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Inhibition of the β-Cyclodextrin Catalyzed Dediazoniation of 4-Nitrobenzenediazonium Tetrafluoroborate. Blocking Effect of Sodium Dodecyl Sulfate

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We have investigated the effects of sodium dodecyl sulfate, SDS, on the reaction between 4-nitrobenzenediazonium, 4NBD, ions and β-cyclodextrin, β-CD, under acidic conditions at $T = 60$ °C by employing a combination of spectrophotometric, chromatographic, and conductometric techniques. Previous studies under acidic conditions indicate that the secondary −OH groups of β-CD solvate 4NBD ions, which are included in the β-CD cavity, leading to the formation of a highly unstable transient diazo ether complex that undergoes homolytic fragmentation with an observed rate constant about 1700 times higher than that in pure aqueous acid solution ($t_{1/2} = 6$ h at $T = 60$ °C) when [β-CD]/[4NBD] = 40. Addition of SDS to a 4NBD/β-CD system makes the k_{obs} values decrease up to its value in a SDS micellar solution, which is similar to that in aqueous acid solution. Dediazoniation product distribution is significantly affected; the reaction between 4NBD and β-CD ([β-CD]/[4NBD] = 40), in the absence of SDS, proceeds exclusively through a homolytic mechanism leading to the quantitative formation of nitrobenzene, ArH, but addition of SDS turns over the mechanism by promoting the heterolytic mechanism. In addition, mixtures of 4-nitrophenol, ArOH, and ArH dediazoniation products are formed; their relative yields depend on the amount of added SDS so that at very high [SDS_T], the heterolytic mechanism becomes the predominant one. Results are consistent with conductometric measurements showing that addition of β-CD to an aqueous surfactant solution inhibits micelle formation and elevates CMC_{app} values because CD encapsulation of surfactant monomers competes with the micellization process and are interpreted in terms of SDS monomers blocking the β-CD cavity by forming a nonreactive complex, releasing 4NBD to the bulk solution.

Introduction

Arenediazonium, ArN_2^+, chemistry has been explored under a wide variety of experimental conditions, but relatively little attention has been given to its reactions in micellar and macromolecular systems.[1−7] During the last years, several groups have investigated (and still they do) the effects of micellar and macromolecular systems on dediazoniations and two major lines of research appear evident; on one hand, the basic physical organic aspects of the reactions have been explored.[4,8−14] Alternatively, new methods to estimate interfacial compositions of weak nucleophiles in colloidal interfaces have been developed on the basis of the atypical and unique characteristics of dediazoniation chemistry.[15−21] To date, literature reports indicate that micellar systems mainly change dediazoniation product distribution but do not modify substantially dediazoniation rate constants,[6,7] in contrast with macromolecular systems such as crown ethers,[3,22−24] which alter significantly the rate constants but not the product distribution. Cyclic oligosaccharides such as cyclodextrins, CDs, may or may not change the rate constants and the product distribution, depending on the nature of the ArN_2^+ ions.[25−27]

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Scheme 1. Basic Representation of the Thermal $D_N + A_N$ Mechanism Operative in Aqueous Acid Solutions, in the Dark, and in the Absence of Reductants

$$Ar\text{-}N_2^+ BF_4^- \xrightarrow{H_2O} (Ar\text{-}N_2^+)solv$$

$$(Ar\text{-}N_2^+)_{solv} \xrightarrow[slow]{k_w} [Ar^+.N_2]_{solv} \xrightarrow{Nu^{n-}} Ar\text{-}Nu^{(n-1)-}$$

Micellar systems are likely to affect dediazoniations by governing their contact with other substrates incorporated in the micelle, with water or with ions present as counterions in the micellar Stern layer.[6,28] Because of electrostatic and hydrophobic interactions, ArN_2^+ ions associate to anionic micelles, but depending on their hydrophobicity, they may also associate to cationic aggregates. Experimental results in anionic, cationic, and nonionic micellar systems are consistent with dediazoniations proceeding through the thermal $D_N + A_N$ mechanism,[6,7] Scheme 1, but recent ab initio calculations also support competitive formation of a S_N2-like transition state.[4]

A striking feature of dediazoniations is the remarkable insensitivity of dediazoniation rates to solvent effects and nucleophile concentrations, suggesting that that the distribution of neutral and anionic nucleophiles in the neighborhood of the ground-state ArN_2^+ ions remains essentially unchanged in the course of the reaction.[8,9,13,14] Thus, product yields reflect concentrations of nucleophiles in the solvation shell of ArN_2^+ ions, and this circumstance has been exploited to estimate interfacial compositions in colloidal aggregates by chemical trapping.[6,21,29,30] In interpreting chemical trapping results, it is assumed that nucleophiles form ion−molecule and ion−ion pairs competitively with ArN_2^+ ions being the exchange rate of nucleophiles in the pairs much faster than that for the thermal dediazoniation such that the pairs are in dynamic equilibrium throughout the time course of the reaction.

An exception for the $D_N + A_N$ reaction mechanism in micellar systems was found for dediazoniation of 4-nitrobenzenediazonium salt (4NBD) in sodium dodecyl sulfate (SDS) systems,[28] where k_{obs} values increase slightly upon increasing [SDS] and micelles promote the homolytic mechanism, although the predominant mechanism is the heterolytic one. Quantitative analyses[31] of the effects of SDS on peak potentials and on peak currents at [SDS] > critical micellar concentration (CMC) allowed estimations of the association constants of the parent 4NBD and of the electrochemically generated nitrobenzene radical, $Ar^{\bullet}$, with SDS micelles; the latter being higher than that of 4NBD by a factor of ∼2, indicating that the nitrobenzene radicals are preferentially located in SDS micelles rather than in the bulk aqueous phase,[31] consistent with the expected higher hydrophobicity of nitrobenzene radicals compared to that of the parent ArN_2^+ ions.

