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Strong Inhibition of Cis–Trans Isomerization of Azo Compounds by Hydroxide Ion

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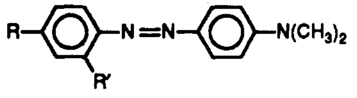
The thermal cis–trans isomerization rate of methyl yellow (1), *p*-phenyl red (2), and *o*-methyl red (3) in aqueous solution was measured at different hydroxide ion concentrations, and it was found that there is a very strong inhibition as the pH increases. For 1 the rate changes from 2.17×10^{-2} s^{-1} at NaOH 6×10^{-3} M to 1.0×10^{-3} s^{-1} at NaOH 0.1 M. The observed rate constant for 2 was too fast for the experimental technique used at a concentration of NaOH lower than 0.01 M. These results are interpreted in terms of a much faster rate of isomerization of the protonated cis compounds than the neutral ones, and values for the pK_a and rate constants for both species are calculated.

The kinetics of thermal cis–trans isomerization of azo benzenes in the liquid phase has been intensely studied during the last 50 years.[1,2] Generally, the trans isomer of an azo compound is the more stable form in solution. The equilibrium may be shifted toward the cis by photoexcitation, and in the dark it undergoes thermal relaxation to trans. This conversion has been shown to be catalyzed by both electrophilic and nucleophilic agents.[3] Only a few systematic studies[4–7] have been reported about the catalysis and almost all of them have been on azobenzene.

The rate of the thermal cis–trans isomerization of azo benzenes is extremely solvent sensitive,[8,9] and many studies have been carried out in various media. In recent years azo compounds have been employed as triggers[10,11] or probes[12,13] for the possible use of this type of compounds in image storage systems.[14] Most of the studies in homogeneous solutions are carried out in organic solvents due to the low solubility in water. We are interested in the photochemical and thermal behavior of azo compounds in water solution, and we found that the hydroxide ion very strongly inhibits the thermal cis–trans isomerization rate of the compounds 1–3.



1: R = R' = H (methyl yellow)
2: R = COO⁻; R' = H (*p*-methyl red)
3: R = H; R' = COO⁻ (*o*-methyl red)

Results and Discussion

Compounds 1–3 were irradiated with a medium-pressure Hg lamp (wavelength of maximum emission 365 nm) until the photostationary state was achieved. There is a bleaching of the solution at the wavelength of maximum absorption. The spectrum recovers the original shape in the dark (Figure 1 is representative). Good isosbestic points are obtained for methyl yellow at 369 and 513 nm. The solutions can be irradiated several times and always revert to the original spectrum which indicates that the reaction is completely reversible. The rate of the reaction is highly dependent on the HO^- concentration at constant ionic strength (Table I). There is a nonlinear dependence of the observed rate constant with the HO^- concentration (Figure 2). The rate of 2 could not be measured at HO^- concentrations lower than 0.01 M because it is too fast for our experimental technique. The reactions of 2 and 3 were studied in water solution, but for the reaction of 1 it was necessary to use an organic cosolvent in order to have enough substrate in solution. In ethanol–water or acetonitrile–water, the reactions show about the same behavior although in the latter solvent they are somewhat slower (see Table I). It has previously been shown that the cis–trans isomerization rate is faster in protic than in aprotic solvent.[15] The effect of the change in the polarity of the reaction was studied using several water ethanol

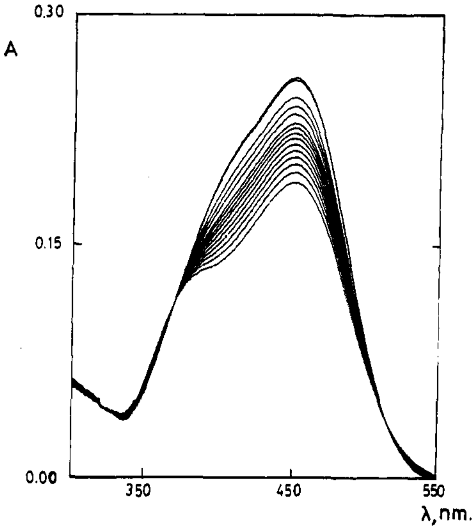


Figure 1. Spectrum of methyl yellow as a function of time. Cycles every 1 min.

