Retardation of Hydrolysis of Aryl Arenesulphonate Esters by Quinuclidine through Complex Formation

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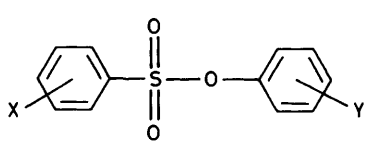
The hydrolysis of aryl arenesulphonate esters is considerably retarded upon the addition of quinuclidine (Quin). Kinetic and spectral data indicate that the protonated form of Quin forms non-covalent complexes with the sulphonate esters and that the complexation partially protects the esters from hydrolysis. Formation constants have been measured with substrates containing various substituents on the benzene ring of either the phenol or the benzenesulphonate portion of the substrate. However, Quin does not affect the hydrolysis of *p*-nitrophenyl methanesulphonate. In addition, other amines such as benzylamine, 4-*N*,*N*-dimethylaminopyridine, triethylamine, and aniline do not affect the hydrolysis of the *p*-nitrophenyl *p*-nitrobenzenesulphonate. Based on these data, a structure has been assigned to the complex formed between the protonated form of Quin and the aryl arenesulphonate esters. In this structure, the polar interaction between the ammonium portion of the protonated Quin and the sulphonyl oxygen of the substrate is involved, together with the hydrophobic interaction between the bicyclic ring of Quin and the benzene ring of the benzenesulphonate moiety of the substrate.

Nucleophilic substitution on aryl sulphonate esters[1–7] involves the cleavage of sulphur–oxygen bonds, and may proceed through either the addition–elimination mechanism or the concerted mechanism. Kinetic data obtained for the nucleophilic reactions on aryl sulphonate esters suggested that the concerted mechanism instead of the addition–elimination mechanism is operative.[6,7]

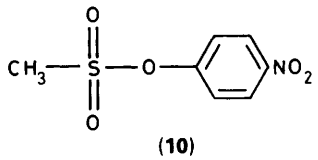
For the ammonolysis of aryl toluene-*p*-sulphonate esters, the magnitude of charge developed on the oxygen atom of the leaving aryl group in the transition state has been assigned.[7] However, the magnitude of positive charge possessed by the nitrogen atom of the attacking amine in the transition state has not been rigorously assigned, but this can be estimated by using amines of different basicities. In the case of aminolysis of carboxylate esters, charge distribution on both the attacking nitrogen atom and the leaving oxygen atom in the transition state and the tetrahedral intermediate has been elucidated by using quinuclidine (Quin) derivatives as the nucleophilic amines.[8] Therefore, we attempted to obtain similar information for the aminolysis of aryl sulphonate esters by using Quin derivatives as the nucleophiles. However, we found that Quin exerts inhibitory effects on the hydrolysis of aryl arenesulphonate esters (**1**)–(**9**). In this article, kinetic data for the retardation of the hydrolysis of (**1**)–(**9**) by Quin are presented, together with a mechanistic analysis.



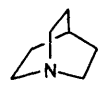
(**1**) X = *p*-NO_2, Y = H
(**2**) X = *p*-NO_2, Y = *p*-Cl
(**3**) X = *p*-NO_2, Y = *m*-Cl
(**4**) X = *p*-NO_2, Y = *p*-CN
(**5**) X = *p*-NO_2, Y = *m*-NO_2
(**6**) X = *p*-NO_2, Y = *p*-NO_2
(**7**) X = *p*-Cl, Y = *p*-NO_2
(**8**) X = H, Y = *p*-NO_2
(**9**) X = *p*-CH_3, Y = *p*-NO_2

