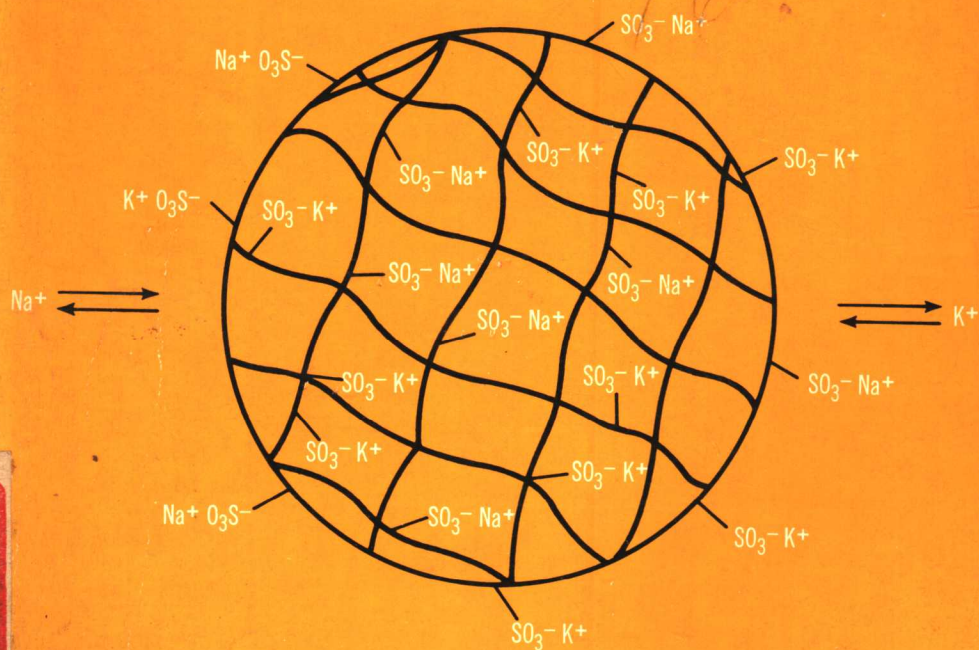


JOSEPH X. KHYM

# ANALYTICAL ION-EXCHANGE PROCEDURES IN CHEMISTRY AND BIOLOGY

Theory, Equipment, Techniques



PRENTICE-HALL BIOLOGICAL TECHNIQUES SERIES

**ANALYTICAL  
ION-EXCHANGE PROCEDURES  
IN CHEMISTRY AND BIOLOGY**  
Theory, Equipment, Techniques

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## PREFACE

Ion-exchange processes can be used in place of or to simplify many of the chemical operations that routinely confront the experimenter. Employment of these techniques has become so commonplace in the laboratory that the advanced student or practicing investigator not well acquainted with them is at a distinct disadvantage. The separation of like elements into distinct groups or the separation of closely related species within a group, concentration of a trace material, synthesis or degradation of compounds, are only a few of the tasks easily performed with ion-exchange materials. One does not have to be a specialist to practice with assurance the techniques of ion exchange. Ordinary laboratory experience is all the background training that is necessary for one to acquire the necessary skills for experimentations with ion-exchange materials.

One purpose of this book is to encourage those investigators inexperienced in the practice of ion-exchange methodology to adapt these time-saving procedures to many of the chemical manipulations that are carried out in the laboratory. It is intended also to serve as a "refresher" source for those who intermittently utilize ion-exchange methods.

Emphasis is placed on practical experimentation with ion-exchange materials. However, to use these materials effectively, some knowledge of theory is necessary. The amount of theory presented here is kept at a minimum, and what is presented is considered as applying to the ideal case (just as the gas laws apply to an ideal gas). It is not the purpose of this book to render complete historical accounts or give complete bibliographies.

I wish to express my gratitude to Dr. Alexander Hollaender, editor of the Biological Techniques Series, for his encouragement during the preparation of this book. I would like to express appreciation also to Drs. Waldo E. Cohn and James W. Holleman, who painstakingly reviewed the manuscript, and to Dr. J. L. Epler for his valuable comments as to the contents of this text.