Relatively little work on dediazoniations in the presence of CDs has been carried out, despite that application and utility of CDs are well recognized and documented in important economic areas[32−34] like the pharmaceutical and food industries, where CDs are dispensed either in the form of oral drug carriers or food additives, and, consequently, CDs can be found in the human body both as free CDs and in the form of inclusion complexes. Fukunishi et al.[35,36] first reported the effects of CDs on dediazoniation of 4-NO_2- and 4-Me-benzenediazonium ions in aqueous acid (pH = 5.4) solution, concluding that the reaction proceeds through a homolytic mechanism yielding the ArH reduction product in an 81−99% yield regardless of the nature of the arenediazonium ion and the atmosphere employed (N_2 or O_2). Results with the 4-Me derivative contrast with those reported later by Bravo-Diaz et al.,[25] who studied the dediazoniation of 2-, 3-, and 4-methylbenzenediazonium ions, at different [HCl], in the presence of α-, β-, or γ-CD. Spectrophotometric, HPLC, and electrochemical kinetic data showed that either $[H^+]$ or [CD] have no effects on the observed rate constant, k_{obs}; values for loss of ArN_2^+ ions are the same, within experimental error, as those obtained for ArOH formation; and HPLC analyses of the reaction mixtures showed that only heterolytic products are formed, suggesting that the reaction proceeds through the $D_N + A_N$ mechanism, Scheme 1.

4NBD reacts with β-CD, Scheme 2, by homolytic scission of a transient diazo ether complex,[26,27] increasing the rate constant for 4NBD decomposition by a factor of ∼1700 compared to that in the absence of CD yielding quantitative amounts of the reduction product ArH when [β-CD]/[4NBD] = 40. Details on the mechanism can be found elsewhere.[26]

To get further insight on the reaction, we investigated the effects of SDS on the β-CD catalyzed dediazoniation of 4NBD because both CD and the SDS surfactant play an important role in dediazoniation of 4NBD by modifying the dediazoniation rate constant and the product distribution. The hydrophobic chains of surfactants tend to reside in the hydrophobic cavity of CDs resulting, for ordinary surfactants, in the formation of 1:1, 1:2, or 1:3 surfactant−CD complexes,[37] which are nonreactive, thus, altering substantially the physicochemical properties of CDs, making investigating a system where competing homolytic and heterolytic mechanisms may coexist simultaneously very attractive.

Experimental Section

Instrumentation. UV−vis spectra and some kinetic experiments were followed on a Beckman model DU-640 UV−vis spectrophotometer equipped with a thermostated cell carrier attached to a computer for data storage. Product analysis was carried out on a WATERS HPLC system, which included a model 560 pump, a model 717 automatic injector, a model 486 VIS−UV detector, and a computer for data storage. Products were separated on a Microsorb-MV C-18 (Rainin) reverse phase column (25-cm length, 4.6-mm internal diameter, and 5-μm particle size) using a mobile phase of 75/25 (v/v) acetonitrile/H_2O. The injection volume was 25 μL in all runs, and the UV detector was set at 220 nm. pH was measured using a previously calibrated Metrohm model 713 or model 744 pH meter, both apparatus equipped

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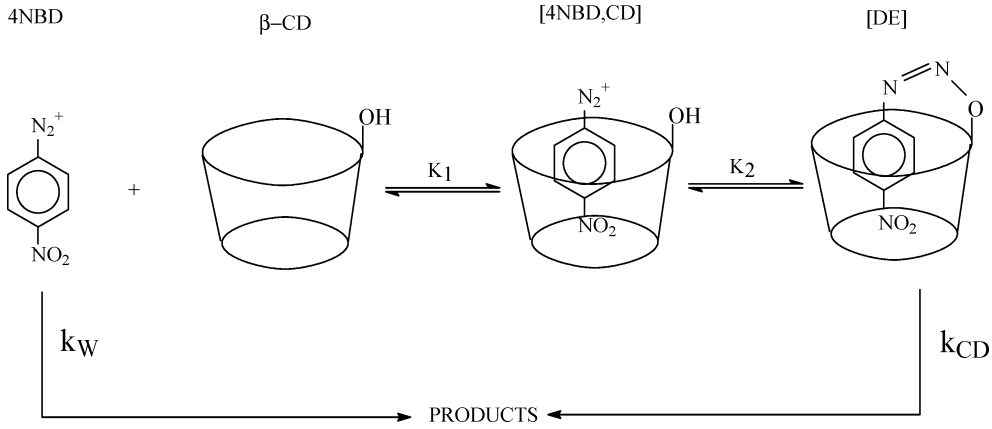
Scheme 2. Proposed Mechanism for the Reaction of 4NBD with β-CD in Aqueous Acid Solution



with temperature sensors. Specific conductivities were obtained by employing a Metrohm model 712 conductometer provided with a four-pole measuring cell (the measured cell factor was equal to 0.82 cm^{-1}) and a Pt-100 temperature sensor attached to a computer for data storage as described elsewhere.[38] Solutions were thermostated in the conductivity cell, equipped with a magnetic stirring device, at $T = 25 \pm 0.1$ °C.

Materials. Reagents were of maximum purity available and were used without further purification. The reagents used in the preparation of 4NBD (as tetrafluoroborate), 4-nitrophenol, ArOH, nitrobenzene, ArH, β-CD, and the surfactant SDS were of the maximum purity available from Aldrich or Fluka and used without further purification. 1-Naphthylamine, employed as the coupling agent in the derivatization protocol, was from Merck. Other materials employed were from Riedel de Häen. All solutions were prepared by using Milli-Q grade water.

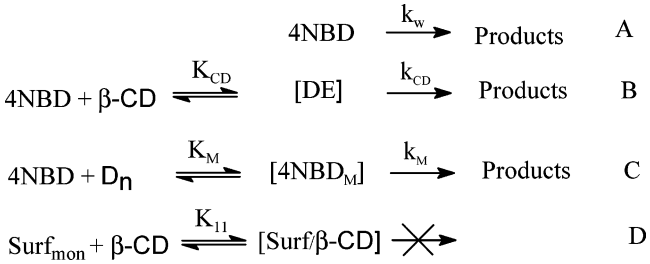
4NBD was prepared under nonaqueous conditions as described in previous work[39,40] and was stored in the dark at low temperature to minimize its spontaneous decomposition. The 4NBD ^1H NMR and the UV−vis spectrum of an aqueous acid (2.0×10^{-3} M HCl) 4NBD solution are consistent with those previously reported.[40] 4NBD stock solutions were prepared by dissolving the diazonium salt in aqueous HCl, to minimize diazotate formation,[41] to give final concentrations of [4NBD] ~ 2×10^{-4} M, and they were freshly prepared and used immediately to minimize their decomposition.

