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Selective Trace Level Analysis of Phenolic Compounds in Water by Flow Injection Analysis−Membrane Introduction Mass Spectrometry

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Flow injection analysis coupled with membrane introduction mass spectrometry (FIA-MIMS) with on-line derivatization is shown to allow fast, accurate, nearly interference-free, and sensitive (low μg/L) quantitation of phenolic compounds in water. On-line FIA derivatization of the phenolic compounds is performed by acetic anhydride acetylation in a K_2CO_3-buffered alkaline medium. The phenol acetates so formed efficiently permeate a silicone membrane and are directly transferred to the mass spectrometer, in which they are analyzed with selectivity and high sensitivity via selected ion monitoring. FIA-MIMS analysis was performed for aqueous solutions of phenol, 2-methylphenol, 4-chlorophenol, 4-chloro-3-methylphenol, 2,4-dichlorophenol, and 2,4,6-trichlorophenol, and detection limits in the 0.5−20 μg/L (ppb) range were observed for an analytical frequency of six samples/h. FIA-MIMS for phenolic compound analysis is considerably less time-consuming and labor intensive than most chromatographic methods based on liquid−liquid extraction and preconcentration procedures and is therefore applicable for on-line and in-situ monitoring of phenols in wastewaters and in the environment. FIA-MIMS employing acetic anhydride derivatization is also virtually free of interferences since it combines chemical, membrane, and enhanced MS selectivity; hence quantitation of phenolic compounds can be performed in the presence of congeners.

Introduction

Phenol and its derivatives are toxic to humans and aquatic organisms and are rated among the most common and serious environmental contaminants (*1*). These priority water pollutants (*2*) are widely used as industrial raw materials and are introduced into the environment directly through industrial wastewaters or indirectly as transformation products from natural and synthetic chemicals. Phenols are naturally found at low and acceptable concentrations in rivers and water reservoirs, but anthropogenic inputs can raise phenol concentrations affecting drastically the organoleptical properties (*3*) of the water and causing potential harm to public health. Routine disinfection of drinking water by chlorination, for instance, produces several chlorophenols which can impart taste and odor to water at concentrations as low as 1 μg/L (*1*). Allowable levels of phenolic compounds in drinking water vary within the 1−10 μg/L range or less (*4*); hence selective and sensitive analytical techniques are needed to monitor these serious water contaminants. Treatment of industrial wastewaters also would benefit greatly from rapid, ideally on-line, analytical techniques for phenol monitoring.

Several analytical techniques are used to identify and to quantitate phenolic compounds in water (*4, 5*). Owing mainly to its high sensitivity in the μg/L range, the classical colorimetric method (4a,h) based on the purplish-red color obtained by condensing phenols with 4-aminoantipyrine (4-AAP) is widely used to measure the total content of phenols in water. The 4-AAP method presents, however, a few drawbacks (*6*): (i) it is nonselective hence unable to differentiate between the many possible phenol contaminants; (ii) some phenols, mainly the *para*-substituted phenols, show limited or no reactivity toward the color reagent, and (iii) sample pretreatments such as distillation are often necessary to remove potential interferences, but several phenols fail to distill completely.

When selectivity is needed, liquid or gas chromatographic methods are employed, but their detection limits without preconcentration steps are often too high (*7*). More commonly, therefore, phenolic compounds are extracted and preconcentrated prior to the chromatographic analysis by liquid−liquid extraction (LLE) or solid-phase extraction (SPE) (*8*). The more polar phenolic compounds are, however, difficult to extract from aqueous samples; hence their recoveries are low. Continuous extraction and several preconcentration procedures have been applied to improve phenol recovery and detection limits (*9*), but these methods with several extraction and solvent exchange steps and with the use of hazardous chlorinated solvents are time-consuming and labor intensive (*4*), hence not applicable for on-line or in-situ monitoring of phenols in the environment.

Both the extraction efficiency of phenols from water and the chromatographic performance can be enhanced considerably by derivatization, and anhydrides (most often acetic or pentafluorobenzoyl anhydrides) have been used to derivatize phenols directly in water (*10*). Recently, Ojala et al. (*11*) showed that off-line acetylation of phenols in water enhances their membrane introduction mass spectrometry (MIMS) (*9*) detection limits by nearly 2 orders of magnitude (typically in the 0.5−10 μg/L range) thus providing a direct, selective, and highly sensitive method for phenol quantitation. The acetylation-MIMS method shows major advantages and is therefore promising for the efficient monitoring of phenols in environmental water samples.

