acid was removed by filtration and washed with 95% ethanol. A benzene slurry of the salt was treated with hydrogen chloride gas, evaporated to dryness, and the residue was extracted with ether. Evaporation of the ether left 0.07 g. (50%) of impure ethylenetetracarboxylic acid, m.p. 155–165° dec. Comparison of the infrared spectrum of this sample with one of an authentic sample of pure ethylenetetracarboxylic acid[3] left no doubt that the spectra are of the same compound.

Methanolysis of Diisopropylidene Ethylenetetracarboxylate.—A methanol solution, which was obtained after 5 hr. at reflux temperature from a slurry of 1.0 g. (3.5 mmoles) of diisopropylidene ethylenetetracarboxylate in 25 ml. of absolute methanol to which a trace of hydrogen chloride gas had been added, was decanted from a trace of undissolved material and concentrated to dryness under vacuum. The residue was dissolved in a minimum amount of 2 *N* potassium bicarbonate, filtered, and acidified with 12 drops of concentrated hydrochloric acid. The product was extracted with ten 5-ml. portions of ether, and the solution was dried over calcium chloride. Evaporation left 0.86 g. of waxy, white 1,2-dimethyl ester of ethylenetetracarboxylic acid, m.p. 189–190° with gas evolution, after recrystallization from an ether–chloroform mixture. The stereochemistry is not known.

Anal. Calcd. for $C_8H_8O_8$: C, 41.39; H, 3.47. Found: C, 41.14; H, 3.54.

Treatment of 0.1 g. of the dimethyl ester with excess diazomethane produced a liquid, but reaction with a limited amount produced tetramethyl ethylenetetracarboxylate, m.p. 121°[21] (lit.[2] m.p. 121°).

Reduction of 33 mg. (0.14 mmole) of the dimethyl ester with hydrogen over platinum in methanol at room temperature, followed by treatment with diazomethane, produced tetramethyl ethanetetracarboxylate, m.p. 137–138°. A mixed melting point with an authentic sample[21] was not depressed.

Hydrogenation of Diisopropylidene Ethylenetetracarboxylate.—The reduction of 0.284 g. (1 mmole) of diisopropylidene ethylenetetracarboxylate in 300 ml. of benzene over platinum under 3400 lb. hydrogen pressure at 85° for about 1 hr. produced a solution which, after evaporation, left a crystalline material and an oil. The oil was later found to be an impurity in the benzene. The residue was slurried with chloroform. By filtration, 45 mg. (16%) of diisopropylidene ethanetetracarboxylate, m.p. 198–200° from benzene, was obtained.

Anal. Calcd. for $C_{12}H_{14}O_8$: C, 50.35; H, 4.93. Found: C, 50.65; H, 4.90.

Isopropylidene Cyclohexylidenemalonate.—A solution of 1.44 g. (10 mmoles) of isopropylidene malonate and 0.98 g. (10 mmoles) of cyclohexanone in 5 ml. of dimethylformamide stood at room temperature for 24 hr. Isopropylidene cyclohexylidenemalonate (0.4 g., 18%) crystallized when the solution was poured into about 20 ml. of ice-water. A preliminary purification was accomplished by pouring a saturated acetone solution of it into water. A product, m.p. 85–86°, was obtained by filtration. An analytical sample, m.p. 87–87.5°, was obtained by recrystallization from methanol.

Anal. Calcd. for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.55; H, 7.39.

URBANA, ILLINOIS

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(21) C. Bischoff, *Ber.*, **29**, 1283 (1896).

[CONTRIBUTION FROM THE OLIN MATHIESON CHEMICAL CORPORATION, HIGH ENERGY FUELS ORGANIZATION]

Concerted Displacement Reactions: The Reaction of Catechol with Acyl Halides[1a,b]

BY J. W. CHURCHILL, M. LAPKIN, F. MARTINEZ AND J. A. ZASLOWSKY

RECEIVED NOVEMBER 14, 1957

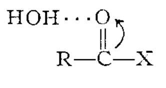
The rates of reaction of catechol with several acyl halides were determined in 95% acetone. The results indicate that the reaction proceeds by a concerted attack of the monocatecholate ion on the acyl halide with the formation of the monoacyl ester of catechol. Benzenesulfonyl fluoride and benzoic anhydride appear to react with catechol by a similar concerted mechanism. Resorcinol, hydroquinone and phenol are, relative to catechol, unreactive toward acyl halides.

