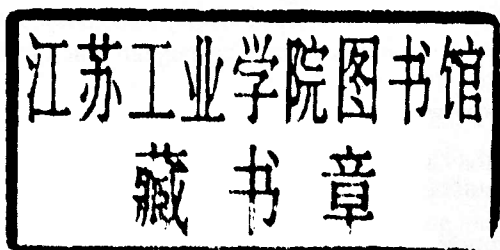
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E. V. Dehmlow, S. S. Dehmlow

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Enlarged Edition



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Prof. Dr. Eckehard V. Dehmlow  
Dr. Sigrid S. Dehmlow  
Fakultär für Chemie der Universität  
P.O. Box 8640  
D-4800 Bielefeld 1  
Germany

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E.V. Dehmlow, S.S. Dehmlow

# Phase Transfer Catalysis





## Preface to the Third Edition

Twenty to twenty-five years have passed since the first publications on phase transfer catalysis found a receptive audience. "PTC" has matured, and has since become widely accepted. Indeed, certain variants are now standard techniques, at least in the laboratory, and phase transfer catalysis may be on the verge of large-scale industrial application. It is therefore timely once more to collect the known body of information in the field within a single volume. The favorable response to the first and second editions of our book further encouraged both publisher and authors to revise the work and bring it up to date.

As in the earlier editions, our aim was to be as comprehensive as possible, and to include practical examples for important reactions. In view of the large number of new publications, however, it would not have been possible to include every single application or investigation. We therefore decided to concentrate on *types of reactions*, *fundamental investigations*, and *important new developments* insofar as this proved manageable. Oftentimes we were forced to be rather concise. Routine applications of known conversions providing little novelty have occasionally been neglected. Furthermore, condensation of the information has been achieved in certain areas by collecting relevant but less fundamental references in the form of tables. Unless they contained items of great novelty, we deliberately excluded many papers from sources not readily available internationally (e.g., papers in "exotic" languages) and traceable only via *Chemical Abstracts*.

The basic organization of the book has been retained, and the original text was reorganized only where it became necessary to add new facts or references, or where a particular paragraph required fundamental revision. References are now arranged (and numbered) alphabetically by first authors throughout the book, thereby eliminating much duplication. A few hundred redundant or out-dated "old" references were removed, and more than 1700 new ones were added (chosen from among well over 3000 in our files).

PTC research trends of the last few years are clearly reflected in the increased size of certain chapters. Key concepts or chapter headings in this context include solid/liquid PTC, enantioselective reactions,  $\beta$ -eliminations, *N*-alkylations, metal-organic reactions, nucleophilic aromatic substitution, reduction, and oxidation reactions.

The literature has been searched up to mid-1990 by reading title lists and browsing through about 40 of the most important primary journals, as well as through weekly CAS search profiles.

In closing, we wish to acknowledge the participation in this project of members of the PTC group within our research team at Bielefeld University. They helped create this third edition in an indirect, but very real way by contributing results that induced additional thought and suggested further investigations. At some time or other during the period 1983-1991 the following individuals either used PTC or carried out PTC

