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Removal of Organic Compounds from Water via Cloud-Point Extraction with Permethyl Hydroxypropyl-β-cyclodextrin

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Abstract

Aqueous solutions of nonionic surfactants are known to undergo phase separations at elevated temperatures. This phenomenon is known as "clouding," and the temperature at which it occurs is referred to as the cloud point. Permethylhydroxypropyl-β-cyclodextrin (PMHP-β-CD) was synthesized and aqueous solutions containing it were found to undergo similar cloud-point behavior. Factors that affect the phase separation of PMHP-β-CD were investigated. Subsequently, the cloud-point extractions of several aromatic compounds (i.e., acetanilide, aniline, 2,2′-dihydroxybiphenyl, *N*-methylaniline, 2-naphthol, *o*-nitroaniline, *m*-nitroaniline, *p*-nitroaniline, nitrobenzene, *o*-nitrophenol, *m*-nitrophenol, *p*-nitrophenol, 4-phenazophenol, 3-phenylphenol, and 2-phenylbenzimidazole) from dilute aqueous solution were evaluated. Although the extraction efficiency of the compounds varied, most can be quantitatively extracted if sufficient PMHP-β-CD is used. For those few compounds that are not extracted (e.g., *o*-nitroacetanilide), the cloud-point procedure may be an effective one-step isolation or purification method.

INTRODUCTION

When subjected to an increase in temperature, aqueous solutions of many nonionic surfactant systems undergo phase separation. The temperature at which this occurs is referred to as the cloud point (*1*, *2*). These phase separations have been used as extraction systems in a manner analogous to liquid–liquid extraction (*3–6*). Surfactant aggregates are considered to be the hydrophobic phase in an aqueous–nonionic surfactant sys-

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tem. The two phases can be separated by raising the temperature above the cloud point followed by centrifugation, decanting, and/or filtration. Most organic molecules are concentrated in the surfactant-rich phase. When the temperature is lowered below the cloud point, the surfactant-rich phase usually becomes clear and homogeneous again.

Removal of organic materials from water has been accomplished with relative success using nonionic surfactants (*7*) and, to a greater extent, activated charcoal (*8–10*). Both of these methods have some drawbacks associated with them, however. Disadvantages of nonionic surfactant extraction include difficulties in obtaining the pure surfactant, degradation of thermally labile analytes at the higher temperatures required for cloud-point separation, narrow ranges of surfactant concentration or pH over which cloud point is observed, decrease of cloud point with increasing ionic strength, and difficulty in monitoring the absorbance of analytes in the UV-visible region because of aromatic moieties present in most nonionic surfactants (*11*). The main disadvantages of using adsorption onto activated carbon to remove organic compounds from water are the limited capacity and the significance of regeneration (*12*).

An alternative cloud-point extraction method was developed which has fewer limitations than previous methods. Specifically, a derivatized form of β-cyclodextrin is shown to undergo phase separations at temperatures slightly above ambient. This derivatized cyclodextrin does not absorb significant amounts of light above 200 nm. Its ability to extract organic solutes from dilute aqueous solution was evaluated.

Cyclodextrins (CD) are cyclic oligosaccharides containing from six to twelve glucopyranose units linked together through α-(1,4)-glycosidic linkages. They have torroidal-shaped apolar cavities which are lined with secondary hydroxyl groups at the mouth and primary hydroxyl groups at the opposite end of the cavity. The internal diameter of the cyclodextrin is sufficient to permit inclusion complexation with a variety of molecules. A combination of things facilitate inclusion complex formation, including hydrophobic effects, hydrogen bonding and dipole–dipole interactions with the cyclodextrin hydroxyl groups, release of high-energy complexed water, ring strain relaxation, and so forth (*13*, *14*). Native cyclodextrins do not undergo phase separations at elevated temperatures (i.e., they have no cloud point). In fact, their solubility in water tends to increase with temperature as do most compounds. However, as previously mentioned, certain derivatives of cyclodextrins, such as permethylhydroxypropyl-β-cyclodextrin, do exhibit cloud-point behavior.