Methods. Product distribution was obtained by employing a chromatographic (HPLC) method as described in previous work.[28,39,42] Kinetic data were obtained by employing spectrophotometric (UV−vis) and chromatographic (HPLC) techniques. Observed rate constants, k_{obs}, were obtained by fitting the absorbance−time or percent yield−time data to the integrated first order eq 1 using a nonlinear least-squares method provided by a commercial computer program, where M is the measured magnitude of the UV−vis absorbance (A) or percent yields. Kinetic runs were done at $T = 60 \pm 0.1$ °C at different acidities (HCl) with 4NBD as the limiting reagent.

$$\ln\left(\frac{M_t - M_\infty}{M_0 - M_\infty}\right) = -k_{obs}t \qquad (1)$$

Spectrophotometric kinetic data were obtained by following the formation of ArOH at an appropriate wavelength.[40] Chromatographic kinetic data were obtained following a well-established procedure that exploits a derivatization method yielding a stable azo dye. Details can be found elsewhere.[43]

Scheme 3. Proposed Dediazoniation Mechanism in the Presence of β-CD and SDS[a]



[a] When [SDS] < CMC_{app}, micelles are not formed and pathway C is not operative. Details on the mechanism involving the pathways A and B are given in Schemes 1 and 2, respectively.

Preliminary HPLC experiments in β-CD systems showed that, under acidic conditions (HCl or Britton−Robinson, BR, buffer), two decomposition products can be formed, ArOH and ArH. Calibration curves for converting HPLC peak areas into concentrations were obtained simultaneously for these dediazoniation products by employing commercial samples dissolved in solutions of similar composition to those used in the HPLC analysis of dediazoniation products at $\lambda = 220$ nm. The percentage of formation, F, of a particular dediazoniation product was obtained from the ratio of the dediazoniation product concentration, [analyte], and the initial diazonium salt concentration, $[4NBD]_0$, estimated by weight, eq 2:

$$F = 100\frac{[\text{analyte}]}{[4NBD_0]} \qquad (2)$$

Results

(1) Effects of β-CD on the Apparent CMC of SDS. Amphiphilic compounds such as surfactants may form stable complexes with CDs,[44,45] Scheme 3D. For the β-CD/SDS system, formation of 1:1 complexes are predominant in view of the reported host−guest binding constants for the 1:1 complex, $K_{11} = 26\,800$ L mol^{-1}, compared to that of $K_{12} = 440$ L mol^{-1} for the 1:2 complex.[46] Because of the surfactant−CD complexation equilibrium, the concentration at which micelles are formed, the *apparent critical micellar concentration*, CMC_{app}, depends on the particular [β-CD] employed. It is usually accepted[45] that the micellization process occurs whenever all of the CD is in the complexed form, and, thus, for a 1:1 complex, the CMC_{app} is expressed[45,47] as the sum of the stoichiometric CD concentration and the CMC in water (CMC_w); knowledge

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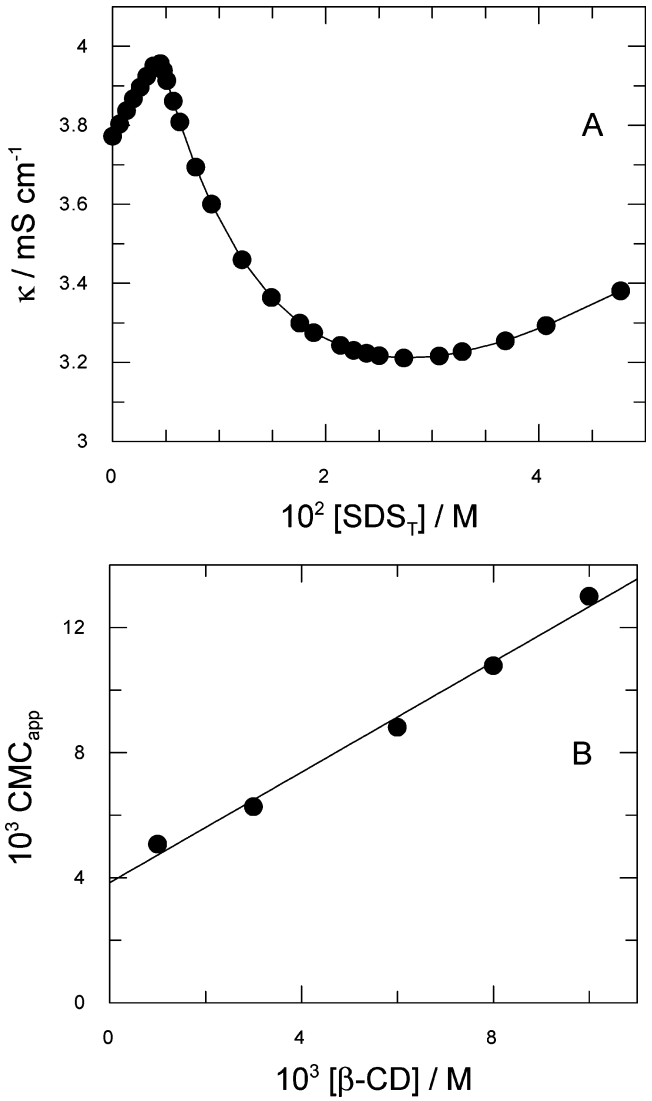

Figure 1. (A) Illustrative variation of κ with [SDS] in aqueous acid solution in the presence of [β-CD] = 0.01 M. (B) Variation of CMC_{app} of SDS with [β-CD]. T = 25 °C, [HCl] = 10^{-2} M.

of it may be crucial to interpret chemical reactivity in mixed surfactant−CD systems.

