

TABLE I
 BENZHYDRYL ESTERS OF HETEROANNULAR SUBSTITUTED FERROCENOIC ACIDS

Substituent	M.p., °C.	Recrystn. solvent	Yield, %	Formula	Carbon, %		Hydrogen, %	
					Calcd.	Found	Calcd.	Found
H	122-124	Hexane	75	C ₂₂ H ₂₀ O ₂ Fe	72.74	73.16	5.08	5.22
COC ₆ H ₅	133-133.5	Cyclohexane	94	C ₃₁ H ₂₄ O ₃ Fe	74.41	74.79	4.83	5.05
CH(OH)C ₆ H ₅	88-89	Hexane	95	C ₃₁ H ₂₆ O ₄ Fe	74.11	74.06	5.22	5.24
CH ₂ C ₆ H ₅	87-87.5	Cyclohexane-hexane	50	C ₃₁ H ₂₆ O ₂ Fe	76.55	76.60	5.39	5.34
						76.35		5.25
CH ₃ CO	103-104.5	Hexane	67	C ₂₆ H ₂₂ O ₃ Fe	71.25	71.02	5.06	5.08
						71.05		5.12
C ₂ H ₅	81.5	Hexane	91	C ₂₆ H ₂₄ O ₂ Fe	73.59	73.67	5.70	5.70

cally⁶⁻¹⁰; the second-order rate constants for this esterification have been correlated with Hammett σ -constants in the aromatic series^{7,9} and with pK 's of bicyclic carboxylic acids.¹⁰ In the present investigation, rate constants were measured under second-order conditions for the esterification of a series of heteroannular substituted ferrocenoic acids with diphenyldiazomethane for comparison with the corresponding acid constants of the ferrocenoic acids in an attempt to establish a linear free energy relationship in the ferrocene series.

Experimental

Substituted Ferrocenoic Acids.—The acids used were prepared according to procedures previously reported.⁴

Diphenyldiazomethane (DDM) was prepared as a stock solution in toluene from the purified hydrazone of benzophenone according to the method of Szmant and McGinnis¹¹ and assayed according to the method described by Hancock and Westmoreland.⁷ Thus it was not isolated, but the stock solution was used in the kinetic experiments.

Benzhydryl Esters of the Substituted Ferrocenoic Acids.—Samples of the product esters were prepared by allowing toluene solutions of ferrocenoic acids containing quantities of diphenyldiazomethane to stand overnight at room temperature. The toluene solutions were extracted with 10% sodium hydroxide, and the toluene was removed. The residues were purified by recrystallization and/or chromatography on Florisil. Table I lists the properties and analyses of the esters prepared. The yields were high except in the early experiments when the techniques of workup of the products were not developed sufficiently for high recovery.

Kinetics.—Toluene solutions of the substituted acids, the esters and the diphenyldiazomethane at various concentrations were scanned over the range between 400 and 700 $m\mu$ in order to confirm Beer's law observance and to determine convenient concentrations of the starting materials for the spectral analyses during the kinetic runs. The 550 $m\mu$ wave length was chosen for the analyses with a Beckman spectrophotometer, model DU. It was originally intended that the kinetics be run pseudo first order in DDM, with the acids present in tenfold excess. However, the acids and product esters absorb significantly at this wave length, and the drop in absorbance during a run under these conditions was too small for precise measurements. Accordingly, the reactions were run under second-order conditions. At least two runs were made on each acid with differing ratios of starting concentrations of the acid and DDM. The starting acid concentrations varied from $1 \times 10^{-3}M$ to $3 \times 10^{-3}M$ and the starting DDM concentrations were approximately $5 \times 10^{-3}M$ in the toluene solvent. These starting concentrations provided significant drops in absorbance during the runs. Synthetic mixtures of DDM, ferrocenoic acids and esters were prepared and analyzed spectrally to confirm

the analytical procedure. Beer's law was followed by each component singly and in mixture.