In this paper we report the synthesis of permethylhydroxypropyl-β-cyclodextrin (PMHP-β-CD) and its use to remove trace amounts of organic compounds from water. The method of removal involves separating the

CD complex using the cloud-point phenomena. The effects of pH, salt, and CD concentration are also evaluated. The results, based upon examinations of a number of analytes, indicate that a cloud-point separation using PMHP-β-CD is a viable alternative for removal of many organic compounds from water. This method is particularly attractive because of the low temperatures required for cloud-point formation, broad ranges of pH in which cloud point is observed, enhancement of removal of organics in high ionic strength solutions, and low absorbance of PMHP-β-CD in the UV-visible region.

EXPERIMENTAL

Materials

Chemicals were obtained from various companies as follows. Aldrich Chemical Company: acetanilide, aniline, *o,p*-chloroaniline, dimethylsulfoxide (99% anhydrous), *o*-nitroacetanilide, *o,m,p*-nitroaniline, nitrobenzene, *o,m,p*-nitrophenol, 4-phenylazophenol, 2-phenylbenzimidazole, 3-phenylphenol, phosphorus pentoxide, and sodium hydroxide; Fisher Chemical Company: methanol, glacial acetic acid, chloroform, methyl iodide, and anhydrous sodium sulfate; Sigma Chemical Company: 2,2′-dihydroxybiphenyl, sodium chloride, and 2-naphthol; Consortium für Elektrochemische Industrie GMBH: hydroxypropyl-β-cyclodextrin (MS 0.9).

Apparatus

A Shimadzu LC-6A liquid chromatographic system with a SPD-2AM variable wavelength spectrophotometric detector and a Linear 1200 strip chart recorder were used to quantitate all samples. C_8 and C_{18} columns (5 mm × 25 cm) from Advanced Separation Technologies Incorporated (Whippany, New Jersey) were used to separate each compound. The detector was operated at the maximum for each analyte. The sample loop size and flow rate were 20 μm and 1.0 mL/min, respectively.

Procedure

All samples were prepared using the following method. Distilled water was added to each analyte to produce the desired concentration. A specified amount (see the tables) of PMHP-β-CD was added to 5 mL of the analyte solution. This mixture was then heated in a water bath at 55°C for 10 min to induce the cloud-point phase separation. The solution was then vacuum filtered for 20 s with a 60 mL, 2–2.5 μm porosity Pyrex Buchner funnel (Aldrich, Milwaukee, Wisconsin) which had been heated in a 200°C oven for 20 min. The filtrate was then injected into the HPLC system without further preparation. Another sample without PMHP-β-CD was also filtered using identical conditions. This filtrate was designated as the sample blank. Sodium hydroxide and acetic acid were used for pH adjustment in the pH study. Sodium chloride was added at specific concentrations for the ionic strength study. The mobile phases were mixtures of methanol and water, filtered through a membrane filter of 0.45 μm pore size and degassed by the vacuum-ultrasonication method prior to use. Peak areas, used to determine the percent of compound removed, were calculated by triangulation.

Synthesis of Permethyl Hydroxypropyl-β-cyclodextrin

Hydroxypropyl-β-cyclodextrin (MS 0.9) was dried overnight to remove hydrated water in a heated vacuum drying chamber with phosphorus pentoxide as the drying agent. HP-β-CD (30 g) was added to 700 mL DMSO and stirred for 10 min (or until completely dissolved) in a stoppered round bottom flask. To this solution, 84 g of finely ground sodium hydroxide that had been dried overnight in a 200°C oven was added. This mixture was stirred vigorously for 4 h in a stoppered flask. Taking care to keep the temperature below 35°C, 130 mL methyl iodide was slowly added. After 2 h of continuous stirring, the solution was decanted into an open vessel and 600 mL water was added. The product was then extracted with 3 × 200 mL chloroform, washed with 3 × 200 mL water, and dried for 2 h over sodium sulfate. After the chloroform was removed by rotoevaporation, the product was dried overnight in the previously described drying chamber and ground using a mortar and pestle.