I wish to thank the library staff of the Biology Division at Oak Ridge National Laboratory, particularly Azolene Vest, for promptness in acquiring desired literature sources, some very difficult to obtain. Also I am grateful to Nancy Trent who patiently typed and retyped the later chapters of this book.

Finally, my deepest appreciation is expressed to Marylou Khym who typed the rough drafts and ensuing manuscript for the earlier chapters and who in addition handled the vast amount of correspondence that is associated with the preparation of a book.

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# Fundamentals of Ion Exchange

# ONE

## A. VERSATILITY OF ION-EXCHANGE MATERIALS

Many of the chemical manipulations routinely encountered in the laboratory can be quickly and efficiently carried out by employing ion-exchange materials. Some of these common operations are listed below.

1. Conversion of one salt to another
2. Desalting
3. Concentration
4. Removal of interfering ions prior to analytical determinations
5. Removal of ionic impurities from organic reagents
6. Rapid quantitative determination of ionic solute concentrations (e.g., standardization of analytical reagents)
7. Catalysis
8. Fractionation or separation of both inorganic and organic ions by chromatographic procedures

As implied by their name and as inferred from the list of reactions given, ion-exchange materials react ionically with other ions. Ion exchangers are termed anionic or cationic depending upon whether they take up the negative or the positive ions of a surrounding electrolyte, respectively.

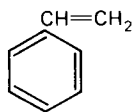
## B. THE CHEMICAL NATURE OF ION EXCHANGERS

A variety of inorganic and organic substances have been used as ion exchangers. For example, such natural products as proteins, celluloses, carbon, common clays, and various minerals contain mobile ions that will exchange with other ions in a surrounding solution. However, these natural substances have low exchange capacities and other unfavorable chemical and physical properties that limit their practical utilization as ion-exchange substances. Consequently, before 1935, the technique of ion exchange was not widely used as a unit process either in the laboratory or on an industrial scale.

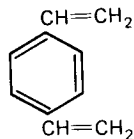
Modern ion-exchange technology began in 1935 with the now classical investigations of Adams and Holmes (1) who discovered that synthetic organic polymers, more commonly referred to as resins, are capable of exchanging ions. These synthetic resins are solids that may be pictured structurally as being composed of two parts. The fundamental framework of these ion-exchange substances is an elastic, three-dimensional hydrocarbon network or matrix; the second part of their structure is hydrophilic in nature and consists of ionizable groups (either acidic or basic) chemically bonded to the hydrocarbon framework. The organic network is fixed, is insoluble in almost all the common solvents used in the laboratory, and is, for all practical purposes, chemically inert. However, the ionizable or functional groups attached to the matrix have active (mobile) ions that can react with or be replaced by other ions. Therefore, if an exchanger particle is brought into contact with an aqueous solution containing ions, the latter may be easily exchanged for those ions initially bound to the resin.

The chemical behavior of an ion-exchange resin is determined by the nature of the functional groups that are attached to the hydrocarbon skeleton. There are two major classes of ion-exchange polymers: *cation exchangers*, whose functional groups can undergo reaction with the cations of a surrounding solution; and *anion exchangers*, whose functional groups can undergo reaction with the anions of a surrounding solution.

A typical cation-exchange resin is prepared by the copolymerization of styrene (I) and divinylbenzene (II). During the polymerization reaction, first linear chains of polystyrene are formed, and these in turn then become covalently bonded to each other, at intermittent points, by divinylbenzene



I



II

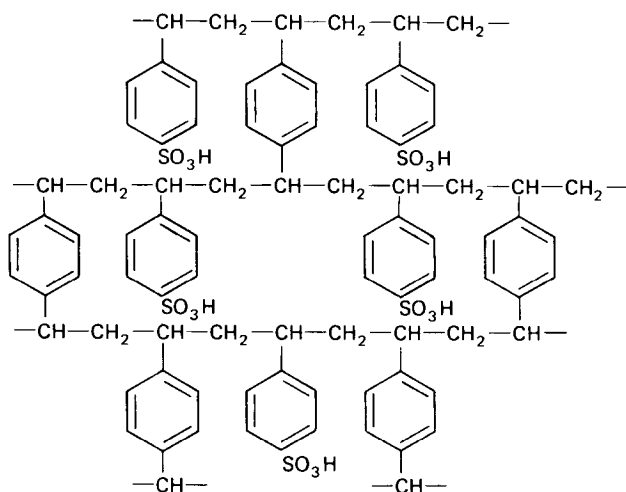


Fig. 1-1. Strong-acid polystyrene type cation-exchange resin.