Experimental

Materials.—Aryl sulphonate esters were prepared by treating the corresponding sulphonyl chloride (5 mmol) with the corresponding phenol (5.3 mmol) in acetone (15 cm^3) in an ice bath. To the stirred mixture were added two portions of aqueous NaOH solution (0.15 g dissolved in 2.5 cm^3 water) at intervals of 30 min. After 2 h, the precipitates formed on addition of excess ice–water were collected and recrystallized from acetone–water. The esters prepared in this way were: phenyl *p*-nitrobenzenesulphonate (**1**); m.p. 113–114 °C (lit.,[9] 113–114 °C). *p*-Chlorophenyl *p*-nitrobenzenesulphonate (**2**); m.p. 119–120 °C. *m*-Chlorophenyl *p*-nitrobenzenesulphonate (**3**); m.p. 117–118 °C. *p*-Cyanophenyl *p*-nitrobenzenesulphonate (**4**); m.p. 152–154 °C. *m*-Nitrophenyl *p*-nitrobenzenesulphonate (**5**); m.p. 130–131 °C. *p*-Nitrophenyl *p*-nitrobenzenesulphonate (**6**); m.p. 152–153 °C. *p*-Nitrophenyl *p*-chlorobenzenesulphonate (**7**), m.p. 110–113 °C (lit.,[10] 110 °C). *p*-Nitrophenyl benzenesulphonate (**8**); m.p. 81–83 °C (lit.,[11] 83 °C). *p*-Nitrophenyl toluene-*p*-sulphonate (**9**); m.p. 95–97 °C (lit.,[12] 97 °C). *p*-Nitrophenyl methanesulphonate (**10**); m.p. 92–93 °C (lit.,[13] 92–93 °C). The compounds newly synthesized in this study gave satisfactory results of elemental analysis (C, H, N).



(**10**)



Quinuclidine

Quin, benzylamine, 4-*N*,*N*-dimethylaminopyridine, triethylamine, aniline, and dioxane were purified by recrystallization or distillation. Distilled water was deionized prior to its use in the kinetic measurements.

Kinetics.—Reaction rates were measured with a Beckman Model 5260 UV–VIS spectrophotometer by following the release of the phenols. Temperature was controlled at 50 ± 0.1 °C with a Lauda/Brinkman Circulator Model RC3. Kinetic measurements were performed at ionic strength 0.5 mol dm^{-3} adjusted with KCl in the presence of 10% (v/v) dioxane. The initial concentration of the sulphonate ester was 0.5–1 × 10^{-4} mol dm^{-3}. The pH measurements were performed with a

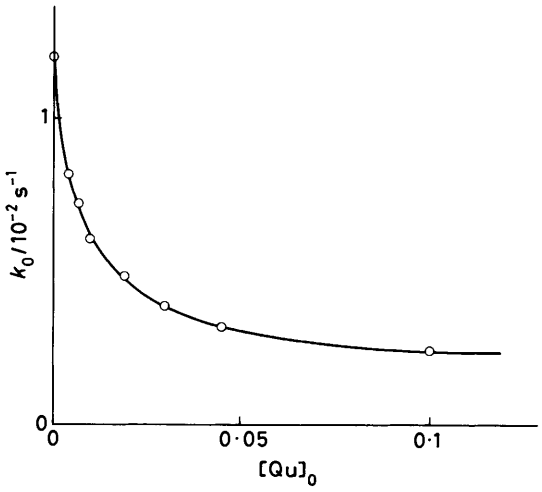


Figure 1. The dependence of k_0 on $[Qu]_0$ for (**5**) at pH 11.08.

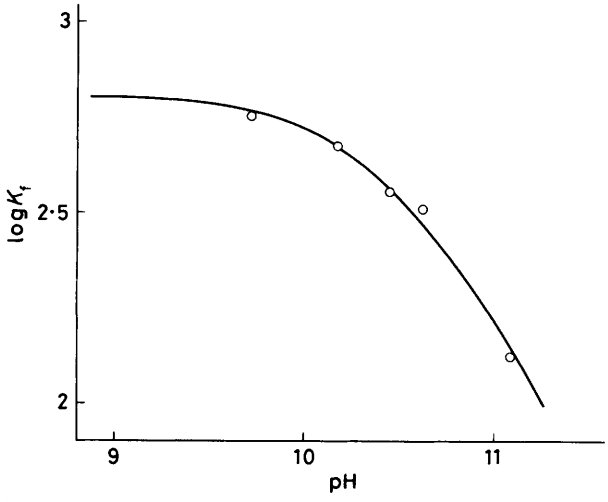


Figure 2. The dependence of K_f on pH for (**6**). The pK_a of Quin estimated from the analysis of the pH profile in terms of equation (4) is 10.50, in agreement with that (10.52) measured by titration under the conditions of kinetic measurements.

