Kinetics of the Alkaline Hydrolysis of Catechol Monoacetate and Some Derivatives

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The rates of the alkaline hydrolysis of acetates of phenol, guaiacol, and catechol (mono- and diester) have been measured at 25° in 0.07 M $KClO_4$. The values for log k_2 were found to be 0.22, 0.01, 3.07, and 0.97, respectively, when k_2 is the second order rate constant in M^{-1} sec^{-1}. The hydrolysis of catechol monoacetate ($pK'_a = 8.56$) is 500 times faster than expected considering only the inductive and resonance effects. It is suggested that the increase is due to intramolecular hydrogen bonding.

In an earlier paper [1] it was reported that the alkaline hydrolysis of tertiary 2- and 3-dialkylaminoalkyl acetates is 20—30 times faster than the hydrolysis of the corresponding quaternary compounds. It was shown that the higher velocity for the tertiary esters is probably due to intramolecular hydrogen bonding. To further investigate the importance of intramolecular hydrogen bonding in alkaline ester hydrolysis, the rates of hydrolysis of catechol monoacetate and some related esters have been studied.

EXPERIMENTAL

Phenyl acetate was prepared according to Vogel's method [2]. B.p. 194—198°; n_D^{25} 1.4992. Vogel has given b.p. 194—197°;

Catechol monoacetate. Green's method [3] was used for the preparation. M.p. 56°. Green found 57—58°.

41.9 mg of catechol monoacetate in 30 ml 0.07 M $KClO_4$ was completely hydrolyzed by adding NaOH at pH 9.0 until the pH of the solution became stable. The

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mixture was then titrated to pH 7 using HCl. The net consumption of NaOH corresponds to an equivalent weight of 151. Calc. for $C_8H_8O_3$: M 152.1.

Catechol diacetate was prepared according to Green's method [3]. M.p. 64°. Green observed m.p. 64°.

2-Methoxy-phenyl acetate (guaiacol acetate) was prepared as described by Freyss [4]. B.p.$_{12}$ 119—119.5; n_D^{25} 1.5093. Wegschneider and Klemenc [5] have reported b.p.$_{13}$. 123—124°. (Found: C 65.0; H 6.06. Calc. for $C_9H_{10}O_3$ (166.2): C 65.0; H 6.07.)

Kinetic method. For the measurements an automatic recording pH-stat [6] was used. The reaction mixture, consisting of 30 ml 0.07 M $KClO_4$ and 0.012—0.015 mmole of ester, was titrated with 0.02 M NaOH at 25°. Except for catechol diacetate, the runs were followed until they were 50—90 % complete and first order rate constants, k_{obs} were calculated using Guggenheim's method [7]. The calculation of the rate constants for catechol diacetate is described in Results.

The infra-red spectra of 2.5—4 % solutions of the esters in CCl_4 (V/V) were recorded at room temperature with a Perkin-Elmer Model 21 spectrophotometer employing a 0.1 mm cell.

RESULTS

The first order rate constants, k_{obs}, for phenyl and guaiacol acetate were found to be proportional to the hydroxyl ion concentration. Values of the second order rate constants, k_2, (Table 1) were calculated using the equations $\log k_2 = \log k_{obs} - \log c_{OH}$ and $c_{OH} = a_{OH}/f_{OH}$, with the constants $K_w = 10^{-14.00}$ and $f_{OH} = 0.80$.

The recorded hydrolysis curves showed that, at the same pH, catechol diacetate is hydrolyzed much more slowly than the monoacetate. The hydrolysis of the diacetate thus involves two consecutive steps. The kinetic equations for such a reaction are quite complicated and k_{obs} cannot be calculated according to Guggenheim's method. Noting that pK'_a of the monoacetate is 8.56 (see below), the initial hydrolysis at pH 8.50 may be written in the following way

$$C_6H_4(OAc)_2 + 1.47\ OH^- \rightarrow 0.53\ HOC_6H_4OAc + 0.47\ {}^-OC_6H_4OAc +$$
$$+ 0.47\ H_2O + AcO^- \tag{1}$$
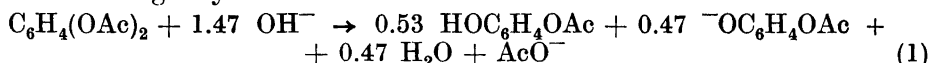
When, after a while, the rates of formation and hydrolysis of the monoacetate have become equal we may consider the following overall reaction (pK'_a of catechol is 9.4).
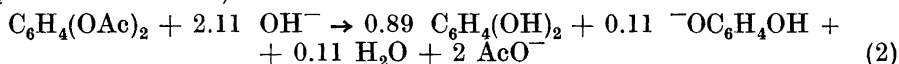
$$C_6H_4(OAc)_2 + 2.11\ OH^- \rightarrow 0.89\ C_6H_4(OH)_2 + 0.11\ {}^-OC_6H_4OH +$$
$$+ 0.11\ H_2O + 2\ AcO^- \tag{2}$$