We investigated the effects of β-CD on the CMC_{app} of SDS by employing a conductometric method. Figure 1A illustrates the variation of κ with [SDS] in the presence of 10^{-2} M β-CD, the first breakpoint indicating micelle formation. Note that, once micelles are formed, κ values decrease upon increasing [SDS] up to a minimun value much lower than that in the absence of SDS, but further addition of SDS causes κ to increase again. Similar Z-shaped profiles are also observed in the absence of β-CD (data not shown), the SDS concentration at which the first breakpoint is observed being dependent on initial [HCl] because of the known electrolyte effects on the CMC. The origin of this Z-shaped variation in κ has been discussed recently elsewhere[38] and attributed to ion exchange (H^+ and Na^+) effects on the conductivity of SDS micellar solutions. Figure 1B shows a linear increase in CMC_{app} upon increasing β-CD, yielding an intercept value of 4×10^{-3} M, in agreement with previous calculations, and a slope of 0.84, consistent with the formation of 1:1 SDS−β-CD complexes.[48]

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(2) Effects of [SDS_T] on the Observed Rate Constant, k_{obs}, for Product Formation and for 4NBD Loss. Kinetic experiments were performed at different pH values by employing both fixed SDS concentrations well below and above its CMC_{app} and different [β-CD]/[4NBD] ratios, a fixed [β-CD]/[4NBD] ratio, and variable [SDS_T].

Previous HPLC studies in the absence of SDS indicate that when [β-CD]/[4NBD] = 2.5 both the homolytic ArH and the heterolytic ArOH are the only dediazoniation products formed, meanwhile when [β-CD]/[4NBD] = 40, ArH is formed quantitatively.[26] The UV−vis spectrum of ArH shows an absorption band in the same region as that for 4NBD, making unadvisable monitoring the reaction by following the decomposition of 4NBD or by following the formation of ArH. For this reason, we investigated spectrophotometrically the effects of [SDS] on k_{obs} by monitoring the changes in the absorbance for ArOH formation (λ = 350 nm) with time. All runs followed first-order kinetics for at least $3t_{1/2}$.

Figure 2A illustrates the effects of [SDS_T] on k_{obs} at a fixed [β-CD]/[4NBD] = 2.5. In the absence of SDS, inset in Figure 2A, $k_{obs} = 6.97 \times 10^{-2}$ min^{-1}; addition of [SDS] results in a decrease in k_{obs} by a factor of 10 when [SDS_T] = 1 mM and by a factor of about 70 when [SDS_T] = 50 mM. k_{obs} values at different [SDS_T] and [β-CD]/[4NBD] ratios are collected in Table 1, showing that addition of SDS clearly inhibits the β-CD catalyzed dediazoniation of 4NBD. It is also remarkable in Figure 2A that the observed A_∞ values increase upon increasing SDS, suggesting that addition of SDS to the system not only inhibits the reaction but also has an effect on the dediazoniation product distribution by promoting the formation of the heterolytic product. This finding prompted us to further investigate the effects of SDS on product distribution by HPLC (see below).

Results in Figure 2B illustrate the effects of [SDS_T] on k_{obs} when [β-CD]/[4NBD] = 40 (Figure 2B also includes data at [β-CD]/[4NBD] = 2.5 for the sake of comparisons). k_{obs} values decrease upon increasing [SDS_T] when [β-CD]/[4NBD] = 40 by a factor of ~35 when [SDS_T] = 50 mM, but further addition of SDS appears to have no significant effect on k_{obs}. Note that A_∞ values increase upon increasing [SDS] up to a limit, Table 1, suggesting again that addition of SDS changes both k_{obs} and the dediazoniation product distribution. Results in Table 1 allow one to compare the effects of increasing [β-CD] on k_{obs} at a fixed [SDS_T]. k_{obs} values increase by a factor of ~2 on going from a [β-CD]/[4NBD] = 2.5 to a [β-CD]/[4NBD] = 40 ratio, the increase being much lower than that observed in the absence of SDS for the same [β-CD]/[4NBD] ratios, which is about 10,[26] substantiating again the inhibitory effect of SDS.

k_{obs} for dediazoniation product formation and for 4NBD loss were determined by employing a published derivatization method that exploits the rapid coupling reaction between 4NBD and β-naphthylamine followed by HPLC analyses of the reaction products.[12,43] Chromatograms were free of extraneous peaks other than the front peak and those for ArOH and ArH. Figure 3 is illustrative and was obtained at two [β-CD]/[4NBD] ratios by employing [SDS_T] = 1 mM, a surfactant concentration well below its CMC_{app}, Figure 1. Data are collected in Table 2.

Both at low or high [β-CD]/[4NBD], the k_{obs} value for ArOH formation is the same as that for ArH formation and equal to that determined indirectly for 4NBD loss by monitoring the formation of the azo dye with time, Figure 4. Similar results were obtained when the dediazoniation reaction was carried out at pH = 5 (data not shown), indicating a negligible effect of the acidity in k_{obs} in the