Table. Values of K_f^{lim} estimated for the complexation of (**1**)–(**9**) with Quin.[a]

Compound	K_f^{lim}/dm^3 mol^{-1}
(**1**)	930
(**2**)	740
(**3**)	720
(**4**)	750
(**5**)	640
(**6**)	680
(**7**)	960
(**8**)	3 100
(**9**)	11 000

[a] Standard deviations are estimated as no more than ±10% of the K_f values.

Dongwoo digital pH meter Model DP-215 at 50 °C in the presence of 10% (v/v) dioxane. Buffers (0.01 mol dm^{-3}) used were sodium borate (pH 9–10), $NaHCO_3$ (pH 10–11) and K_2HPO_4 (pH 11–12). The pH of a stock solution of an amine was adjusted to a desired value and then diluted with a buffer solution of the same pH prior to the kinetic measurements. The

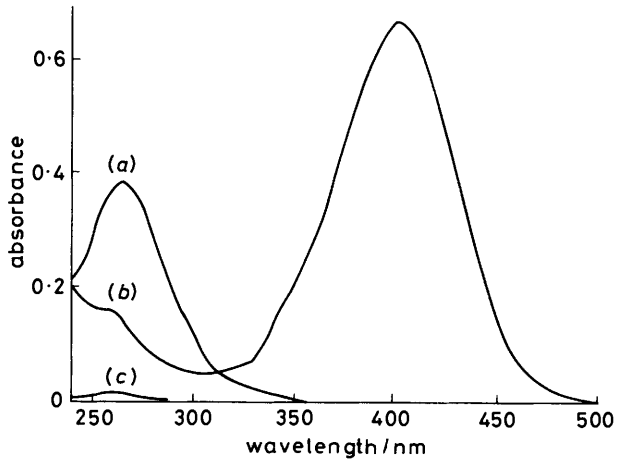


Figure 3. The electronic spectra of 7.5 × 10^{-4} mol dm^{-3} (**9**) (*a*), *p*-nitrophenol (*b*), or *p*-toluenesulphonate (*c*) at pH 10.44.

pK_a values of the amines were determined by titration under the conditions of kinetic measurements. UV–VIS spectra of the reaction products were identical with those of the corresponding hydrolysis products.

Results

Pseudo-first-order rate constants (k_0) for the hydrolysis of (**1**)–(**9**) decreased when the total concentration of Quin ($[Qu]_0$) was raised, as exemplified by the typical plot of k_0 against $[Qu]_0$ illustrated in Figure 1. The dependence of k_0 on $[Qu]_0$ was analysed in terms of equations (1) and (2), where K_f is the

$$\begin{array}{ccc} S + Quin & \overset{K_f}{\rightleftharpoons} & SQuin \\ \Big\downarrow k_{sp} & & \Big\downarrow k_{com} \\ \multicolumn{3}{c}{\text{hydrolysis products}} \end{array} \quad (1)$$

$$k_0 = (k_{sp} + k_{com}K_f[Qu]_0)/(1 + K_f[Qu]_0) \quad (2)$$

formation constant for SQuin [complex formed between a sulphonate ester (S) and Quin]. Thus, retardation of the hydrolysis of the sulphonate esters by Quin occurs through complex formation. The value of k_{com} (k_0 for the complexed substrate) was 3–20% of that of k_{sp} (k_0 for the uncomplexed substrate), depending on pH and the nature of the substrate.