research with us as members of the technical staff, as students working toward the diploma thesis or doctoral dissertation, and as postdoctoral coworkers: Dr. Dietmar Balschukat, Dipl.-Chem. Christof Bollmann, Dr. Witold Broda, Dr. Rubin Cyrankiewicz, Dipl.-Chem. Renate Dedert, Chemielaborantin Katharina Drechsler, Dr. Veneta Dryanska, Dipl.-Chem. Uwe Fastabend, Dipl.-Chem. Manoucher Godarzani, Chemotechniker Michael Keßler, Dr. Volker Knufinke, Dr. Roland Kramer, Dr. Ernst Kunesch, Dipl.-Chem. Bertold Lipka, Dr. Manfred Lissel, Dr. Jagdish K. Makrandi, Dr. Iris Nachstedt, Dr. Y. Ramachandra Rao, Dr. Hans-Christian Rath, Dipl.-Chem. Rolf Richter, Dr. Christiane Sauerbier, Dr. Sabine Schrader-Bunte, Chem.-Ing. Johanna Soufi-Siavash, Dr. Thomas Stiehm, Dr. Jörg Stütten, Dr. Rainer Thieser, Prof. Gagik O. Torossian, Dr. Burghard Vehre, Dr. Jürgen Wilkenloh, Dr. Andreas Winterfeldt, and Dr. Alexej Zhivich. Special thanks are due to Mrs. A. Gaestel who typed the new text passages from E.V.D.'s poor handwriting, helped in locating references, and assisted in transferring old references into a data file. Last but not least we should like to acknowledge the valuable and effective work of Prof. William E. Russey. On behalf of the editor and the publisher, he read and polished this third edition and prepared copy and layout for print.

Bielefeld, December 1992

Eckehard Volker Dehmlow  
Sigrid Sonja Dehmlow

# From the Preface to the Second Edition

Despite the existence of competing publications, our monograph was so well received that the publisher asked us to prepare a second edition only one year after the first had appeared. We welcomed this opportunity to bring our material up to date. The field has continued to expand rapidly; hence we now include about 55 % more references after a relatively short time. (Original closing date for literature: early 1979; for the Second Edition: May 31, 1981. Selected further references were added in April 1982). In order to keep costs reasonably low, we tried not to break up the original text too often. Since some of the new papers merely extend existing work, they could be dealt with briefly or by simply adding reference numbers. In some areas, however, so many fundamentally new facts have emerged that we could not avoid adding new sections or rewriting old ones. Again, a virtually comprehensive, but concise review was our aim. The new literature was evaluated on the basis of the *Science Citation Index* (complete through the end of 1980), *Chemical Abstracts* [machine search program of computer tapes, through Volume 96, issue 6 (1982)] and by scanning recent issues of about 50 journals up to April 1982. For the Second Edition the patent literature was not searched beyond *Chemical Abstracts*.

Major changes in the text are:

- (i) A more practical breakdown of Chapter 3. The original arrangement according to reaction with or without extra base proved both difficult for classification and inconvenient to the reader seeking specific information. The arrangement now is according to type of reaction, and respective section titles appear at the top of each odd-numbered page.
- (ii) Material on the application of *chiral catalysts* and of *polymer-bound catalysts* is now collected in specific sections.
- (iii) The large increase of material on *nucleophilic aromatic substitution* and *organo-metallic reactions* prompted us to include new sections on these subjects.
- (iv) The subject index was enlarged and improved. After long consideration, we again decided not to provide an author index as we do not believe it to be of use to the general reader.

We should like to thank our research collaborators, Dr. S. Barahona-Naranjo, Dr. M. Prashad, Dr. A. R. Shamout, Dr. P. Singh, Dipl.-Chem. W. Broda, Dipl.-Chem. E. Kunesch, Dipl.-Chem. R. Thieser, K. Drechsler, U. Fastabend, R. Meier, J. Soufi, and especially Dr. Manfred Lissel, for their enthusiastic experimental work and their help in establishing the group in Bielefeld after the move from Berlin in 1979. Further thanks are due to Mrs. A. Stoffels who helped with clerical work and in typing the major manuscript additions.

Bielefeld, February 1983

E. V. Dehmlow  
S. S. Dehmlow

# From the Preface to the First Edition

One hundred and fifty years of organic synthesis since Wöhler's first successful experiments have provided the chemist with a confusingly large arsenal of sophisticated methods. However, on considering the ease with which a living organism produces complex structures in essentially aqueous surroundings at temperatures only a little above room temperature, the chemist realizes that he has not progressed very far and endeavors to advance further. Thus, organic chemists are constantly on the alert for faster, simpler, and cheaper preparative methods. This book, therefore, is an attempt to collect the somewhat scattered examples of a new technique that has emerged only in the last decade or so. In many cases, the new procedure eliminates the customary requirement of running an organic reaction in a homogeneous, often "absolute" (i.e., perfectly dry) medium.