A second permethylation was then performed using the previously synthesized permethyl HP-β-CD in place of HP-β-CD. The procedure was followed as before using 30 g permethyl HP-β-CD, 69 g NaOH, 108 mL methyl iodide, 600 mL DMSO, 600 mL water, and 600 mL chloroform (*15*).

RESULTS AND DISCUSSION

The cloud-point behavior of PMHP-β-CD is described by the phase diagram in Fig. 1. Note that phase separation is dependent on the concentration of PMHP-β-CD and that cloud points can be observed at temperatures as low as 28°C. This makes cloud-point extractions using PMHP-β-CD much easier to accomplish than some other analogous procedures where much higher temperatures must be reached before phase separation occurs (*16*). Although clouding occurs at temperatures lying on the boundary line in Fig. 1, it is recommended that slightly higher temperatures

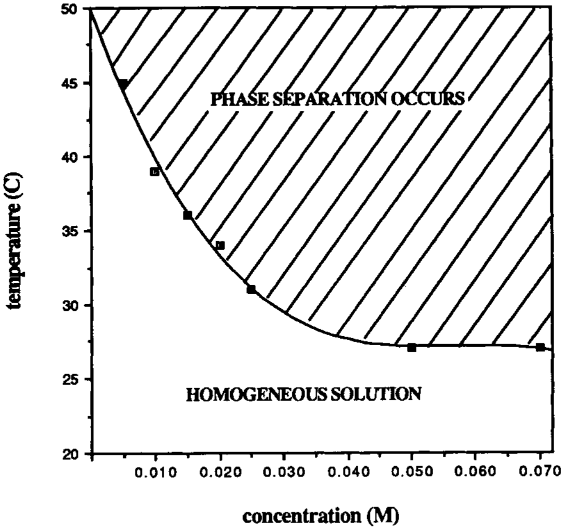

FIG. 1. Permethyl hydroxypropyl-β-cyclodextrin phase diagram.

(~10°C) be used for quick and efficient separations. It is also recommended that concentrations of PMHP-β-CD above 0.005 M be employed for best results.

Although pH changes from 3 to 13 had no effect on clouding, the addition of salt, organic solvents, or chlorinated analytes affected clouding ability and therefore the separation. Upon observing the effects of salt on clouding, it seemed that some additional coagulation of the clouded CD occurs with the addition of as little as 0.01 M NaCl. As higher concentrations of salt are added, there is more of an effect. At 0.5 M NaCl, almost all clouded PMHP-β-CD has settled to the bottom of the container within a few minutes. This allows for much easier separation of the clouded CD from the bulk water. On the other hand, the use of miscible organic solvents or chlorinated analytes tended to inhibit the phase-separation process. An addition of 1 mL methanol or acetonitrile in 5 mL clouded aqueous 0.01 M PMHP-β-CD turned the solution completely clear. This is probably a result of higher solubility of PMHP-β-CD in the hydro-organic solvent mixture than in water. When analyzing chloroanilines, the cloud point was somewhat diminished even at a low concentration of chloroaniline (1×10^{-5} M). These results indicate that moderate amounts of polar organic solvents and some chlorinated analytes interfere with the clouding phenomenon, while the addition of salt enhances the phase separation of PMHP-β-CD from water.