For each substrate, the dependence of k_0 on $[Qu]_0$ was measured at several pHs. The dependence of K_f on pH was consistent with equations (3) and (4), as illustrated in Figure 2.

$$SQuin \overset{K_f^{lim}[S]}{\rightleftharpoons} QH^+ \overset{K_a(pK_a = 10.52)}{\rightleftharpoons} Q^b \quad (3)$$

$$K_f = K_f^{lim}/(1 + K_a/[H^+]) \quad (4)$$

In equation (3), QH^+ stands for the protonated form of Quin and Q^b the neutral basic form of Quin. Thus, the kinetic data indicate that (**1**)–(**9**) form complexes with QH^+ much more readily than with Q^b. The values of K_f^{lim} measured for (**1**)–(**9**) are summarized in the Table.

In order to examine whether Quin forms covalent intermediates with (**1**)–(**9**), the electronic spectra of the esters were measured in the presence of Quin. As exemplified by the spectra illustrated in Figure 3, the aryl arenesulphonate esters absorb quite strongly in the UV region, while the corresponding arenesulphonic acids exhibit very weak spectra. This indicates

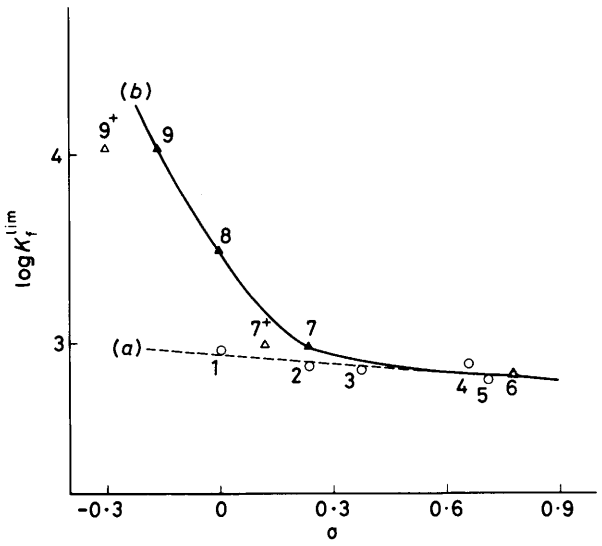


Figure 4. The Hammett plot for K_f^{lim}: Line (*a*) (○), (**1**–**6**); line (*b*) (▲), (**6**–**9**). For (**7**) and (**9**), data points △ are based on σ^+ instead of σ. Slope of line (*a*) is -0.15 ± 0.05.

that substitution at the sulphonyl sulphur leads to sensitive changes in the UV spectra. At $[Qu]_0 \gg 1/K_f$, the substrate is almost fully complexed by Quin. Under these conditions, however, the UV spectra of the sulphonate esters were identical with those measured in the absence of Quin.

Rates of the hydrolysis of methanesulphonate ester (**10**) were not affected by the addition of up to 0.03 mol dm^{-3} Quin at pH 10.18, 10.52, or 11.67, in marked contrast with the hydrolysis of arenesulphonate esters (**1**)–(**9**).

The effects of other amines on the kinetics of the hydrolysis of the sulphonate esters were also examined. Addition of up to 0.02–0.03 mol dm^{-3} benzylamine (pK_a 8.85) at pH 8.89, 4-*N*,*N*-dimethylaminopyridine (pK_a 9.03) at pH 9.08, 9.68, and 10.25, triethylamine (pK_a 10.14) at pH 9.68 and 10.48, or aniline at pH 8.98 did not affect the rate of hydrolysis of (**6**).

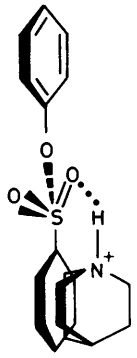
Previous studies revealed that the nucleophilic reaction of ammonia[7] or triethylamine[3] on (**9**) is extremely slow in accordance with the present results. The k_0 for the hydrolysis of (**9**) in a 4:1 triethylamine–triethylammonium buffer containing 20% acetonitrile was 8×10^{-5} s^{-1} at 70 °C.[3] However, k_0 measured in the present study for the hydrolysis of (**9**) at pH 10.63 and 50 °C in the absence of any added amine was 3.1×10^{-4} s^{-1}. The pK_a of triethylamine would be lowered considerably upon the addition of 20% acetonitrile. The hydroxide concentration of the reaction medium employed in the previous study, therefore, might be appreciably smaller than that in the present study, leading to the lower rate.