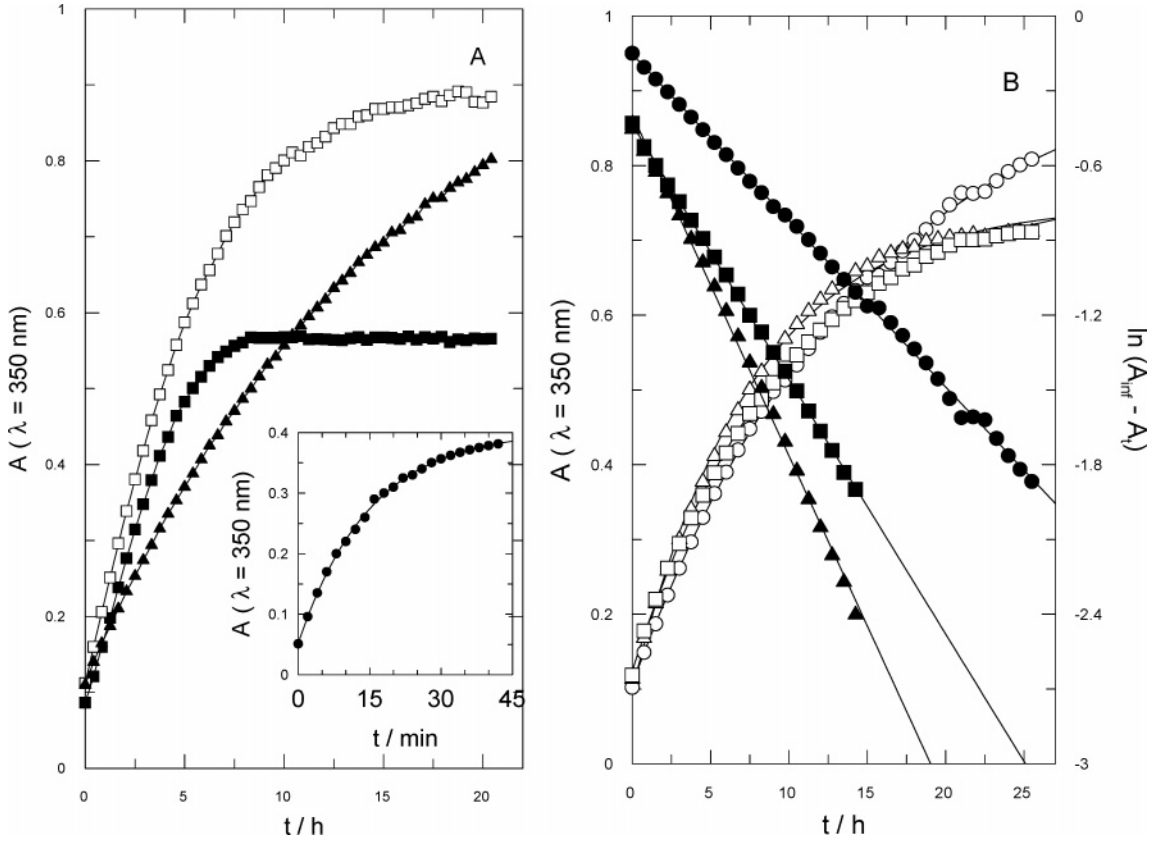

Figure 2. (A) Effects of [SDS] on ArOH formation in the presence of [β-CD] = 2.5 [4NBD]. ●, [SDS] = 0 M; ■, [SDS] = 10 mM; □, [SDS] = 30 mM; ▲, [SDS] = 50 mM. (B) Effects of [SDS] on ArOH formation and ln plots. ○, [SDS] = 50 mM and [β-CD]/[4NBD] = 2.5; △, [SDS] = 50 mM and [β-CD]/[4NBD] = 40; □, [SDS] = 100 mM and [β-CD]/[4NBD] = 40. [4NBD] = 2×10^{-4} M, [HCl] = 0.01 M, T = 60 °C.

Table 1. Values of k_{obs} for ArOH Formation Determined by UV−Vis and by HPLC under Different Experimental Conditions

run	[SDS], mM	[β-CD]/[4NBD]	[SDS]/[β-CD]	$10^3 k_{obs}$, min^{-1}	A_∞[a]
1	0	2.5		69.71[b]	0.40
2	1	2.5	2	6.67[b]	0.58
3	5	2.5	10	6.64[b]	0.57
4	10	2.5	20	3.12[b]	0.88
5	30	2.5	60	1.17[b]	0.95
6	50	2.5	50	1.11[b]	
7	50	2.5	100	1.05[b]	0.94
8	50	40	62.5	2.20[b]	0.71
9	100	40	125	1.71[b]	0.71
10	1	2.5	1.4	14.1[c]	
11	1	40	0.1	114[c]	
12	50	2.5	71.4	2.88[c]	
13	50	40	6.25	3.20[c]	

[a] By nonlinear regression from absorbance/time kinetic runs. [b] By UV−vis (λ = 350 nm). [c] By HPLC after derivatization. [4NBD] ~ 2×10^{-4} M, [HCl] = 0.01 M, and T = 60 °C.

investigated pH range. These findings are suggestive of competing homolytic and heterolytic mechanisms taking place simultaneously. Note the remarkable decrease in $t_{1/2}$ upon increasing [β-CD], $t_{1/2} \sim 60$ min when [β-CD]/[4NBD] = 2.5; meanwhile, $t_{1/2} \sim 7$ min when [β-CD]/[4NBD] = 40, suggestive of the notable effect of [β-CD] on the dediazoniation of 4NBD as well as of the inhibitory effect of SDS.[26]

Figure 3A also shows that, when [β-CD]/[4NBD] = 2.5, the major dediazoniation product is ArOH, and only moderate amounts of ArH are formed; meanwhile, when [β-CD]/[4NBD] = 40 the major dediazoniation product is ArH and very low amounts of ArOH are detected, Figure 3B. Similar results were obtained when employing [SDS_T] concentrations well above its CMC_{app} as illustrated in Figure 5 (data in Table 2). Note that only ArOH and ArH dediazoniation products are detected, ArOH being the major one, and that the obtained k_{obs} values are equal to those reported for 4NBD dediazoniation in a SDS micellar solution under the same experimental conditions,[28] suggesting that dediazoniation is mainly taking place in a micellar environment.

(3) Effects of [β-CD] and [SDS] on 4NBD Dediazoniation Product Distribution. Product distribution was determined by HPLC analyses of reaction mixtures once dediazoniations were finished, that is, at infinite time. Figure 6 shows the effects of [SDS_T] on the product distribution at a fixed pH = 2 and [β-CD]/[4NBD] = 40. Only two dediazoniation products where detected, ArOH and ArH, its relative yield being dependent on [SDS_T]. When no SDS is present, the major dediazoniation product is ArH, in keeping with previous findings,[26] and addition of SDS results in a reduction in the percentage of formation of ArH with a parallel increase in ArOH yield. Note that, when [SDS] = 160 mM, the product distribution is very similar to that obtained previously, Figure 7, under similar experimental conditions.