MIMS (*12*), a powerful technique for the analysis of volatile (*13*) and semivolatile (*14*) organic compounds in water, is fully compatible with continuos monitoring using flow injection analysis (FIA) (*15*) methods of sample handling. The coupling of FIA with MIMS (FIA-MIMS) is benefitial since it presents excellent quantitative precision and accuracy, high analytical frequency, simplicity of the experimental setup, and economy of sample (*12, 16*).

We herein describe the use of FIA coupled with MIMS with on-line acetic anhydride derivatization for the trace level quantitation of phenolic compounds in water. The FIA-MIMS method shows several advantages: it allows nearly interference-free monitoring of many phenolic compounds in water with no extraction or preconcentration steps and with high selectivity (combined chemical, membrane and enhanced mass spectrometric discrimination), speed, accuracy, and sensitivity (detection limits in the μg/L range).

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TABLE 1. Selected Ions Used for MS Quantitation and Confirmation, Linear Range, and Detection Limits (DL) for FIA-MIMS Analysis of Phenolic Compounds as Acetates in Water

phenolic compd	MW (ArOAc)	$ArOH^{+\cdot}$ *m/z* (RA)[a]	$ArOAc^{+\cdot}$ *m/z* (RA)[a]	linear range (μg/L)	DL[b] (μg/L)
phenol	136	94 (100)	136 (18)	5−1000	2
2-methylphenol	150	107 (100)	150 (23)	5−1000	5
4-chlorophenol	170	128 (100)	170 (18)	1−1000	0.5
4-chloro-3-methyl-phenol	184	142 (100)	184 (17)	2−1000	2
2,4-dichlorophenol	204	162 (100)	204 (16)	5−1000	5
2,4,6-trichlorophenol	238	196 (100)	238 (16)	20−1000	20

[a] Relative abundance in the 70 eV EI mass spectrum. [b] Defined for a sinal-to-noise ratio of 3:1.

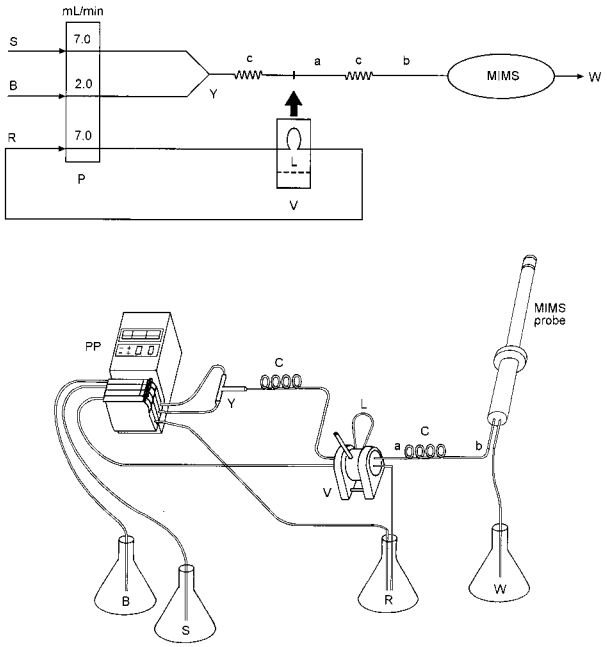

FIGURE 1. Diagrams of the experimental setup used for the FIA-MIMS integrated on-line derivatization analysis of phenols in water. *PP*: peristaltic pump; *V*: FIA valve; *C*: mixing glass coils; *L*: reagent loop (defines the volume of acetic anhydride), *R*: derivatization reagent (pure acetic anhydride); *B*: aqueous K_2CO_3 buffer solution; *S*: aqueous phenol solution; *W*: waste. Lengths *a* and *b* are 15 and 30 cm, respectively. The sheet silicone membrane is placed at the tip of a conventional MIMS probe, for details see ref *17*.