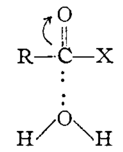
Introduction

The rates of hydrolysis and alcoholysis of acyl halides in inert solvents have been claimed to vary with the square of the concentration of water or alcohol.[2a,b]

$$\text{rate of reaction} = k(H_2O)^2\ (\text{acyl halide})$$

Water or alcohol can act by virtue of their amphoteric character either as electrophilic or nucleophilic reagents in the solvolysis of acyl halides.


electrophilic attack


nucleophilic attack

The possibility that the reaction in such systems involves a simultaneous electrophilic and nucleophilic attack on the substrate was recognized by Lowry and Faulkner[3] in their study of the mutarotation of tetramethylglucose. In inert solvents a mixture of pyridine and cresol markedly increased the rate of mutarotation even though both reagents were relatively ineffective by themselves. The hypothesis of a termolecular reaction mechanism was, therefore, advanced. Swain used the term "concerted displacement" to describe the phenomenon.[4,5] A concerted mechanism in general gives rise to third-order kinetics. The observed third-order kinetics can also arise from two consecutive bimolecular reactions.

$$A + B \underset{k_2}{\overset{k_1}{\rightleftarrows}} C$$

$$C + D \xrightarrow{k_3} E$$

If k_3 is the rate-determining step, the rate of reaction is

$$\frac{k_1k_3}{k_2}\ (A)\ (B)\ (D)$$

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(1) (a) This document is based upon work performed under Contract Number DA-18-108-CML-5635 for the Chemical Corps, Department of the Army; (b) presented before the 132nd Meeting of the American Chemical Society, New York, N. Y., September, 1957.

(2) (a) G. Zimmerman and C. Yuan, THIS JOURNAL, **77**, 332 (1955); V. Gold and J. Hilton, *J. Chem. Soc.*, 838 (1955), disagree with Z and Y. (b) A. A. Ashdown, THIS JOURNAL, **52**, 268 (1930).

(3) T. Lowry and I. J. Faulkner, *J. Chem. Soc.*, **127**, 2883 (1925).

(4) C. G. Swain, THIS JOURNAL, **70**, 1124 (1948).

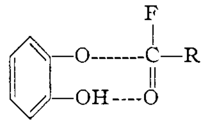
(5) C. G. Swain, *ibid.*, **72**, 4678 (1950).

Substances containing both electrophilic and nucleophilic substituents in the proper steric configuration partake in some chemical reactions at rates which exceed the combined reactivities of the individual functional groups on two different molecules. This has been explained[6] on the basis of a concerted mechanism which requires a bimolecular instead of a termolecular collision. The most carefully documented study in this connection is the work of Swain and Brown[6] on the catalysis of the mutarotation of tetramethylglucose by phenol, pyridine and hydroxypyridines. The catalytic effect of 2-hydroxypyridine in benzene on the rate of mutarotation far exceeds that of a solution of phenol and pyridine in the same solvent; 3-hydroxypyridine was almost devoid of activity relative to the 2-isomer. This phenomenon has been called polyfunctional catalysis.[6]

The above concept of concerted reactions and polyfunctional reactivity, if valid, should be perfectly general and would not be restricted to catalytic reactions.

If the solvolysis of acyl halides involves a concerted attack by both nucleophilic and electrophilic groups, a phenomenon akin to the one noted with tetramethylglucose and 2-hydroxypyridine could occur. A molecule containing both an electrophilic and nucleophilic substituent in the proper configuration would react much faster than two monofunctional reactants.

Half-neutralized dihydroxybenzenes contain both nucleophilic and electrophilic substituents on the same molecule. Sterically, it might be expected that the 1,2-isomer would be the most effective for concerted action on the acyl halide.



The rates of reaction of Sarin (methyl isopropylfluorophosphonate) with catechol and substituted catechols have been reported recently.[7] The rate of reaction was found to vary with the concentration of the singly dissociated catecholate ion.

This paper deals with an investigation of the concept of polyfunctional reactivity as it relates to the reactions of catechol with acid derivatives in a 95% acetone–5% water (by volume) solvent system.

Experimental

Materials.—The chemicals required for this study were either the purest commercially available materials or were synthesized in these laboratories.

Propionyl fluoride (b.p. 43–44°) and benzoyl fluoride (b.p. 157–159°) were prepared by the method of Mashentsev[8] from the acid anhydride and anhydrous potassium fluoride.

Apparatus.—The experiments were conducted at constant "*p*H" employing a Beckman model K automatic titrimeter with glass and calomel electrodes. The reaction temperature was regulated to ±0.1° by the use of a jacketed reaction flask through which constant temperature water was circulated.

