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The solvolysis of benzoyl halides as a chemical probe determining the polarity of the cavity of dimethyl-β-cyclodextrin

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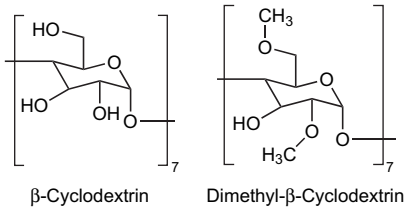
Abstract—The solvolysis of benzoyl halides (BzX) in the presence of dimethyl-β-cyclodextrin (DM-β-CD) was studied. Methylation or hydroxyalkylation of the hydroxyl groups in β-cyclodextrin increases their solubility and the highest possible concentration of DM-β-CD that can be dissolved in water is 0.2 M. The ability to use more readily soluble CDs may allow one to determine the stoichiometry of their complexes and the properties of water held in their cavity with increased precision. Based on the experimental results, this cyclodextrin forms host–guest complexes of variable stoichiometry where two reaction pathways are considered: in water and in the internal cavity of the cyclodextrin. We determined the rate constants for the halides in their reaction inside the internal cavity. This allowed the influence of the substituent and leaving group on the reactions in the bulk water and the internal cavity of DM-β-CD to be compared. Depending on whether the solvolysis reaction is preferentially associative or dissociative, the presence of the cyclodextrin has a catalytic or inhibitory effect, respectively.

1. Introduction

Naturally occurring cyclodextrins (CDs) are homochiral cyclic oligosaccharides the most common of which consist of 6, 7 or 8 α-1,4-linked D-glucopyranose units. These compounds result from the degradation of starch by the enzyme CD glucosinyltransferase. The most widely studied CDs are α-, β-, and γ-CD, which possess 6, 7, and 8 glucopyranose units, respectively, and are commercially available in natural or modified forms.[1]

The use of CDs for investigating some chemical reactions has attracted much interest from chemists.[2–5] The practical use of cyclodextrins is restricted by their low solubility in water; this is especially true for β-cyclodextrins. The aggregation of cyclodextrins and their interaction with neighboring water molecules, together with the lattice energy in the solid state, may be the origin of the solubility differences among cyclodextrins.[6] Methylation or hydroxyalkylation of the hydroxyl groups in β-cyclodextrin has been used to increase their solubility. However, when hydroxyl groups in cyclodextrins are substituted with alkyl groups longer than the methyl group via an ether or ester linkage, the solubility of these compounds decreases in proportion to their degree of substitution.[7]

In this work, we used heptakis(2,6-di-*O*-methyl)-β-cyclodextrin (i.e., dimethyl-β-cyclodextrin, DM-β-CD). This cyclodextrin (see Scheme 1), which is commercially available and widely used by the pharmaceutical industry, possesses a cavity of size close to the optimum size for accommodating a phenyl group. As experimentally measured, the highest possible concentration of β-CD that can be dissolved in water is ca. 1.5×10^{-2} M; on the other hand, that for DM-β-CD is 0.2 M (i.e., roughly 13 times greater). The ability to use more readily soluble CDs is especially attractive for kinetic studies as it may allow one to determine the stoichiometry of their complexes and the properties of water held in their cavity with increased precision.



Scheme 1.

Although acyl-transfer reactions are by now widely documented, they continue to attract much attention for reaction mechanism studies, particularly in biomimetic media.[8–13] Cyclodextrins constitute an effective choice for examining the solvolysis of substituted benzoyl chlorides. The presence of α-, β-, and γ-cyclodextrin alters these reactions in a way

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that is related to the stability of the substrate–CD complex and its stoichiometry. In a previous study we showed that solvolysis reaction of benzoyl chlorides in the presence of cyclodextrins shows two clearly differentiated behaviors: when the solvolysis mechanism occurs through an associative path the presence of cyclodextrins catalyzes the process through the reaction with its hydroxyl group. The substituted benzoyl chlorides with electron-donating groups, which undergo solvolysis through a dissociative path, show a reduction in the rate constant caused by the presence of the cyclodextrins. This behavior is due to the complexation of the substrates with the cyclodextrins and also to the limited value of the rate constant in the cavity of the cyclodextrin, due to its low capacity to solvate the leaving group, Cl^-.[4] The study of these reactions can be substantially improved by using DM-β-CD. Thus, this modified cyclodextrin has allowed the Hammett correlation to be applied to reactions in the DM-β-CD cavity with a view of determining the nucleophilicity and electrophilicity of the reaction medium.

