Protonation Study and Mechanism of Hydrolysis of 2-[(*p*-Methoxyphenyl)azo]-1,3,4-thiadiazole in Aqueous Sulfuric Acid at 60 °C

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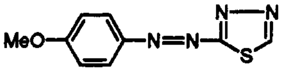
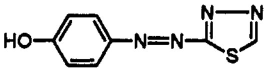
2-[(*p*-Methoxyphenyl)azo]-1,3,4-thiadiazole has been found to be associated with a single protolytic equilibrium, its pK_a value for the protonation equilibrium has been evaluated, and the structure of the protonated species has been determined. The compound hydrolyzes from the monopronated substrate by the A–S_E2 mechanism of the S_NAr type.

The compound 2-[(*p*-methoxyphenyl)azo]-1,3,4-thiadiazole is an azo dye, and some azo dyes are somehow sluggish toward S_NAr reaction due to the energetic requirements of such reactions. This compound (I)is such an azo dye since it has been found to conform to a slow A–S_E2 rather than any other mechanism(s) of the S_NAr type. This is a typical example of the insensitive reaction of alkyl aryl ethers toward hydrolysis in acid media. This category of azo dyes can be made active and susceptible to hydrolysis in acid media by subjecting the aromatic ring to phenylazo substitution[1,2] (see III–V in Scheme 1 and VII in Scheme 2). In accordance with Cox and Yates[3] work in the determination of reaction mechanism, the acid protonation constants of weak bases from ionization ratio measurements in strong acid solution are evaluated using the excess acidity method (X functions), and this method on analysis gives reliable pK_{SH} values in either the presence or the absence of medium effects on the spectra used to obtain the ionization ratios. In a related work, Buncel and Onyido[4] studied the protonation equilibrium and spectroscopic properties of some (phenylazo)pyridines relative to the mechanism of the acid-catalyzed Wallach rearrangement of azoxy compounds, and their report alerted several workers to the use of absorption spectra in sulfuric acid and other strong acids in the determination of the basic dissociation constants of weak bases.[5] This method is also adopted in this paper. In an earlier work, Bunnett et al.[2] had observed a much less sensitive acid-catalyzed hydrolysis of 4-[(*p*-sulfophenyl)azo]anisole. They obtained a k_ψ of 1.57 × 10^{-6} S^{-1} for the hydrolysis of the benzene-series azoether in 1.015 M HCl at 46.2 °C, while the naphtalene-series azoether 4-[(*p*-sulfophenyl)azo]-1-naphthyl methyl ether) hydrolyzes 6890 times faster under the same conditions.

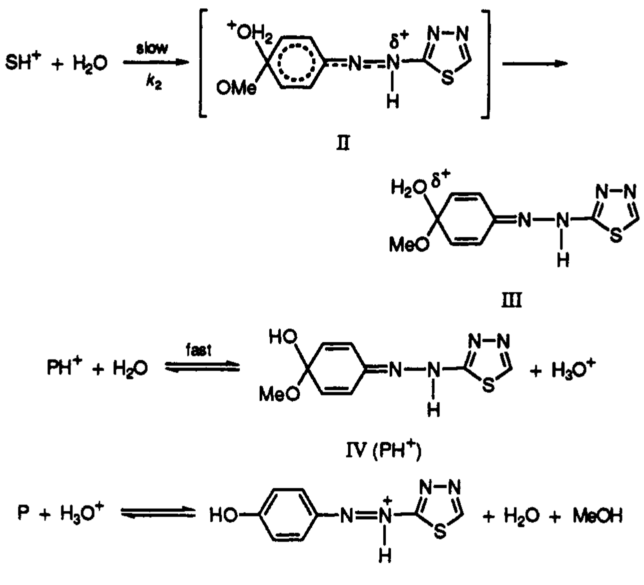


I

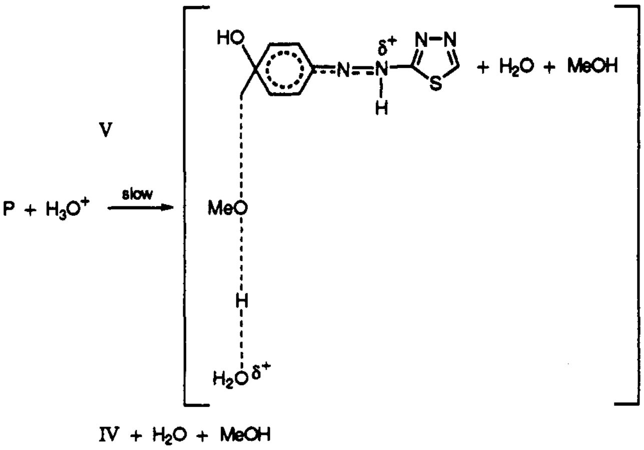


II

Scheme 1



Scheme 2



This was said to be due to the fact that the rate of hydrolysis of this benzene-series azoether was studied as a function of hydrochloric acid concentration in the concentrated range only and that the slow rate of hydrolysis observed in the benzene-series azoether is a typical example of the sluggish reactions of some azo dyes which is in connection with the energetic demands of such reactions mentioned above. In this paper, a k_ψ of 5.65 × 10^{-6} S^{-1} for

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[•] Abstract published in *Advance ACS Abstracts,* March 15, 1994.

