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MICROENCAPSULATION

II. INTERFACIAL REACTIONS[1]

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ABSTRACT

In recent years a number of papers and patents describing the use of interfacial reactions as a means of microencapsulation have been reported in the literature. This paper discusses the technique of microencapsulation by interfacial reactions and the effect of variables which may influence the integrity of the microcapsules. Variations of the basic interfacial polymerization techniques are described with special reference to interfacial polycondensation, the formation of polymer material by induced catalyzation, vapor deposition technique, and in-situ polymerization. Examples of some processes used and/or the types of reacting species are also included.

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[1] Part I of this paper dealing with phase separation (coacervation) appeared in volume 4 number 1 of THIS JOURNAL.

The feasibility of using interfacial reaction as a means of preparing microcapsules is believed to have resulted from a demonstration of preparing a nylon film by the process of interfacial polymerization (1). The basic chemistry involved in interfacial reactions is the interaction between an organic solution of an acid halide with an aqueous solution of a diamine resulting in the production of a film at the interface of the two liquids. In order to employ this technique for the preparation of microcapsules, one simply incorporates the core material in the system. The basic design of the system may be considered to be similar to the coacervation process in that the preparation of the microcapsules involves the following three steps:

1. Dispersion of the material to be encapsulated in a vehicle containing one of the reactants
2. Addition of the second reactant
3. Collection of the microcapsules

The technology of preparing microcapsules utilizing interfacial reactions has grown considerably in recent years and a number of variations have been reported in the literature. These variations have resulted primarily due to the many diverse applications of the microcapsules and/or because of the specific nature of the material being encapsulated (Table I). Some of the common procedures employed are discussed here.

TABLE I

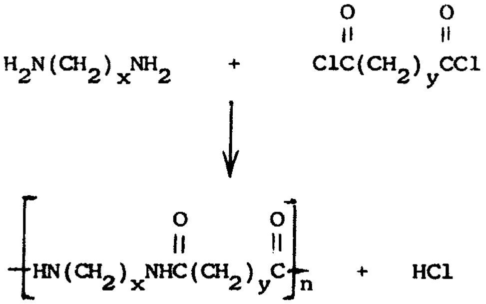
INDUSTRIAL APPLICATIONS OF INTERFACIAL REACTIONS

COMPANY	PROCESS
BATTELLE DEVELOPMENT CORPORATION	VAPOR DEPOSITION
FUJI PHOTO FILM CO.	INTERFACIAL POLYMERIZATION
FUJI PHOTO FILM CO.	IN-SITU POLYMERIZATION
IMPERIAL CHEMICAL INDUSTRIES	INTERFACIAL POLYMERIZATION
INTERNATIONAL BUSINESS MACHINES CORPORATION	INTERFACIAL POLYMERIZATION
MINNESOTA MINING AND MANUFACTURING COMPANY	INTERFACIAL POLYMERIZATION
MOORE BUSINESS FORMS	INTERFACIAL POLYMERIZATION
NATIONAL CASH REGISTER	DISSOLVED MONOMER POLYMERIZATION
NATIONAL LEAD CO.	IN-SITU POLYMERIZATION
PENWALT CORPORATION	INTERFACIAL POLYMERIZATION
POLAROID CORPORATION	INTERFACIAL POLYMERIZATION
STANFORD RESEARCH	IN-SITU POLYMERIZATION
UNION CARBIDE CORPORATION	VAPOR DEPOSITION

INTERFACIAL POLYMERIZATION

The formation of a polymer at the interface between two liquids phases is known as interfacial polymerization (2). The most common and widely used application of interfacial polymerization technique of microencapsulation is the interfacial polycondensation reaction.

The most popular illustration of microencapsulation by interfacial polycondensation is an example of the Schotten-Baumann reaction of an acid halide with a compound containing an active hydrogen atom (-OH, -NH, -SH). The reaction is believed to take place by an SN^2 (nucleophilic) mechanism to form a protonated amide from which a proton is rapidly eliminated by the presence of an added base. An example of this reaction is the interaction of an acid dihalide with a diamine:

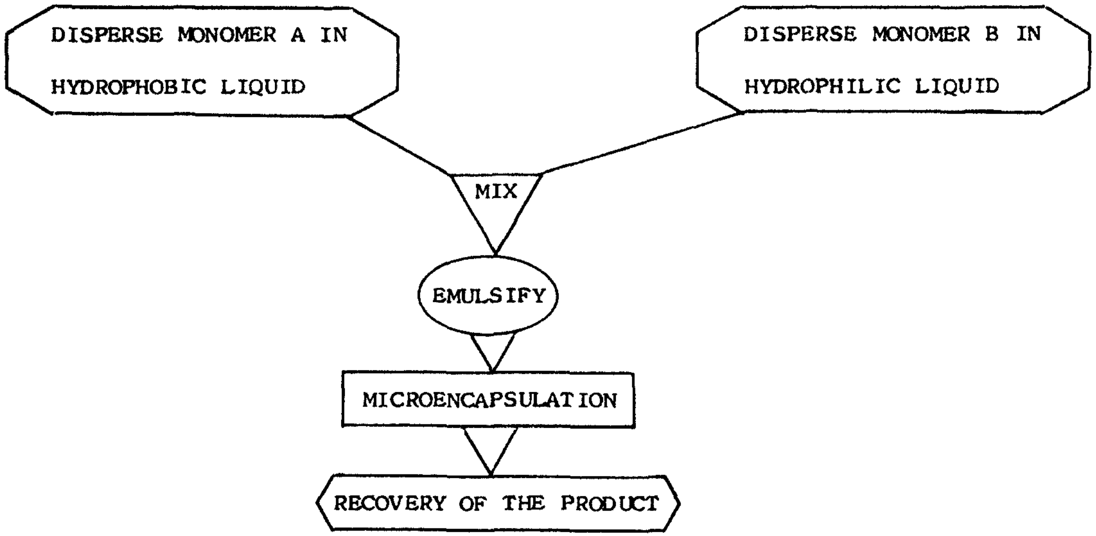


$$H_2N(CH_2)_xNH_2 + Cl\overset{\overset{O}{\|}}{C}(CH_2)_y\overset{\overset{O}{\|}}{C}Cl \Big\downarrow \left[HN(CH_2)_xNH\overset{\overset{O}{\|}}{C}(CH_2)_y\overset{\overset{O}{\|}}{C} \right]_n + HCl$$

The resulting polymer (polyamide) is popularly known as nylon. The nylon formed is identified by the reacting species involved. For example, if the reaction involved the polymerization of 1:6-hexanediamine [$H_2N(CH_2)_6NH_2$]and sebacoyl chloride [$ClCO(CH_2)_8COCl$], the resulting polyamide would be called nylon 6-10. The first number in the nylon represents the carbon atoms of the diamine and the second number represents the total carbon atoms of the acid dihalide.

In order to prepare the nylon microcapsules of a water-soluble drug, an aqueous solution of the diamine containing the drug is emulsified in an organic liquid to form a water-in-oil emulsion. The dicarboxylic acid halide is dissolved in the organic liquid and added to the water-in-oil emulsion. The dicarboxylic acid halide is dissolved in the organic liquid and added to the water-in-oil emulsion with constant stirring (Scheme I). The nylon walls of the microcapsules are thus formed due to the interfacial polymerization reaction between the diamine and the acid dihalide.

Ordinarily, one would expect that the reaction between the diamine and the acid dihalide is not suitable for polymerization since hydrolysis of the acid halide groups would be expected to upset the balance of the functional groups. However, the success of the reaction depends on the fact that polymerization takes place in the organic phase and therefore the partitioning of the components involved in the reaction becomes important. Thus, polymerization will occur only if the rate of polymerization greatly exceeds the rate of partitioning of the acid dihalide in the aqueous phase. In other words, by choosing an acid dihalide which is nearly insoluble in water and therefore will partition only slowly, and a water-soluble diamine having an appreciable partition



SCHEME I: MICROENCAPSULATION BY INTERFACIAL POLYCONDENSATION coefficient towards the organic phase, one can cause polymerization to occur near the interface. Experiments have shown that an acid dihalide having less than eight carbon atoms does not produce satisfactory microcapsules (3). For example, using 1:6-hexanediamine as one of the reacting components, it was virtually impossible to prepare microcapsules with either succinoyl chloride ($ClOCH_2CH_2COCl$) or adipoyl chloride ($ClOCH_2CH_2CH_2CH_2COCl$). While sebacoyl chloride $[ClO(CH_2)_6-COCl]$ gave permeable microcapsules, terephthaloyl chloride ($ClOC_6H_4COCl$) produced microcapsules which had very strong walls.