2. Results

The study of the influence of the DM-β-CD concentration on the solvolysis rate constant for the benzoyl halides (BzX) studied revealed three different types of action of the cyclodextrin, namely: inhibition, catalysis, and a combination of the previous two.

2.1. Inhibition

Figure 1 shows the effect of the presence of DM-β-CD on the solvolysis reaction for most of the benzoyl chlorides studied. Thus, k_o decreased with increasing DM-β-CD concentration. This behavior was observed in **3-CF$_3$**, **3-Cl**, **4-Cl**, **3-MeO**, **4-H**, **3-Me**, **4-Me**, **4-MeO**, **BzF**, and **BzBr**. As can be seen, there were differences in the strength of the inhibitory effect, which was much greater on **4-MeO** than that on **4-Cl**. Such an effect increased with increasing electron-releasing character of the substituents in the benzoyl chloride and was 465, 278, and 26 times greater for **4-MeO**, **4-H**, and **3-Cl**, respectively, than that for the parent compound. These differences can explained in the light of the reaction

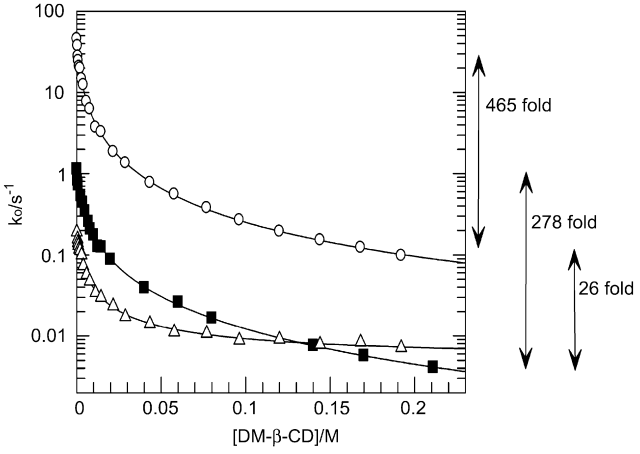


Figure 1. Influence of the DM-β-CD concentration on the *pseudo* first-order rate constant for the solvolysis of **4-MeO** (○), **4-H** (■), and **3-Cl** (△) at 25.0 °C.

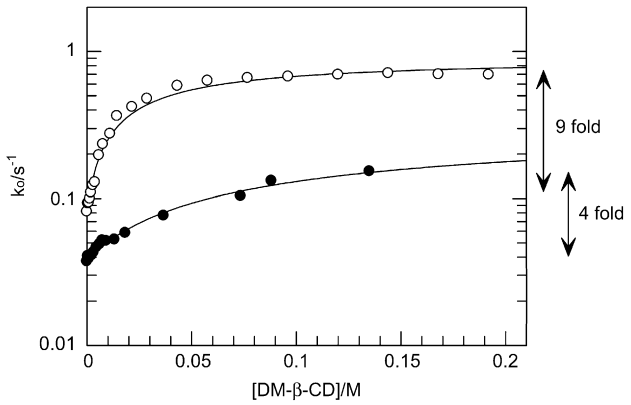


Figure 2. Influence of the DM-β-CD concentration on the *pseudo* first-order rate constant for the solvolysis of **4-NO$_2$** (○) and **3-NO$_2$** (●) at 25.0 °C.

mechanism involved, the stoichiometry of the CD–BzX complex, and the properties of water inside the CD cavity.

2.2. Catalysis

The reactants **4-NO$_2$** and **3-NO$_2$** exhibited a rather different behavior as regards the influence of the DM-β-CD concentration on k_o. In fact, the results (Fig. 2) suggest the involvement of a different mechanism in the reaction of these benzoyl chlorides. As noted earlier, solvolysis reactions are highly sensitive to changes in the reaction medium. In this case, the presence of the cyclodextrin acted differently on the reaction because its mechanism was preferentially associative. Also, the catalytic effect was greater on **4-NO$_2$** than on **3-NO$_2$**, which is consistent with the stronger electron-withdrawing character of former, even though the geometry of the inclusion complex formed may also be influential here.