Table 1. Rate constants and infra-red absorption frequencies, ν, for some compounds $ROCOCH_3$. k_2 is the second order rate constants in $M^{-1}\ sec^{-1}$ for reactions with hydroxyl ions in 0.07 M $KClO_4$ at 25°.

R	$\log k_2$	Studied pH-range	pK_a of corresp. phenol at 25°	ν_{CO} cm^{-1}
C_6H_5O	0.22 ± 0.02 0.14 [8]	9.5—10.4	9.9 [9]	1775
2-HOC_6H_4O	3.07 ±0.03	7.6— 8.8	9.5 [9]	1745 1775 (weaker)
2-$CH_3COOC_6H_4O$	0.97 ± 0.04	8.5	8.66	1780
2-$CH_3OC_6H_4O$	0.01 ± 0.02	9.5—10.07	10.0 [9]	1775

The increase from 1.47 to 2.11 moles of NaOH required to neutralize 1 mole of hydrolyzed diacetate gave the curve of NaOH consumed against time a peculiar shape. The rate of NaOH consumption first increased and then decreased. In a normal pseudo monomolecular reaction the rate steadily decreases. Thus, for a solution containing 10.3 mg of diacetate in 30 ml of solvent at pH 8.50 the rate was 3.04×10^{-6} mmoles sec^{-1} at the beginning of the run and 3.68×10^{-6} mmoles sec^{-1} when 9×10^{-3} mmoles of NaOH had been consumed. Using the first value and reaction 1 the first order rate constant k_{obs} was found to be 3.90×10^{-5} sec^{-1}. This is only 1.5 % of the value of k_{obs} for the monoacetate at the same pH. When using the higher rate of NaOH consumption, reaction 2 and the initial amount of diacetate, allowing for the small amount that had been hydrolyzed, $k_{obs} = 3.58 \times 10^{-5}$ sec^{-1} was calculated. When the hydroxyl ion concentration of the reaction mixture is suddenly doubled, the result was that the rate of NaOH consumption was also doubled. This shows that the rate of hydrolysis of catechol diacetate is first order with respect to hydroxyl ions. Therefore, k_2 was calculated from k_{obs} as described for phenyl acetate.

When the hydroxyl ion concentration of a solution of catechol monoacetate is raised, the rate of hydrolysis increases, but the increase is less than proportional to the change of the hydroxyl ion concentration. This is because, in the presence of a weakly acid phenol group, the ester exists in a neutral and an ionized form one of which is hydrolyzed more rapidly than the other. The $pK_a' = a_{H^+} \times c_{A^-}/c_{HA}$ of the phenol group was determined by comparing a plot of log k_{obs} against pH with a standard curve as previously described [10] and found to have the value 8.56 ± 0.03 ($pK_a = a_{H^+} \times a_{A^-}/a_{HA} = 8.66$).

The above described relationship between log k_{obs} and pH has been also found for other esters possessing acid groups e.g. acetyl salicylic acid [11]. For this compound it has been shown that hydrolysis in the range pH 3 to 9 involves first an intramolecular transacylation giving 2-hydroxybenzoic acetic anhydride and then a rapid decomposition [12] of this intermediate. A similar transacylation may occur in the anion of catechol monoacetate but results in
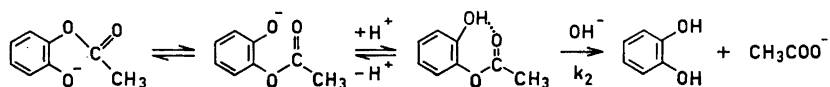
the same anion. The hydrolysis must then be caused by an attack of a hydroxyl ion on the carboxyl group. The rate constant for this reaction, k_2, was calculated from k_{obs} and pK_a' using the equation

$$\log k_2 = \log k_{obs} - \log c_{OH} + \log (1 + K_a'/a_{H^+}).$$

All the aromatic esters showed IR-absorption at $1775-1780$ cm^{-1} because of the C=O group. In catechol monoacetate this absorption was weaker than in the other compounds but instead there was a strong C=O band at 1745 cm^{-1}. The OH absorption band was also split. A weak but sharp absorption band was found at 3580 cm^{-1} which is close to the OH absorption frequency of phenol (3600 cm^{-1}), and a rather strong broad band also occurred at 3410.