In phase transfer catalysis (PTC) a substrate in an organic phase is reacted chemically with a reagent present in another phase which is usually aqueous or solid. Reaction is achieved by means of the transfer agent; this agent or catalyst is capable of solubilizing or extracting inorganic and organic ions, in the form of ion pairs, into organic media.

This book attempts to provide a comprehensive survey of work done so far in this area. It developed out of two review articles published in 1974 and 1977 [E. V. Dehmlow, *Angew. Chem.*, **86**, 187 (1974); *Angew. Chem. Int. Ed. Engl.*, **13**, 170 (1974), reprinted in "New Synthetic Methods," Vol. 1, p. 1, Verlag Chemie, Weinheim, 1975, and in slightly shortened form in *Chemical Technology*, **1975**, 210; and E. V. Dehmlow, *Angew. Chem.*, **89**, 521 (1977); *Angew. Chem. Int. Ed. Engl.*, **16**, 493 (1977), reprinted in "New Synthetic Methods", Vol. 6, p. 205, Verlag Chemie, Weinheim, 1979]. A review booklet by A. Brändström, containing much theoretical derivation on extraction equilibria along with some applications, is available in mimeographed form. [A. Brändström, "Preparative Ion Pair Extraction—An Introduction to Theory and Practice," Apotekersocieteten/Hässel Läkemedel, Stockholm, 1974.]

Of the many possible phase transfer catalysts, quaternary ammonium and phosphonium salts are most widely used. In the past such salts have been utilized for purposes other than those presented in this work:

- (a) as **catalysts** for a multitude of reactions in homogeneous media;
- (b) as aqueous/organic **extractants** mostly for quantitative-analytical, but to some extent for preparative purposes also;
- (c) —less frequently— as **reagents** in homogeneous media; and
- (d) in micellar catalysis.

We can exclude (a) as not pertaining to the subject covered here. The material under (b) and (c) has a strong bearing on our subject, and will be considered here to some extent, since PTC has to do with both extraction into the organic phase and any chemical transformations occurring therein. Micellar catalysis is mechanistically and preparatively different from standard PTC. The demarcation between PTC and micellar catalysis will be elucidated as far as presently possible.



The present book is written with the practicing organic chemist in mind. Typical experimental procedures for the more frequently used PTC reactions are given, and care is taken to mention pertinent data of reaction conditions even in the less important cases.

Since the subject is being actively pursued from many angles and since many of its potential fruits have not yet been harvested, the following will provide an introduction rather than a final evaluation of the technique. PTC is defined in the introductory Chapter 1. This is followed by a presentation of the fundamental theoretical aspects of ion pairs in general and the factors influencing the aqueous/organic extraction equilibria. Chapter 2 concerns the mechanism of PTC in different fields, the evaluation of catalysts, and its differences from micellar catalysis. The main part of the book, Chapter 3, deals with applications, grouped according to various reaction types, with tabular surveys and details of typical practical procedures.

Originally, a comprehensive literature coverage through the end of 1977 was our aim, but—due to production delays—as many references as came to our attention in 1978/79 (several hundred!) could be included. All additions, however, had to be concise and were put at the ends of paragraphs. The journal literature has been surveyed on the basis of *Chemical Abstracts Indexes*, *Science Citation Index*, and by browsing through the 1978–79 issues of about 50 of the more important primary journals. Literature evaluation in this field is not straightforward since relevant keywords have only recently been introduced and since in the early years isolated groups in the field did not cite each other. Thus, undoubtedly interesting observations are buried in old volumes of journals and patents, and may not have been recognized. Patent literature was searched with the aid of a computer program through the facilities of IDC, Internationale Dokumentationsgesellschaft für Chemie m.b.H., Frankfurt, W. Germany.