Experimental Section

All chemicals were of analytical-reagent grade, and Milli-Q water was used throughout. Aqueous standard solutions of the phenols were prepared by dilutions of 1000 mg/L methanol stock solutions. The FIA-MIMS experimental setup (Figure 1) employs polyethylene tubing (0.8 mm i.d.) and propulsion tubes (Technicon) with different internal diameters selected according to the desired flow rate. A single-quadrupole ABB Extrel (Pittsburgh, PA) mass spectrometer equipped with a conventional MIMS probe (*17*) with a 125 μm silicone sheet membrane (Silastic 500-3 from Dow Corning Co.) was used. Pumping was provided by an Ismatec multichannel peristaltic pump (PP). For the FIA-MIMS analysis, the sample (S) is continuously buffered to pH 11.5 with a 10 g/L potassium carbonate solution (B) (*10*). At the Y intersection, the sample stream is mixed with the buffer stream, but more effective mixing occurs at coil (C). The acetylating reagent (99% acetic anhydride, R) is injected into the buffered sample stream at valve (V) and efficient mixing occurs at the second coil (C). Both mixing glass coils were 4.2 cm long with an internal diameter of 0.2 cm. Under optimized conditions, the sample and buffer were pumped at flow rates of 7.0 and 2.0 mL min^{-1}, respectively, and 50 μL of acetic anhydride (L) was added at (V). To clean the lines, to speed analysis and, hence, to increase analytical frequency, the buffered sample stream was replaced by Milli-Q water a few seconds after MS response reached its maximum.

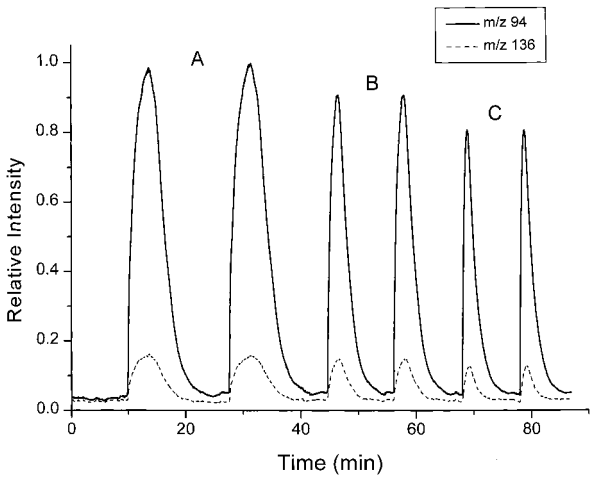

FIGURE 2. FIA-MIMS responses (two repetitions) using SIM (*m/z* 94 and 136) for the analysis of a 1000 μg/L phenol aqueous solution as a function of system total flow rate [A: 5.0, B: 9.0, and C: 10.5 mL/min]. Experimental conditions are listed in Table 2, experiments 7−9.

Results and Discussion

MS Detection and Quantification. Table 1 lists the 70 eV electron ionization (EI) ions used in selected ion monitoring (SIM) to quantitate and to confirm the identity of the six phenolic compounds as their acetates. The most intense peak in the 70 eV EI mass spectra of the acetylated phenols (ArOAc) is the fragment ion $ArOH^{+\cdot}$ formed by the loss of neutral ketene (CH_2CO) from the molecular ion ($ArOAc^{+\cdot}$), whereas the relative abundance of $ArOAc^{+\cdot}$ is typically near 20%. The $ArOH^{+\cdot}$ base peak was therefore used in SIM for quantitation, and the molecular ion ($ArOAc^{+\cdot}$) was used to confirm the identity of the analyte, hence to enhance selectivity.

The higher masses of the $ArOAc^{+\cdot}$ ions (than those of $ArOH^{+\cdot}$ ions used by MIMS analysis of nonderivatized phenols) are also benefitial for selectivity since most VOCs that efficiently permeate the membrane (*12*−*14*) display either lower mass ions or ions not isobaric with $ArOAc^{+\cdot}$. When attention is directed to some selected phenols, selectivity can be further improved by comonitoring other characteristic ions. For the chlorophenols, selectivity can be greatly improved by monitoring, for both $ArOH^{+\cdot}$ and $ArOAC^{+\cdot}$, their ^{35}Cl and ^{37}Cl isotopomers.

