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β-Propiolactone. XVI. Reaction Rates with Anilines and *para*-Substituted Anilines

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Bimolecular rate constants have been determined for the reaction of β-propiolactone at 25° in water with aniline and six of its *para*-substitution products. The data fit the Hammett equation yielding a value of $\rho = -1.18$. From the behavior *of p-aminobenzoic acid at pH 7 and at pH 3, the σ-value for the carboxylate ion appears to be +0.31, being opposite in sign* from its value as determined from the dissociation constants of terephthalic acid. The considerable reactivity of aniline at the β-position of propiolactone is in accord with predictions from the Edwards equation.[3] From the slow attack of aniline and the rapid attack of hydroxyl ion at the carbonyl group of β-propiolactone the rate of these ester type reactions appears to be governed largely or entirely by the basicity (Edwards' *H*) of the reagent.

Ammonia, primary and secondary amines are able to react with β-propiolactone either at the carbonyl group yielding hydracrylamides or at the β-carbon atom yielding β-alanines.[1] The relative rates of formation of the two types of product vary greatly with the individual amine and with the solvent. In the course of a general study of the factors governing the point and rate of attack of amines upon β-propiolactone, we have studied the rate of formation of N-phenyl-β-alanine and certain of its *para*-substituted derivatives in aqueous solution where this product appears to be formed almost exclusively.[1,2]

The fact that the reaction takes this course is itself of some interest in view of the fact that water as a solvent favors the attack of ammonia and primary aliphatic amines upon the carbonyl group rather than upon the β-carbon atom of the lactone.[1]

The rates of displacement reactions at the β-position of propiolactone recently have been correlated with others by means of the equation[3]

$$\log (K/K_0) = \alpha E_n + \beta H$$

where for β-propiolactone $\alpha = 2.00$ and $\beta = 0.069$. Thus the "nucleophilic" term E_n is much more important than the "basic" term H in determining the reaction rate relative to water. From the values given by Edwards for E_n and H of hydroxyl ion and aniline, and our estimated rate constants of 1.17 and 10^{-4}, respectively, for the reaction of these agents at the carbonyl group of the lactone, we conclude that attack at the carbonyl group is governed far more largely by basicity (H) than is any of the displacement reactions correlated by Edwards.

Method of Measurement

The method used in part IX of this series[4] in which β-propiolactone was titrated with thiosulfate was applicable to these systems, but was not advantageous. The reaction is slow enough so that it is advantageous to have one component present in excess over the other. Propiolactone is best taken in excess because of its greater solubility in water compared to that of the aromatic amines. However, since its concentration then changes by only a small fraction, it is desirable to titrate the aniline rather than the lactone. For this purpose we adopted the colorimetric determination described by English[5] in which the aniline is diazotized and allowed to couple with H-acid (1-amino-8-naphthol-3,6-disulfonic acid), the color intensity being determined photometrically.

Preliminary experiments gave curved lines when the reaction was plotted for second-order kinetics and it was discovered that hydrolysis of the lactone was an important competing reaction. In order to keep the hydroxyl ion concentration at a minimum consistent with the aromatic amine being in its basic form, the solutions were buffered with sodium bicarbonate and carbon dioxide. The concentration of the anilines was of the order of 0.002 *M*, that of the lactone varied from 0.04 to 1.2 *M* for different anilines. With such large excesses of propiolactone, the changing lactone concentration can be treated as if it were the result solely of hydrolysis which is kinetically of the first-order in lactone. The rate of this hydrolysis could be determined in each instance by making a few determinations of the lactone concentration during each run. The following kinetic treatment then served for the evaluation of k_2, the bimolecular reaction rate constant for the formation of substituted β-alanine.

Let x = concentration of aniline, and y = concentration of lactone = $y_0e^{-\alpha t}$ where α = the rate constant for hydrolysis under the particular conditions of the run. The rate of decrease of amine concentration is then expressed by the equation

$$-\mathrm{d}x/\mathrm{d}t = k_2xy = k_2xy_0e^{-\alpha t}$$

The integrated form of this equation is

$$\ln x = (k_2y_0/\alpha)e^{-\alpha t} + (\ln x_0 - k_2y_0/\alpha)$$

A plot of $\log_{10} x$ against $e^{-\alpha t}$ yields k_2 as slope $\times$ $2.303\alpha/y_0$.