2.3. Catalysis and inhibition

At low DM-β-CD concentration the solvolytic rate constant of **4-CF$_3$** increased to a peak level (Fig. 3). This behavior is similar to that of **4-NO$_2$**. However, above a certain DM-β-CD

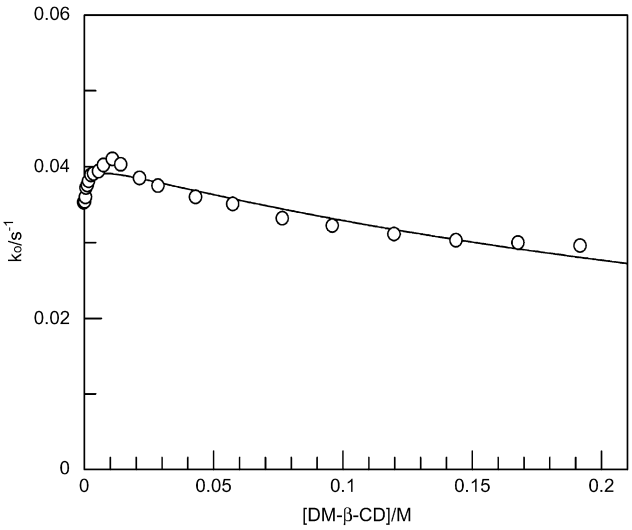


Figure 3. Influence of the DM-β-CD concentration on the *pseudo* first-order rate constant for the solvolysis of **4-CF$_3$** (○) at 25.0 °C.

concentration, the solvolysis of **4-CF$_3$** was inhibited in a manner similar to that for most of the benzoyl chlorides. Therefore, this benzoyl halide clearly exhibits competition between the two reaction mechanisms for the solvolysis reaction.

3. Discussion

There are two essential issues to be considered in interpreting our experimental results. Thus, the presence of the cyclodextrin can lead to the formation of complexes of variable stoichiometry with the benzoyl halides depending on their geometry. Also, as stated above, the solvolysis mechanism for these compounds is highly sensitive to changes in the solvent and reaction medium such as the presence of CDs, which can be strongly influential and causes a switch to a different mechanism. These two factors are mutually related and complicate the analysis of the results.

3.1. Complexation model

Benzoyl halides can form 1:1 or 2:1 CD–BzX complexes[4] that can react either in the bulk water or within the CD cavity. If both mechanisms occur, the overall rate constant will be a combination of the solvolysis constants for the free benzoyl halide in water and its CD-complexed form. One can therefore discuss the experimental results in the light of different reaction mechanisms and previous results obtained in the presence of α-, β- and γ-CD.[4] The increased solubility of DM-β-CD relative to β-CD allows one to operate on a broader concentration range in order to obtain a more precise interpretation of the complexation models potentially applicable.

If Benzoyl halides form 1:1 CD–BzX complexes the equation obtained is:

$$k_o = \frac{k_w + k_{CD}K_{1:1}[\text{DM-β-CD}]}{1 + K_{1:1}[\text{DM-β-CD}]} \quad (1)$$

Table 1 lists the equilibrium formation constants for the host–guest complexes and the observed rate constants for the reaction within the CD cavity. Inhibition occurs because complexation with DM-β-CD removes substrate from bulk solution and the solvolytic rate constant inside the cyclodextrin cavity is much slower than that in bulk water.

The experimental results obtained regarding the influence of the presence of CD concentration on the solvolysis reaction of **3-NO$_2$** and **4-NO$_2$** are shown in Figure 2. Raising the CD concentration increased the observed rate constant. This behavior departs from that observed in other benzoyl halides. The stoichiometry of the CD–benzoyl chloride complex continued to be 1:1 as the hydrophobic forces governing the formation of the CD complex with the substrates are independent of the particular mechanism for the solvolysis reaction. Figure 2 illustrates the good fit of the experimental results to Eq. 1, which confirms the assumed stoichiometry (1:1) despite the fact that the reaction mechanism for the previous two halides is preferentially associative. As can be seen from the kinetic parameters in Table 1, the rate constant for the reaction in the cyclodextrin exceeds that for the reaction in water ($k_{CD}>k_w$). This behavior is a consequence of the solvolysis mechanism for **3-NO$_2$** and **4-NO$_2$** being largely of the associative type.