FIA-MIMS: Optimization of Operational Parameters. Reaction Path, pH of the Buffered Sample, and Temperature. The lengths of the tubing connecting valve V and the MIMS probe (a and b, Figure 1) were varied, and the highest sensitivity was obtained for a 45 cm long reaction path (a +

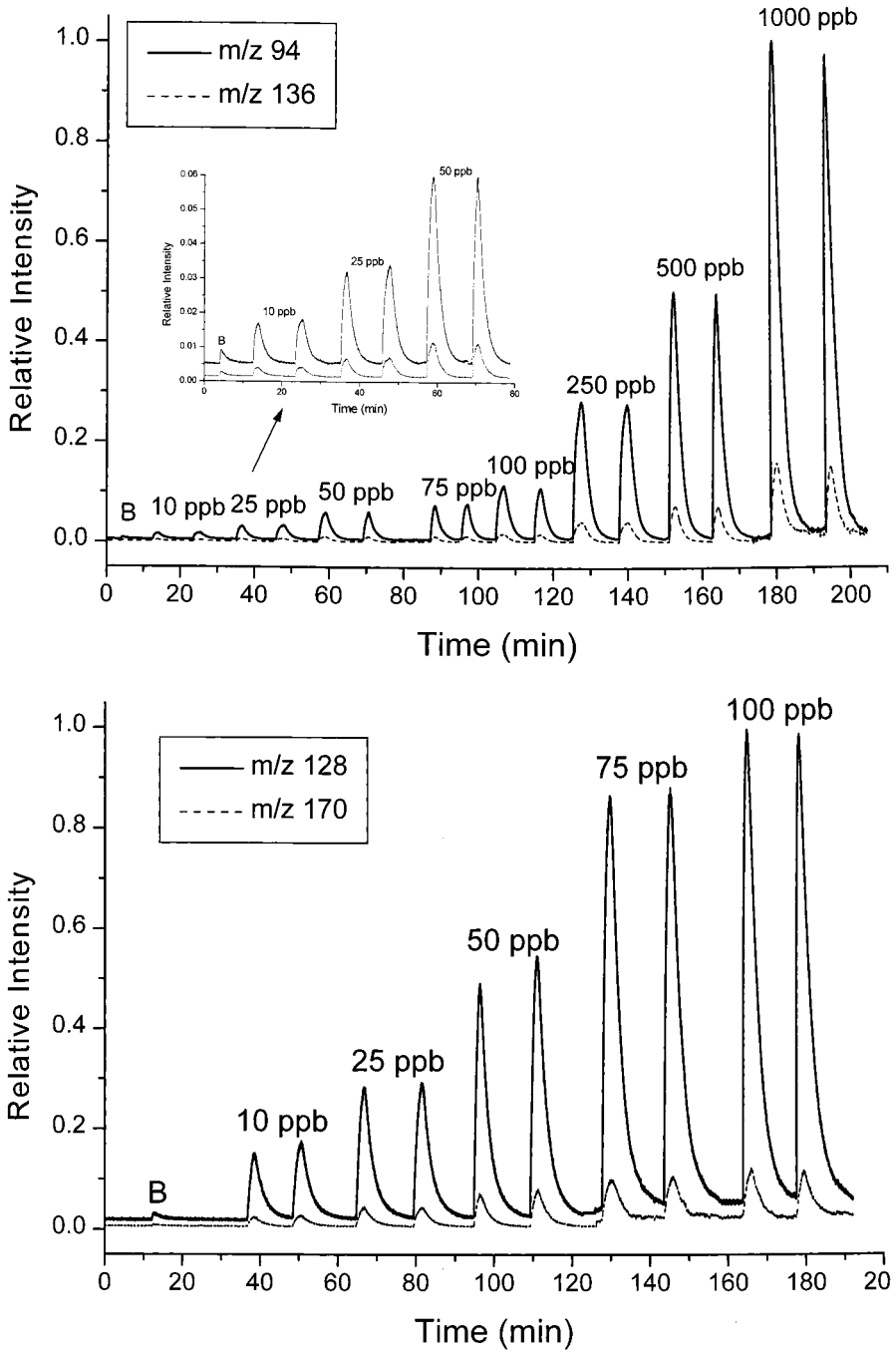

FIGURE 3. FIA-MIMS responses (two repetitions) using SIM at optimized conditions for (a) successive analysis of phenol solutions and (b) of 4-chlorophenol solutions of various concentrations. B is blank.

b). A highly concentrated aqueous K_2CO_3 solution (10 g/L) was used so as to buffer the phenol solution at pH 11.5 while avoiding excessive sample dilution. Although sample heating normally increases the sensitivity of analytical methods based on membrane diffusion (*18*), responses obtained at 60 °C showed minor analytical gain. For simplicity therefore, analyses were performed with solutions at room temperature.