Eckehard V. Dehmlow  
Sigrid S. Dehmlow

## Frequently Used Abbreviations

Adogen 464	methyltrioctylammonium chloride (technical grade)
Aliquat 336	same product as Adogen 464
Bu	<i>n</i> -butyl
Hex	<i>n</i> -hexyl
Hep	<i>n</i> -heptyl
Katamin AB	(mixed higher) alkylbenzyltrimethylammonium chloride
Oct	<i>n</i> -octyl
Pent	<i>n</i> -pentyl
Prop	<i>n</i> -propyl
PTC, PT	phase transfer catalysis, phase transfer
Q	quaternary ammonium cation
TDA-1	tris (3,6-dioxaheptyl) amine
TEBA	benzyltriethylammonium chloride
TEBA-bromide	benzyltriethylammonium bromide

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# Contents

<b>1</b>	<b>Ion Pairs and Ion Pair Extraction . . . . .</b>	<b>1</b>
1.1	Introduction: The Nature of Phase Transfer Catalysis . . . . .	1
1.2	Ion Pairs in Organic Media . . . . .	3
1.3	Extraction of Ion Pairs from Aqueous Solution . . . . .	6
1.3.1	Principles . . . . .	6
1.3.2	Influence of the Solvent . . . . .	10
1.3.3	Influence of the Onium Cation . . . . .	12
1.3.4	Influence of the Anion . . . . .	14
1.4	Crown Ethers, Cryptates, and Other Chelating Agents as Extractants .	22
1.5	Solid-Liquid Anion Exchange . . . . .	25
<b>2</b>	<b>Mechanism of Phase Transfer Catalysis . . . . .</b>	<b>29</b>
2.1	Mechanistic Investigations . . . . .	29
2.1.1	Mechanism under Neutral Conditions . . . . .	29
2.1.2	Mechanisms in the Presence of Alkali Metal Hydroxides . . . . .	39
2.1.3	Mechanisms in the Presence of Other Bases . . . . .	49
2.2	Empirical Catalyst Evaluations . . . . .	50
2.3	Unusual and Polymer-Supported Catalysts . . . . .	61
2.4	Extraction into the Water Phase ("Inverse PTC") . . . . .	63
2.5	Cation Extraction . . . . .	63
2.6	Extraction by Anionic Complex Formation or Hydrogen Bonding . .	64
<b>3</b>	<b>Practical Applications of Phase Transfer Catalysis . . . . .</b>	<b>65</b>
3.1	General Experimental Procedures . . . . .	65
3.1.1	The Common Catalysts . . . . .	65
3.1.2	Reaction Conditions . . . . .	71
3.1.2.1	Solvent . . . . .	72
3.1.2.2	Stirring . . . . .	72
3.1.2.3	Amount of Catalyst . . . . .	72
3.1.2.4	Stability of the Catalyst . . . . .	73
3.1.2.5	Choice of Catalyst . . . . .	75
3.1.2.6	Separation and Regeneration of the Catalyst . . . . .	75
3.1.2.7	Miscellaneous . . . . .	76
3.1.3	General Remarks on Reactions in the Presence of Additional Bases .	77
3.1.4	Polymer-Bound Catalysts . . . . .	79
3.1.5	Optically Active Catalysts; Enantioselective Reactions . . . . .	80
3.2	Formation of Halides . . . . .	93
3.2.1	Halide Exchange . . . . .	93
3.2.2	Exchange for Fluoride . . . . .	97