Table 1. Kinetic parameters for the solvolysis of various benzoyl chlorides in the presence of DM-β-CD

Substrate	k_w (s^{-1})	k_{CD} (s^{-1})	$K_{1:1}$ (M^{-1})	$K_{2:1}$ (M^{-1})
4-NO$_2$	$8.2\pm0.3\times10^{-2}$	$9.0\pm0.4\times10^{-1}$	30±3	—
3-NO$_2$	$3.8\pm0.2\times10^{-2}$	$2.9\pm0.5\times10^{-1}$	5±2	—
4-CF$_3$	$3.5\pm0.1\times10^{-2}$	$4.1\pm0.1\times10^{-2}$	610±100	5±1
3-CF$_3$	$3.3\pm0.1\times10^{-2}$	$1.8\pm0.1\times10^{-2}$	115±20	—
3-Cl	$4.7\pm0.2\times10^{-1}$	$1.3\pm0.1\times10^{-2}$	345±30	—
4-Cl	$1.9\pm0.1\times10^{-1}$	$4.8\pm0.2\times10^{-3}$	435±10	—
3-MeO	$5.9\pm0.2\times10^{-1}$	$1.4\pm0.2\times10^{-3}$	1120±30	—
4-H	1.14±0.05	$3.0\pm1.0\times10^{-3}$	470±30	10±1
3-Me	2.51±0.07	$6.0\pm2.1\times10^{-3}$	810±60	10±3
4-Me	6.3±0.2	$3.5\pm1.0\times10^{-2}$	1050±25	25±5
4-MeO	46±1	$3.7\pm0.9\times10^{-1}$	730±35	30±4

The following equation can be derived for 2:1 CD–BzX complexes:

$$k_o = \frac{k_w + k_{CD}K_{1:1}[\text{DM-β-CD}]}{1 + K_{1:1}[\text{DM-β-CD}] + K_{1:1}K_{2:1}[\text{DM-β-CD}]^2} \quad (2)$$

A comparison of the k_{CD} and k_w values obtained is quite revealing irrespective of the particular reaction scheme adopted. Thus, when $k_w>k_{CD}$, the presence of CD decreases the reaction rate; such is the case with the benzoyl halides, the solvolysis mechanism for which is preferentially dissociative. For a solvolysis reaction taking place by a largely associative mechanism (as observed with **3-NO$_2$** and **4-NO$_2$**) $k_{CD}>k_w$ resulting in an observed catalysis. Finally, **4-CF$_3$** exhibits a combination of the two mechanisms and its k_{CD} and k_w values are similar in magnitude.

3.2. Cyclodextrin promoted mechanistic changes

The influence of the substituent on the reaction mechanism was assessed via the Hammett correlation (Table 1). Figure 4 illustrates the good Hammett correlation obtained for our system. The slope of the Hammett plot for the solvolysis of benzoyl chlorides in water changed from negative values suggesting a dissociative mechanism to positive values suggesting an associative mechanism somewhere in between the

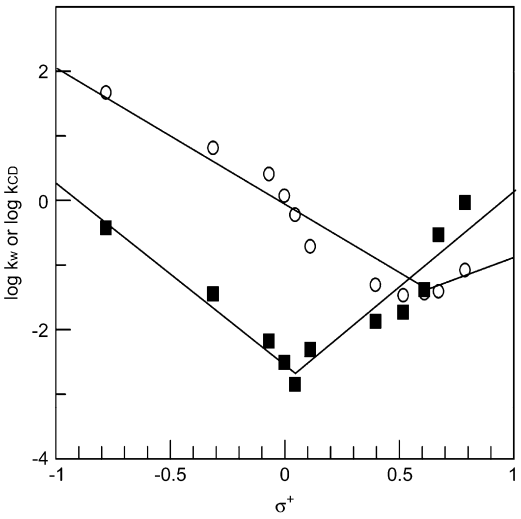
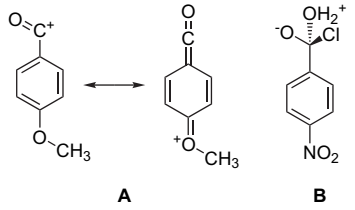