By working at both *p*H 3 and 7 with *p*-aminobenzoic acid it was possible to obtain rate constants for aniline substituted by COOH and also by COO$^-$ in the *para* position. In order to obtain the former constant, it was necessary to correct the observed rate at *p*H 3 for that fraction of the amino group which exists in the form of the conjugate acid, NH_3^+ under those conditions. This might be done accurately by making a series of rate determinations over a range of *p*H's. Instead, an approximate correction (of the order of 20%) was made by assuming identical basic strengths for *p*-aminobenzoic acid and for *p*-aminoacetophenone. The rate of reaction of the latter compound with propiolactone was measured at *p*H 3 and 7 and the ratio of the two values was used as a correction factor to obtain the rate constant listed in Table I.

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[1] Part XI of this series, T. L. Gresham, J. E. Jansen, F. W. Shaver, R. A. Bankert and F. T. Fiedorek, THIS JOURNAL, **73**, 3168 (1951).

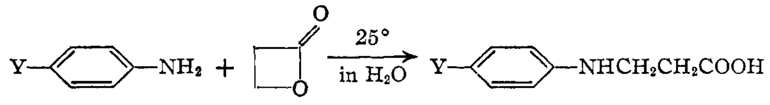
[2] C. D. Hurd and S. Hayao, *ibid.*, **74**, 5889 (1952).

[3] J. O. Edwards, *ibid.*, **76**, 1540 (1954).

[4] P. D. Bartlett and G. Small, Jr., *ibid.*, **72**, 4867 (1950).

[5] F. L. English, *Anal. Chem.*, **19**, 457 (1947).

TABLE I



concn. of $ArNH_2$ *ca.* 0.002 *M*

p-Substituent (Y)	Run no.	β-Propiolactone concn., *M*	*p*H (approx.)	k_2, l. m.$^{-1}$ sec.$^{-1}$	k_2 (ave.), l. m.$^{-1}$ sec.$^{-1}$	σ-Values[a]
$-OCH_3$	54	0.0449	7	1.86×10^{-2}	1.90×10^{-2}	−0.268
	64	.0586	7	1.93×10^{-2}		
$-CH_3$	51	.0619	7	1.65×10^{-2}	1.70×10^{-2}	− .170
	65	.0791	7	1.75×10^{-2}		
$-H$	49	.0697	7	1.09×10^{-2}	1.08×10^{-2}	.000
	50	.1060	7	$1\ 06 \times 10^{-2}$		
$-Cl$	53	.1084	7	6.90×10^{-3}	6.97×10^{-3}	+ .227
	66	.149	7	7.03×10^{-3}		
$-CO_2^{\ominus}$	56	.241	7	4.57×10^{-3}	$4\ 59 \times 10^{-5}$	+ .16[e]
	62	.331	7	4.61×10^{-3}		+ .31[c]
$-COOH$	57	.626	3	1.21×10^{-3}	1.50×10^{-3}[d]	+ .728[b]
	60	.807	3	1.19×10^{-3}		
$-COCH_3$	59	.857	3	8.85×10^{-4}	8.83×10^{-4}	
	63	.701	3	8.80×10^{-4}		
$-COCH_3$	52	.621	7	1.09×10^{-3}	1.10×10^{-3}	+ .874[b]
	61	.597	7	1.10×10^{-3}		
$-NO_2$	55	1.226	7	2.93×10^{-4}	2.90×10^{-4}	+1.27
	58	1.602	7	2.86×10^{-4}		

[a] Ref. 6. [b] Ref. 6, "Tested only on phenol derivatives, probably valid only for these and for aniline derivatives." [c] Obtained from line of Fig. 2. [d] 1.20×10^{-3} $(1.10 \times 10^{-3}/8.83 \times 10^{-4}) = 1.50 \times 10^{-3}$. [e] Ref. 7.