---

3.2.3	Halides from Alcohols, Ethers, and Diazomethanes . . . . .	101
3.3	Preparation of Nitriles . . . . .	103
3.4	Ester Formation . . . . .	106
3.5	Miscellaneous Displacements . . . . .	117
3.6	Thiols and Sulfides . . . . .	122
3.7	Preparation of Ethers . . . . .	126
3.8	<i>N</i> -Alkylations . . . . .	136
3.9	<i>C</i> -Alkylation of Activated CH Bonds . . . . .	149
3.9.1	Alkylation of Arylacetonitriles . . . . .	149
3.9.2	Alkylation of Other Activated Cyanides and Isocyanides . . . . .	156
3.9.3	Alkylation of Malonic Esters . . . . .	158
3.9.4	Alkylation of Benzyl Ketones and Arylacetic Esters and Amides . . . . .	159
3.9.5	Alkylation of Other Doubly Activated CH Bonds . . . . .	164
3.9.6	Alkylation of Carbonyl and Other Less Activated Derivatives . . . . .	166
3.9.7	Alkylation of Hydrocarbons . . . . .	168
3.10	Alkylation and Acylation of Ambident Anions . . . . .	170
3.11	Isomerizations and H/D Exchange . . . . .	184
3.12	Additions across Multiple CC Bonds . . . . .	187
3.12.1	Additions to Acetylenes . . . . .	187
3.12.2	Michael Additions . . . . .	190
3.12.3	Additions across Nonactivated Double Bonds . . . . .	197
3.13	Addition to C=O and C=N Bonds . . . . .	199
3.13.1	Benzoin Condensation . . . . .	199
3.13.2	Aldol-Type Reactions . . . . .	199
3.13.3	Other Types of Reactions . . . . .	204
3.14	$\beta$ -Eliminations . . . . .	209
3.15	Hydrolysis Reactions . . . . .	215
3.15.1	Miscellaneous Hydrolysis Reactions . . . . .	215
3.15.2	Saponification of Esters . . . . .	218
3.16	Generation and Conversion of Phosponium and Sulfonium Ylides . . . . .	222
3.16.1	Wittig Reactions . . . . .	222
3.16.2	Horner (PO-Activated) Olefination . . . . .	226
3.16.3	Sulfonium Ylide and Oxosulfonium Ylide Reactions . . . . .	233
3.17	Nucleophilic Aromatic Substitution . . . . .	237
3.18	Miscellaneous Reactions in the Presence of Bases . . . . .	245
3.18.1	Diazo-Group Transfer . . . . .	245
3.18.2	$\gamma$ -Elimination . . . . .	246
3.18.3	Preparation of Acid Fluorides and Anhydrides . . . . .	246
3.18.4	Rearrangements . . . . .	248
3.18.5	Radical Reactions . . . . .	251
3.18.6	Reactions with Carbon Tetrahalides and Hexahaloethane . . . . .	251



3.18.7	Special Reactions of Certain Sulfur Compounds . . . . .	254
3.18.8	Generation of Nitrenes . . . . .	255
3.18.9	PTC Reactions of Diazonium Salts . . . . .	256
3.18.10	Hydrazones by and in PTC . . . . .	258
3.18.11	Electrochemistry . . . . .	258
3.18.12	Other Reactions . . . . .	259
3.19	Organometallic PTC Applications . . . . .	260
3.19.1	Extraction of Metals, Metal Salts, and Metal Carbonyls . . . . .	260
3.19.2	Metal-Organic Reactions of Sulfur Compounds . . . . .	261
3.19.3	Preparation of Complexes, Ligand Exchange . . . . .	262
3.19.4	Carbonylations . . . . .	264
3.19.5	Metal-Organic Coupling Reactions . . . . .	268
3.19.6	Isomerizations and Other Reactions . . . . .	270
3.20	$\alpha$ -Eliminations . . . . .	271
3.20.1	Generation and Addition Reactions of Dichlorocarbene . . . . .	271
3.20.2	Other Reactions of Dichlorocarbene and Trichloromethylide Anion . . . . .	287
3.20.3	Dibromocarbene . . . . .	303
3.20.4	Other Dihalocarbenes . . . . .	309
3.20.5	Other Carbenes . . . . .	315
3.21	Reduction Reactions . . . . .	321
3.21.1	Complex Hydrides and Diborane . . . . .	321
3.21.2	Dithionite . . . . .	330
3.21.3	Alkali Metals and Hydrides . . . . .	331
3.21.4	Metal Carbonyls . . . . .	331
3.21.5	Hydrogenations and Transfer Hydrogenations . . . . .	333
3.21.6	Other Reducing Agents . . . . .	334
3.22	Oxidation Reactions . . . . .	335
3.22.1	Oxidation with Permanganate . . . . .	335
3.22.2	The Role of Hydrogen Peroxide and Alkyl Hydroperoxides in PTC Reactions . . . . .	344
3.22.3	Reactions with Potassium Superoxide . . . . .	349
3.22.4	Chromate . . . . .	359
3.22.5	Hypochlorite/Hypobromite . . . . .	361
3.22.6	Potassium Hexacyanoferrate(III) . . . . .	365
3.22.7	Periodate . . . . .	366
3.22.8	Peroxy Acids . . . . .	368
3.22.9	Oxygen as Oxidant . . . . .	369
3.22.10	Peroxymono- and Peroxydisulfate . . . . .	373
3.22.11	Other Oxidizing Agents . . . . .	374
<b>References</b>		<b>379</b>
<b>Subject Index</b>		<b>481</b>