Discussion

The kinetic and the spectral data indicate the formation of non-covalent complexes between the sulphonate esters and Quin. Furthermore, it is the protonated form of Quin instead of the basic form that is involved in the complexation.

The Hammett plot for log K_f^{lim} for (**1**)–(**9**) is illustrated in Figure 4, revealing that K_f^{lim} does not vary considerably when the substituent on the phenol portion of the substrate is changed. However, the substituent, especially *p*-CH_3 and H, attached to the benzenesulphonate moiety of the substrate considerably affects K_f^{lim}. The hydrophobicity of the benzene ring of the benzenesulphonate moiety would be considerably greater for (**8**) and (**9**) compared with (**6**) and (**7**). It appears that the complex formation involves hydrophobic interaction between the benzene ring of the benzenesulphonate portion of the substrate and Quin. This is also in agreement with the failure of complex formation between (**10**) and Quin.

Based on the kinetic data obtained in the present study, structure (**A**) is assigned to the complex formed between the aryl arenesulphonate esters and Quin. Here, the sulphonate oxygen atom is the site which interacts with the ammonium cation of Quin. In addition, the complexation is further facilitated by the hydrophobic interaction between the benzene ring of the benzenesulphonate portion of the substrate and the bicyclic ring of Quin.

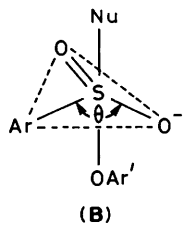


(**A**)

Importance of the hydrophobic interaction between the benzene ring of the substrate and the bicyclic ring of Quin in the complex formation is further supported by the failure of complex formation of (**1**)–(**9**) with other amines. Neither the protonated nor the neutral form of benzylamine, triethylamine, 4-*N*,*N*-dimethylaminopyridine, or aniline contains a ring with the geometry necessary for hydrophobic interaction. Examination of space-filling models indicates that only the bicyclic ring of the protonated form of Quin can make proper contact with the benzene ring of the benzenesulphonate moiety of the substrate while the ammonium portion interacts with the sulphonyl oxygen.

If Quin does not interact with the benzene ring of the phenol portion of the substrate in the complex as illustrated by (**A**), Quin might also form complexes with alkyl arenesulphonate esters. Kinetic studies on the hydrolysis of alkyl arenesulphonates in the presence of Quin, however, were not performed in the present investigation as the nucleophilic reactions on alkyl arenesulphonates would involve the cleavage of alkyl–oxygen bond resulting in the substitution at the alkyl carbon.

In the nucleophilic substitution reactions on the sulphonate sulphurs, the rate-determining transition state would resemble (**B**) for either the addition–elimination mechanism or the concerted mechanism, although several lines of evidence have been presented in support of the concerted mechanism.[6,7] Conversion of the substrate into the transition state is, therefore, accompanied by an increase in the angle (θ) of the bond connecting the sulphonyl oxygen, the sulphonyl sulphur, and the phenyl carbon atoms. Complexation of the substrate with Quin to form (**A**) would hamper this structural change, leading to the retardation of the overall reaction.



(**B**)

Benzylamine, triethylamine, 4-*N*,*N*-dimethylaminopyridine, or aniline (up to 0.03 mol dm^{-3}) do not affect the rate of the expulsion of *p*-nitrophenol from (**6**). Similarly, triethylamine (up to 0.08 mol dm^{-3}) did not alter the rate of the hydrolysis of (**9**).[3] However, the hydrolysis of (**9**) in 60% aqueous 1,2-dimethoxyethane (glyme) at 115 °C was accelerated [3] (up to two fold) by the addition of *N*-ethylpyrrolidine (NEP), a tertiary amine less hindered than triethylamine. It was suggested that NEP acts as a nucleophile.[3] Quin is less hindered than NEP, but its primary effect on the hydrolysis of aryl arenesulphonates is retardation through complex formation instead of acceleration through aminolysis. This is attributable to the geometry of the protonated form of Quin, as discussed above.

Acknowledgements

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