Stock solutions of the acids, 1.111 times the desired initial concentrations, were prepared. To 45 ml. of the acid stock solutions in the reaction vessels (50-ml. volumetric flasks) were added 5 ml. of stock solutions of DDM that were ten times the desired initial concentrations. The stock solutions and the reaction vessels were thermostated at 30°. Zero time was taken when half the DDM solution was delivered from the pipet. After addition of the DDM, the flasks were withdrawn from the thermostat, quickly wrapped in a towel, and shaken well to mix, and returned to the thermostat. The whole operation required but 15 sec. From time to time samples were withdrawn and placed in the spectrophotometer, thermostated at 30°, for analysis. Since in all runs the acid concentration was limiting, infinity absorbance values were calculated by measuring the absorbance of ester solutions prepared at the same concentration as the starting acids and adding the absorbance of the calculated excess of DDM.

In all experiments, except one, initial concentrations of DDM and acid were different, and second-order rate constants were calculated from the slope of plots of $\log B/A$ according to the equation¹²

$$\frac{1}{B_0 - A_0} \ln \frac{A_0 B}{B_0 A} = kt$$

where A and B are concentrations of acid and DDM, respectively, and A_0 and B_0 are initial concentrations.

In the one run where initial concentrations were the same ($A = B$), the usual second-order equation was used ($1/A = kt$).

Discussion

Figure 1 shows a typical second-order plot for the kinetic runs. All the runs showed the same typical behavior: Initially the plots were linear, but after 20 to 50% of the materials had reacted the plots

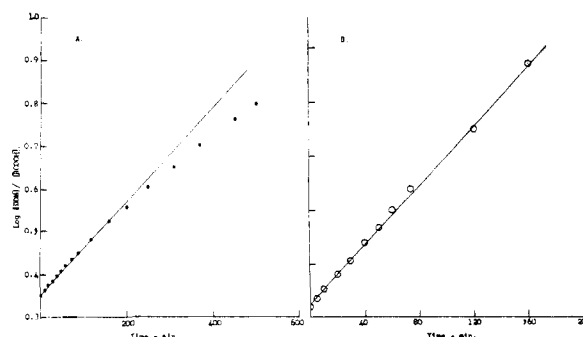


Fig. 1.—Reaction of 1'-acetyl-1'-ferrocenoic acid with diphenyldiazomethane: A, entire run; B, first 47% of reaction.

took on a curvature concave downward. Consistent rate constants could be obtained, however, by considering the initial portions of the plots, including experiments with different initial concentration

(6) J. F. Norris and W. H. Strain, *J. Am. Chem. Soc.*, **57**, 187 (1933).

(7) C. K. Hancock, R. F. Gilby, Jr., and J. S. Westmoreland, *ibid.*, **79**, 1917 (1957).

(8) A. B. Hoefelmeyer and C. K. Hancock, *ibid.*, **77**, 4746 (1955).

(9) J. D. Roberts, E. A. McElhill and R. Armstrong, *ibid.*, **71**, 2923 (1949).

(10) J. D. Roberts and W. T. Moreland, *ibid.*, **75**, 2167 (1953).

(11) H. H. Szmant and C. McGinnis, *ibid.*, **72**, 2890 (1950).

(12) S. W. Benson, "The Foundations of Chemical Kinetics," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, pp. 20-21.

TABLE II
RATE CONSTANTS FOR THE REACTION OF HETEROANNUAR SUBSTITUTED FERROCENOIC ACIDS WITH DIPHENYLDIAZOMETHANE
IN TOLUENE AT 30°

Substituent	Init. concentrations, moles/liter $\times 10^3$		k_2 , l. mole ⁻¹ min. ⁻¹	% of reacn. considered	pK of acid ⁴ in 50% EtOH
	Acid	DDM			
H	3.000	3.000	0.1027	24 37 37 35 32	6.29
	3.000	5.980	.0994		
	3.004	6.000	.1032		
	2.054	5.790	.0997		
	2.056	4.937	.1048		
COCH ₃	2.390	6.639	.9061	58 47	5.76
	2.242	4.995	.9158		
COC ₆ H ₅	3.050	4.730	.7533	52 49	5.90
	2.079	5.174	.7560		
C ₂ H ₅	2.083	6.256	.0556	29 30	6.34
	3.036	7.286	.0576		
CH ₂ C ₆ H ₅	1.829	4.254	.0593	18 17	6.25
	2.307	5.243	.0596		
CH(OH)C ₆ H ₅	1.768	5.074	10.18	33 36	5.84
	1.506	5.740	9.90		

ratios of reactants. Table II lists the constants obtained, the initial concentrations, and the percentage of reaction over which the plots were linear.