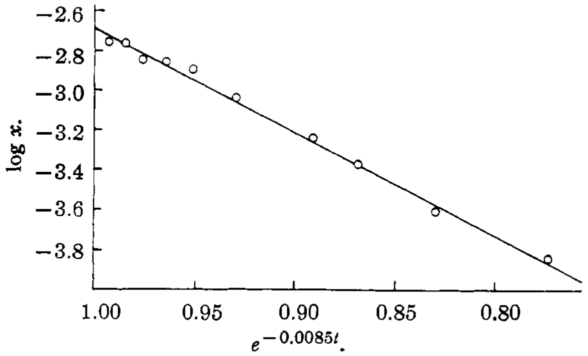


Fig. 1.—Reaction of β-propiolactone (0.0619 *M*) with *p*-toluidine (0.002 *M*) at 25° in an aqueous solution containing 0.1 *M* sodium bicarbonate, saturated with carbon dioxide.

The effect of *para*-substitution upon the rate of the aniline–propiolactone reaction is well expressed by the Hammett equation. Figure 2 shows a plot of log k_2 against the Hammett σ-constants for the several substituents. The constant used for the *p*-nitro group is the special one applicable to phenols and amines.[6] All the others are σ-constants applicable to all types of compounds. The σ-constant for the COO^- group which has been used in Fig. 2 is that of +0.16 determined[7] from three quite different types of reaction. Our series suggests the value of $\sigma = +0.31$ for the COO^- group which increases further the previously noted discord between the sign of this value determined from kinetics and from the ionization constants of terephthalic acid.

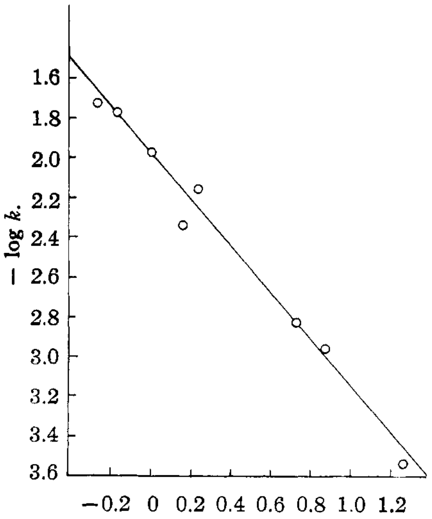


Fig. 2.—Logarithm of second-order rate constant for reaction of β-propiolactone with *para*-substituted anilines in water at 25°, plotted against the Hammett σ-constant of the substituent. The most deviant point is for COO^-, its σ-value taken as +0.16 (ref. 7).

The Hammett plot as shown in Fig. 2 yields a value of ρ for this reaction of −1.18.

Experimental

Materials.—β-Propiolactone was supplied by the B. F. Goodrich Co. and was redistilled under diminished pressure. Analysis by the thiosulfate method[4] showed it to be 99% pure. Aniline was dried over pellets of potassium hydroxide and distilled from zinc dust through a 24-in. Vigreux column. It boiled at 183°. It was stored over potassium hydroxide.

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(6) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 188.

(7) E. Berliner and L. C. Monack, THIS JOURNAL, **74**, 1574 (1952).

The *p*-substituted anilines were all Eastman Kodak white label grade and were recrystallized as follows:

Substance	Solvent for recrystn.	M.p., °C.
p-Anisidine	Ethanol–water	57
p-Toluidine	Ethanol–water	39
p-Chloroaniline	Ligroin (30–60°)	69–70
p-Aminoacetophenone	Water	104–105
p-Nitroaniline	Water	150
p-Aminobenzoic acid	Water	187–188

The *p*-toluidine obtained was the monohydrate and was used as such.

Kinetic Procedure.—The lactone was weighed accurately from a dropping bottle into a dry 100-ml. volumetric flask which was then placed in a thermostat at 25.00 ± 0.02°. In a 250-ml. glass-stoppered erlenmeyer flask a weighed amount of the amine was dissolved, warming if necessary, in about 100 ml. of water, giving a concentration of approximately 0.002 *M*. A weighed amount of sodium bicarbonate was introduced and the solution was saturated with carbon dioxide by bubbling the gas into the solution at 10°. After being brought to temperature in the thermostat, it was added to the flask containing the lactone exactly to the mark. The flask was vigorously shaken and the timer started. At measured time intervals, 5-ml. aliquots were taken and added to measured amounts of sodium hydroxide solution which were more than sufficient to react with the lactone and to neutralize the buffer. After standing for ten minutes, the samples were acidified with hydrochloric acid and transferred to 25- to 50-ml. volumetric flasks. From these 5, 10, 15 or 20 ml. was pipetted and diazotized as described below. The lactone concentrations were determined in the usual manner with thiosulfate solution, separate samples being taken and acidified with 1 *N* acetic acid before titration with iodine solution.

