The Effect of Para Substitution on the Rate of Alkaline Hydrolysis of Ethyl 5-Ethyl-2,4-pentadienoates[1]

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Ethyl 5-phenyl-2,4-pentadienoate and its *p*-nitro and *p*-dimethylamino derivatives have been prepared and the alkaline hydrolysis rate of these esters has been investigated at 30, 40, and 50° in a solvent mixture consisting of (by volume) acetone 70%, ethanol 20%, and water 10%. The hydrolysis showed second-order kinetics with activation energies in the range of 13.7–15.4 kcal mol^{-1}. The results of para substituents were correlated by the Hammett equation, ρ +0.83. A qualitative comparison of the hydrolysis rate of ethyl 5-phenyl-2,4-pentadienoate ($k_{30} = 7.18 \times 10^{-3}$ l. mol^{-1} sec^{-1}), and that of the reported values of ethyl cinnamate ($k_{30} = 1.99 \times 10^{-3}$ l. mol^{-1} sec^{-1}) and ethyl benzoate ($k_{30} = 0.85 \times 10^{-3}$ l. mol^{-1} sec^{-1}) indicates that the saponification rate increases with increasing conjugation. The effect of para substituents, however, decreases as conjugation increases.

The studies on the alkaline hydrolysis of para-substituted ethyl benzoates have been reported and the effect of such substituents on the rate of such hydrolysis was well documented.[3,4] In similar studies made on the para-substituted cinnamic esters the effect of the substituent was found to be parallel to those in the benzoate but to a lesser degree.[4] In this paper we wish to report the effect of some para substituents in a more extended conjugated structure, ethyl 5-phenyl-2,4-pentadienoate, and the comparison between the para substituent effect in these three types of esters.

The kinetic data of Ingold and Nathan[3] and Kindler[4] both indicated that in these series of reactions the Arrhenius equation has a common pre-exponential value and the effect of substituents on the rate of saponification is due largely to their influence on the activation energy. The hydrolysis rate of cinnamates was about three times that of benzoate in the same solvent, 87.83% ethanol at the same temperature 30°, but the effect of para substituents is higher in benzoates than that in cinnamates. By extending the conjugation in the system, the distance between the substituent and the site of the reaction will be increased; thus the expected rate of hydrolysis should be higher and the para-substituent effect lower than that in the cinnamates. The average values of the second-order rate constants for the alkaline hydrolysis of the ethyl 5-phenyl-2,4-pentadienoate and two of its derivatives are summarized in Table I.

The relative constancy of the values of log A in these three ester hydrolyses suggests that in these esters, as in the case of hydrolysis of benzoates and cinnamates, the principal effect of the para substituent is to change the activation energy. An exact comparison of the reaction rate constants and the effect of para substituents of the three types of ester is not achievable, since the present experiment was carried out in a different solvent medium (for reasons given in the Experimental Section), ethanol–acetone–water instead of 87.83% ethanol,[4] but the trend of change in both the rate constant and the effect of para substituents against the length of conjugation is apparent. To illustrate that the effect of para substituents decreases with increase of conjugation, the saponification rate at 30° of the *p*-nitro substituted ester against the unsubstituted esters in each case are given in Table II.

This effect is, of course, also reflected from the ρ values of the corresponding series.[3,4] That the rate of alkaline hydrolysis of these esters increases with increase of conjugation can be best illustrated with the comparison of the rate constants of the three unsubstituted esters at 30° in Table III.

It is expected that in the alkaline hydrolysis of an ester, the initial addition of the hydroxide ion to the carbonyl carbon is facilitated by electron-withdrawing groups. The extent to which the electron recession occurs would be a function of polarizibility of the molecule and would increase with an increase in the length of the conjugation.

Experimental Section[5]

Materials.—The following reagents were obtained from Eastman, White Label: 5-phenyl-2,4-pentadienoic acid, mp 166–168°; *trans*-cinnamaldehyde, mp −7°, bp 253°; malonic acid, mp 134–136° dec; *p*-nitrobenzaldehyde, mp 104–106°; *p*-dimethylaminobenzaldehyde, mp 74–75°; acetaldehyde, bp 20°.

Ethyl 5-Phenyl-2,4-pentadienoate.—A mixture of 54 g (0.31 mol) of 5-phenyl-2,4-pentadienoic acid and 90 g of absolute ethanol was refluxed for 6 hr while a slow stream of hydrogen chloride was passed into it. Then the excess alcohol was distilled off and the ester was distilled under reduced pressure at 141° (1 mm). The yield was 45.7 g (73%), refractive index $N^{29.5}\text{D}$ 1.6018 (lit.[6] $N^{30}\text{D}$ 1.5769).

Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.22; H, 6.9. Found: C, 77.3; H, 7.0.

***p*-Nitrocinnamaldehyde.**—To a cold mixture of 58.5 g (0.38 mol) of *p*-nitrobenzaldehyde and 117 g (2.65 mol) of acetaldehyde, a 25% solution of potassium hydroxide in methanol was added drop by drop until the suspension had disappeared. To the solution, 200 ml of acetic anhydride was added. The excess acetaldehyde was evaporated off and the content was poured to an excess amount of water containing 90 ml of concentrated hydrochloric acid. A dark yellow crystalline solid was obtained. Recrystallization of the solid from ethanol gave 47 g (70%) of *p*-nitrocinnamaldehyde, mp 140–142° (lit.[7] 141–142°).

5-(*p*-Nitrophenyl)-2,4-pentadienoic Acid.—A mixture of 23.5 g (0.132 mol) of *p*-nitrocinnamaldehyde, 125 ml of acetic anhydride, and 7.2 g of fused sodium acetate was refluxed at 145–150° for 6 hr. After cooling, the reaction mixture produced a yellow solid. The solid was dissolved in dilute potassium hy-

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[1] This research was initiated by N. Wang at St. Louis University under the direction of Professor K. H. Adams.

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[3] C. K. Ingold and W. S. Nathan, *J. Chem. Soc.*, 222 (1936); 1430 (1937).

[4] K. Kindler, *Justus Liebigs Ann. Chem.*, 450, 1 (1926); 452, 90 (1927); *Ber.*, **69B**, 2792 (1936).

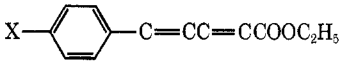
[5] Melting points are uncorrected. Elementary analysis were performed by Dr. C. K. Fitz, Needham Heights, Mass., and Galbraith Laboratories, Inc., Knoxville, Tenn.

[6] I. F. Eijkman, *Chem. Zentral.*, **11**, 1209 (1907).

[7] C. F. Göhring, *Ber.*, **18**, 372 (1885).

TABLE I

ALKALINE HYDROLYSIS RATES OF ETHYL 5-PHENYL-2,4-PENTADIENOATES[a]



X	Registry No.	Temp, °C	k, l. mol^{-1} sec^{-1}	Log A^b	E, kcal/mol
NO_2	15542-23-1	30	2.72×10^{-2}	8.35	13.7 ± 0.9
		40	6.06×10^{-2}		
		50	1.12×10^{-1}		
H	1552-95-0	30	7.18×10^{-3}	8.29	14.5 ± 0.4
		40	1.44×10^{-2}		
		50	2.97×10^{-2}		
$(CH_3)_2N$	15542-27-5	30	2.43×10^{-3}	8.48	15.4 ± 0.5
		40	4.65×10^{-3}		
		50	1.15×10^{-2}		

[a] All hydrolyses were carried out in two concentrations of potassium hydroxide, 1.8×10^{-2} and 3.6×10^{-2} M, with the ester concentration ranging from 0.75×10^{-2} to 1.06 M in a solvent mixture consisting of (by volume) acetone 70%, ethanol 20%, and water 10%. [b] The pre-exponential factor in the Arrhenius equation obtained based on the rate constant of each at 30°.

TABLE II[a]

COMPARISON OF THE HYDROLYSIS RATES OF p-NITRO-SUBSTITUTED ESTERS AGAINST THE UNSUBSTITUTED ESTERS

Ethyl ester	Δ log k (log k − log k_0)	ρ
p-Nitrobenzoate	2.11	+2.498
p-Nitrocinnamate	0.99	+1.329
5-(p-Nitrophenyl)-2,4-pentadienoate	0.59	+0.83

[a] k is the rate constant for p-nitro ester; k_0 is the rate constant for the corresponding unsubstituted ester.

TABLE III

HYDROLYSIS RATE CONSTANTS OF THE THREE UNSUBSTITUTED ESTERS

Ethyl ester	k_{30}, l. mol^{-1} sec^{-1}
5-Phenyl-2,4-pentadienoate	7.18×10^{-3}
Cinnamate	1.99×10^{-3}
Benzoate	0.85×10^{-3}

droxide and reacidification with hydrochloric acid gave 9 g (31%) of the pure acid, mp 270°.

