Tetrahedron Letters,Vol.30,No.47,pp 6477-6480,1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Pergamon Press plc

α-CYCLODEXTRIN COMPLEXATION AS A PROBE OF HETEROLYTIC GENERAL BASE-CATALYZED PHOTO-SMILES REARRANGEMENTS

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Abstract: α-Cyclodextrin complexation of $3\text{-}O_2NC_6H_4O(CH_2)_nNH_2$ inhibits by 40 and 15%, respectively, the efficiency of base-catalyzed and uncatalyzed photo-Smiles rearrangement for n = 2; α-CD complexation inhibits the photorearrangement efficiency of n = 3 by 40% in the base-catalyzed regime but enhances the efficiency by 67% in the uncatalyzed regime.

Our quantitative kinetic[1] and nanosecond transient[2] studies of photo-Smiles rearrangement of **1a** and **1b** conclude that the primary photochemical process is heterolytic nucleophilic attack on the triplet state to give a high energy σ-complex . We attribute the observed general base catalysis to irreversible deprotonation of the ammonium group of the σ-complex (**MH**), as shown in Scheme 1. Both uncatalyzed and base-catalyzed rearrangements take place. We felt that α-cyclodextrin (α-CD) complexation of **1a** and **1b** would cause interesting perturbations of the photorearrangement kinetics, the interpretation of which might provide mechanistic insight, as it had in a previous case.[3]

The hydrochloride salt of **1b** was synthesized by the methods reported for **1a**.[4] Photolysis of **1b** in aqueous 0.01 M NaOH caused UV spectral changes identical with those reported for **1a**,[4] which indicates that clean photo-Smiles rearrangement occurs for this substance, as it does for **1a**. Kinetic studies were carried out by irradiating samples (0.001 M) at 21°C in cuvettes at 335 nm with light from a monochromator illuminated by a 75-W xenon lamp. The actinimeter was Aberchrome 540 in toluene, and reaction progress was followed by product absorbance at 405 nm (ε 1110). Carbonate-free water was used and ionic strength was maintained at μ = 0.10 by adding KCl.

Table 1 shows the effect of α-CD concentration on the efficiency of photo-Smiles rearrangement of **1a** at 0.01 M NaOH. We have not directly measured the dissociation constant of the α-CD·**1a** complex, but the inhibitory effect is over 90% achieved at 0.036 M α-CD, indicating that K_D is ≅ 0.004 M. This agrees with K_D

Table 1. Cyclodextrin Inhibition of Photo-rearrangement of **1a** at pH 12.

[α-CD], **M**	Φ
0	0.25
0.018	0.17
0.036	0.15
0.072	0.14

reported for m-$O_2NC_6H_4OH$ and m-$O_2NC_6H_4CO_2H$ (both 0.0066 M at 20°C).[5] These molecules complex by inserting the m-nitrophenyl moiety into the wider opening of the α-CD cavity,[5] a binding mode that is very likely for **1a** and **1b**.

Figures 1 and 2 show the variation in quantum yield for photo-Smiles rearrangement of **1a** and **1b** as NaOH concentration is varied. The data indicate that uncatalyzed photorearrangement occurs for both cases at $[OH^-] < 0.0005$ and 0.002, respectively, and OH^- -catalyzed photorearrangement occurs at higher OH^- concentrations.[6] Also shown are the dependencies of efficiency on the OH^- concentration in the presence of 0.036 M α-CD, at which concentration **1a** and **1b** are over 90% complexed. Photorearrangement of **1a** is inhibited by complexation to the extent of 40% in the catalyzed regime and about 15% in the uncatalyzed regime. Base-catalyzed photorearrangement of **1b** is inhibited by complexation to the extent of 40%, but the uncatalyzed reaction is enhanced by complexation by 67%.

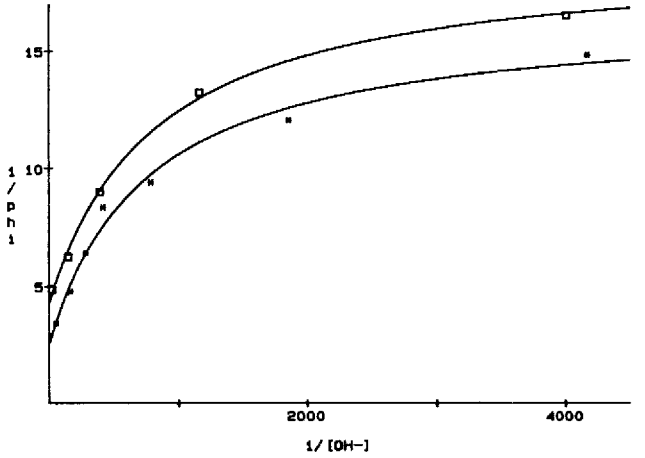


Figure 1. Effect of $[OH^-]$ on Efficiency of Photo-Smiles Rearrangement of **1a** in the absence of (*) and presence of (□) 0.036 M α–CD.