Diazotization.—Some slight modifications were introduced into the procedure of English. The reagents used were as follows: (1) sodium nitrite–sodium bromide solution: 3 g. of sodium nitrite, 5 g. of sodium bromide, 100 ml. of water; (2) 1.2 *N* hydrochloric acid: 10 ml. of concentrated C.P. hydrochloric acid and 90 ml. of water; (3) sulfamic acid solution: 10 g. of sulfamic acid and 100 ml. of water (the sulfamic acid was recrystallized from water according to "Inorganic Syntheses," Vol. II, p. 178); (4) sodium acetate solution: 100 g. sodium acetate trihydrate and 100 g. of water; (5) H-acid solution: 1.0 g. of H-acid and 100 g. of water, 2 ml. of concd. hydrochloric acid. The H-acid solution was found to be stable in a brown bottle for at least a week. It was prepared fresh for each determination, however. The H-acid was purified by the same procedure as given by English for the Chicago acid (1-amino-8-naphthol-2,4-disulfonic acid) used by him on account of its greater stability and despite its less intensely colored coupling products. To the amine solution (10–20 ml. diluted if necessary) in a 100-ml. volumetric flask was added 1 ml. of 1.2 *N* hydrochloric acid and the flask was immersed in an ice-bath to the neck. When the temperature was below 5° at least five minutes, 1 ml. of sodium nitrite–sodium bromide solution was added and the reaction was allowed to proceed for one minute (two minutes in the case of *p*-substituted anilines which give more stable diazonium salts).[8] Then 1 ml. of sulfamic acid solution was added and the stoppered flask shaken vigorously once or twice, then immediately re-immersed in the ice-bath. After addition of 2 ml. (for *p*-anisidine, 4 ml.) of the H-acid solution and 10 ml. of sodium acetate solution, the flask was allowed to remain in the ice-bath for at least 10 minutes. In the case of *p*-anisidine which has a very stable diazonium salt, the solution was warmed to 20° and allowed to stand for 15 minutes, omitting the standing in the ice-bath. Then 25 ml. of methanol was added, the solution diluted to 100 ml. with water, and its absorption read from a Coleman junior model 6A spectrophotometer against distilled water at the wave length of maximum absorption using 0.75-cm. round cells.

N-Phenyl-β-alanine when treated with nitrous acid gave a yellow color, the solution being transparent at 535 mμ. *p*-Nitroaniline absorbs at 420 mμ, but is transparent at 500 mμ and up. Its diazonium salt was colorless. *p*-Nitrophenyl-β-alanine was yellow but did not interfere with the determination. All the other anilines gave colorless diazotization products. Table II summarizes the optical determinations on the coupling products.

TABLE II

D is optical density; *C* is concn. of $ArNH_2$

p-Substituent in $Y\text{-}C_6H_4NH_2$	λmax,[a] mμ	Eq. for calibration curve	
–OMe	545	$D = 1.965 \times 10^4 C$	+ 0.030
–Me	540	1.82	.033
–H	535	1.66	.031
–Cl	535	1.85	.040
–COOH	535	2.05	.040
–COMe	535	2.23	.050
–NO_2	540	2.17	.035

[a] Due to the photometer scale of 5 mμ divisions and the rather wide slit, no attempt was made to get any closer peak value. The optical density readings were found to be insensitive to changes of ±2 mμ at the vicinity of the λ_{max}. For the λ_{max}. of the coupling product from *p*-aminoacetophenone (diazotization, etc.), the Beckman model DU quartz spectrophotometer gave a value of 536 mμ.

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[8] M. L. Crossley, R. H. Kienle and C. H. Benbrook, THIS JOURNAL, **62**, 1400 (1940).