Figure 7, chosen as representative, shows the changes in product distribution on increasing [β-CD] at two [SDS_T] well below and above its CMC_{app}. In the absence of β-CD, the major dediazoniation product is ArOH, and negligible amounts of ArH are found, indicating that the predominant mechanism is the heterolytic one, in agreement with previous reports.[28] When [SDS] = 1.6 mM, Figure 7A, addition of β-CD makes the ArOH yield decrease with a concomitant increase in ArH so that when [β-CD]/[4NBD] > 5, the homolytic mechanism predominates over the

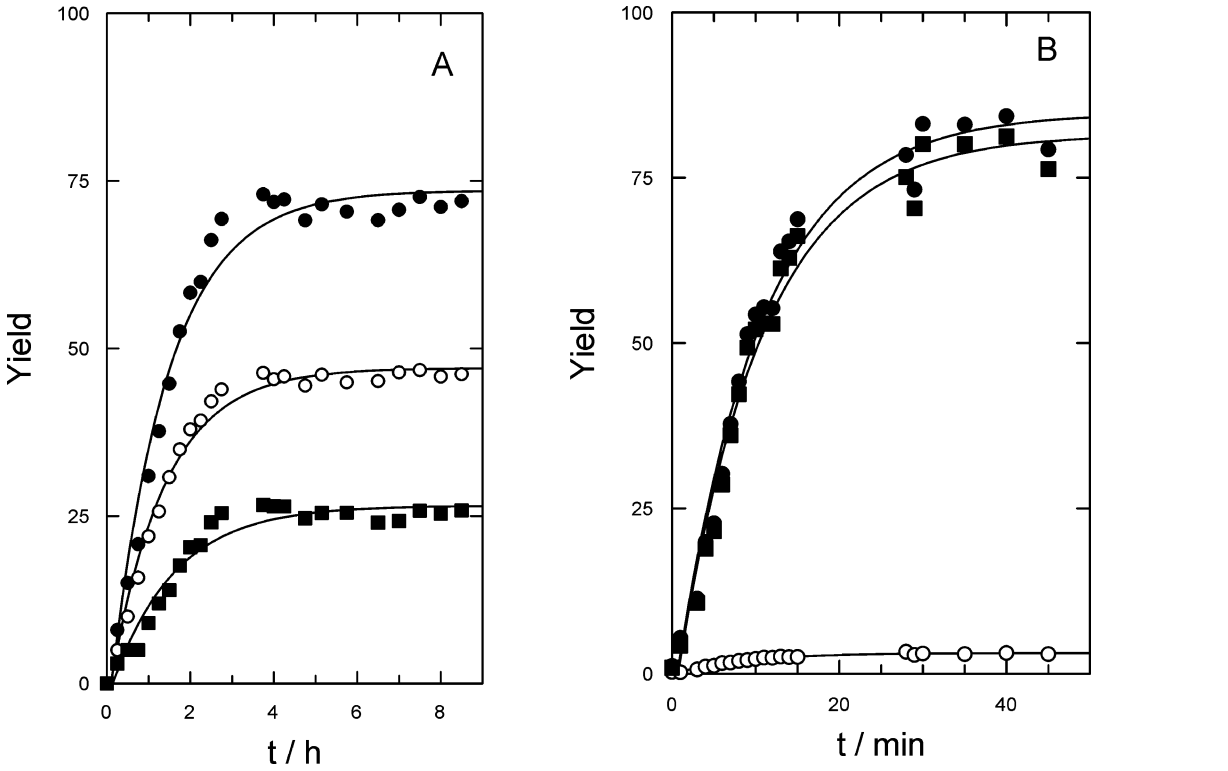

Figure 3. Percentage of formation of (○) ArOH, (■) ArH, and (●) total ArOH + ArH with time. (A) [SDS]/[β-CD] = 1.3, [β-CD]/[4NBD]= 2.5. (B) [SDS]/[β-CD] = 0.1, [β-CD]/[4NBD] = 40. [SDS] = 10^{-3} M, [HCl] = 0.01, [4NBD] ~ 2.1 × 10^{-4} M, T = 60 °C.

Table 2. k_{obs} Values for Dediazoniation Product Formation and 4NBD Loss Obtained by HPLC and Indirectly after Derivatization, Respectively

	$10^3\ k_{obs}$,[a] min^{-1}	$10^3\ k_{obs}$,[b] min^{-1}	$10^3\ k_{obs}$,[c] min^{-1}
ArOH	14.2	110	3.8
ArH	14.7	120	3.6
total yield	14.1	121	3.2
4NBD[d]	14.5	115	

[a] From Figure 3A; [β-CD]/[4NBD] = 2.5 ([SDS]/[β-CD]) = 1.2). [b] From Figure 3B; [β-CD]/[4NBD] = 40 ([SDS]/[β-CD]) = 0.1). [c] From Figure 5, [β-CD]/[4NBD] = 40 ([SDS]/[β-CD] = 6). [d] Determined indirectly by measuring changes in absorbance of the azo dye with time (Figure 4). Other conditions as in Figure 3.

heterolytic one. However, when [SDS_T] = 160 mM, Figure 7B, product distribution remains basically constant upon increasing [β-CD] and the heterolytic mechanism is predominant in the investigated [β-CD] range.

Discussion

The chromatographic product distribution, Figures 6 and 7, shows that both the homolytic ArH and the heterolytic ArOH are the only dediazoniation products detected, their relative yields being dependent on [SDS] and, hence, on the [SDS]/[β-CD] ratio. Spectrophotometric and HPLC kinetic data, Figures 3−5, show that k_{obs} values for ArOH formation are the same as those for ArH formation and 4NBD loss, strongly suggesting that competitive homolytic and heterolytic mechanisms coexist in the SDS/β-CD system.

Conductometric studies on the β-CD/SDS system, Figure 1, show a linear increase in CMC_{app} upon increasing [β-CD] with a slope d(CMC_{app})/d([β-CD]) = 0.84, very similar to those reported in the literature, d(CMC_{app})/d([β-CD]) = 0.70[48] and d(CMC_{app})/d([β-CD]) = 0.86,[49] consistent with

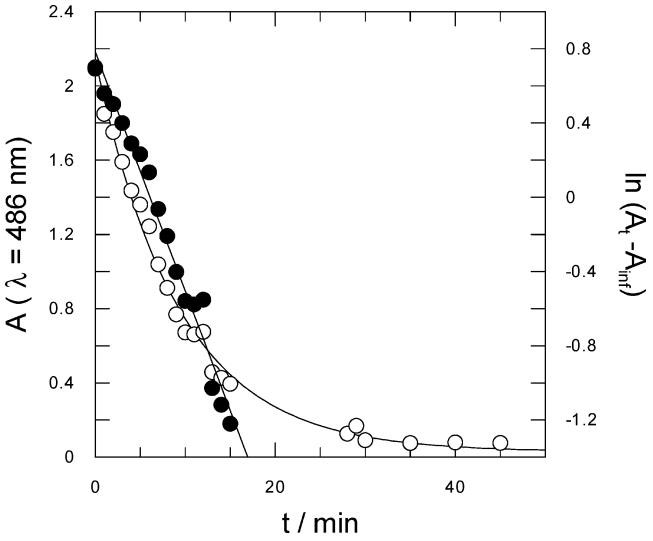

Figure 4. Variation in the absorbance of the azo dye formed from reaction of 4NBD with 1-naphthylamine (see text) with time. Experimental conditions as in Figure 3B.

the formation of 1:1 surfactant−CD complexes. The results are in complete agreement with previous studies on CD−surfactant systems[45,47,48,50,51] and can be interpreted in terms of CDs siphoning away surfactant monomers from the bulk aqueous solution competing with the micelle formation process.