TABLE 1

Percent Removal of Various Aromatic Compounds from Water Using PER-HP-β-CD[a]

Compound	Percent[b] removed	Analyte concentration $(M \times 10^{-5})$	PMHP-β-CD concentration (M)
Acetanilide	45	1.0	0.017
Aniline	59	2.5	0.014
o-Chloroaniline	—	5.0	0.017
p-Chloroaniline	—	5.0	0.017
2,2′-Dihydroxybiphenyl	71	1.0	0.017
N-Methylaniline	74	190	0.017
2-Naphthol	99	1.0	0.017
o-Nitroacetanilide	0	1.0	0.017
o-Nitroaniline	73	1.0	0.017
m-Nitroaniline	34	1.0	0.017
p-Nitroaniline	70	1.0	0.017
Nitrobenzene	91	100	0.017
o-Nitrophenol	59	1.0	0.017
m-Nitrophenol	71	1.0	0.017
p-Nitrophenol	61	1.0	0.014
4-Phenazophenol	95	1.0	0.017
3-Phenylphenol	72	1.0	0.017
2-Phenylbenzimidazole	77	1.0	0.017

[a] A 5-mL aqueous sample is used in all cases.

[b] The percent removed is subject to the concentration of PMHP-β-CD added.

[c] Concentrations that removed between 40–90% of most compounds studied were chosen so that removal comparisons could be made between compounds.

Table 1 is a list of the percent removal of various aromatic compounds from water using the cloud-point separation technique. It should be noted that most compounds which possess more than one aromatic ring have higher extraction rates than those with only a single ring. One-ring compounds are included into the CD cavity but do not form as tight a "fit" as most two-ring compounds (*17*). All compounds were removed from water to some extent except for *o*-nitroacetanilide and the chloroanilines. As previously mentioned, chlorinated substances seem to inhibit cloud-point formation. Hence the chloroanilines were not removed because no phase separation occurred. The case of *o*-nitroacetanilide is very interesting. An excellent phase separation occurs in the presence of this compound. However, little or none of it is concentrated into the PMHP-β-CD phase (Table 1). This is the only compound of those tested where this occurred. Size cannot be a factor since compounds both larger and smaller than *o*-nitroacetonilide were effectively extracted.

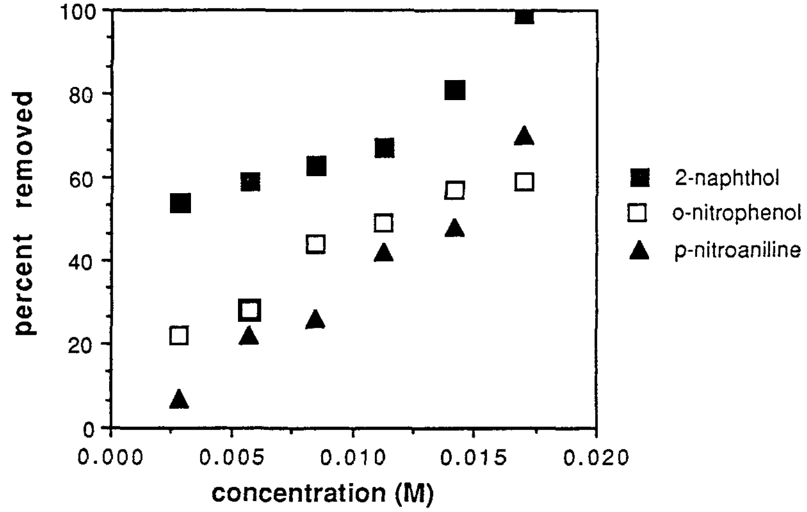

FIG. 2. Concentration effect of PMHP-β-CD on removal.

Figure 2 illustrates the effect of PMHP-β-CD concentration on percent removal. As expected, a higher percentage of the analyte is removed as more derivatized cyclodextrin is introduced into the system. It is obvious that almost all materials which have at least some affinity for the cyclodextrin phase could be removed at nearly 100% as long as high enough concentrations of PMHP-β-CD are used. Figure 2 also shows the preferential extraction of 2-naphthol as compared to other compounds.

As seen in Table 2, the addition of anywhere from 0.01 to 0.50 M of sodium chloride either improves or has little effect on the extraction efficiency of the three test compounds (i.e., 2-naphthol, *o*-nitroaniline, and nitrobenzene). These test compounds were respectively acidic, basic, and neutral. Ionizable analytes, in particular, seemed to be salted out of the aqueous phase and into the cyclodextrin phase. This, coupled with the fact that salt enhances the phase-separation process (*vide supra*), make this technique even more effective for solutions of high ionic strength.