[1] Bunnett, J. F.; Hoey, G. B. Dealkylation in connection with diazo coupling of phenol ethers. *J. Am. Chem. Soc.* **1958**, *80*, 3142.

[2] Bunnett, J. F.; Buncel, E. Kinetics of the Acid-catalysed Hydrolysis of 4-(p-sulphophenylazo)-1-naphthylether and 4-(p-sulphophenylazo)-anisole. *J. Am. Chem. Soc.* **1961**, *83*, 1117.

[3] Cox, R. A.; Yates, K. Kinetics equations for reaction in concentrated aqueous acids based on the concept of excess acidity. *Can. J. Chem.* **1981**, *59*, 2853.

[4] Buncel, E.; Onyido, I. Studies of Azo and azoxy dye stuffs. Part 18. Kinetics and mechanism of the hydrolysis of 3- and 4-(p-methoxyphenylazo) pyridines in aqueous sulphuric acid media. *Can. J. Chem.* **1986**, *64*, 2115.

[5] Davis, C. T.; Geissman, T. A. Basic dissociation constants of some substituted flavones. *J. Am. Chem. Soc.* **1954**, *76*, 3507.

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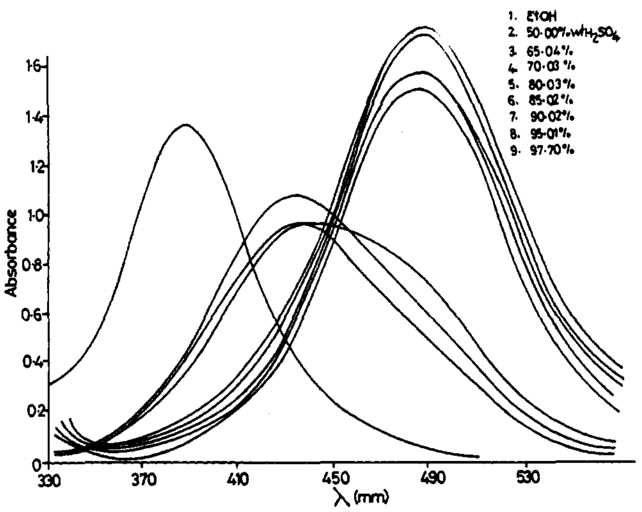


Figure 1. Plot of absorbance vs wavelength for 50–97 wt % H_2SO_4.

Table 1. Selected k_ψ Values at Varying wt % H_2SO_4[a]

acid (wt % H_2SO_4)	k_ψ (values × 10^{-6} s^{-1})	acid (wt % H_2SO_4)	k_ψ (values × 10^{-6} s^{-1})
35.04	5.15	55.04	5.72
40.02	5.43	60.02	5.75
45.01	5.46	65.04	5.84
50.00	5.66	70.20	6.20

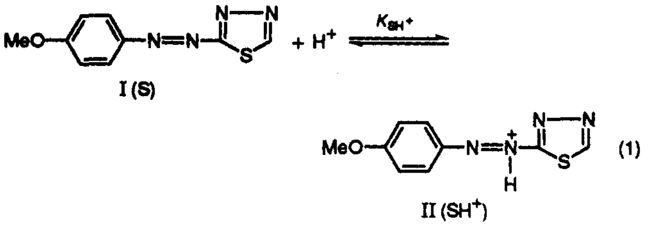
the hydrolysis of the title compound in 1.033 M H_2SO_4 at 60 °C was obtained (see Table 1). This is in good agreement with the report of Bunnett et al.[2] on the hydrolysis of the benzene-series azoether mentioned above. Bunnett and Hoey worked at 46.2 °C, and while this work was carried out at 60 °C, the rate of hydrolysis of this compound (I) is still comparable to that of the naphthalene-series azoether. Just as Bunnett et al.[2] rightly pointed out the reasons for the inactiveness of azo dyes/azoethers, the same reasons account for the slow rate of hydrolysis of 2-[(p-methoxyphenyl)azo]-1,3,4-thiadizole in aqueous media since the rate depends on the sulfuric acid concentration and temperature; in addition, a different rate of hydrolysis is expected if the temperature is changed.