Figure 4. Hammett plot for the solvolysis of substituted benzoyl chlorides in water (○) and DM-β-CD (■).

points for **3-CF$_3$** and **3-NO$_2$**. With DM-β-CD, the change in the reaction mechanism occurred at smaller σ^+ values (specifically, with **4-H**). This shift in the mechanism break point to lower σ^+ values can be ascribed to the properties of water being altered inside the cyclodextrin cavity.

As previously stated, **4-MeO** was the benzoyl chloride most clearly followed a dissociative mechanism. The reaction intermediate, shown in Scheme 2A, was amenable to stabilization by resonance of the acyl ion formed in the dissociative mechanism. The reaction within the inclusion complex must involve the release of the leaving group under the assistance of the cyclodextrin. The properties of the water inside the cavity and in its close environment are quite different from those of the bulk water.[14] Despite the lack of uniformity, the inside of the cyclodextrin cavity is much less polar than pure water. The solvolysis reactions of benzoyl chlorides, which take place via a dissociative mechanism are highly sensitive to the solvent polarity. In fact, k_o for the solvolysis of **4-H** decreases with increasing proportion of methanol in the reaction medium; thus, the reaction is inhibited approximately 190 times in the transition from water to mixtures of methanol–water containing a 90% (v/v) proportion of the alcohol.[15] This difference in reactivity is more marked with **4-MeO**, a benzoyl chloride that is closer to the dissociative mechanism, where k_o decreases roughly 2900 times in the transition from the bulk water to a 95% (v/v) methanol–water mixture.[16] In our case, the rate constant was about 500 times greater in water than in the presence of [DM-β-CD]=0.20 M, which confirms the dissociative mechanism involved and the polarity change in the water within the cyclodextrin cavity.



Scheme 2.

The solvolysis of **4-NO$_2$** exhibits a catalytic effect (Fig. 2). The reaction intermediate is shown in Scheme 2B. The origin of the disparate behavior of **4-NO$_2$** and **4-MeO** is the different mechanism behind their reactions; thus, electron-releasing substituents favor a dissociative mechanism where the reaction rate within the cyclodextrin is much lower than that in the bulk water, so the addition of DM-β-CD to the medium produces an inhibitory effect. The results of Figure 2 expose the catalytic effect of DM-β-CD on the solvolysis of the benzoyl chlorides with electron-withdrawing substituents. The disparate behavior in this case is a result of the hydroxyl group (C3) in the cyclodextrin acting as efficient nucleophile if the reaction takes place via an associative mechanism. Three effects arise from methylation of half of the secondary OH's: steric hindrance to proton transfer, reduction in the number of reactive sites, and the raising of effective pK_a of the CD.[17] The C(3) group is exposed at the wider end of the cyclodextrin cavity, such that when they deprotonate under basic conditions, the resultant alkoxide often react readily and selectively as nucleophile.[4]

3.3. Influence of the leaving group

The influence of the leaving group on the solvolysis of benzoyl chlorides was examined under the assumption that the reaction took place both in the bulk water and within the CD cavity. The kinetic parameters in Table 2 were obtained by fitting the k_o values obtained to Eq. 2.

It should be noted that the presence of DM-β-CD caused no switch in the major solvolytic mechanism. The cyclodextrin exerted an inhibitory effect, the rate constant in the bulk water invariably exceeding that within the CD cavity. The ratio $k_o^{[CD]=0}/k_o^{[CD]=0.211}$ was 26, 267, and 487 for **BzF**, **BzCl**, and **BzBr**, respectively. The magnitude of the inhibitory effect decreased with increasing ability of the leaving group. Also, as previously noted for **4-MeO**, the results echoed the polarity changes in the water inside the CD cavity.

