Mechanism of Acyl Transfer between 1-Acetoxy-8-Hydroxynaphthalene and Phenolate Ions; Investigation of a Leaving Group with Potential Hydrogen Bond Stabilisation

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The kinetics of the acyl transfer between 1-acetoxy-8-hydroxynaphthalene and substituted phenol buffers have been studied and the rates are compared with those for the reaction of 1-acetoxynaphthalene. The variation of the first-order rate coefficient with buffer concentration at different buffer ratios is compatible with reaction between undissociated 1-acetoxy-8-hydroxynaphthalene and phenolate ion or with reaction of the anion of 1-acetoxy-8-hydroxynaphthalene with undissociated phenol. Analysis of the data according to the latter reaction gives a rate coefficient for reaction of the anion of 1-hydroxy-8-acetoxy-naphthalene with phenol which is larger than that for the reaction of 1-acetoxynaphthalene with phenolate ion and is, therefore, rejected. The rate coefficients calculated for the preferred reaction of undissociated 1-acetoxy-8-hydroxynaphthalene with substituted phenolate ions give a linear Brønsted plot of slope β 0.48. The rate coefficients for reaction with phenolate and 3,4-dichlorophenolate ions are respectively 5.5 and 13 times higher than the values for the reaction of 1-acetoxynaphthalene with the same ions. The enhanced rate may be the result of weak assistance of the departure of the leaving group by partial formation of an intramolecular hydrogen bond involving the 8-hydroxy group.

New examples of intramolecular catalysis are of relevance to an understanding of enzyme-catalysed reactions.[1,2] The hydrolysis of 1-acetoxy-8-hydroxynaphthalene to 1,8-dihydroxynaphthalene in aqueous solution gives a dependence of rate coefficient on hydroxide ion concentration that requires two kinetic pathways: reaction of ionised 1-acetoxy-8-hydroxynaphthalene with hydroxide ion, and either reaction of ionised 1-acetoxy-8-hydroxynaphthalene with solvent or reaction of the unionised species with hydroxide ion.[3] If the second pathway is assumed to be the solvent reaction of ionised 1-acetoxy-8-hydroxynaphthalene, the magnitude of the rate coefficient (3.7×10^{-3} s^{-1}), in comparison with that estimated for 1-acetoxynaphthalene (7.0×10^{-8} s^{-1}) requires the operation of efficient intramolecular base catalysis by the ionised hydroxy group. On the assumption that the second pathway consists of reaction of undissociated 1-hydroxy-8-acetoxynaphthalene with hydroxide ion, the value of the rate coefficient calculated for this process is *ca* 40-fold higher than that predicted from a σρ plot for the similar reaction of other esters with substituted naphthol leaving groups. Hence, whichever pathway is used to account for the kinetic behaviour, evidence for intramolecular participation by the hydroxy group is obtained, either as a base catalyst in assisting the attack of solvent or as an acid catalyst in assisting the attack of hydroxide ion. The former mechanism was preferred, in line with the conclusions of previous studies.[4]

In the hydrolysis of 1-hydroxy-8-methoxymethoxynaphthalene, evidence was obtained[5] for intramolecular acid catalysis of the expulsion of the leaving group by the hydroxy group. This was attributed to stabilisation of the leaving group by the formation of an intramolecular hydrogen bond as charge is developed in the transition state. The same leaving group is involved in the reactions of 1-acetoxy-8-hydroxynaphthalene. To investigate whether similar catalysis can operate in the reaction of an ester we have now extended studies of 1-acetoxy-8-hydroxynaphthalene to reaction with phenolate nucleophiles for which departure of the leaving group is expected to make a more important contribution than for reaction with hydroxide ion. Evidence has recently been obtained[6,7] that acyl transfer between esters with

phenolic leaving groups and substituted phenolate ions occurs by a concerted mechanism and for reactions where the leaving group and attacking nucleophile are of similar pK_a, bond forming and breaking in the transition state are almost equally advanced.