Flow Rates. SIM responses were then tested by varying total flow rates (Table 2). Figure 2 exemplifies the FIA-MIMS responses (for two replicates) for a 1000 μg/L phenol solution analyzed using variable flow rates. As expected, sensitivity (maximum peak height) decreases with increasing flow rates (from A to C), and higher sensitivity was observed for a 5.0 mL/min flow rate (A). But, due to the expected decrease in dispersion within the FIA-MIMS system by reduced codilution, higher flow rates (from A to C) considerably sharpen the analyte SIM signal. The intermediate flow rate of 9.0 mL/min (B) was therefore selected; it combines almost as good sensitivity with high analytical frequency.

Volume of the Acetylating Reagent. While continuously pumping a 1000 μg/L aqueous phenol solution at 7 mL/min through the FIA-MIMS system together with a 10 g/L aqueous K_2CO_3 buffer solution at 2 mL/min, variable volumes (25, 50 and 100 μL) of the acetylation reagent (99% acetic anhydride) were injected at the FIA valve (V) directly into the buffered phenol solution stream (Table 2). Response increased considerably in changing from 25 μL to 50 μL, but no significant increase in response was observed in changing from 50 μL to 100 μL; hence, 50 μL of acetic anhydride is sufficient to derivatize phenols in water at total concentrations up to 1000 μg/L.

TABLE 2. Operational Parameters Tested for Optimal Performance of FIA-MIMS for the Analysis of Phenolic Compounds in Water and the Respective SIM-MS Responses

expt[a]	acetic anhydride vol. (μL)	flow rates K_2CO_3/sample (mL min^{-1})	total flow rate (mL min^{-1})	rel. response (SIM)[c]
1	50	0/7.0[b]	7.0	1.00
2	50	4.0/4.0	8.0	0.47
3	50	2.0/7.0	9.0	0.92
4	25	2.0/7.0	9.0	0.68
5	50	2.0/7.0	9.0	0.94
6	100	2.0/7.0	9.0	1.00
7	50	1.0/4.0	5.0	1.00
8	50	2.0/7.0	9.0	0.91
9	50	2.5/8.0	10.5	0.81

[a] Analysis of an aqueous phenol solution of 1000 μg/L buffered on-line at pH 11.5 with aqueous K_2CO_3 solution. [b] Ten grams of K_2CO_3 was added directly to the sample. [c] Response for phenol acetate was measured for its $PhOH^{+\cdot}$ fragment ion of *m/z* 98.

TABLE 3. FIA-MIMS Recoveries of Phenol Acetate from Groundwater Samples

sample	initial concn (μg/L)	added (μg/L)	found (μg/L)	% recovery
1	54.1	50	110.5	106.1
2	110.5	50	153.5	95.6
3	75.7	50	129.2	102.8
4	129.2	50	181.5	101.3
5	158.9	100	260.1	100.5
6	260.1	100	357.0	99.1
7	242.7	150	398.9	101.6
8	398.9	150	533.0	97.1
9	360.2	200	506.7	90.5
10	506.7	200	662.9	93.8

Analytical Performance. Linearity. Figure 3 shows FIA-MIMS responses (two replicates) using SIM for aqueous solutions of phenol (Figure 3a, *m/z* 94 and 136) and 4-chlorophenol (Figure 3b, *m/z* 128 and 170). The data demonstrates the good linearity and reproducibility of the method. Correlation coefficients higher than 0.999 were obtained.

Detection Limits. Table 1 lists the detection limits (DL) and the linear range tested for the analysis of the selected phenolic compounds by FIA-MIMS under optimized conditions. Detection limits in the 0.5−20 μg/L range were easily attained, which match those reported for the off-line method (*11*).

Repeatability. The method repeatability was tested by comparing the responses for 15 consecutive injections of solutions of the phenolic compounds at either 1000 μg/L and 50 μg/L. The relative standard deviations were about 5% in all cases.

Recovery. Quantitative recoveries were also investigated (Table 3). Groundwater samples spiked with known amounts of phenol were analyzed by the FIA-MIMS method. High recoveries, between 90.5 and 106.1%, were obtained for concentrations ranging from 50 μg/L to 700 μg/L.

