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EFFECT OF α-CYCLODEXTRIN COMPLEXATION ON A GENERAL-BASE-CATALYZED PHOTO-SMILES REARRANGEMENT

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Abstract. α-Cyclodextrin complexation suppresses the efficiency of base-catalyzed photo-Smiles rearrangement of p-$O_2NC_6H_4OCH_2CH_2NHPh$ by 80% in aqueous solution. α-CD does not restrict the electron transfer; it inhibits by enhancing the decay of an intermediate.

We have found[1] that the photo-Smiles rearrangement of p-$O_2NC_6H_4OCH_2CH_2NHPh$ (1) to p-$O_2NC_6H_4NPhCH_2CH_2OH$(2)[2,3] occurs cleanly in 25% DMSO-75% water (v:v) and is subject to general base catalysis. Mutai, et al,[3] have formulated the primary photochemical event for this system in acetonitrile, an intramolecular one-electron transfer, as involving overlap of the π-electron clouds of the two aromatic moieties. We sought to provoke this putative activated complex by α-cyclodextrin inclusion complexation of one of the rings, which we felt would severely disrupt this electron transfer complex.

Alpha- and β-cyclodextrins (α- or β-CD) inhibit the photorearrangement in aqueous solution, as shown by the data of Table I. Despite the solubility limitation of 0.02 M for β-CD, both CD's appear to cause a maximum reduction of efficiency of about 80%. This and the observation that the suppression in the presence of 0.036 M α-CD is maximal and the same as the efficiency at 0.072 M α-CD implies that nearly complete complexation of 1 has occurred in both cases. These results appear reasonable in view of reported CD binding constants for benzene derivatives.[4]

Table 1. Inhibition by cyclodextrins in 20% DMSO-80% water at 1.0 x 10^{-4} M [OH^-]

[α-CD],M	REL. Φ	[β-CD],M	REL. Φ
0	1.0	0	1.0
0.018	0.5	0.018	0.4
0.036	0.2	0.020	0.2
0.072	0.2		

Cyclodextrin complexation of benzoic acid and p-nitrophenol causes downfield shifts of the nmr signals of the aromatic ring protons.[4] We have determined the effect of α-CD on these shifts for 1 at 360 MHz.[5] For a

solution of 1 at 1.0×10^{-4} M in 30% DMSO-d_6 and 70% D_2O, the proton nmr spectrum in the region of 6.5 to 8.5 δ shows a doublet (J = 9 cps) at 8.258, a triplet (J ≈ 7 cps) at 7.250, a doublet (J = 9 cps) at 7.141, and a multiplet (J ≈ 7 cps) at 6.824 δ. We attribute the two doublets to the nitrophenyl ether group, and the triplet and multiplet to the anilino group. When 0.036 M α-CD is present, the two doublets shift downfield by 9 cps, whereas the triplet and multiplet are not shifted. These results indicate that inclusion complexation occurs on the nitrophenyl ether and that the anilino group is not complexed. These conclusions are in accord with reported α-CD binding constants for the groups involved.[4]

The dependence of the quantum yield at 313 nm of photo-Smiles rearrangement of 1 on the concentration of hydroxide ion is shown in Figure 1. The linearity of the double reciprocal plot establishes that the α-CD inhibited reaction is subject to base catalysis. If the pH is held constant and a weak base such as acetate ion or an amine is present, the quantum yield increases. This indicates that the α-CD-inhibited reaction is subject to general base catalysis, as is the normal reaction.[1]

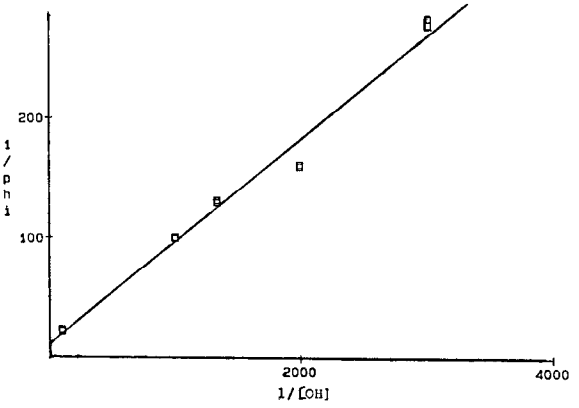


Figure 1. Quantum yield of photo-Smiles rearrangement of 1 in 25% DMSO-75% water in the presence of 0.036 M α-cyclodextrin.

The mechanistic scheme for the photorearrangement shown in Scheme 1 is based on evidence reported by Mutai[2] and by us.[1] We have argued elsewhere[1] that ZH is not an intermediate in this reaction. Thus, for the pathway not involving ZH, the quantum yield expression is given by eq. 1, where $f = (k_8/(k_7 + k_8))(k_{10}/(k_9 + k_{10}))$. Eq. 1 assumes that

$$\frac{1}{\Phi} = \frac{1}{\Phi_{ISC}} \frac{1}{f} \left(1 + \frac{k_1}{k_2}\right)\left(1 + \frac{k_3 + k_4}{\sum_i k_{5_i}[B_i]}\right) \qquad (1)$$

$k_6[BH^+] \ll k_7 + k_8$, because general base catalysis is observed, and that $k_{12} \ll k_{11}$, because uncatalyzed photorearrangement is very inefficient. The deprotonation rate constant for each base can be calculated by using the measured quantum yield at a particular pH and an assumed rate constant[6] of $1.0 \times 10^{10} M^{-1}s^{-1}$ for OH^- in k_5 to calculate the overall product of the remaining constants of eq. 1; the quantum yield at the same pH with a base present is

then combined in eq. 1 with the calculated overall constant to get the rate constant k_5 for the base. These data are plotted in Fig. 2 according to the Bronsted Catalysis Law (eq. 2).

$$\log k_{cat} = \beta(pKa_{BH}) + \text{const.} \quad (2)$$

The least squares regression line (not shown) has a slope of 0.22 (corresponding to β in eq. 2), though it is unlikely that the correlation is linear.