One usual practice in studying the influence of the leaving group is to examine the variation of the ratios k_i^{BzBr}/k_i^{BzF}, k_i^{BzCl}/k_i^{BzF}, and k_i^{BzBr}/k_i^{BzCl}. In this work, the variation of these ratios inside a cyclodextrin was examined for the first time thanks to the ability to determine k_{CD} for each benzoyl halide. However, no mechanism switch from the bulk water to DM-β-CD was observed. Figure 5 shows the variation of the previous ratios with the DM-β-CD concentration. Based on it, changes in the properties of water inside the DM-β-CD cavity affect the solvolysis reaction occurring via a dissociative mechanism; the effect, however, depends largely on the nature of the particular leaving group.

3.4. Determination of the ionizing power and nucleophilicity in the DM-β-CD cavity

The solvolysis of benzoyl halides in solvent mixtures has been widely studied. In these media, the following variant

Table 2. Kinetic parameters for the solvolysis of benzoyl halides in the presence of DM-β-CD

Substrate	k_w (s^{-1})	k_{CD} (s^{-1})	$K_{1:1}$ (M^{-1})	$K_{2:1}$ (M^{-1})	k_w/k_{CD}
BzF	$1.45\pm0.05\times10^{-3}$	$1.7\pm0.1\times10^{-4}$	135±10	10±1	9
BzCl (4-H)	1.14±0.04	$3.0\pm1.0\times10^{-3}$	470±25	10±2	380
BzBr	81±3	$3.8\pm0.2\times10^{-1}$	925±50	15±5	215

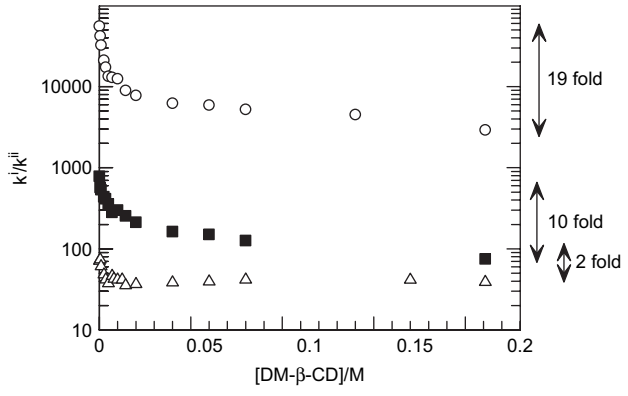


Figure 5. Variation of k_i^{BzBr}/k_i^{BzF} (○), k_i^{BzCl}/k_i^{BzF} (■), and k_i^{BzBr}/k_i^{BzCl} (△) with the DM-β-CD concentration.

of the Grunwald–Winstein equation provides especially good results:[18a]

$$\log\left(\frac{k}{k_o}\right)_{BzX} = mY_X + lN_{OTs} \quad (3)$$

where Y_X is the ionizing power and N_{OTs} the nucleophilicity of the solvent. Our aim was to determine both parameters within the CD cavity. With this aim we used previously reported values of the solvolysis rate constants for **4-MeO**, **4-Me**, **4-H**, and **4-Cl** in acetone–water, methanol–water, and ethanol–water mixtures containing 20–90% (v/v) water.[18b] As can be seen from Figure 6, all four benzoyl halides exhibited excellent linear correlation between the reported experimental $\log(k/k_o)_{BzX}$ values and those calculated by using appropriate values of Y_X and N_{OTs} for each halides in Eq. 3.

Because we had previously determined the experimental value of k_{CD} for DM-β-CD, $\log(k_{CD}/k_o)_{BzX}$ was known. By fitting the experimental data to Eq. 3, we determined parameters m and l for each benzoyl halide. Using a combination of two equations in two unknowns allowed us to obtain Y_X and N_{OTs} for DM-β-CD. The mean value for Y_X was Y_{Cl}=2.12 and that for N_{OTs} was N_{OTs}=−0.85. These values suggest that the water inside the CD cavity has an ionizing power similar to that of an ethanol–water mixture containing 40–50% water and a nucleophilicity similar to that of a 50:50 TFE–water mixture. An alternative scale, N_T, can be used for the solvent nucleophilic power. Based on published results of Kevill and D'Souza[19] for solvolysis of substituted benzoyl chlorides the Y_{Cl}, Y_{Cl}=1.94, and N_T, N_T=−0.80, values for the cavity of the cyclodextrin can be obtained.