All evidence is, thus, consistent with Scheme 3, which considers the spontaneous decomposition of 4NBD in aqueous acid solution, the formation of reactive 4NBD−β-CD and nonreactive SDS−β-CD complexes, and the

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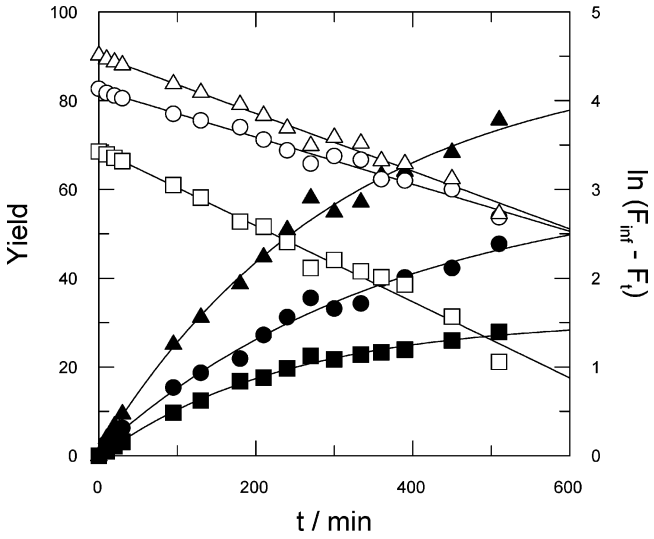


Figure 5. Illustrative determination of k_{obs} values by HPLC after derivatization for dediazoniation product formation and ln plots. ●, ArOH (○, ln plot); ■, ArH (□, ln plot); ▲, total ArH + ArOH (△, ln plot). [SDS] = 5×10^{-2} M, [β-CD]/[4NBD] = 40, [4NBD] = 2.1×10^{-4} M, [HCl] = 60 °C.

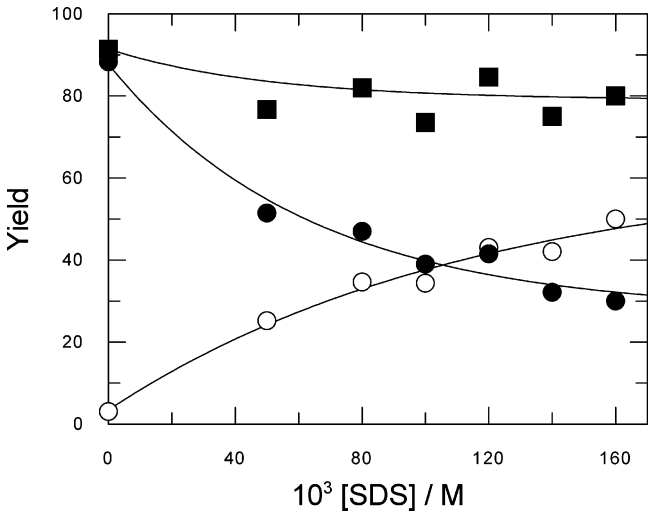


Figure 6. Effects of [SDS] on 4NBD dediazoniation product distribution in the presence of [β-CD] = 40[4NBD]. [HCl] = 0.01 M, [4NBD] = 2×10^{-4} M, T = 60 °C.

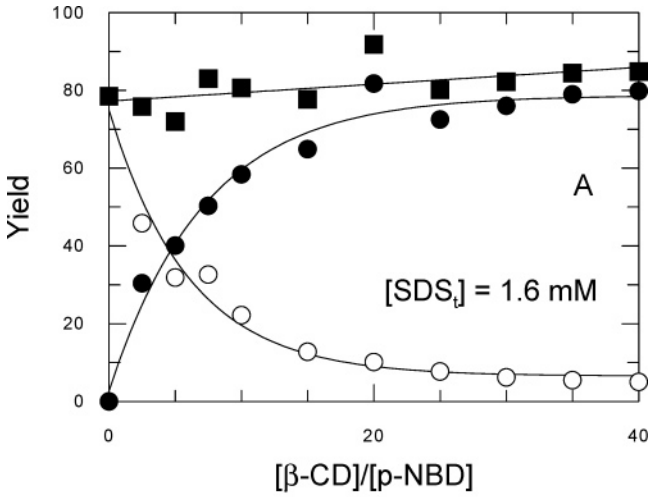
possibility of 4NBD being incorporated to micellar aggregates whenever they exist. Basic aspects of the reaction mechanisms involved in the A, B, and C pathways are given in Schemes 1 and 2, and further details can be found elsewhere.[26,28,42]

According to the above mechanism, the rate for 4NBD loss is given by eq 3

$$v = -\frac{\mathrm{d[4NBD]}}{dt} = k_w[\mathrm{4NBD_F}] + k_{CD}[\mathrm{DE}] + k_M[\mathrm{4NBD_M}] \quad (3)$$

where k_w and k_M are the rate constants in water, Scheme 3A, and in the micellar aggregate, Scheme 3C, respectively, and k_{CD} stands for the rate constant for the unimolecular decomposition of the diazo ether DE formed by reaction of 4NBD with β-CD, Scheme 3B.[26] The mass balance for 4NBD is given by eq 4

$$[\mathrm{4NBD_T}] = [\mathrm{4NBD_F}] + [\mathrm{DE}] + [\mathrm{4NBD_M}] \quad (4)$$