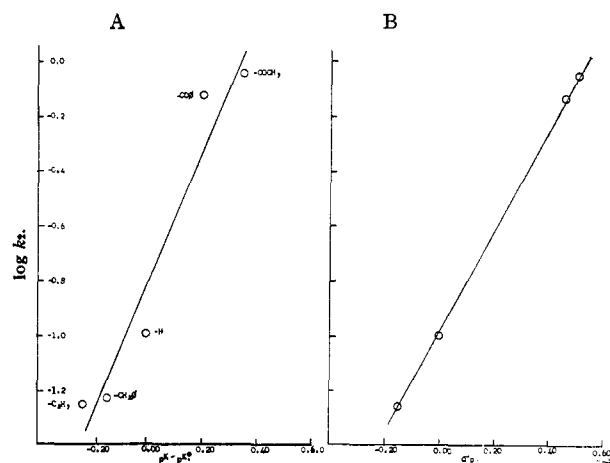


Fig. 2.

It would seem that the possible dimerization of the carboxylic acids in the toluene solvent should be taken into consideration in the kinetics of the reaction. In benzene, for example, benzoic acid is approximately 50% dimerized at $1 \times 10^{-3} M$.¹³ While the dimerization of carboxylic acids in toluene has not been reported, Norris and Strain⁶ reported the esterification of aromatic acids with DDM in toluene to give excellent second-order kinetics over several half-lives, using concentrations of acids at $10^{-2} M$, a tenfold larger concentration than that used in these experiments, which should exhibit the effect of dimerization even more than our experiments if dimerization is important. Other workers^{7,8} have converted pseudo-first-order rate constants (in DDM) to second-order constants in toluene without regard to possible dimerization and have correlated these calculated second-order constants with pK 's. These previous reports and the constancy of the present second-order rate con-

(13) F. T. Wall and F. W. Banes, *J. Am. Chem. Soc.*, **67**, 898 (1945).

stants with varying ratios of initial concentrations lends confidence to the procedures used in this work.

Table II shows that the rate constants for esterification of the substituted acids parallel their acid strengths, with the exception of the α -hydroxybenzyl substituted acid, which reacts much faster than its acid constant would indicate.

That linear free energy relationships can be applied to heteroannular substituted ferrocenoic acids is demonstrated in Fig. 2. The logarithms of the rate constants of the DDM reaction *versus* the difference in pK 's between the substituted acids and ferrocenoic acid are linear with a correlation coefficient of 0.95, indicating a "satisfactory fit."¹⁴ Only the rate constant for the α -hydroxybenzylferrocenoic acid does not fit on this plot. The success of this correlation indicates that there is no steric interaction between the carboxyl group and the substituent group in the transition state, and might imply that the heteroannular substituents prefer a conformation with the groups distal to each other during the reaction; however, it is not certain that an opposed conformation of the groups would produce significant steric effects. It should also be pointed out that in the ferrocene series, in view of the free rotation of the system, the time-average distance separation of the substituent groups may be a function of the identity of the groups; and thus the direct field effect of a given substituent on reactions occurring on the other ring, though a function of the substituent, might be variable from one reaction series to another. This is not a significant problem with rigid benzene derivatives, for which the Hammett equation was originally devised.

It is interesting to note that the correlation is even better in Fig. 2B, where the logarithms of the rate constants are plotted *versus* Hammett *para* sigma constants for the four groups whose σ -values have been reported.¹⁵ The significance of the correlation

(14) H. H. Jaffé, *Chem. Revs.*, **53**, 191 (1953).

(15) Jaffé's¹⁴ *para* sigma constants were used. A more recent compilation of σ -constants is available (D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, **23**, 420 (1958)), but Jaffé's values were used since McDaniel and Brown did not list a value for the *p*-benzoyl group, and, of the groups used, only the acetyl group showed a slight difference in the

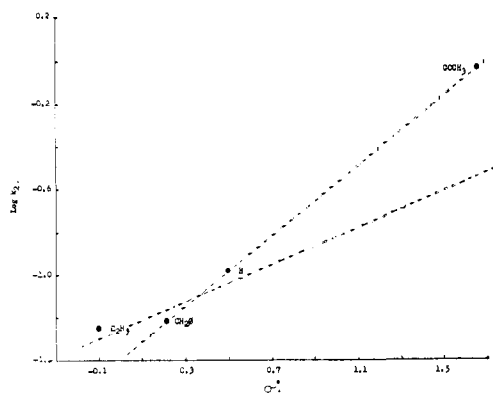


Fig. 3.