Procedure.—Catechol (5–10 meq. representing at least a 5-fold excess) was dissolved in 200 ml. of solvent (95% acetone–water). A sufficient quantity of base was added to give the desired "*p*H".[9] About 1 meq. of acyl halide was added to the reaction mixture at time zero. The rate of addition of base by the titrimeter at constant "*p*H" was used as a measure of the rate of reaction. Reaction rate constants were obtained by the conventional graphical method for pseudo-first-order reactions. Second-order constants were obtained by dividing the first-order constant by the catecholate ion concentration.[10] The results are summarized in Table I. Inasmuch as the rates of reaction with catechol under the investigated conditions were at least 100-fold greater than the self-hydrolysis reaction of propionyl and benzoyl fluoride, no correction for the self-hydrolysis was necessary. In the case of benzoyl chloride such a correction was made. At the termination of the reaction a large volume of water was added to the reaction mixture and the total quantity of acid generated was determined. This step was necessary because any carboxylic acids that might have formed by the reaction were not titratable in 95% acetone up to a "*p*H" of 8.4.

TABLE I

SPECIFIC REACTION RATE CONSTANTS OF ACID HALIDES WITH CATECHOL AT VARIOUS "*p*H" VALUES IN 95% AQUEOUS ACETONE AT 25°[a]

Acid halide[b]	"*p*H"	k_2', liters mole^{-1} sec.$^{-1}$ [c]	k_2, liters mole^{-1} sec.$^{-1}$
Propionyl fluoride	7.4	Self-hydrolysis	($k_1 < 4.2 \times 10^{-6}$ sec.$^{-1}$)
	7.4	$1.09 \pm 0.05 \times 10^{-2}$	1.7×10^3
	8.0	$5.0 \pm 0.5 \times 10^{-2}$	2.0×10^2
	8.5	14.0×10^{-2}	1.8×10^2
		Av.	$1.83 \pm 0.1 \times 10^2$
Benzoyl fluoride	7.4	Self-hydrolysis	($k < 4.2 \times 10^{-6}$ sec.$^{-1}$)
	7.4	1.07×10^{-2}	1.7×10^2
	8.0	$3.2 \pm 0.5 \times 10^{-2}$	1.3×10^2
		Av.	$1.5 \pm 0.2 \times 10^2$
Benzoyl chloride	5.0	Self-hydrolysis	$k_1 = 2 \times 10^{-4}$ sec.$^{-1}$
	6.0	Self-hydrolysis	$k_1 = 2 \times 10^{-4}$ sec.$^{-1}$
	7.5	Self-hydrolysis	$k_1 = 2 \times 10^{-4}$ sec.$^{-1}$
	7.4	$9.0 \pm 0.3 \times 10^{-2}$	1.45×10^2

[a] Catechol concn.: 2.5 to 5.0×10^{-2} mole/liter. [b] 5×10^{-3} mole/liter. [c] k_2' = constant based upon total catechol; k_2 = constant based upon catecholate ion.

One equivalent of acid was liberated by the reaction, and no additional acid was liberated upon the addition of water.

Similar experiments were conducted using resorcinol, hydroquinone and phenol. The rates of reaction were too slow to be conveniently measured and no rate constants were determined.

The rate of hydrolysis of benzoyl chloride in the "*p*H" range 5 to 7.5 was determined. The rate was independent of the "*p*H." At "*p*H" 7.5 resorcinol did not affect the rate of acid liberation; catechol markedly increased this rate (see Table I).

Discussion

The relationship between the monocatecholate ion and total catechol can be expressed by the equation

$$\frac{[\mathrm{Cat}^-]}{[\mathrm{Cat}^0]} = \frac{K_a}{K_a + [\mathrm{H}]}$$

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(6) C. G. Swain and J. F. Brown, THIS JOURNAL, **74**, 2538 (1952).

(7) J. Epstein, D. H. Rosenblatt and M. M. Demek, *ibid.*, **78**, 341 (1956).

(8) A. I. Mashentsev, *J. Gen. Chem.* (*U.S.S.R.*), **15**, 915 (1945).

(9) The meaning of "*p*H" in a 95% acetone solution may be ambiguous. It is used in this paper to signify a reproducible value which is given by the measuring instrument. Titration curves of acetic and hydrofluoric acids in the 95% acetone with 0.1 *N* sodium hydroxide were determined. The curves are normal in shape and the titrations have sharp end-points. The "*p*Ka" of the acid is displaced to the basic side by about 2–3 units. Titration of catechol in this medium gave a titration curve with half-neutralization point of 11.6. This corresponds to the "*p*Ka" of catechol.

(10) The following equations were used for calculations

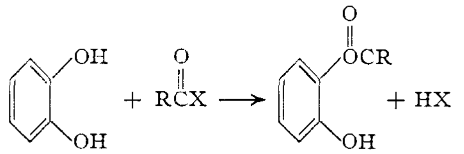
$$\log \frac{A}{A - X} = \frac{k_1t}{2.3};\ k'_2 = k_1/\mathrm{Cat}^0;\ k_2 = k_1(\mathrm{Cat}^-)$$

$A - X$ = acid halide concentration at time t, moles/liter; Cat^0 = catechol, total, moles/liter; Cat^- = catechol, moles/liter.

where [Cat⁻] is the concentration of monocatecholate ion, and [Cat⁰] is the initial concentration of catechol. At the "*p*H" values investigated [H] is large relative to the value of K_a and the concentration of catecholate ion varies inversely with [H]. Table I indicates that only k_2, which is based upon the monocatecholate ion concentration, gives a consistent second-order specific rate constant over the "*p*H" range studied.