Polyamide is only one of the many polymers used in the interfacial polycondensation reactions. Some of the commonly used chemical classes of polymers used in microencapsulation by interfacial polycondensation are listed in Table II.

In general, the interfacial polycondensation reactions are very rapid chemical reactions and the rate constants of the order of 10^2 to 10^6 liters $mole^{-1}$ sec^{-1} are not uncommon (4). However, the rate of reaction decreases as the polymer precipitates and greater the polymer formed, greater is the reduction in the rate of reaction. The polymer yield, polymer quality, and the molecular weight of the polymer formed depend on various parameters, including the concentration of the reactants, the choice of the solvents, the rate of stirring, the additives present, etc. (5). By carefully controlling the manufacturing variables, one can prepare microcap-

TABLE II

CHEMICAL CLASSES OF POLYMERS IN INTERFACIAL POLYCONDENSATION

REACTING GROUPS			LINKING STRUCTURE	POLYMER
$-O-H$ BISPHENOL	+	$Cl-\overset{O}{\overset{\|}{C}}-$ DICARBONYL CHLORIDE	$-O-\overset{O}{\overset{\|}{C}}-$	POLYESTER
$-O-H$ BISPHENOL	+	$O=C=N-$ DI-ISOCYANATE	$-O-\overset{O}{\overset{\|}{C}}-\overset{\mid}{N}-$	POLYURETHANE
$-O-H$ BISPHENOL	+	$Cl-\overset{O}{\underset{O}{S}}-O$ DISULFONYL CHLORIDE	$-O-\underset{\underset{O}{\|}}{\overset{O}{\overset{\|}{S}}}-$	POLYSULFONATE
$-O-H$ BISPHENOL	+	$Cl-\overset{O}{C}-Cl$ PHOSGENE	$-O-\overset{O}{\overset{\|}{C}}-O$	POLYCARBONATE
$-\overset{\mid}{N}-H$ DIAMINE	+	$Cl-\overset{O}{C}-$ DICARBONYL CHLORIDE	$-\overset{\mid}{N}-\overset{O}{\overset{\|}{C}}-$	POLYAMIDE
$-\overset{\mid}{N}-H$ DIAMINE	+	$Cl-\overset{O}{\underset{O}{S}}-O$ DISULFONYL CHLORIDE	$-\overset{H}{\overset{\mid}{N}}-\underset{\underset{O}{\|}}{\overset{O}{\overset{\|}{S}}}-$	POLYSULFONAMIDE

sules having a sufficiently narrow range of particle size, anywhere from about 2 microns to about 3 mm. (6). A number of reports describing the process and the effect of various variables on the release and/or properties of the microcapsules have been reported in the literature (7-10).

POLYMERIZED MONOMER MATERIAL

A process for making minute substantially spherical individual pressure-rupturable, oil-containing microcapsules has been described (11) in which the capsule walls are of solid artificial polymer material formed of polymerized monomer material. At least one selected monomer material, which is polymerizable to a solid, is dissolved in an oil in which the solid polymer material is insoluble. The solution is dispersed as droplets in a polar liquid, such as water, where polymerization of the monomer material takes place under the influence of a catalyst. The catalyst may either be introduced into the oil, into the monomer material before solution, into the monomer solution, into the polar liquid, or into the dispersion. The formation of the polymer material is induced by catalyzation. Because the polymer is insoluble in the oil, it deposits at the interface of the oil droplets and polar liquid, and thus forms an individual solid wall around each oil droplet. The resulting product is discrete pressure-rupturable, substantially spherical, oil-containing microcapsules.

A variety of monomers, catalysts, and emulsifying agents may be used to achieve microencapsulation by this method. These are listed in Table III.

VAPOR DEPOSITION

The vapor deposition technique of microencapsulation differs from the conventional methods of preparing microcapsules in that while most microencapsulation methods (12) employ liquid techniques (phase separation, coacervation, interfacial polymerization, spray-drying etc.), vapor deposition of polymeric materials is usually accomplished dry in vacuum environment without a liquid carrier. Microencapsulation of the material is accomplished by tumbling it within an evacuated cylinder. In the case of liquids, the material is formed in droplets, frozen, and held at temperatures below the melting point. Deposition of the polymer from the reactive monomer due to the polymerization of the shell forming capsule membrane upon dispersed frozen droplets or suspended solid particles takes place until the reaction ceases due to the build up of a chemically impervions layer. The tumbling particles are thus uniformly coated and form the microcapsules.