The results listed in Table 3 show the effect of pH on the extraction efficiency of several organic compounds. In most cases the pH effect was relatively small. However, for some compounds, particularly those where the organic ion and neutral molecule have significantly different binding constants, pH had a noticeable effect on extraction efficiency. *m*-Nitrophenol is a case in point. Clearly the protonated, neutral *m*-nitrophenol is more completely extracted into the cyclodextrin phase (i.e., Table 3, pH

TABLE 2
Effect of Salt on the Cloud-Point Extraction of Organic Compounds[a]

Compound	Salt concentration (M)	Percent removal
2-Naphthol	0.00	82
	0.01	96
	0.05	94
	0.10	92
	0.50	94
o-Nitroaniline	0.00	52
	0.01	67
	0.05	65
	0.10	72
	0.50	70
Nitrobenzene	0.00	91
	0.01	88
	0.05	81
	0.10	87
	0.50	82

[a] Concentration of all compounds is 5×10^{-5} M, except for nitrobenzene which is 1×10^{-3} M. A 5-mL aqueous sample is used in all cases. PMHP-β-CD concentration is 0.017 M for all compounds.

3) than the corresponding anion (i.e., Table 3, pH 10). Different thermodynamic binding constants of *m*-nitrophenol and its conjugate base to various cyclodextrins are well documented (*18*). However, it should be noted that even at pH 10, *m*-nitrophenol can be quantitatively removed from solution as long as a sufficient excess of PMHP-β-CD is used. These results indicate that PMHP-β-CD cloud-point extraction can be performed successfully under either basic or acidic conditions for a wide range of compounds.

The separation of aromatic compounds using this method is particularly attractive because PMHP-β-CD, if properly purified, shows little or no absorbance in the UV-visible region. Many other substances that are used for removal of organic material from water possess an aromatic ring, making detection in the UV-visible range difficult or impossible (*11*). In this study the maximum absorbance wavelength for all compounds was used without encountering significant background absorbance from the extractant (i.e., PMHP-β-CD). The ability to use nearly any wavelength in the

TABLE 3
Effect of pH on the Cloud-Point Extraction of Organic Compounds[a]

Compound	pH	Percent removed
2-Naphthol	3.0	86
	7.0	82
	10.0	87
o-Nitroaniline	3.0	50
	7.0	52
	10.0	47
Nitrobenzene	3.0	85
	7.0	91
	10.0	98
m-Nitrophenol	3.0	67
	7.0	60
	10.0	40
m-Nitroaniline	3.0	69
	7.0	63
	10.0	61

[a] Concentration of all compounds is 5×10^{-5} M except for nitrobenzene which is 1×10^{-3} M. A 5-mL aqueous sample is used in all cases. PMHP-β-CD concentration is 0.017 M for all compounds.

UV-visible region is important if extremely low detection limits are desired. Another advantage of using PMHP-β-CD is that temperatures as low as 35°C or as high as 90°C can be used for separation, with no change in cloud-point behavior. This broad temperature range means that no stringent control of temperature is necessary to conduct a successful separation.

CONCLUSIONS

It has been shown that PMHP-β-CD can be used to remove a variety of organic compounds from water without encountering many of the problems that occur in other analogous techniques. The cloud-point separation is conducted at relatively low temperatures over a broad concentration range and is not adversely affected by pH or ionic strength. The objective of this study was the removal of trace organics from water, but obviously this method could also be an effective analytical method to concentrate numerous compounds, thereby lowering detection limits. The fact that PMHP-β-CD shows little absorbance in the UV-visible region and can enhance fluorescence as well will increase its usefulness in areas of analytical importance. These results indicate that this method could be incorporated into a large-scale wastewater cleanup operation or in any general operation to concentrate and separate organic material from bulk aqueous solution.

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