Experimental Section

A 0.0167 M solution of 2-[(p-methoxyphenyl)azo]-1,3,4-thiadiazole was used as the stock for the pK_a determination. Six μL of the stock solution was withdrawn and added to 2 mL of sulfuric acid solution already in the cuvette. The absorbance of the resulting solution mixture was monitored over a wavelength of 335 to 550 nm. This was repeated for acid solutions of varying concentration(s) (i.e., wt %) as well as in neutral solvent (ethanol). From the data and plot of absorbance versus wavelength (Figure 1), the pK_a for the sample (I) is found to be 6.51 at 60 °C.

Discussion

The monoprotonation behavior of I in aqueous sulfuric acid solution in this experiment with respect to eq 1



(1)

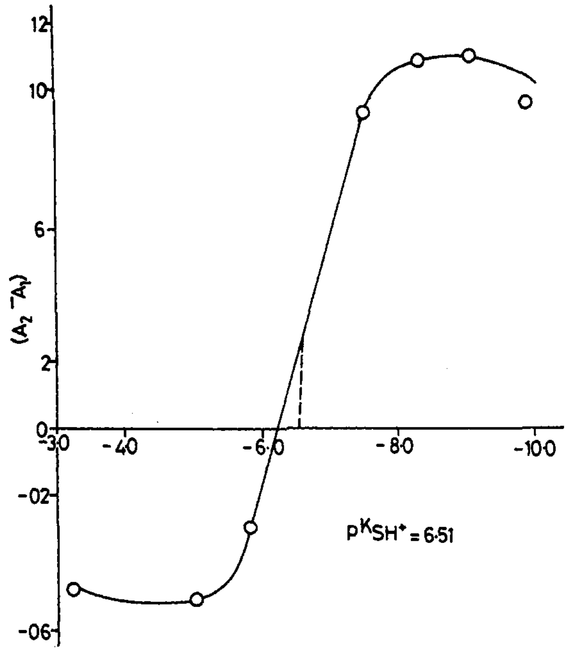


Figure 2. Plot of $(A_2 - A_1)$ vs H_o.

Table 2. pK_a Determination

wt % H_2SO_4	$A_2 = A_{490}$	$A_1 = A_{435}$	$A_2 - A_1$	H_o
50.00	0.505	0.985	−0.480	−3.30
65.04	0.615	1.115	−0.500	−5.10
70.03	0.730	0.975	−0.245	−5.83
80.03	1.580	0.650	0.930	−7.46
85.02	1.720	0.640	1.080	−8.28
90.02	1.750	0.660	1.090	−9.00
95.01	1.580	0.620	0.960	−9.84
97.70	1.510	0.660	0.850	−10.28

presents no convincing evidence for further protonation from spectroscopic data; this is most probably due to both steric and electronic effects. The steric effect is a result of a six-carbon-containing methoxyphenyl group which is farther from the protonated N atom than the unprotonated one; in addition, the five-membered thiadiazole group can enter into resonance with the protonated N atom though the probability of the S atom being protonated is less than that of thiadiazole N atoms.[1,2,6–8] However, the pK_{SH^+} value for the title compound was evaluated to be −6.51. For methyl aryl ethers, an A1 mechanism has been reported to be unsuitable due to the participation of high-energy Me^+ species in the "slow step" of their reactions.[4] According to Bunnett and co-workers,[1,2,7] the azo linkage when protonated is a strong activating group for S_NAr reactions, and for the present work, a proton-transfer reaction (eq 1) is being carried along to the rate-determining step (slow step) of the reactions shown in Scheme 1; this reaction then conforms to general acid catalysis, thereby ruling out the possibility of an A1 mechanism.[4]

The hydrolysis of compound I follows the same pattern as reported for azo dyes, and now that the A1 mechanism

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(6) Buncel, E.; Keum, S. R. Investigation of the protonation and Tautomeric equilibria of 4-(p-hydroxyphenylazo) pyridine and related substrates. *Tetrahedron* **1983**, *39*, 1091.

(7) Bunnett, J. R.; Buncel, E.; Nahabedian, K. Y. The mechanism of acid-catalysed hydrolysis of Azoaryl ethers. *J. Am. Chem. Soc.* **1962**, *84*, 4136.

(8) Hart, S. *Organic Chemitry-A short course*; Houghton Mifflin: London, 1978; pp 189–214. Chapter 10.