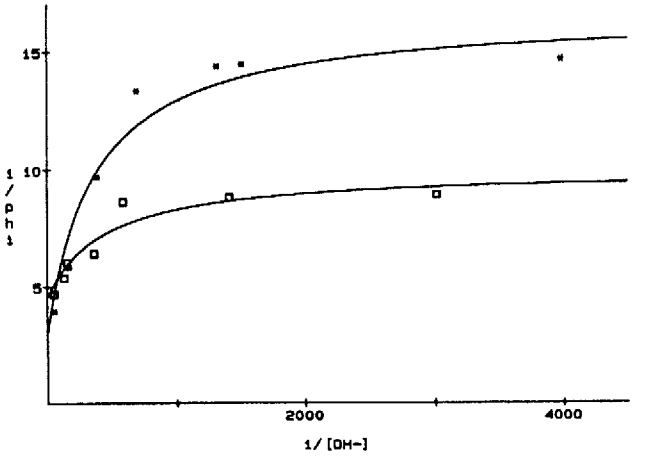
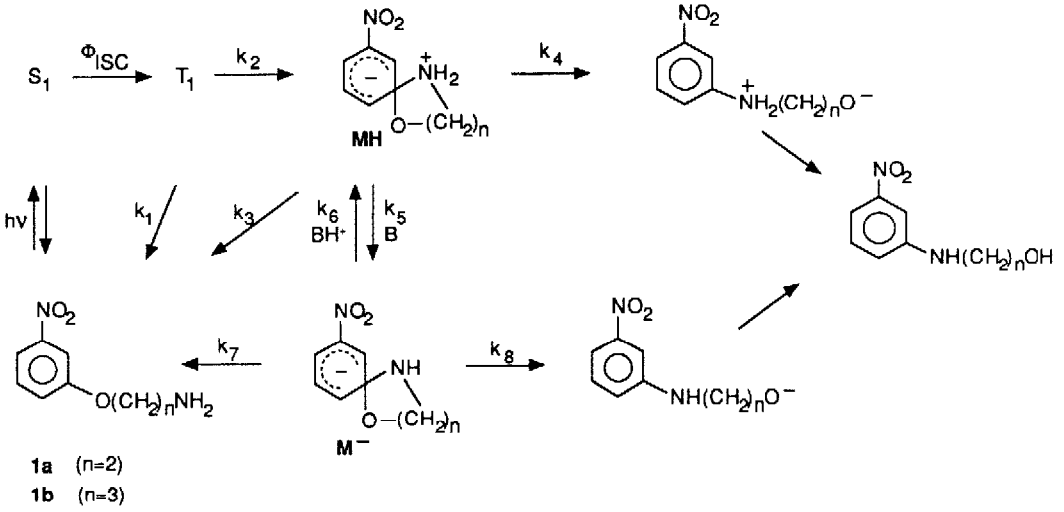


Figure 2. Effect of $[OH^-]$ on Efficiency of Photo-Smiles Rearrangement of **1b** in the absence of (*) and presence of (□) 0.036 M α–CD.

The curves of Fig. 1 and 2 were obtained with RS/1 software (BBN Software Products) that calculates by iteration to a convergent best fit of the data points to the mathematical general form of the quantum yield

SCHEME 1



expression (eq. 1). By assuming that the rate of proton transfer from **MH** to OH^- is diffusion controlled (k_5 = 1.4 x 10^{10} $M^{-1}s^{-1}$),[7] we obtain from the fits the absolute rate constants for k_3 and k_4. Typical standard deviations of the parameters found by the fits are shown by the results for **1a** at [α-CD] = 0 in Figure 1: intercept = 2.36 ± 0.30, k_3 = 1.16 ± 0.28 x $10^8 s^{-1}$, and k_4 = 1.93 ± 0.26 x $10^7 s^{-1}$ Results are listed in Table 2 along with values for the limiting quantum yield at the intercept (infinite catalyst concentration) and the quantum yield of uncatalyzed photorearrangement. These data afford rationalizations of the effects of complexation.

$$\frac{1}{\Phi} = \frac{1}{\Phi_{ISC}}\left(1 + \frac{k_1}{k_2}\right)\left(1 + \frac{k_3}{k_4 + k_5[OH^-]}\right) \qquad (1)$$

At infinite catalyst concentration, partitioning at the stage **MH** does not occur because **MH** goes exclusively to M^- , which in turn goes exclusively to product.[1] The 40% suppression of efficiency of the catalyzed photorearrangement by α-CD in both cases therefore seems likely to reflect lowered

Table 2. Efficiency and Kinetic Data for Photorearrangement of **1a** and **1b**

n	[α-CD], M	Φ_{lim}	Φ_{uncat}	$k_3 \times 10^{-7}$ s^{-1}	$k_4 \times 10^{-7}$ s^{-1}	k_4/k_3
2	0.000	0.42	0.061	11.6	1.9	0.17
2	0.036	0.24	0.052	6.1	1.7	0.28
3	0.000	0.36	0.060	19.0	3.8	0.20
3	0.036	0.22	0.100	3.8	3.1	0.82

success of k_2 versus k_1, an effect reasonably attributed to steric encumbrance of the attack (k_2) by the α-CD rim. It seems unlikely that this inhibition could be caused by reduction of Φ_{ISC} (see eq. 1) since a medium effect of this size on intersystem crossing of a nitrophenyl ether would be unprecedented.