A procedure using vapor deposition technique and employing the poly-p-xylenene family of polymers was first reported by Szwarc (13) who used xylene as the starting material. Later it was shown that improved polymer quality and process

TABLE III

COMPONENTS USED IN MICROENCAPSULATION

BY POLYMERIZED MONOMER MATERIAL

MONOMERS	EMULSIFYING AGENTS	CATALYSTS
ETHYL ACRYLATE	ACACIA	ACETYL PEROXIDE
ETHYL METHACRYLATE	SODIUM ALKYL SULFATES	ALPHA-ALPHA-AZO-DIISOBUTYRONITRILE
METHYL ACRYLATE	SORBITAN MONOLAUREATE	BENZOYL PEROXIDE
METHYL METHACRYLATE	SORBITAN MONOPALMITATE	CALCIUM PEROXIDE
STYRENE	SODIUM MYRISTATE	DITERTIARYBUTYL PEROXIDE
VINYL ACETATE		HYDROGEN PEROXIDE
		SODIUM PYROPHOSPHATE PEROXIDE
		ZINC PEROXIDE

control could be achieved by vacuum pyrolysis of di-p-xylylene. Various chemical derivatives of di-p-xylylene have been synthesized, many of which can be converted to polymer in a similar manner. Examples of the reactions are shown in Fig. 1.

In another process (14), solid particles are coated by vaporizing the coating material in a body of hot moving gas. The coating material is then condensed onto the solid particles which are maintained in a fluidized bed. For example, copper particles (about 100 microns) are coated with alumina which enters the fluidized bed through a generator at about 200°C. It is claimed that the temperature of application of the coating influences the integrity of the microcapsules obtained.

The physical properties of the microcapsules prepared by vapor deposition make them attractive choices for use where chemical resistance, low moisture permeability, and high use temperature are important. Most techniques produce microcapsules which are insoluble in organic solvents at ordinary temperatures and are not affected by most acids and alkalis. In addition, the process can produce microcapsules ranging from about 200 microns to about 2,000 microns (6) having a wall thickness which can be made to range from a few angstroms to about 100 microns.

IN-SITU POLYMERIZATION

In-situ polymerization is a variation of the chemical vapor deposition technique. Here also the core particles