Anal. Calcd for $C_{11}H_9NO_4$: C, 62.5; H, 4.26; N, 6.63. Found: C, 62.6; H, 4.3; N, 6.59.

Ethyl 5-(p-Nitrophenyl)-2,4-pentadienoate.—The procedure used here paralleled the one used in the preparation of the unsubstituted ester. The time required to complete the esterification was 3.5 hr and the yield was 70% of the theoretical. The ester was recrystallized from ethanol, mp 120–122°.

Anal. Calcd for $C_{13}H_{13}NO_4$: C, 65.27; H, 5.44; N, 5.8. Found: C, 65.3; H, 5.4; N, 5.7.

p-Dimethylaminocinnamaldehyde.—To 150 ml of concentrated sulfuric acid, 30 g (0.2 mol) of p-dimethylaminobenzaldehyde was added gradually. To this mixture, 26.6 g (0.6 mol) of acetaldehyde was added dropwise with stirring over a period of 3 hr at 0°. The dark-colored reaction mixture was poured onto an excess of ice. A yellow precipitate was formed when the solution was neutralized with 10% sodium hydroxide solution. The precipitate was dried and extracted with petroleum ether (bp 60–90°) and further recrystallized from petroleum ether. The yield was 14 g (40%), mp 140–141° (lit.[8] 133°).

5-(p-Dimethylaminophenyl)-2,4-pentadienoic Acid.—The procedure used here paralleled the one used in the preparation of the unsubstituted acid. The time required to complete the reaction was 20 hr of reflux at 110–115°. The yield of the acid was 40%.

Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.89; H, 6.9; N, 6.4. Found: C, 72.0; H, 7.1; N, 6.3.

Ethyl 5-(p-Dimethylaminophenyl)-2,4-pentadienoate.—The esterification of 5-(p-dimethylaminophenyl)-2,4-pentadienoic acid was accomplished in the same manner as in the preparation of other esters. The time for completing the reaction was 9 hr and the yield was 65%. The ester was recrystallized from ethanol, mp 112–114°.

Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.4; H, 7.75; N, 5.7. Found: C, 73.6; H, 7.8; N, 6.0.

Hydrolysis Rate Measurement.—The esters used in this investigation were found to be practically insoluble in water and of low solubility in ethanol. They are soluble in acetone and adequately soluble in a 9:1 (by volume) mixture of acetone and water. However, the addition of sodium or potassium hydroxide to the latter mixture caused separation of an aqueous phase which retained a major portion of the alkali. Consequently, a mixed solvent was adopted which consisted of (by volume) acetone 70%, ethanol 20%, and water 10%. In this solvent mixture it was possible to produce solutions containing 0.02 M of potassium hydroxide and 0.01 M in ester concentration.

Acetone was purified by fractionating analytical grade acetone previously dried over potassium carbonate. Absolute ethanol was purified by fractionating analytical grade absolute ethanol over magnesium turnings and a small amount of iodine. The fraction boiling at 77.5° was collected.

In a typical kinetic run, 0.1881 g of ethyl 5-phenyl-2,4-pentadienoate was dissolved in 90 ml of a solvent mixture (77.7% acetone, 22.3% ethanol by volume) in a 100-ml volumetric flask. The flask was then stoppered and immersed in the thermal bath at 50°. After 45 min, 5.00 ml of prewarmed (50°) 0.366 N potassium hydroxide was added. Time was recorded in seconds when the last drop of potassium hydroxide had run into the solution. The mixed solution was diluted with water (prewarmed to bath temperature) to the 100-ml mark. The reaction flask was gently shaken in the thermostat. At appropriate intervals 10-ml aliquot portions of the solution was removed and transferred immediately into 5.00 ml of 0.0520 N hydrochloric acid. The mixture was then titrated against 0.0636 N sodium hydroxide solution with cresol red as indicator. Bromthymol blue was used in the case of ethyl 5-(p-dimethylaminophenyl)-2,4-pentadienoate because the red color of the ester obscured the cresol red end point. Each end point was matched against a color standard consisting of a freshly prepared solution of 0.03 M of sodium salt of the corresponding 5-phenyl-2,4-pentadienoate in 20 ml of the reaction solvent mixture containing the same amount of indicator as used in the titration.

Registry No.—5-(p-Nitrophenyl)-2,4-pentadienoic acid, 31235-98-0; 5-(p-dimethylaminophenyl)-2,4-pentadienoic acid, 31235-99-1.

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(8) F. Sachs and W. Weigort, *Ber.*, **40**, 4368 (1907).