Experimental

Reactions were begun by injection of 0.01 cm^3 of a concentrated solution of the ester in dioxane into a buffer solution contained in a quartz cuvette which had been thermostatted at 25 °C in the cell housing of a Unicam SP8 100 UV spectrophotometer. The esters were present initially at concentrations of *ca.* 5×10^{-5} mol dm^{-3}. The subsequent reaction was observed by following the increase in absorbance at 340 nm (1-acetoxy-8-hydroxynaphthalene) or 330 nm (1-acetoxynaphthalene). Absorbance data from the spectrophotometer were transferred directly to a microcomputer. First-order rate coefficients (k_{obs}) were calculated from linear regression analysis of plots of $\log_{10}(A_\infty - A_t)$ against time where A_t is the absorbance at time t during the reaction and A_∞ is the absorbance after *ca.* ten half lives. The rate coefficients were calculated from absorbance readings taken for at least two half lives and were generally reproducible to within $\pm 3\%$ of the mean. Rate coefficients were determined in each buffer at several buffer concentrations in the range 0.001 to 0.1 mol dm^{-3} and usually at three buffer ratios. Plots of k_{obs} against buffer anion concentration were linear and the values of the gradients and intercepts at different buffer ratios in each of the buffers are given in the Table.

Table. Analysis of kinetic results for acyl transfer.[a]

Phenol	pK_a^{0b}	r^c	Gradient[d]/dm^3 mol^{-1} s^{-1}	Intercept[e] 10^{-4} s^{-1}	k_2^f/dm^3 mol^{-1} s^{-1}	k_3^g/dm^3 mol^{-1} s^{-1}
1-Acetoxy-8-hydroxynaphthalene						
4-MeC$_6$H$_4$OH	10.26	2.0	0.0373	31.5	0.172	0.0954
		1.0	0.0639	27.5	0.179	0.0995
C$_6$H$_5$OH	9.99	2.0	0.0383	27.5	0.112	0.116
		1.0	0.0652	22.6	0.128	0.133
		0.5	0.0813	15.3	0.121	0.125
4-ClC$_6$H$_4$OH	9.42	2.0	0.0435	19.2	0.0662	0.254
		1.0	0.0479	16.3	0.0604	0.231
		0.5	0.0635	8.22	0.0718	0.275
3,4-Cl$_2$C$_6$H$_3$OH	8.59	2.0	0.0274	3.15	0.0295	0.774
		1.0	0.0307	1.86	0.0319	0.836
		0.5	0.0285	1.21	0.0290	0.762
3,5-Cl$_2$C$_6$H$_3$OH	8.19	2.0	0.0101	2.06	0.0104	0.685
		1.0	0.0111	1.27	0.0113	0.741
		0.5	0.0130	0.84	0.0131	0.862
3,4,5-Cl$_3$C$_6$H$_2$OH	7.75	4.0	0.0128	0.87	0.0131	2.35
		2.0	0.0130	0.51	0.0131	2.36
1-Acetoxynaphthalene						
C$_6$H$_5$OH	9.99	2.0	0.0218	4.07	0.0218	
		1.0	0.0240	3.57	0.0240	
		0.5	0.0193	2.72	0.0193	
3,4-Cl$_2$C$_6$H$_3$OH	8.59	2.0	0.002 17	0.185	0.002 17	
		1.0	0.002 15	0.0921	0.002 15	
		0.5	0.002 51	0.0552	0.002 51	

[a] Aqueous solution, 298.3 K, and ionic strength 0.2 mol dm^{-3}. [b] Values are taken from reference 8 and refer to infinite dilution and 298.3 K. [c] Buffer ratio r = [phenolate ion]/[phenol]. [d] Gradient of plot of k_{obs} against [phenolate]. [e] Intercept of plot of k_{obs} against [phenolate]. [f] Calculated from equation (4). [g] Calculated from equation (5).