These facts indicate that there is hydrogen bonding between the hydrogen atom of the phenol group and carbonyl oxygen atom (see Table 1 and addendum).

DISCUSSION

Table 1 shows that catechol monoacetate is hydrolyzed 700 times faster than phenyl acetate. Two factors may contribute to this difference in the rate constants, (a) the inductive and the resonance effects of an oxygen atom in the ortho-position, and (b) the possibility of intramolecular hydrogen bonding.

By replacing the hydrogen atom of the phenol group of catechol mono-acetate with an aceto group (diacetate) or a methyl group (guaiacol acetate), the sum of the negative resonance and inductive effects of the phenol group should be somewhat increased and diminished respectively but still remain negative [13]. Thus, in the absence of a hydrogen bonding effect the diacetate should be the compound that is most rapidly hydrolyzed. Table 1 shows that this is not the case. Consequently, hydrogen bonding must be the main reason why catechol monoacetate is hydrolyzed much more rapidly than phenyl acetate. The importance of steric hindrance has been neglected because the ortho substituents are relatively far removed from the carboxyl group attacked by the hydroxyl ion.

The presence of intramolecular hydrogen bonding in catechol monoacetate in water solution cannot be demonstrated using infra-red spectra. However, the infra-red spectrum of the monoacetate in CCl_4 shows the occurrence of strong hydrogen bonding to the carbonyl oxygen atom of the carboxyl group. Cf. addendum.

The influence of hydrogen bonding on the reaction rate may also be demonstrated in another way. After careful alkaline hydrolysis of resorcinol diacetate the monoacetate can be isolated [14]. As mentioned previously it is not possible to isolate catechol monoacetate as a hydrolysis product from the diacetate. It may be expected that the rate constants of the hydrolysis of the two diacetates have approximately the same values. Consequently resorcinol mono-acetate, in which the steric conditions for hydrogen bonding are unfavourable, must be hydrolyzed much more slowly than catechol monoacetate.

The rates of hydrolysis increase in the order guaiacol acetate < phenyl acetate < catechol diacetate. The acidity of the phenols formed during hydrolysis increase in the same order. There is apparently a relationship between the rate constants and pK_a, a phenomenon that often has been observed. Assuming that this relationship would also hold true for catechol monoacetate if there were no hydrogen bonding, log k_2 for this compound may be estimated to be 0.35 by linear interpolation. As it is found that log $k_2 = 3.07$, the catalytic effect of the hydrogen bond may be estimated to be approximately 500 times. This seems to be higher than any value previously reported.

The alkaline hydrolysis of the monoacetates of 1,2-cyclopentanediols is known to be catalyzed by intramolecular hydrogen bonding [15]. In these cases the catalytic effect is 20—30 times, which is 15—25 times less than for catechol monoacetate. The difference in the rates between the aliphatic and the aromatic systems may be mainly due to the formation of stronger hydrogen bonding in the catechol monoacetate as phenols are stronger acids than alcohols.

An indication of this is that for catechol monoacetate the $C=O$ absorption frequency in the infra-red region is 30 cm^{-1} below normal but for trans cyclopentanediol monoacetate [15] the difference is only 9 cm^{-1}.

Addendum. Whilst this paper was in the press, Biggins *et al.*[16] published some investigations on catechol monoacetate. They had previously observed that the ester bonds in gallotannins are subject to rapid methanolysis also at neutral pH. Gallotannins are monoesters of complex 4-substituted catechols. Biggins *et al.*[16] assumed that intramolecular hydrogen bondings might occur in the gallotannins and that these hydrogen bonds could be involved in the methanolysis.

In their recent paper [16] Biggins *et al.* have studied the intramolecular hydrogen bonding in some model compounds, amongst others catechol monoacetate. By infra-red technique they have shown that intramolecular hydrogen bondings occur in this compound. They found that in a very diluted solution (1.65 mM) in carbon tetrachloride the absorbtion at 3585 cm^{-1} is stronger than at 3410 and that in the $C=O$ region, two equally strong bonds occur at 1778 and 1736 cm^{-1}. These values are somewhat different from those reported in the present paper. The differences may be attributed to differences in concentrations (the values in Table 1 refer to $100-200$ mM solutions), which may indicate some intermolecular hydrogen bonding, and to different amounts of impurities as different methods of preparation were used. The catechol monoacetate actually is difficult to synthesize and purify.

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