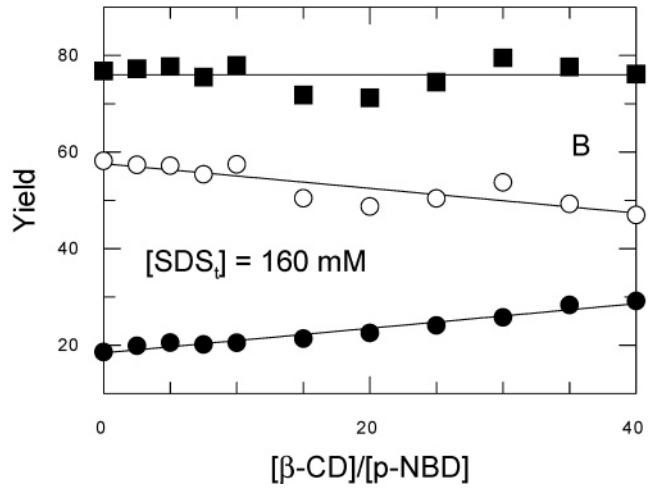


Figure 7. Effects of [β-CD] on 4NBD dediazoniation product distribution in the presence of a fixed [SDS_T]. ●, ArH; ○, ArOH; ■, total (ArOH + ArH). (A) [SDS_T] = 1.6×10^{-3} M. (B) [SDS_T] = 0.16 M. [4NBD] ~ 2×10^{-4} M, [HCl] = 0.01 M, T = 60 °C.

Taking into consideration the different pathways reflected in Scheme 3, [$4NBD_F$] can be obtained from eq 4, in terms of [$4NBD_T$], and bearing in mind that pseudo-first-order conditions apply, the obseved rate constant is given by eq 5

$$k_{obs} = \frac{k_w + k_{CD}K_{CD}[\beta\mathrm{-CD_F}] + k_M K_S[\mathrm{D_n}]}{1 + K_{CD}[\beta\mathrm{-CD_F}] + K_S[\mathrm{D_n}]} \quad (5)$$

where [D_n] stands for the concentration of micellized surfactant and [β-CD] stands for the concentration of "free" CD. Note that above the micellization point, [SDS_T] = [D_N] + CMC_{app} = [D_N] + [Surf/β-CD] + [$Surf_{mon}$], where [Surf/β-CD] stands for the nonreactive surfactant−CD complex.

[CD_F] can by obtained from the total β-CD, SDS, and 4NBD concentrations by considering the corresponding mass balances, resulting in the third order eq 6

$$[\beta\mathrm{-CD_T}] = A[\beta\mathrm{-CD_F}]^3 + B[\beta\mathrm{-CD_F}]^2 + C[\beta\mathrm{-CD_F}] \quad (6)$$

where the parameters A, B, and C are given by eqs 7, 8, and 9, respectively

$$A = K_{11}K_S \quad (7)$$

$$B = K_{11} + K_S + A([SDS_T] + [4NBD_T] - [\beta\text{-}CD_T]) \quad (8)$$

$$C = 1 + K_{11}([SDS_T] - [\beta\text{-}CD_T]) + K_S([4NBD_T] - [[\beta\text{-}CD_T]) \quad (9)$$

Figures 2 and 3 and Table 1 show that addition of SDS to an aqueous acid solution containing a fixed amount of β-CD results in a decrease in k_{obs}, which can be explained qualitatively on the basis of Scheme 3 by recognizing that the equilibrium constant for SDS/β-CD complex formation,[50] $K_{11} = 26\,800$ L mol^{-1}, is larger by a factor of $\sim$15, with respect to that for the 4NBD/β-CD complex,[26] $K_{CD} = 2700$ L mol^{-1}. Thus, SDS monomers are likely to be included in the CD cavity impeding inclusion of 4NBD, blocking the CD cavity, inhibiting pathway B in Scheme 3 because the SDS/β-CD complex is nonreactive, Scheme 3D, causing 4NBD to be released from the CD cavity, and reacting through the thermal $D_N + A_N$ mechanism in the bulk solvent where water, surfactant monomers, and micelles may be present depending on the experimental conditions.

This blocking effect is apparent on analyzing the effects of [SDS_T], Figure 6, and [β-CD], Figure 7, on the dediazoniation product distribution. When [SDS] $\ll CMC_{app}$, Figure 7A, only a fraction of the β-CD is being blocked and further addition of β-CD promotes the homolytic dediazoniation (ArH formation) over the heterolytic one (ArOH formation); however, when [SDS] $\gg CMC_{app}$, an increase in [β-CD_T] has no significant effect on the product distribution because most of the β-CD molecules are blocked and, thus, the reaction is mainly taking place in a micellar environment. The assumption is supported by the fact that the k_{obs} values, Figure 5, are the same as those previously reported in absence of β-CD.[28] Alternatively, addition of SDS at a given [β-CD_T] causes ArH yields to decrease with a concomitant increase in ArOH. Figure 6 also shows that a turnover from the homolytic mechanism, which is the predominant one at low [SDS], takes place at [SDS] $\sim$ 100 mM when [β-CD_T] = 40 [4NBD], causing the heterolytic one to predominate at high [SDS_T].

In conclusion, we have shown that addition of SDS to the 4NBD/β-CD mixture leads to a turnover of the homolytic dediazoniation mechanism to the heterolytic one by complete inhibition of the reaction and changing the dediazoniation product distribution. The main reason of this behavior is the formation of a nonreactive SDS/β-CD complex that releases 4NBD out of the CD cavity. The value of the binding constants K_{11} of surfactants with CDs depend, among others, on the possibility of formation of hydrogen bonds between the surfactant headgroups and the hydroxyl groups of the larger rim of CD and the length of their hydrophobic chain,[51] so the expected effects of cationic and zwitterionic surfactants on the 4NBD/β-CD reaction may be somewhat different depending on the particular K_{11} value. Our results may have some importance in drug release control.[52,53] The natural CDs and their synthetic derivatives have been successfully utilized to improve various drug properties, such as solubility, dissolution, stability, bioavailability, and release rates. CDs may form noncovalent complexes with a large number of chemicals, so that complexation can be considered a dynamic process. The drug−CD complex is generally formed outside of the body and, after administration, it dissociates, releasing the drug into the organism in a fast and nearly uniform manner. A drug included within the CD cavity may, therefore, be dissociated upon addition of amphiplilic compounds by displacing them to the targeted place. Our results show that surfactants may also inhibit chemical reactions with CDs, leading to formation of covalent complexes.

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