Results

Previous studies[6] have shown that acyl transfer occurs when an ester with phenolic leaving group is introduced into a solution of dissociated and undissociated phenol. The linearity of the plots of k_{obs} against buffer concentration in the reaction of 1-hydroxy-8-acetoxynaphthalene shows that the reaction is of the first order with respect to buffer. The change in the gradient of the plots with buffer ratio for buffers of 4-methylphenol, phenol, and 4-chlorophenol (see Table) is due to ionisation of 1-acetoxy-8-hydroxynaphthalene, equation (1), and can be accounted for in two ways, shown in equations (2) and (3). In
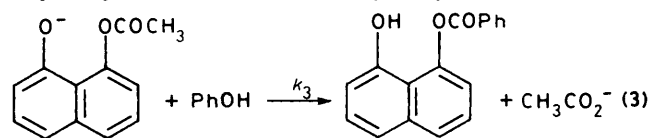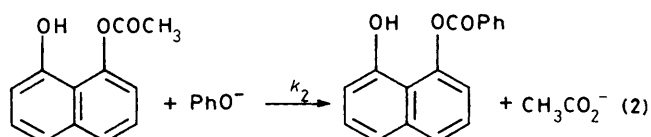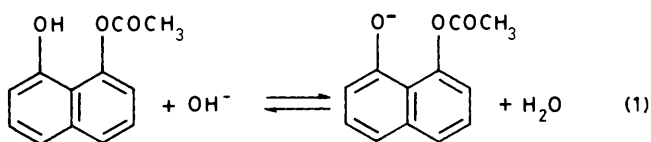

equation (2) it is assumed that undissociated 1-acetoxy-8-hydroxynaphthalene reacts with buffer anion and in (3), dissociated 1-acetoxy-8-hydroxynaphthalene is assumed to react with the buffer acid. For the reactions in equations (2) and (3), expressions (4) and (5) are obtained respectively by assuming that reaction of 1-acetoxy-8-hydroxynaphthalene

$$k_{obs} = k_2[\text{PhO}^-]/(1 + KrK_w/K_a) \qquad (4)$$

$$k_{obs} = k_3[\text{PhO}^-](KK_w/K_a)/(1 + KrK_w/K_a) \qquad (5)$$

with hydroxide ion, equation (1), occurs rapidly in comparison with the acyl transfers. In equations (4) and (5), the value K 1.14 ± 0.1 × 10^4 dm^3 mol^{-1} has been measured previously[3] as the equilibrium constant for the reaction in equation (1). The buffer ratio is defined as r = [phenolate]/[phenol], K_a is the acid dissociation constant of the phenol and K_w is the ionic product of water under the experimental conditions (298 K and ionic strength 0.2 mol dm^{-3}). Values of K_a^0 referring to infinite dilution were taken from tables[8] and pK_a^0 was corrected to an ionic strength I = 0.2 mol dm^{-3} by addition of the value[9] of log γ = $-0.51(I)^{\frac{1}{2}}/[1 + (I)^{\frac{1}{2}}]$ = -0.315. The value of K_w at 298.3 K and ionic strength 0.2 mol dm^{-3} was taken[9] as 1.797 × 10^{-14}. The results for k_2 and k_3 calculated from the gradients using equations (4) and (5) respectively are given in the Table. In buffers of 4-methylphenol, phenol, and 4-chlorophenol the gradients of the plots of k_{obs} against the concentration of buffer anion vary with buffer ratio. For each buffer the values of k_2 and k_3 calculated from the different gradients using equations (4) and (5) respectively are constant within experimental error, showing that equations (2) and (3) give a satisfactory explanation of the kinetic results. In buffers of 3,4- and 3,5-dichlorophenol and 3,4,5-trichlorophenol, the term KrK_w/K_a is at least 13 times lower than unity and the gradients of the plots of k_{obs} against the concentration of buffer anion are independent of buffer ratio as required by equations (4) and (5). Arguments to provide a choice between the reactions in equations (2) and (3) will be given in the Discussion. For reaction of 1-acetoxynaphthalene in phenol and 3,4-dichlorophenol buffers, the gradients of the plots of k_{obs} against buffer anion concentration were found to be independent of buffer ratio and the data, therefore, refer to reaction of the ester with the buffer anion. The calculated
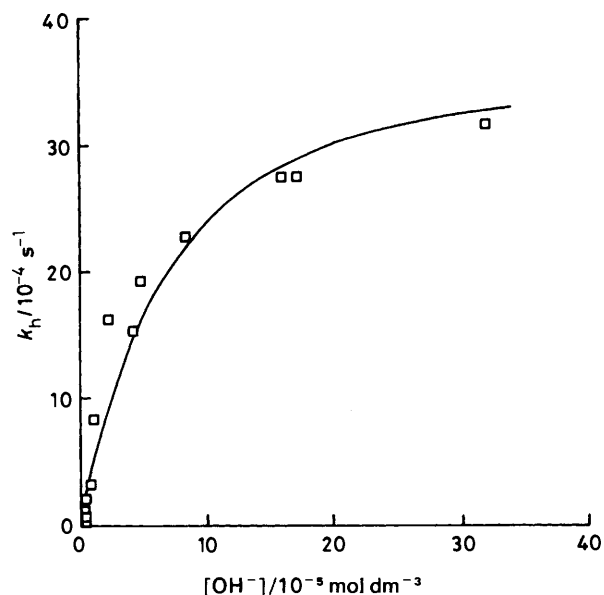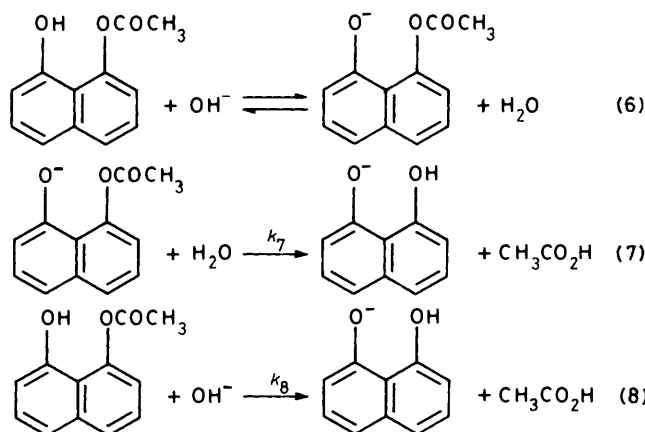
Figure 1. Variation of k_h with [OH$^-$]. The curve is a best fit of equation (9) using $(k_7K + k_8) = 56$ dm^3 mol^{-1} s^{-1} and $K = 1.4 \times 10^4$ dm^3 mol^{-1}.