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Table I. Effect of Hydroxide Ion Concentration on the Cis–Trans Isomerization Rate of Compounds 1–3

[NaOH], M	*p*-methyl red[a] k_{obs}, s^{-1}	methyl yellow[b] k_{obs}, s^{-1}	methyl yellow[c] k_{obs}, s^{-1}	*o*-methyl red[d] k_{obs}, s^{-1}
0.001			0.0748	
0.003			0.0215	
0.006		0.0217	0.0089	
0.008		0.0162		
0.010	0.510	0.0088	0.0049	0.297
0.016		0.0060		
0.020	0.151	0.0040		
0.025				0.135
0.030	0.123	0.0038	0.0022	
0.040	0.113			
0.050	0.097			0.066
0.060		0.0014	0.0009	
0.075	0.083			0.061
0.100	0.100	0.0010	0.0006	0.051
0.125				0.018
0.200	0.097			

[a] Solvent: H_2O; *T*, 25 °C, $[\mathbf{2}]_0 = 6.8 \times 10^{-5}$ M. [b] Solvent: EtOH/H_2O (20:80 v/v); *T*, 25 °C; $[\mathbf{1}]_0 = 1.22 \times 10^{-5}$ M. [c] Solvent: ACN/H_2O (20:80); *T*, 25 °C; $[\mathbf{1}]_0 = 1.22 \times 10^{-5}$ M. [d] Solvent: H_2O; *T*, 25 °C, $[\mathbf{3}]_0 = 7.8 \times 10^{-5}$ M.

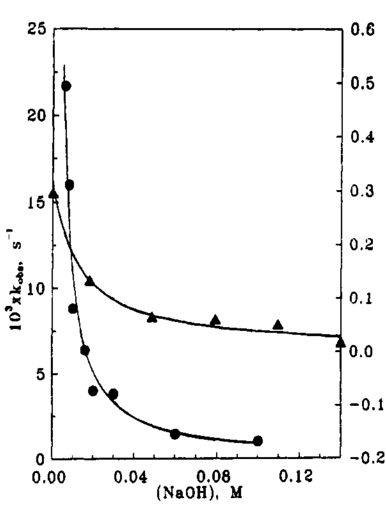


Figure 2. Effect of the HO^- concentration on the rate of cis–trans isomerization rate of **1**, ■ (left ordinate), and **3**, ▲ (right ordinate).

Table II. Effect of the Polarity of the Solvent on the Thermal Cis–Trans Isomerization Rate of *o*-Methyl Red at 25 °C[a]

EtOH, %	k_{obs}, s^{-1}	EtOH, %	k_{obs}, s^{-1}
2.00	0.022 ± 0.001	20.00	0.010 ± 0.002
5.00	0.021 ± 0.001	30.00	0.0036 ± 0.0001
7.50	0.020 ± 0.003	50.00	0.0008 ± 0.0001
10.00	0.016 ± 0.002	dioxane[b]	0.0041 ± 0.0004

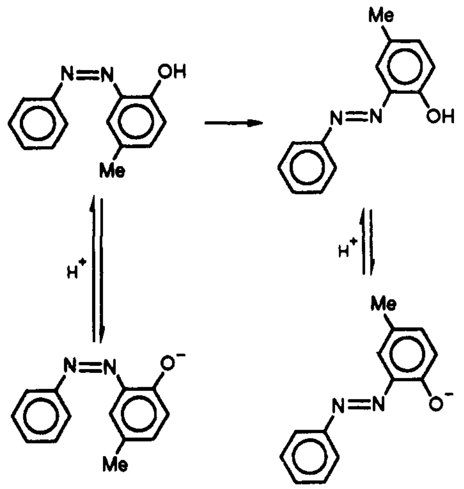
[a] $[\text{Substrate}]_0 = 7.5 \times 10^{-5}$ M, [NaOH] = 0.1 N. [b] Dioxane/water (20:80 v/v).

mixtures between 2 and 50% at constant HO^- concentration (Table II).

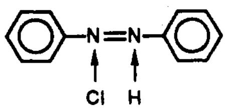
Since it is very common that dyes are associated when they are dissolved in water,[16] we determined the spectra of substrates **1–3** at several concentrations. There was no evidence for association in this range of concentration, and there was a very good fit to the Lambert–Beer law.

The reaction of several azobenzenes in several solvents was studied many years ago and catalysis by traces of acid was noticed,[17] but no further efforts were made to determine the mechanism. Most studies of the cis–trans isomerization reactions were directed toward the differentiation of the inversion or rotation mechanism.[8,18] The behavior of compounds **1–3** in the presence of HO^- might indicate that the substrate interact with hydroxide ion leading to a compound that isomerizes at slower rate. There is a slight change in the spectrum of the substrate when HO^- is added, and an equilibrium constant of about 80 M^{-1} can be calculated assuming 1:1 interaction for methyl yellow, but this value is too low to account for the observed effect on the rate.

Scheme I



The cis–trans isomerization of azobenzene was shown to be catalyzed by HCl and $HClO_4$, and the results were interpreted considering the formation of an addition compound like **4**;[6] however, the observed catalysis takes place at high acid concentration and it is not as strong as the inhibition reported here. For instance, the ratio of observed rate constants at 1 M and zero concentration of $HClO_4$ is 1.9.



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The thermal isomerization of 2-hydroxy-5-methylazobenzene was studied as function of pH, and the mechanism described in Scheme I was postulated.[19] The authors suggest that the anion does not isomerize and the only pathway is that corresponding to the neutral substrate. If a similar mechanism is responsible for the inhibition observed in these reactions we could write Scheme II.