The hydrolysis of benzoyl chloride at "*p*H" 5.0 proceeded at the same rate as at "*p*H" 7.5 ($k_{25^0} = 2.0 \times 10^{-4}$ sec.$^{-1}$) indicating no [OH⁻] catalysis of the reaction over this "*p*H" range.

Only one mole of acid is liberated by the reaction of catechol with acid halides.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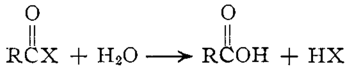
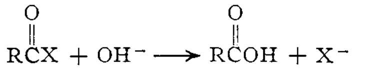
If the reaction involved water, two moles of acid would be liberated


$$\mathrm{R\overset{\overset{O}{\|}}{C}X + H_2O \longrightarrow R\overset{\overset{O}{\|}}{C}OH + HX} \qquad (2)$$

If the reaction involved the hydroxide ion the equivalent of two moles of acid would be liberated.

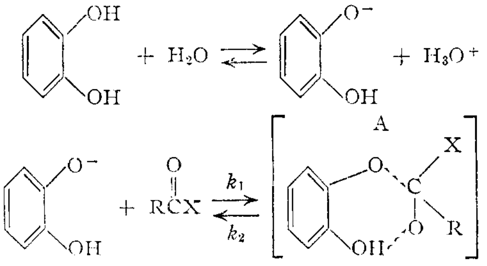

$$\mathrm{R\overset{\overset{O}{\|}}{C}X + OH^- \longrightarrow R\overset{\overset{O}{\|}}{C}OH + X^-} \qquad (3)$$

Reaction 1 is written as if the catechol itself is the reactive species. This is merely a representation of the stoichiometry of the reaction at the "*p*H" values used.

The importance of the undissociated *o*-hydroxyl group is proven by the lack of reactivity of phenol, resorcinol and hydroquinone toward acyl halides under conditions in which the *o*-derivative is reactive.

The specificity of the monocatecholate ion is interpreted on the basis of a concerted attack upon the carbonyl group of the acid halide.

A mechanism which is consistent with the experimental facts is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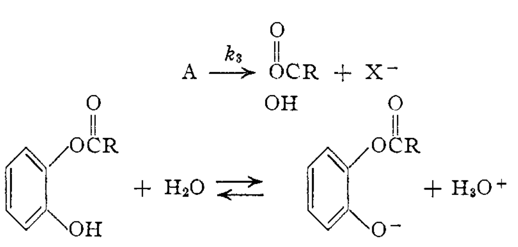
(3)

(4)

The kinetic measurements were conducted under conditions where there was very little catecholate ion present (less than 0.1%). Under these conditions the base required for step 1 (at constant "*p*H") was a measure of experimental rate of reaction. Step 4 is not significant when the pK_a of the product is of approximately the same order of magnitude as that of catechol.[11]

Either reaction 2 or 3 can be rate determining. The rate of acid evolution is determined by the disappearance of catecholate ion. This can occur either by a rate-controlling complex formation step followed by a rapid decomposition, or by an equilibrium complex formation step followed by the rate-determining decomposition. The latter case is discussed by Swain and Brown.[7] In any event, the rate of acid liberation with catechol is much greater than the rate with other dihydroxybenzenes.

Equation 2 is written with the hydroxyl group complexing with the carbonyl oxygen rather than with the halogen because dipole–dipole interactions noted with chlorine atoms are ordinarily too weak to be classified as true hydrogen bonds and it is not reasonable to suppose that the mechanism changes when fluorine is substituted for chlorine.

It was qualitatively observed that in aqueous solution the rates of reaction of benzoic anhydride and benzenesulfonyl fluoride with catechol were much faster than with resorcinol. It is probable that a "concerted" mechanism accounts for the greater reactivity of catechol in these cases.

It seems probable that the increased reactivity of phosphonyl halides, acid halides, sulfonyl halides and carboxylic acid anhydrides with catechol relative to other phenols can best be explained on the basis of the above concerted polyfunctional mechanism.

NIAGARA FALLS, N. Y.

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[11] If appreciable quantities of catecholate ion were present, the value of the K_a's of the product of the reaction and catechol would have to be very close to obtain an accurate rate of reaction by this method. Effectively only the rate of acid evolution by reaction 1 has been measured experimentally. Catechol monoacetate was prepared by the method of A. Green, *J. Chem. Soc.*, 500 (1927), b.p. 123–126° at 8 mm. The "pK_a" was approximately the same as catechol.