In the uncatalyzed regime, partitioning at the **MH** stage becomes significant. The partitioning k_4/k_3 is increased by complexation by a factor of 1.6 for n = 2 and a factor of 4.1 for n = 3 (see Table 2). In both cases the increased partitioning toward product is achieved mainly by suppressing k_3, decay to starting material by expulsion of H_2NR, rather than by enhancing k_4.

The medium represented by the α-CD cavity is well established to be highly apolar.[8] Replacement of the polar medium of water by this medium should destabilize the anion part of $\mathbf{M}^-$, causing it to be even less selective than it is in water in expelling H_2NR in preference to ^-OR. (Conjugate acid pK_a's are ca. 10 and 16, respectively). This effect must be small, however, since k_4 is not changed by complexation that causes k_4/k_3 to increase. The major effect of complexation is to lower k_3. Hydrogen bonding of $-N^+H_2R$ to a 2- or 3-hydroxyl group of the α-CD rim would be a plausible means of stabilizing the nitrogen group against expulsion. The reason the stabilizing effect is so much larger for n = 3 than for n = 2 may be that the intermediate, **MH**, for n = 3 makes a more stable complex with α-CD. Examination of models reveals that **MH** for n = 3 can adopt a chair conformation of the cyclohexane-like moiety that places the methylene hydrogens well away from interference via van der Waals interactions with the atoms of the α-CD rim. **MH** for n = 2 cannot adopt a conformation that as effectively reduces such non-bonded repulsions; this intermediate, consequently, may be forced slightly out of the α-CD cavity, which may reduce the strength of the stabilizing hydrogen bond of its ammonium moiety.

The effects of α-CD complexation on this system and on $4\text{-}O_2NC_6H_4OCH_2CH_2NHPh$ **3** support a crucial mechanistic distinction. The latter Smiles photorearrangement was proposed[3,9] to involve intramolecular electron transfer in the triplet state to give $4\text{-}\bar{O}_2\dot{N}C_6H_4OCH_2CH_2\dot{N}\overset{+}{H}Ph$, irreversible deprotonation of $-\dot{N}\overset{+}{H}Ph$, and coupling of the radicals (amino N at C-1) to make a spiro σ-complex. Uncatalyzed rearrangement does not occur for the N-phenyl case. Complexation affects the cyclization efficiencies of the current case (**1a** and **1b**) and the N-phenyl case differently. For the current case, nucleophilic attack in the triplet state is postulated to complete with rapid decay of the triplet. Encumbering the attack with α-CD complexation indeed causes a 40% reduction in the efficiency of making **MH**. For the N-phenyl case, however, one sees no such effect, the rationale being that the σ-complex is formed by radical coupling that has no effective competition; thus any reduction of its rate by complexation does not show in the quantum yield.

Acknowledgment is made to the National Science Foundation (CHE-8605343) for support of this research.

References

1. G. G. Wubbels and D. W. Celander, *J. Am. Chem. Soc.*, 103, 7669-70 (1981).

2. G. G. Wubbels, P. H. M. van Zeyl, and C. A. G. O. Varma, *Abstracts of 185th National Meeting*, Am. Chem. Soc., Seattle, March 1983; ORGN-50.

3. G. G. Wubbels, B. R. Sevetson, and S. N. Kaganove, *Tetrahedron Lett.*, 27, 3103-06 (1986).

4. G. G. Wubbels, A. M. Halverson, J. D. Oxman, and V. H. De Bruyn, *J. Org. Chem.*, 50, 4499-504 (1985).

5. R. I. Gelb, L. M. Schwartz, B. Cardelino, H. S. Fuhrman, R. F. Johnson, and D. A. Laufer, *J. Am. Chem. Soc.*, 103, 1750-7 (1981).

6. The meaning of "catalyzed" here is defined in G. G. Wubbels, *Acc. Chem. Res.*, 16, 285-91 (1983).

7. M. Eigen, *Angew. Chem. Int. Ed. Engl.*, 3, 1-19 (1964).

8. H.-J. Schneider, R. Kramer, S. Simova, and U. Schneider, *J. Am. Chem. Soc.*, 110, 6442-8 (1988).

9. a. Yokoyama, IK.; Nakagaki, R.; Nakamura, J.; Mutai, K.; Nagakura, S. *Bull. Chem. Soc. Jpn.*, 53, 2472-75 (1980); b. G.G. Wubbels, B.R. Sevetson, and H. Sanders, *J. Am. Chem. Soc.*, 111, 1018-22 (1989).

(Received in USA 1 August 1989)