# 1 Ion Pairs and Ion Pair Extraction

## 1.1 Introduction: The Nature of Phase Transfer Catalysis

Phase transfer catalysis (PTC) is concerned with conversions between chemical species situated in different phases. Common cases are reactions between, on the one hand, salts dissolved in water or present in the solid state, and, on the other, substances dissolved in organic media. Without a catalyst such a reaction is usually slow and inefficient or does not occur at all. The traditional procedure involves dissolving the reactants in a homogeneous medium. If a hydroxylic solvent is used the reaction may prove slow due to extensive solvation of the anion. Solvolytic side reactions sometimes reduce the efficiency even further. Polar aprotic solvents are often superior, but they tend to be expensive and difficult to remove after the reaction and may present environmental problems in large scale operations. In some cases, such as O vs. C alkylation with ambident anions, polar aprotic solvents may even hinder rather than promote the desired reaction by encouraging formation of an alternative product.

According to the original definition, phase transfer catalysis permits or accelerates reactions between ionic compounds and organic, water-insoluble substrates in solvents of low polarity. The catalysts most commonly used are onium salts or complexing agents that can mask and thereby solubilize alkali metal ions. The basic function of the catalyst is to transfer anions of the reacting salt into the organic medium in the form of ion pairs. In aprotic solvents these are virtually unsolvated and unshielded (except, perhaps, by their counter ions) and consequently very reactive.

It is clear, therefore, that PTC offers significant advantages over conventional procedures:

- no need for expensive anhydrous or aprotic solvents
- improved reaction rates and/or
- lower reaction temperatures
- easier work-up in many cases
- aqueous alkali metal hydroxides replace alkoxides, sodamide, sodium hydride, or metallic sodium.

Other special advantages apply as well, e.g.:

- occurrence of reactions that would not otherwise proceed
- modification of selectivity
- changes in product ratios (e.g., O vs. C alkylation)
- increased yields through suppression of side reactions.

Although most reactions considered in this book involve the extraction of anions into organic solvents mediated by catalyst cations, the general concept of PTC is broader, since it includes extraction of cations, even neutral molecules, from one phase into another with the help of a catalyst. Alternatively, one phase might be a gas, there can be more than two phases, etc.

PTC is a relatively new field of chemistry that originated in research work from three independent groups. The foundations were laid in the mid to late 1960s by M. Mąkosza, C. M. Starks, and A. Brändström.