crosslinks; the result is a three-dimensional insoluble hydrocarbon network. If sulfuric acid is then allowed to react with this copolymer, sulfonic acid groups ( $-\text{SO}_3^-\text{H}^+$ ) are introduced into most of the benzene rings of the styrene-divinylbenzene polymer, and the final substance formed is a cation-exchange resin (2, 3) whose structure is given in Fig. 1-1.

A typical anion-exchange resin is prepared by first chloromethylating the benzene rings of the three-dimensional styrene-divinylbenzene copolymer to attach  $-\text{CH}_2\text{Cl}$  groups and then causing these to react with a tertiary amine, such as trimethylamine. This gives the chloride salt of a strong-base exchanger (2, 3), which has the structure given in Fig. 1-2.

These crosslinked vinylbenzene resins have remarkable chemical and physical properties. For instance, they are insoluble in concentrated acids, bases, and salts and are resistant to oxidation, reduction, and radiation. The resins have excellent thermal stability and have a high "exchange capacity," which means that a high percentage of the benzene rings of the styrene-divinylbenzene matrix must contain the added ionic functional groups (3). These ionic groups, covalently bonded to the resin matrix, maintain the same chemical properties that they display in aqueous solution; they behave as if they were in the free monomeric form. Consequently, the ionic group fixed to the polymer determines the nature of the ion-exchange material (4). Therefore, just as there are strongly and weakly ionized acids and bases, so can there be these classes of ion-exchange resins. Since there obviously can be many types of ion exchangers, this brings up the question of how best to classify ion-exchange materials.

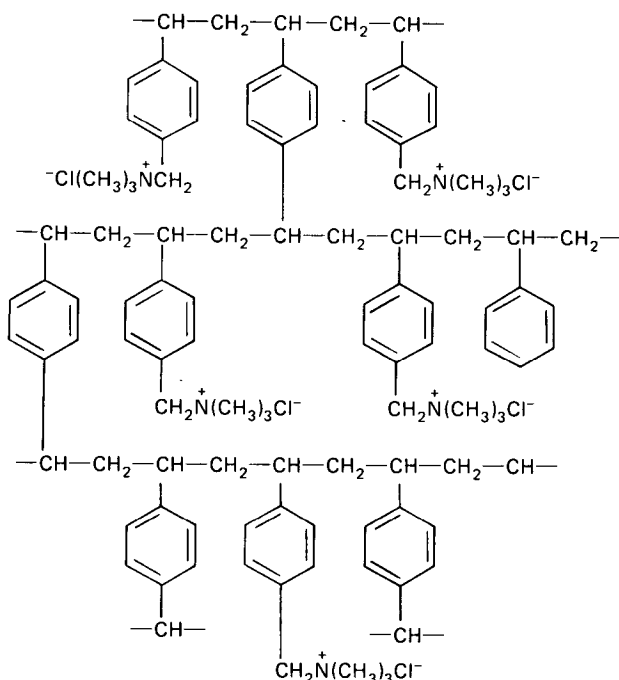
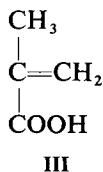


Fig. 1-2. Strong-base quaternary ammonium polystyrene type anion-exchange resin.

Thus far, the modern types of ion exchangers have been considered as being of a resinous nature. For all practical purposes, the lattice material of these synthetic polymers is of only two kinds. The so-called polystyrene resins are of the type illustrated in Figs. 1-1 and 1-2. The other variety of resinous exchanger is prepared by the copolymerization of methacrylic acid (III) and divinylbenzene (II). The result of this reaction gives the weak-acid, acrylic type of ion exchanger (2, 3) that has the structure shown in Fig. 1-3.