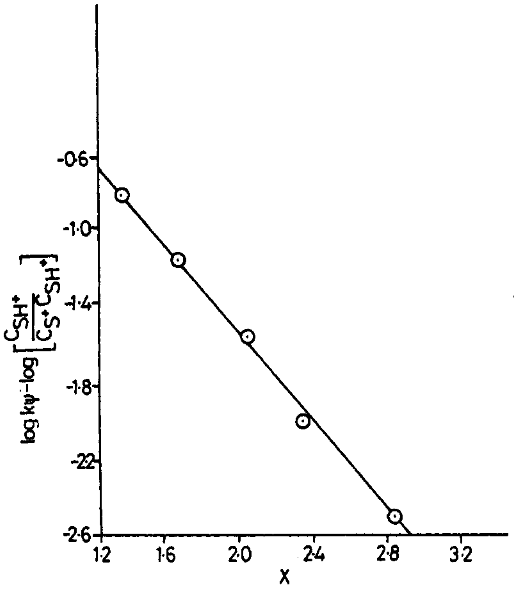

Figure 3. Plot of $\log k_u - \log[C_{SH^+}/C_S + C_{SH^+}]$ vs X.

is known to be unsuitable, further discussion is considered with respect to A2 and A–S_E2 mechanisms of the S_NAr-type involving monoprotonated species. Schemes 1 and 2 explain the two mechanisms; however, the general acid-catalyzed detachment of MeOH in the "fast step" from V, leading to the formation of the product in VI, as well as the addition of H_2O to II, might be subject to general base catalysis (Scheme 1).

Since the monoprotonated species acts as the reactive species, the present result is discussed with reference to the Cox–Yates excess acidity treatment which has been found to be suitable for the mechanism of azoether hydrolysis.[4] For an A2 mechanism to operate here, a plot of the left hand side of eq 2 versus X is expected to give

$$\log k_\psi - \log[C_{SH^+}/(C_S + C_{SH^+})] = (m^{\ddagger} + 1)m^*X + r \log a_{H_2O} + \log k_2 \quad (2)$$

a downward curve. According to Figure 3, this was not obtained, and as a result, the A2 mechanism is not appropriate for this work thereby leaving the A–S_E2 mechanism for full consideration.

In the A–S_E2 mechanism, a rapid nucleophilic attack by water precedes a fast, proton-transfer equilibrium giving the intermediate V after which the leaving group is detached in a slow step under general acid catalysis (Scheme 2). A plot of the left hand side parameters of eq 3 versus X shown in Figure 4 gives a slope, $m^{\ddagger}m^* = 0.471$; this follows the expected trend of plots/graphs in accordance with an A–S_E2 mechanism.

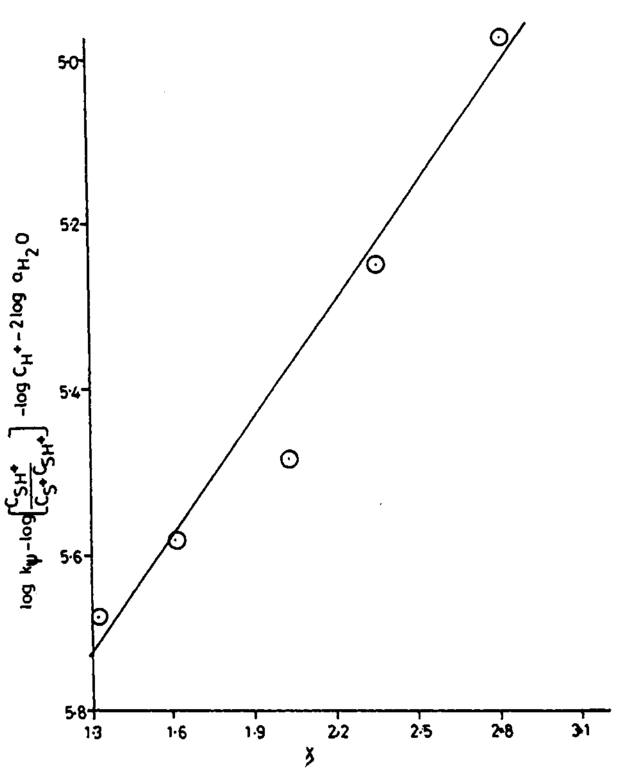

Figure 4. Cox–Yates plot for A–S_E2 mechanism of hydrolysis of I in which the electrophilic catalyst is H_3O^+.

$$\log k_\psi - \log [C_s/C_S + C_{SH^+}] - \log C_{H^+} - 2 \log a_{H_2O} = \log k' + m^{\ddagger}m^*X \quad (3)$$

The linearity obtained in Figure 4 coupled with the value of the slope parameter $m^{\ddagger} = 0.477$ as well as the magnitude of the slope parameter falling between 0 and 1 for a rate-limiting proton-transfer mechanism makes the A–S_E2 mechanism of the S_NAr type suitable for this work.

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