Reactions involving phase transfer phenomena were, of course, performed even earlier, and undoubtedly a considerable number of such reactions are buried in the older literature [187, 1583, 2160] and especially in patents [625, 631, 957, 1846, 2421, 2422]. The earliest one presently known dates from 1913. Some of the original authors entered the field more or less incidentally and apparently did not reflect on the catalytic mechanisms involved. None realized the potential and scope of the new technique.

PTC techniques as we know them today originated in the work of Mąkosza and coworkers in 1965 [2225]. They initiated a systematic exploration of alkylations and subsequently of other reactions in two-phase systems containing mainly concentrated aqueous alkali metal hydroxides. The descriptive terms they originally used included "catalytic two-phase reactions," "catalytic alkylation of anions," and "catalytic generation of carbenes." Mąkosza still prefers these terms for mechanistic reasons. This work became more widely known with the publication in *Tetrahedron Letters* 1969 [2235] of Mąkosza's discovery of dichlorocarbene generation.

Brändström started from a more physicochemical and analytical point of view. His first papers relevant to our subject appeared in 1969 [392]. Brändström uses the term "extractive alkylation" for alkylation reactions in a two-phase mixture in the presence of molar amounts of catalyst.

The term "phase transfer catalysis" was coined by Starks and first used in patents in 1968 [3179]. Recognition of the new technique and the term "phase transfer catalysis" probably originates in Starks' 1971 paper published in the *Journal of the American Chemical Society* [3172]. For the first time the scope of the method was clearly outlined and extended beyond the original applications: alkylation and carbene generation. Furthermore, a mechanistic concept unifying all of these reactions was proposed. This provided an enormous impetus for the development of the field. Since then a flood of papers has appeared expanding PTC to new types of reactions (e.g., liquid-solid PTC and polymer-bound catalysis) and introducing new catalytic reagents such as crown ethers. These will be discussed in subsequent sections.

The term "phase transfer catalysis" is now the most widely accepted name. It appears in general textbooks and works of reference, in abstract sources and thesauri, as well as in *Organic Syntheses*. Certain modifications of the original definition are now required: in the extended view not all PTC reactions obey the above-mentioned unifying mechanism. Mąkosza prefers to exclude some reactions from the category of "true" PTC reactions, calling them instead "so-called PTC reactions" or "catalytic two-phase reactions." For the purpose of this review, however, the present

authors prefer to include under the heading "phase transfer catalysis" all two-phase reactions between solid or aqueous salts, acids, bases, or even neutral molecules and substrates in organic solvents with catalysis by onium salts, crown ether/alkali metal salts, or similar chelated salts. This permits classification of reactions involving similar catalytic effects or similar catalysts, irrespective of whether a mechanism is known or is always the same, providing a practical, phenomenological definition. It does not imply a specific action of the catalyst and depends only on the presence of two phases together with a catalyst. Reactions occurring exclusively or primarily at the interphase are also included provided they are accelerated by a catalyst. Many such reactions are known. Also covered is a (still small) group of reactions in which the substrate is extracted from an organic to an aqueous phase for reaction ("inverse PTC").

The question may arise as to whether micellar catalysis should be included in a monograph on PTC. Where must one draw the line? Micellar reactions have been reviewed extensively [1020, 1021, 1022]. Since they are normally carried out in a homogeneous or pseudohomogeneous phase, these reactions do not fall under our definition of PTC reactions and consequently have been largely omitted here. However, it is possible that a PTC reaction as defined in this book could proceed mechanistically in a micellar or inverted micellar environment. This would not be a typical PTC reaction, but there are some indications that such processes can occur.

Earlier thorough reviews of PTC are found in Brändström's 1974 booklet *Preparative Ion Pair Extraction* [379] and the books *Phase Transfer Catalysis in Organic Synthesis* by Weber and Gokel [3501] and *Phase Transfer Catalysis; Principles and Techniques* by Starks and Liotta [3177], published in 1977 and 1978, respectively.