with the *para* sigma constants cannot be fully determined, since a reasonably good correlation is also obtained by plotting the data *versus meta* sigma constants as well; but this latter plot suffers from the fact that *meta* sigma constants are available for but three of the substituents used, namely H, C₂H₅ and COCH₃. While, to a first approximation, a better correlation with *para* sigma's, as opposed to *meta* sigma's, would suggest resonance contributions of the substituent groups across the rings, a much better criterion for resonance contributions is the comparison of rate correlations with Hammett *para* constants and Taft's polar sigma constants.¹⁶ Indeed, these rate constants correlate better with Hammett sigmas than with Taft sigmas. Figure 3 shows the greater deviations from linearity for polar sigma's.

Similar conclusions can be drawn from the studies reported by Kuwana, *et al.*¹⁷ These workers measured chronopotentiometric quarter wave potentials, $E_{1/4}$, for a series of substituted ferrocenes, and correlated the potentials with Taft σ -constants, explaining sharp deviations for acetylferrocene and diacetylferrocene from linearity as an effect of resonance. Retreatment of their data using Hammett σ -constants, using data of Brown and McDaniel (see ref. 15), shows that either *para* or *meta* sigma's give much better correlations than that reported with Taft's constants, again suggesting that resonance contributions of substituents is important in the reactions at the iron atom of ferrocene.

For homoannular substituted derivatives, however, Rinehart¹⁸ has suggested that it is the inductive effect of substituents that is important.

two compilations. This difference is hardly perceptible on the scale used in Fig. 2B.

(16) R. W. Taft, Jr., in M. S. Newman, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, pp. 578-580 and 594-597.

(17) T. Kuwana, D. E. Bublitz and G. Hoh, *J. Am. Chem. Soc.*, **82**, 5811 (1960).

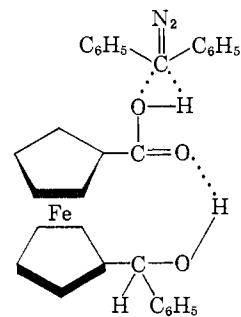


Fig. 4.

The very large reaction rate of the α -hydroxybenzyl substituted ferrocenoic acid cannot be explained on grounds of electronic effects alone. Although σ -constants are not available for this group, Kuwana found the quarter wave potential of α -hydroxybenzylferrocene to lie between ferrocene and benzoylferrocene, but quite close to that of ferrocene itself, indicating only a slight electron-withdrawing effect for this group. The failure to fit the rate constant of the α -hydroxybenzylferrocenoic acid in Fig. 2, due to its much faster rate, is reminiscent of the much larger rate of reaction of salicylic acid⁶ with DDM in toluene than its acid constant would predict. While *o*-chloro- and *o*-bromobenzoic acids are both slightly stronger acids than salicylic acid¹⁹ and react with DDM in toluene 16.5 and 21.8 times faster than benzoic acid, respectively, salicylic acid reacts 300 times as fast as benzoic acid; *o*-methoxybenzoic acid reacts only 0.044 times as fast as benzoic acid.⁶ Hancock and Westmoreland⁷ have presented evidence that the attack of DDM on carboxylic acids occurs at the O-H bond. The great reactivity of salicylic acid and the α -hydroxybenzylferrocenoic acid might be explained in terms of intramolecular hydrogen bonding (Fig. 4) between the substituent OH groups and the carbonyl oxygen of the carboxyl groups, freezing the rotation of the carboxyl group, and speeding the reaction with DDM. This should be reflected in a more positive entropy of activation than the non-hydrogen bonded substrates exhibit. Work is underway in this Laboratory to measure entropies of these reactions and dimerization constants of these acids in non-polar solvents.

Acknowledgment.—The authors wish to thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for a grant in support of this work.

(18) K. L. Rinehart, Jr., K. L. Motz and S. Moon, *ibid.*, **79**, 2749 (1957).

(19) E. A. Braude and F. C. Nachod, "Determination of Organic Structures by Physical Methods," Academic Press, Inc., New York, N. Y., 1955, p. 588.