The expression for the observed rate constant for Scheme II is given in eq 1, if k_2 is very small compared to k_1.

$$k_{obs} = k_1 \frac{K_w/K_A}{K_w/K_A + [HO^-]} \tag{1}$$

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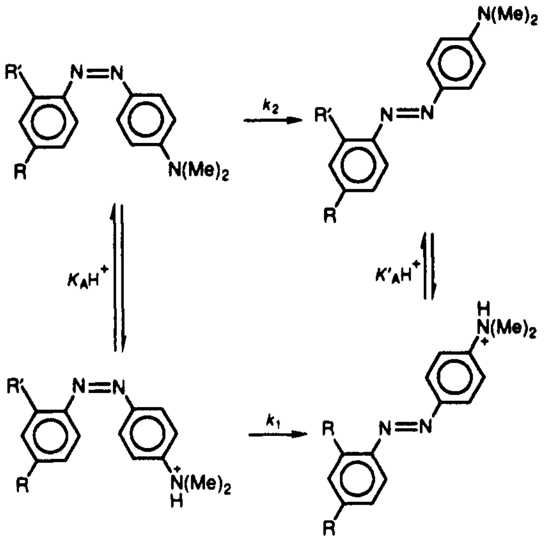
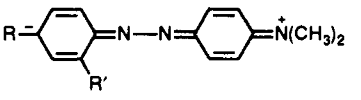
Scheme II



Nonlinear adjustment of the data to eq 1[20] for the methyl yellow reaction yields $k_1 = (1.6 \pm 0.9) \times 10^5$ s^{-1} and $K_A = (1.3 \pm 0.8) \times 10^{-4}$ M (pK_a = 3.9). The latter is a quite reasonable value considering that the pK_a of the trans isomer of a similar compound, *p*-(diethylamino)azobenzene, is 2.7[21] and in the cis isomer the contribution of structures like **5** may not contribute as much as in the trans isomer. From molecular mechanics calculations,[22] the two aryl rings are not coplanar in the cis form, and this noncoplanarity occurs even in compounds 1 and 2 which do not have substituents in the ortho position.



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For *o*-methyl red the data can not be fitted to an equation of the form of eq 1 but are better represented by eq 2 with $k_2 = 1.4 \times 10^{-2}$ s^{-1} and $k_1/K_A = (2.8 \pm 0.1) \times 10^{11}$.

$$k_{obs} = \frac{K_w k_1}{K_A[HO^-]} + k_2 \qquad (2)$$

If K_A has about the same value as for 1, we can estimate $k_2 \approx 4 \times 10^7$ s^{-1}. In Table III the values of k_1 and k_2 for the three substrates are compared. We can see that both values increase in the order 2 > 3 > 1.

Table III. Rate Constants for the Isomerization of the Protonated and Unprotonated Forms of 1–3

substrate	k_1, s^{-1}	k_2, s^{-1}
1	$(1.6 \pm 0.9) \times 10^5$	$<1 \times 10^{-3}$ [a]
3	4×10^7	1.4×10^{-2}
2		9×10^{-2}

[a] Value at the highest HO⁻ concentration.

The very strong inhibition of the rate of isomerization of compounds 1–3 indicates that great care should be taken in the interpretation of results when the rate of isomerization is measured in organized media if the pH is not appropriately controlled.

Experimental Section

Materials. *o*-Methyl red (RP Carlo Erba) and methyl yellow (Aldrich) were commercial samples and were recrystallized from ethyl alcohol, whereas *p*-methyl red was synthesized from diazotized *p*-aminobenzoic acid and *N,N*-dimethylaniline and was recrystallized from toluene.[23] Their purity was controlled by HPLC, thin-layer chromatography, and IR. The solutions were prepared at the highest concentration which gave constant absorption for 1–2 h, which indicates that there was no precipitation. Several spectra were done at concentrations in the range of (0.75–3.84 × 10^{-5} M, (0.75–3.02) × 10^{-5} M, and (0.122–1.2) × 10^{-5} M for *o*-methyl red, *p*-methyl red, and methyl yellow, respectively, to check for association of the substrate. There was a good fit to the Lambert–Beer law. Sodium or potassium hydroxide solutions were standardized against primary standard potassium acid phthalate.

Kinetics. A solution in pure water or in ethanol water of the appropriate substrate was irradiated with a medium-pressure Hg lamp for 10 min, and then the cuvette was placed in the thermostated cell of a spectrophotometer (Shimadzu UV 260) and the absorbance at the maximum of the substrate (429, 463, and 450 nm for *o*-methyl red, *p*-methyl red, and methyl yellow, respectively) was measured as a function of time. The experiments were repeated at least three times. The spectrum of the final solution matches that of the solution without irradiation.

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