Selectivity. The quantitation of phenolic compounds in water by FIA-MIMS with on-line acetic anhydride derivatization displays high selectivity since it allows for combined chemical (an acetylation reaction must occur), membrane (the analyte must pervaporate the membrane), and mass spectrometric discrimination using SIM of higher mass ions (higher than those used for nonderivatized phenol monitoring). These combined discriminations make the analysis virtually free of interferences. The MS monitoring of higher mass ions is beneficial for selectivity since it eliminates inteferences from low mass volatile organic compounds that may efficiently copermeate the membrane, whereas acetic anhydride derivatization also increases selectivity by allowing SIM of *two* specific ions: $ArOH^{+\cdot}$ and $ArOAc^{+\cdot}$, separated in mass by 42u.

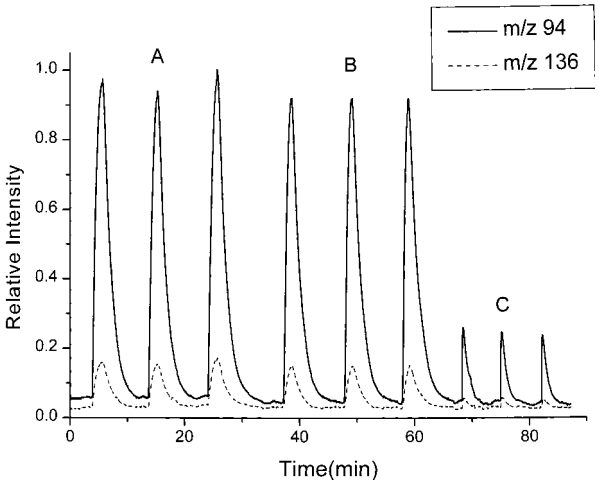

FIGURE 4. FIA-MIMS responses (three repetitions) for the analysis of a 1000 μg/L aqueous phenol solution using SIM at optimized conditions and different sequences of pumping. A: phenol solution/acetic anhydride/phenol solution; B: water/acetic anhydride/phenol solution; and C: phenol solution/acetic anhydride/water.

Analytical Frequency. The whole analytical cycle takes about 10 min per sample, which equates to an analytical frequency of six samples/h. The FIA-MIMS method is therefore considerably less time-consuming (and less labor intensive) than most chromatographic methods based on liquid−liquid extraction or other preconcentration procedures, being applicable for on-line and in-situ monitoring of phenols in wastewaters and in the environment. We are currently applying the method for real samples of wastewaters, groundwaters, and industrial effluents.

The Membrane as the Major Reaction Site. Responses (three replicates each) were measured for an aqueous phenol solution analyzed by FIA-MIMS using three different sequences of pumping (see below). In (A), therefore, the usual pumping sequence was used: a 50 μL of acetic anhydride was injected into the buffered phenol solution stream continuously pumped through the system. In (B), however, water was initially pumped through the system, then a 50 μL acetic anhydride plug was injected, and immediately after the injection of acetic anhydride, the water stream was replaced by the phenol solution; that is, the acetylating agent was sandwiched between water and the phenol solution. In (C), as in (A), 50 μg/L of pure acetic anhydride was injected into the buffered phenol solution stream continuously pumped through the system, but immediately after the acetic anhydride injection, the phenol solution stream was replaced by water.

phenol solution	acetic anhydride	phenol solution	A
phenol solution	acetic anhydride	water	B
water	acetic anhydride	phenol solution	C

Response in (B) was only 10% lower than that in (A) (Figure 4). But in (C), response dropped drastically compared with that in (A), by nearly 80%. This interesting finding suggests, therefore, that the acetylation reaction occurs predominantly at the membrane. Acetic anhydride, a compound of relatively

low polarity, is efficiently adsorbed into the silicone membrane. We propose therefore that, when the aqueous phenolic solution reaches the membrane, the phenols are adsorbed into the acetic anhydride-impregnated membrane, and efficient mixing and acetylation occur in the more concentrated environment of the hydrophobic membrane. This process facilitates (i) phenol adsorption as its acetate into the membrane; (ii) acetylated phenol migration through the membrane; and (iii) acetylated phenol desorption from the membrane surface to the gas phase.

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