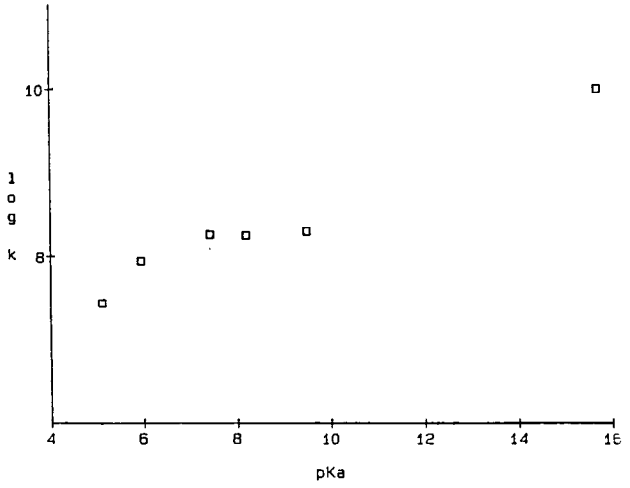
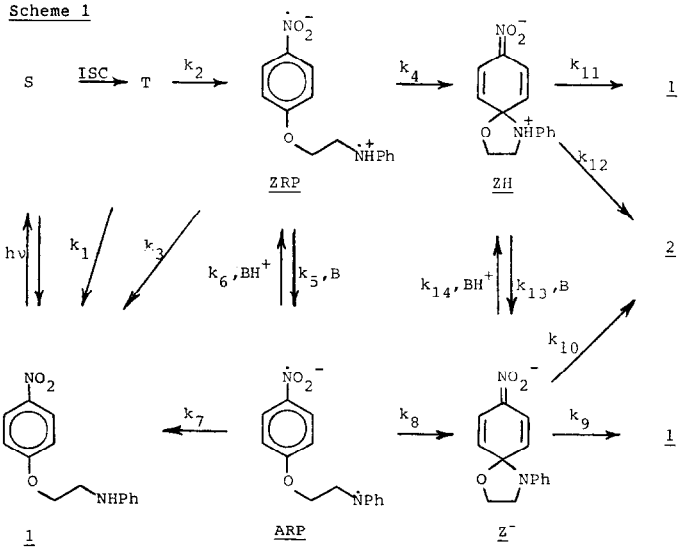


Figure 2. Bronsted plot for base catalysts of the α-CD inhibited Smiles photorearrangement of 1. Bases (BH pKa) are (l to r): acetate (5.10), hydroxylamine (5.95), 2,4,6-collidine (7.43), glycinamide (8.20), ethanolamine (9.50), hydroxide (15.7).

The intercept of Fig. 1 corresponds to infinite $[OH^-]$, under which condition the quantum yield (0.085 ± 0.02) is approximately the same as that for the photorearrangement of 1 in the absence of α-CD (0.10 ± 0.01).[1] This result implies that α-CD complexation has no net effect on the product of the partitionings of the intermediates S, T, ARP, and Z^-. Of these, intersystem crossing from S is likely to be little changed or slightly enhanced by the apolar CD cavity, and CD complexation is unlikely to alter the high efficiency with which Z^- should reach 2. Disruption by CD complexation of the putative electron transfer complex involving π-electron overlap of the two rings would cause $k_2/(k_1 + k_2)$ to become much smaller, and it seems unlikely that $k_8/(k_7 + k_8)$ would be changed by the complexation in the opposite direction and to the same extent. We conclude that the electron transfer involves not π-electron overlap but tunnelling through the σ-bonds, a process well documented by spectroscopic observations on other systems.[7]

Scheme 1



Interpretation of the nature of the Bronsted relationship (Figure 2) awaits further work, but the plot shown and the corresponding one without CD[1] are similar in shape and

coextensive. For example, the deprotonation rate constants for acetate ion, based on an assumed rate constant in each case of $1.0 \times 10^{10} M^{-1}s^{-1}$ for hydroxide ion, are $2.8 \times 10^{7} M^{-1}s^{-1}$ with no CD, and $2.7 \times 10^{7} M^{-1}s^{-1}$ with 0.036 M α-CD. This indicates that the proton transfer is not affected by complexation and implies that enhancement of the decay of ZRP is the cause of CD inhibition. The slope to intercept ratio of Fig. 1 (0.0073) represents $(k_3 + k_4)/k_5$; the corresponding ratio with no CD present is 0.0014.[1] If k_5 for hydroxide ion is $1.0 \times 10^{10} M^{-1}s^{-1}$, $k_3 + k_4$ is $7.3 \times 10^{7} s^{-1}$ with α-CD and $1.4 \times 10^{7} s^{-1}$ without CD. Since the α-CD cavity is apolar, it seems reasonable that the anion radical moiety of ZRP would be destabilized by complexation, which might enhance the rate of ZRP decay by reverse electron transfer or radical coupling to make an unproductive intermediate, ZH. That the analysis reveals an effect of α-CD on the partitioning of an intermediate indicates that the lifetime of the α-CD complex is long enough that it persists through the mechanistic evolution of the reaction. This conclusion agrees with previous work indicating that the lifetime of the p-nitrophenol-α-CD complex is 10^{-5}s.[4]

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5. We thank Dr. Bruce Hawkins of the NSF Regional NMR Facility at Colorado State University for assistance with these experiments.

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