and either the reaction in equation (7) or (8). If equation (8) is ignored, the fit to the present results gives k_7 4.0×10^{-3} s^{-1} and K 1.4×10^4 dm^3 mol^{-1}. If (7) is ignored, the results

$$k_h = (k_7K + k_8)[\text{OH}^-]/(1 + K[\text{OH}^-]) \qquad (9)$$

give k_8 56 dm^3 mol^{-1} s^{-1} and K 1.4×10^4 dm^3 mol^{-1}. These situations correspond to reaction of the anion of 1-acetoxy-8-hydroxynaphthalene with solvent and to reaction of undissociated 1-acetoxy-8-hydroxynaphthalene with hydroxide ion respectively.

values of the rate coefficients (k_2) for this reaction are given in the Table.

In all buffers, the intercepts of the plots of k_{obs} against buffer concentration varied with buffer ratio. The intercepts (k_h) refer to the rate coefficient for reaction of 1-acetoxynaphthalene and 1-acetoxy-8-hydroxynaphthalene with species derived from the solvent. For 1 acetoxynaphthalene, nucleophilic substitution by hydroxide ion is involved and this reaction has been studied previously in aqueous sodium hydroxide. The values of the intercepts at three buffer ratios in phenol and 3,4-dichlorophenol buffers were plotted against the hydroxide ion concentration calculated for each buffer. The data were scattered because hydroxide ion makes a small contribution to the overall rate in phenol buffers. Linear regression analysis gave a value k_{OH} 2.5 ± 1 dm^3 mol^{-1} s^{-1} for the rate coefficient for nucleophilic substitution by hydroxide ion to be compared with the result k_{OH} 1.40 ± 0.05 dm^3 mol^{-1} s^{-1} determined from studies in aqueous sodium hydroxide.[3] In view of the errors involved in the intercepts of the plots of k_{obs} against buffer concentration in the present studies and the limited data, the agreement is considered satisfactory.