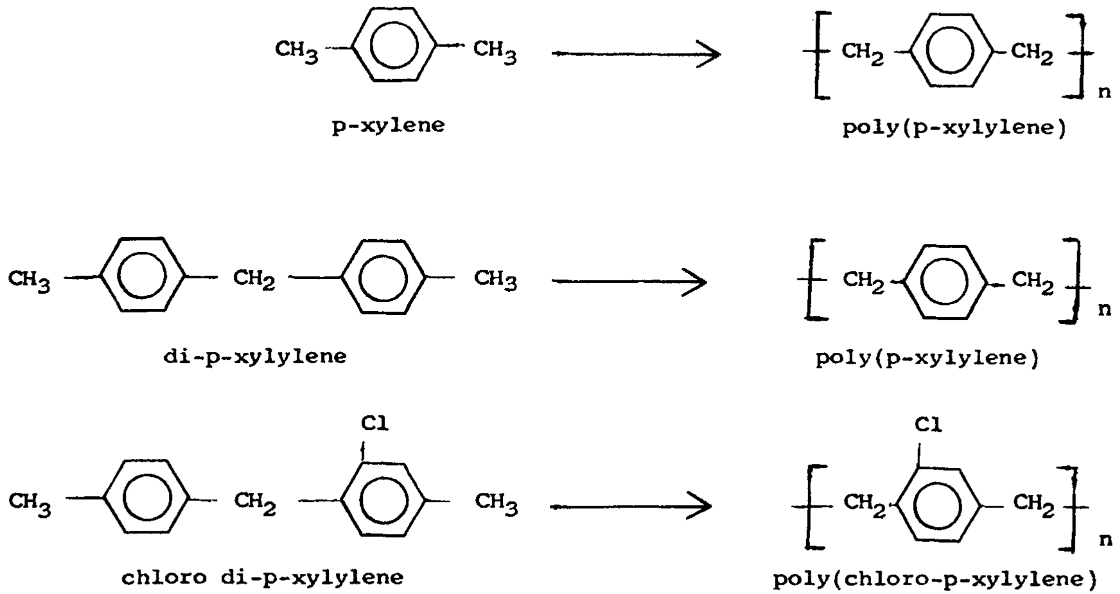


Figure 1

POLYMERIZATION BY VAPOR DEPOSITION

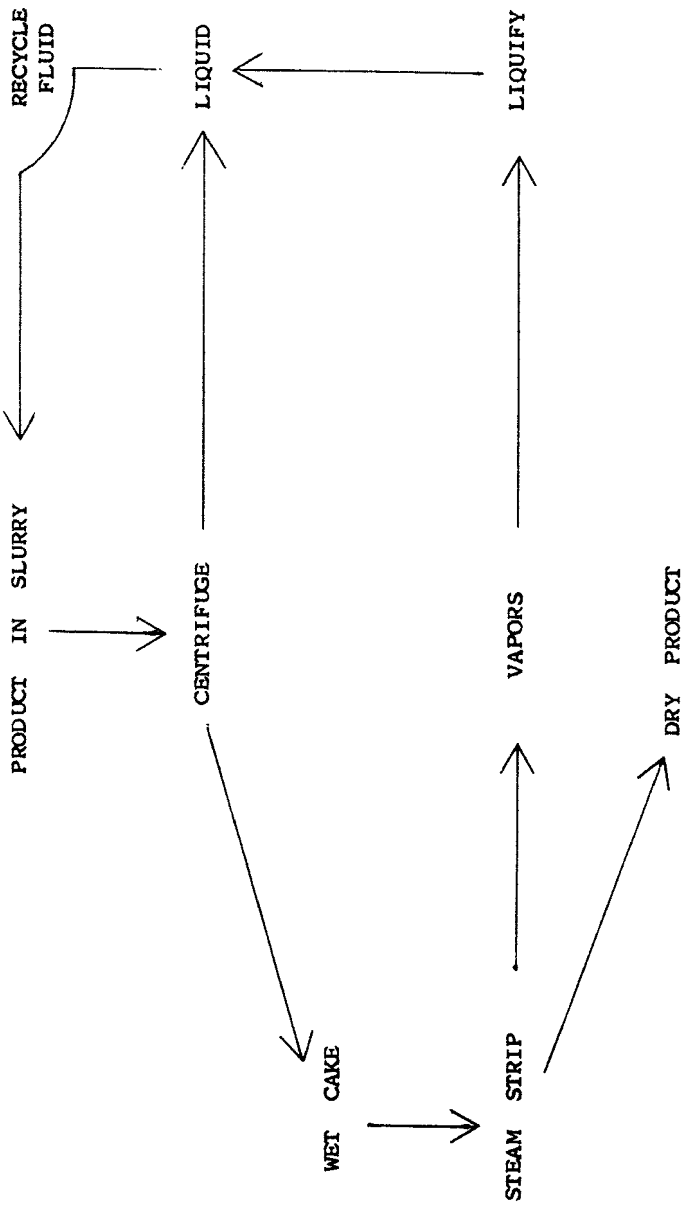


Figure 2

CONTINUOUS PROCESS FOR IN-SITU POLYMERIZATION can be either solid or liquid, but lower temperatures are generally employed. In this process the polymerization of an elofin, usually ethylene, is conducted directly upon the particle surface. Briefly, the process involves the dispersion of the particles in a liquid vehicle, such as toluene followed by the addition of a catalyst. The function of the catalyst is to create activated sites on the particles to be encapsulated. An olefin, such as ethylene, is then bubbled into the mixture to cause polymerization. Polymerization takes place directly on the surface of the core material and as polymerization proceeds, the polymer gradually surrounds the nucleus material (15). As shown in Fig. 2, the process can be made continuous (15).

A somewhat similar process has been described for encapsulating aerosol particles by in-situ polymerization (16). This process utilizes the aerosol as the condensation nuclei upon which organic monomers polymerize. In yet another variation of in-situ polymerization, a cyclic di-p-xylelene is pyrolyzed to form reactive diradicals which can be made to polymerize on the surface of moving core particles (17-20).

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