The properties of water inside a cyclodextrin cavity or in its vicinity differ markedly from those of bulk water.[14,20,21] Uno et al.[22] concluded that the cavity environment was similar to that of methanol or ethanol, depending on the particular probe. A series of 1,4-disubstituted benzenes exhibited no consistent spectral shifts in α-CD solutions compared with spectra for the compounds in pure solvents, and it was decided that UV spectral probes could not provide unambiguous evidence of the cavity's polarity.[23] Some studies have exploited the fact that fluorescence quantum yields are sensitive to the polarity of the probe environment.[24,25] Ramamurthy and Eaton,[26] and Turro et al.,[25] showed that the polarity of the CD cavity is close to that of alcohols. Thus, parameter E_T was found to be similar to those for *tert*-butyl alcohol and ethylene glycol.[27]

Heredia et al.[28] used correlations of diphenylamine fluorescence energy with $E_T(30)$ and Kosower's Z-value; they assigned a Z value of 88 (similar to that for ethanol) to the β-CD cavity. Street and Acree[29] related the emission wavelength of pyrene-3-carboxaldehyde to the solvent dielectric constant and concluded that ε was 55 for α-CD and 48 for β-CD. Fluorescence enhancement studies, however, constitute no unambiguous routes for estimating accurate cyclodextrin polarity values because the fluorescence quantum yield dependents not only on the polarity of the environment, but also on the restrictions of the motional freedom or collisional probability of the fluorescent probe.[30]

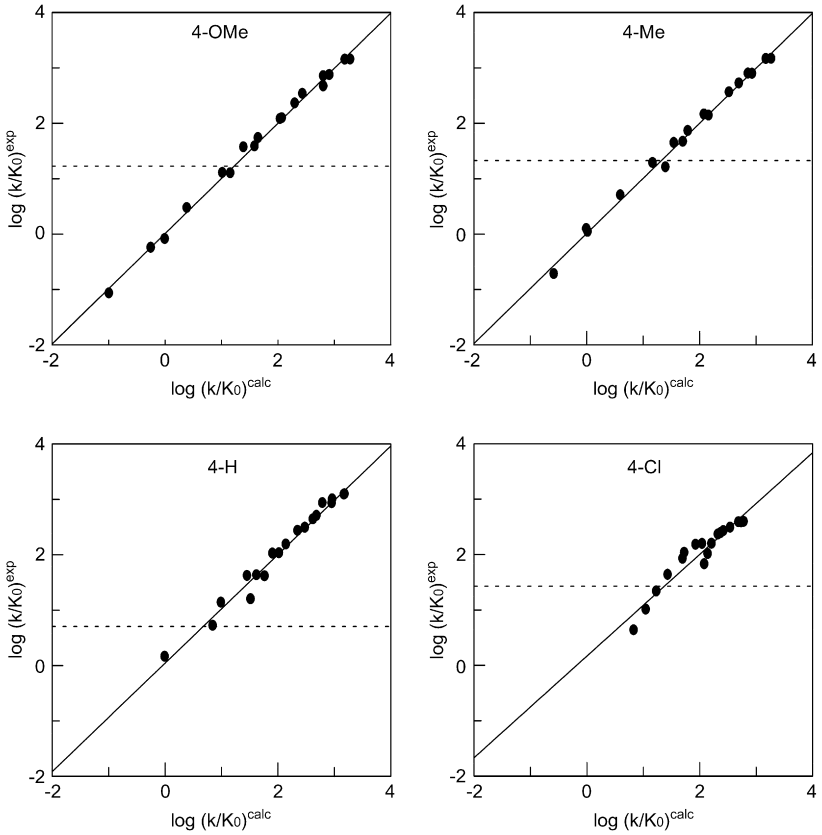


Figure 6. Plots of $\log(k/k_o)^{exp}$ versus $\log(k/k_o)^{calc}$ for acetone–H_2O, MeOH–H_2O, and EtOH–H_2O mixtures. The dotted line represents $\log(k_{CD}/k_o)^{exp}$.