The plots of k_{obs} against buffer concentration for 1-acetoxy-8-hydroxynaphthalene gave intercepts (k_h) which showed a complex dependence on hydroxide ion concentration, Figure 1. A similar dependence was found[3] previously for the observed rate coefficient for reaction of 1-acetoxy-8-hydroxynaphthalene in solutions of hydroxide ion and was explained in terms of the reactions in equations (6), (7), and (8). At higher hydroxide ion concentrations it was also necessary to include a reaction between the dissociated form of 1-acetoxy-8-hydroxynaphthalene and hydroxide ion. For the mechanism in equations (6), (7), and (8), the observed rate coefficient (k_h) for the first-order disappearance of the ester is given by the expression in equation (9). The fit of equation (9) to the experimental results is shown as the curve in Figure 1 calculated with the values $(k_7K + k_8) = 56$ dm^3 mol^{-1} s^{-1} and $K = 1.4 \times 10^4$ dm^3 mol^{-1}. The data in sodium hydroxide previously obtained[3] gave best fit values of $(k_7K + k_8)$ 42 ± 9 dm^3 mol^{-1} s^{-1} and K $1.14 \pm 0.1 \times 10^4$ dm^3 mol^{-1}, in satisfactory agreement with the present results. Actually the data can be fitted using the reaction in equation (6)

Discussion

The dependence of k_{obs} on buffer concentration and buffer ratio for reaction of 1-acetoxy-8-hydroxynaphthalene in phenol buffers can be explained either by a process involving reaction of the undissociated form of the ester with phenolate ion or by reaction of the ester anion with the buffer acid. Similarly the dependence of k_h on hydroxide ion concentration shown in Figure 1 and found previously in solutions of sodium hydroxide can be accounted for by reaction of the undissociated ester with hydroxide ion or by reaction of the ester anion with solvent. The evidence to distinguish between the two possibilities for the variation of k_h is ambiguous[3] but a definite choice of mechanism can be made for reaction with buffer.

The values of k_2 obtained by assuming that the undissociated ester reacts with phenolate anion, reaction (2), and the values of k_3 calculated by assuming that the dissociated ester reacts with undissociated phenol, reaction (3), are given in the Table. The values of k_2 decrease as the phenolate becomes a weaker base as would be expected for a nucleophilic substitution and a plot of log k_2 against pK_a^0 is linear with slope, β 0.48. A plot of the values of log k_3 against pK_a^0 is also linear with slope -0.52. The variations of log k_2 and log k_3 with pK_a^0 do not permit a choice between reactions (2) and (3), however a choice between the two possibilities can be made on the basis of the relative rate coefficients for reaction of 1-acetoxy-8-hydroxynaphthalene and 1-acetoxynaphthalene. For 1-acetoxynaphthalene the kinetic data in phenol buffers are only compatible with reaction of the ester with the phenolate ion.

By assuming that the acyl transfer of 1-acetoxy-8-hydroxynaphthalene in phenol buffers involves reaction of the ester anion with the buffer acid a second-order rate coefficient of k_3 0.125 ± 0.009 dm^3 mol^{-1} s^{-1} for nucleophilic attack of phenol at the carbonyl group of 1-acetoxy-8-hydroxynaphthalene anion is obtained. This rate coefficient is to be compared
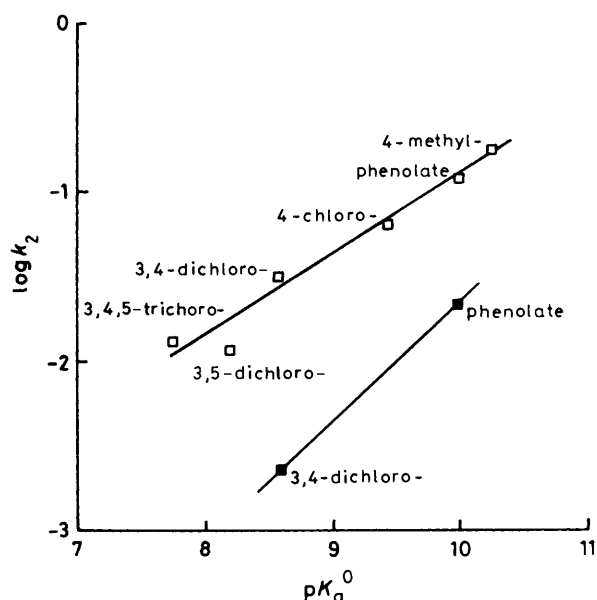
Figure 2. Brønsted plot for the reaction of undissociated 1-hydroxy-8-acetoxynaphthalene (□) and 1-acetoxynaphthalene (■) with substituted phenolate ions; the substituents are shown alongside the data points.