In addition to the two kinds of crosslinked vinylbenzene polymers, there are other types of exchange substances of high capacity, such as inorganic ion-exchange crystals and exchange materials made by introducing functional groups into polyacrylamide gels, celluloses, or dextrans. These latter ion-

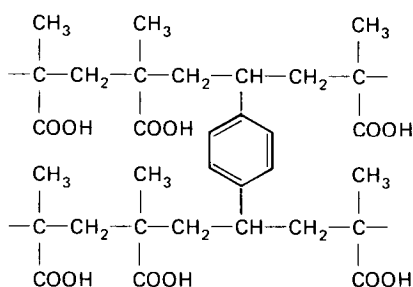


Fig. 1-3. Weak-acid acrylic type cation-exchange resin.

exchange materials have specialized uses, such as high selectivities for certain ions, or are useful in fractionating macromolecules, such as serum proteins, nucleic acids, and enzymes; these types of exchange materials are considered in a later section (Chapter 3) on "Selecting the Proper Ion-Exchange Material." Many of their properties are given in tabular form in that chapter.

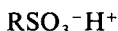
The crosslinked vinylbenzene resins are more versatile and are utilized more than any other exchange material available. For this reason, they will be considered, for the remainder of this book, in more detail than other types of exchangers. Nevertheless, the principles and concepts associated with the synthetic crosslinked resins can readily be applied to other ion-exchange substances.

### C. CHEMICAL FORMULAS FOR ION-EXCHANGE RESINS

Ion-exchange resins can be considered as insoluble acids, bases, or salts and, as such, their roles in chemical reactions are easier to visualize if they are assigned chemical formulas. Once the matrix material is specified and is then given a symbol, various kinds of ion exchangers can be classified by formula. Symbols such as  $\phi$  or R are commonly used to represent the lattice material of an ion-exchange substance. By attaching to such symbols the known chemical structure of functional groups, ion-exchange materials are thus conveniently characterized according to their formulas. For example, formulas IV and V represent a weak-acid and a strong-acid cation-exchange resin,



IV

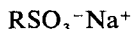


V

respectively. The sodium salts of IV and V, in turn, have the formulas given in VI and VII



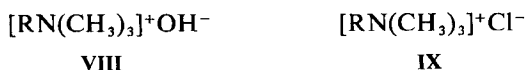
VI



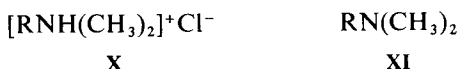
VII



A strong-base exchanger is represented by formula VIII, and if it were converted to the chloride form, it would then have the formula denoted by IX. A weak-base exchanger is highly ionized only when

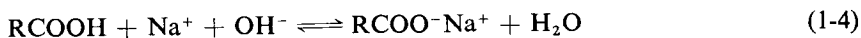
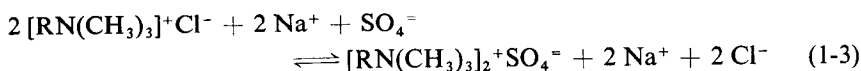
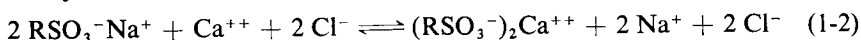
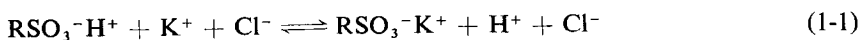


in a salt form such as that represented by formula X. In the free base form, the formula would simply be that given for XI, which is the formula for a tertiary amine. Being a weak base, it would tend to



lose its ion-exchange properties at pH values much above 7. It follows then that ion exchangers have chemical properties similar to those of other ionic substances. Exchangers with highly ionized functional groups are similar to strong acids and bases, while those with weakly ionized functional groups behave like weak acids or bases.

Chemical equations can be written in the usual manner for the reactions between ion exchangers and other ionic substances. This is illustrated in the following set of equations.



## D. PHYSICAL PROPERTIES OF ION-EXCHANGE RESINS

### 1. Particle Size and Form

Most ion-exchange resins are sold in the form of spherical beads. In a typical preparation, the particles may range from 1 mm to less than 0.04 mm. The resin beads are graded in a range of sizes by manufacturers and suppliers. The coarser particles (50–100 mesh)\* are usually used in batch operations in which slurry contact of the exchanger and solution is made. Following the reaction, the resin beads may be separated from the solution phase by filtration, settling, or centrifugation. The finer resin particles (200–400 mesh or smaller)\* are utilized in chromatographic procedures wherein

\*See Chapter 3.