Important book or series chapters on fundamentals and applications by Brändström [387, 389, 390], Montanari and coworkers [2387], and Mąkosza [2172, 2183] are also available, as are two Russian language books: *Mechanism of Phase Transfer Catalysis* (1984) by S. S. Yufit [3593] and a 1989 monograph by Y. Sh. Goldberg. The latter was translated into English in 1992: *Phase Transfer Catalysis; Selected Problems and Applications* [1200]. Special reviews concerning the role of PTC in preparation and chemical modification of polymers deserve attention [1053, 3033]. This is an area not covered in depth in the present text.

## 1.2 Ion Pairs in Organic Media

In many cases, PTC entails the extraction of ionic molecules into an organic solvent, or their solubilization therein. It is therefore of interest to know something about the state and properties of such solutions. A complete review of the subject is beyond the scope of the present book, but a concise and qualitative summary will be presented in this section. For a more thorough, in-depth treatment of physicochemical concepts, methods, and results the reader is referred to textbooks of physical and physical organic chemistry [e.g., 1318] or recent monographs [2576, 3248, 3249]. The structure and



reactivity of carbanions in ion pairs and of carbanionoid metal organic compounds have been treated in a review [950] and special monographs [648, 951, 2947].

Typical inorganic sodium and potassium salts do not dissolve in nonpolar organic solvents. The same is true for salts of inorganic anions with small organic cations, (e.g., tetramethylammonium). Such ammonium salts often can be dissolved in dichloromethane and chloroform, however. Moreover, the use of rather large organic anions may make alkali metal salts soluble in solvents such as benzene. For example, sodio diethyl-*n*-butylmalonate gives a 0.14 M solution in benzene. This solution shows no measurable freezing point depression, indicating a high degree of association. Similarly, large onium cations (e.g., tetra-*n*-hexylammonium) solubilize in hydrocarbons salts with even small, organophobic anions (e.g., hydroxide ions). Ionophores, which are molecules made up of ions in the crystal lattice, dissociate (or partially dissociate) into solvated cations and anions in solvents of high dielectric constant. Such solutions in water are good conductors. Even strong electrolytes may dissolve in other, less polar, solvents to give solutions of low electrical conductance, indicating that only a fraction of the dissolved salt is dissociated into free ions. To account for this behavior Bjerrum advanced the ion pair hypothesis in 1926. His original hypothesis was subsequently refined by Fuoss [1084] and a number of other researchers. Ion pairs are neutral entities formed by the association of oppositely charged ions. Basically, ion pairs are held together by Coulombic forces, but strong interactions with the medium also contribute occasionally. Ion pairs are thermodynamically distinct species coexisting in equilibrium with the free ions:



An important distinction between free ions and ion pairs is that solutions containing only the latter do not conduct electricity. Thus, conductivity measurements can be used to estimate the proportion of free ions present. Ion pairs behave as single entities with respect to cryoscopy and vapor pressure measurements. Dissociation constants are known for ion pairs in many solvents. As a general rule, and at low concentrations, solvents of dielectric constant greater than 40 contain mainly dissociated ions. In solvents of dielectric constant lower than 10–15 almost no free ions exist, even at high dilution.

In any given solvent, the larger the ions the greater the degree of dissociation. For example, the equilibrium constant for ion pair formation  $K$  in nitrobenzene is  $K = 80$  for tetraethylammonium chloride,  $K = 62$  for the bromide, too small to estimate for tetra-*n*-butylammonium picrate, and  $K = 7$  for tetraethylammonium picrate [3527].

The behavior and structure of ion pairs and higher complexes have been studied extensively with physical techniques such as conductivity, UV, visible, IR, and Raman spectroscopy, and electron and nuclear magnetic resonance. A review of methods and results is available [3248].

Solvents cannot be regarded as continuous, structureless substances. Ion-dipole interactions occur on contact between solute and solvent molecules. The solvation number is an indication of the extent of such an interaction. The closer the contact between solute and solvent, the greater the interaction. Dipole, dispersion, induction, and hy-