with that for the attack of phenolate ion at the carbonyl of 1-acetoxynaphthalene (k_2 0.0217 ± 0.0016). Presumably the rate coefficient for reaction of phenolate ion with the anion of 1-acetoxy-8-hydroxynaphthalene would be lower still. Hence if the value of k_3 refers to the reaction between undissociated phenol and 1-acetoxy-8-hydroxynaphthalene anion, attack of the weak nucleophile, phenol, must be assisted by the ionised hydroxy group through intramolecular base catalysis. However, it seems extremely unlikely that intramolecular assistance by proton removal from the attacking phenol to generate an incipient phenolate ion could occur with a larger rate coefficient than attack of phenolate ion itself. For 3,4-dichlorophenol as buffer, the calculated value of the rate coefficient k_3, assuming that the reaction in equation (3) occurs, would be 350 times higher than the rate coefficient for reaction of 1-acetoxynaphthalene with 3,4-dichlorophenolate ion. In intramolecular base catalysis of reaction of ionised 2-hydroxyphenyl acetate[1,4,10] with water, the calculated second-order rate coefficient is 1.6 × 10⁴ times lower than the rate coefficient for reaction of phenyl acetate[11] with hydroxide ion. These arguments effectively rule out the occurrence of reaction (3) and the kinetic results will be explained in terms of the reaction of undissociated 1-acetoxy-8-hydroxynaphthalene with phenolate ions, equation (2).

The linear Brønsted plot for this reaction, Figure 2, is similar to those which have been found for acyl transfer from aryl acetates to phenolate ions.[6,7] These and other linear Brønsted plots for the reaction of esters with nucleophiles whose pK_a^0 values span the pK_a^0 value of the leaving group of the ester have been interpreted in terms of a concerted mechanism for acyl transfer[6,7,12] and a similar mechanism may operate in the reactions of 1-acetoxynaphthalene and 1-acetoxy-8-hydroxynaphthalene.

The rate coefficients for the reactions of 1-acetoxy-8-hydroxynaphthalene with phenolate and 3,4-dichlorophenolate ions are respectively 5.5 and 13 times higher than the rate coefficients for the same reactions of 1-acetoxynaphthalene. By comparison with the results that have been found for acyl transfer between arylacetates and phenolate ions,[7] a much

smaller effect would have been expected for a hydroxy substituent. For example, a 3-chloro substituent (σ_m 0.37) increases the rate coefficient for reaction of 4-nitrophenyl acetate with various phenolate ions by a factor of 2.6. A 3-nitro substituent (σ_m 0.74) has a 4.9-fold effect. Based on these results, a 3-hydroxy substituent (σ_m 0.13) would be expected to increase the rate coefficient by a factor of ca. 1.3 to 1.4. The higher observed effects could indicate the operation of weak intramolecular catalysis of the acyl transfer. This may arise because the leaving group, 1,8-dihydroxynaphthalene monoanion possesses an intramolecular hydrogen bond which is partially developed in the transition state for the reaction. The transition state is thereby stabilised and the greatest stabilisation will arise for reactions in which bond breaking to the leaving group is most advanced. The higher effect of the hydroxy substituent for reaction with 3,4-dichlorophenolate ion compared with phenolate ion is compatible with a more product-like transition state in which the intramolecular hydrogen bond is more fully formed and this is in the expected direction for reaction of the weaker nucleophile.

The maximum rate effect due to stabilisation of the transition state by formation of an intramolecular hydrogen bond will be similar to the effect of the hydrogen bond on the stability of 1,8-dihydroxynaphthalene monoanion. Rough estimates of the strength of this intramolecular hydrogen bond can be made from the first and second pK_a^0 of 1,8-dihydroxynaphthalene which have values[8] of 6.7 and > 14 respectively. The first pK_a^0 is lower and the second pK_a^0 is higher than for typical naphthols because the monoanion is stabilised by the hydrogen bond. The maximum rate effect that could arise from hydrogen bond stabilisation of the leaving group is 1 × 10³ to 1 × 10⁴ in this case. The present rate effects are much smaller than this, and smaller than the ca. 40-fold effect found[5] in the hydrolysis of 1-hydroxy-8-methoxymethoxynaphthalene which possesses the same leaving group. The largest rate effects which are thought to arise by hydrogen bond stabilisation have been found[13] for reactions in which salicylate ion is the leaving group in which case enhancements in rate of up to 10³-fold have been observed.

Acknowledgements

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