The results obtained in this work show that the polarity of the cyclodextrin cavity is similar to that of alcohol–water mixtures. Our polarity values exceed previously reported ones, which, as can be seen, are rather disperse. Another factor to be considered is the presence of water molecules inside the CD cavity. It is not known exactly how many water molecules are displaced in the cavity of natural cyclodextrins, nor how many water molecules are released from the cavity upon complexation, but for α-CD, these numbers are estimated to be 2 or 3 and ≤2, respectively.[31] In the case of β-CD,[32] 6 to 7 water molecules are distributed within the cavity, even though the cavity is big enough to accommodate up to 11 of them. There is no accurate information regarding the number of water molecules inside the cavity after guest complexation exists as such a number must depend on how the guest is accommodated in the cavity. Our benzoyl chlorides are easily accommodated within the DM-β-CD cavity; however, they allow a certain number of water molecules to be accommodated as well.

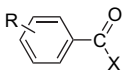
4. Conclusions

We studied the solvolysis of benzoyl halides in the presence of DM-β-CD, the high solubility of which substantially facilitated the conduct of kinetic tests. By choosing an appropriate reaction scheme for each halide, we obtained accurate estimates for the different kinetic parameters. Two possible reaction sites were identified in all cases, namely: the bulk water and the CD cavity. Hammett correlation was for the first time successfully used to examine the reaction mechanism within the internal cavity of cyclodextrins. The presence of a CD increases the reaction rate for those halides that are solvolyzed via a preferentially associative mechanism by the effect of hydroxyl group in the cyclodextrin acting as efficient nucleophile. In those halides where the reaction mechanism is preferentially dissociative, the reaction rate is much more sensitive to changes in the polarity of water inside the CD cavity, an increase in polarity substantially decreases the rate. Finally, the reaction rate additionally depends, strongly, on the ability of the leaving group.

5. Experimental

The DM-β-CD was commercial available (purity >98%) and was used without further purification. In preparing the solutions the water content supplied by the manufacturer was taken into account. The benzoyl chlorides (Scheme 3) had purities between 97 and 98% and were used without further purification. Stock solutions of benzoyl chlorides were prepared daily in dry acetonitrile at the appropriate concentration in order to get a final concentration of 1.0×10^{-4} M.

The solvolysis reactions were followed by monitoring the UV absorbance of substrate solutions using a spectrophotometer or a stopped flow spectrophotometer with unequal mixing. When the kinetics was carried out in a stopped flow spectrophotometer the benzoyl chloride dissolved in dry acetonitrile was placed in the smaller syringe (0.1 mL) and aqueous solution of cyclodextrins was placed in the larger syringe (2.5 mL). The total acetonitrile concentration



4-NO_2:	X = Cl, R = 4-NO_2	**4-H** or **BzCl**:	X = Cl, R = H
3-NO_2:	X = Cl, R = 3-NO_2	**3-Me**:	X = Cl, R = 3-CH_3
4-CF_3:	X = Cl, R = 4-CF_3	**4-Me**:	X = Cl, R = 4-CH_3
3-CF_3:	X = Cl, R = 3-CF_3	**4-MeO**:	X = Cl, R = 4-CH_3O
3-Cl:	X = Cl, R = 3-Cl	**BzF**:	X = F, R = H
4-Cl:	X = Cl, R = 4-Cl	**BzBr**:	X = Br, R = H
3-MeO:	X = Cl, R = 3-CH_3O		

Scheme 3.

was always 3.85% (v/v) and all experiments were carried out at 25.0 °C.

The wavelengths used to monitor the reactions were between 250 and 300 nm. The kinetic data always fitted the first-order integrated rate equation satisfactorily (r>0.999); in what follows, k_o denotes the *pseudo* first-order rate constant. All the kinetic experiments could be reproduced within an error margin of 3%. In all cases it was checked that the final spectrum of the product of the reaction coincided with another obtained in pure water, guaranteeing that the presence of the cyclodextrin did not alter the product of the reaction.

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Supplementary data

A compilation of k_o data as a function of the cyclodextrin concentration is available. Supplementary data associated with this article can be found in online version, at doi: 10.1016/j.tet.2006.12.083.

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