Rates of Addition of Styrene to 9-Substituted Acridizinium Ions

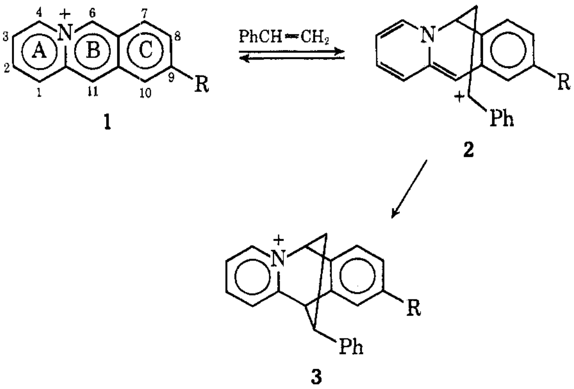
I. JOHN WESTERMAN[1] AND CHARLES K. BRADSHER*

Department of Chemistry, Duke University, Durham, North Carolina 27706

Received August 10, 1970

The rates of cycloaddition of styrene with acridizinium perchlorate and with nine 9-substituted acridizinium derivatives 1 have been determined. A well-correlated Hammett plot was obtained and interpreted as being consistent with a two-step mechanism.

Earlier evidence showed that the addition of ethylene derivatives to the acridizinium ion 1 occurred with "inverse electron demand."[2,3] It also suggested that the reaction does not fall into the classical pattern of a concerted (but two stage) reaction[4] but has reached the limiting case in which two discrete steps are involved and configuration may not be retained.[5]



The first step in the proposed mechanism involves a nucleophilic attack by the alkene on the electron-deficient 6 position of the acridizinium ion (1). Presumably factors influencing the electron deficiency at position 6 would also influence the rates. Frost and Saylor[6] have shown that the polarographic reduction of the acridizinium ion (presumably at position 6) occurs at lower negative potential when electron-attracting groups are present in ring C.

The purpose of the present work was to measure the rate of addition of styrene to acridizinium salts having substituents at position 9. This orientation was selected because resonance effects could be readily transmitted to position 6 while steric effects would be minimal. Fortunately the nine-substituted acridizinium salts required had been synthesized previously in this laboratory.[7] As in previous studies[3,5] reaction rates were followed by measuring the disappearance of the longer wavelength absorptions in the acridizinium spectrum rather than by isolation of addition products.

Experimental Section

Rate Determinations.—Rate determinations were carried out by a slight modification of that described earlier.[3] Stock solutions were made in dimethyl sulfoxide.[8] Due to the rapidity with which some salts reacted, samples slightly large than 0.1 ml were withdrawn rapidly using disposable pipets fitted with eye-dropper bulbs, the resulting sample was cooled rapidly in an ice bath, and then exactly 100 μl of cool liquid was withdrawn carefully with a microsyringe and diluted to 50 ml immediately with either water or 95% ethanol. The concentration of the acridizinium salt remaining was determined by measuring the absorbance (A) at the wavelength of maximum absorption beyond 300 mμ. Good pseudo-first-order plots were obtained, and in nearly all cases rates were reproducible to within 5%. An average trial followed the rate over 1–2 half-lives and, as judged by the linearity of the plots, pseudo-first-order conditions were maintained. The rate reported is a simple average of the trials.

9-Substituted Acridizinium Perchlorates (1).—The salts, with the exception of the 9-isopropyl, were prepared by methods published earlier,[7] and the observed and literature melting points are recorded in Table I.

9-Isopropylacridizinium Perchlorate [1, R = $(Me)_2CH$].[9]—The quaternization of 6.04 g of 2-(1,3-dioxolan-2-yl)pyridine[10] with 8.52 g of *p*-isopropylbenzyl bromide in 4 ml of tetramethylene sulfone was carried out in 3 days. Addition of ethyl acetate precipitated an oil which was dissolved in 40 ml of 48% hydrobromic acid and heated on a steam bath for 6 hr. Removal of the acid under reduced pressure left an oil which crystallized on addition of 35% perchloric acid. The salt (51% yield) was crystallized as pale yellow needles from methanol–ethyl acetate, mp 144–146°.

Anal. Calcd for $C_{16}H_{16}ClNO_4$: C, 59.72; H, 5.01; N, 4.35. Found: C, 59.93; H, 5.11; N, 4.65.

Results

As may be seen in Table I, changes in the substituent at position 9 have a significant effect (up to 50-fold) on the rate of addition. The compounds when tabulated in the order of their increasing Hammett substituent constants are approximately in the order of their increasing rate of reaction. A Hammett plot using the available primary σ values of the McDaniels and Brown[11] as well as the recommended[11,12] consistent treatment of the data is shown in Figure 1.

An analysis of the significance of the plot was made as recommended by Jaffé,[13] and in Table II will be seen the results obtained when only the seven primary σ values were used and when the three secondary values were used in addition. The standard deviation of ρ is less than 4% of the total value of ρ, an excellent agreement.

Discussion

Both the sign and magnitude of the reaction constant (ρ) are unusual for a 4 + 2 cycloaddition reaction.

---

(1) National Science Foundation Trainee, 1967–1969.

(2) D. L. Fields, T. H. Regan, and J. C. Dignan, *J. Org. Chem.*, **33**, 390 (1968).

(3) C. K. Bradsher and J. A. Stone, *ibid.*, **33**, 519 (1968).

(4) R. B. Woodward and T. J. Katz, *Tetrahedron*, **5**, 70 (1959).

(5) C. K. Bradsher and J. A. Stone, *J. Org. Chem.*, **34**, 1700 (1969).

(6) J. Frost and J. H. Saylor, *Recl. Trav. Chem. Pays-Bas*, **83**, 340 (1964).

(7) (a) C. K. Bradsher and L. E. Beavers, *J. Amer. Chem. Soc.*, **77**, 4812 (1955); (b) C. K. Bradsher and J. C. Parham, *J. Heterocycl. Chem.*, **1**, 30 (1964); (c) C. K. Bradsher, J. P. Shearer, and J. C. Parham, *J. Chem. Eng. Data*, **10**, 180 (1965); (d) J. C. Parham, Ph.D. Dissertation, Duke University, 1963.

(8) An obvious typographical error in the published directions: ". . . placed in a 2-ml volumetric flask . . . was made up to 20 ml." This should read ". . . to 2 ml."

(9) Based in part upon the work of J. C. Parham, ref 7d.

(10) C. K. Bradsher and J. C. Parham, *J. Org. Chem.*, **28**, 83 (1963).

(11) D. H. McDaniel and H. C. Brown, *ibid.*, **23**, 420 (1958).

(12) J. F. Bunnett, "Techniques of Organic Chemistry," part I, Vol. VIII, Interscience, New York, N. Y., 1961, pp 177–278.

(13) H. H. Jaffé, *Chem. Rev.*, **53**, 191 (1953).

TABLE I

RATES OF ADDITION OF STYRENES TO 9-SUBSTITUTED ACRIDIZINIUM PERCHLORATES (1) AT 65°

R	Mp, °C	Lit. mp, °C	Lit. ref	n^c	$k \times 10^{-3}$ min$^{-1\,d}$	$\sigma_p{}^e$
Me	196–198	203–205	7a	4	2.0 ± 0.1	−0.170 ± 0.02[f]
CH(Me)$_2$	144–146	145–146	7d	3	2.8 ± 0.1	−0.151 ± 0.02[f]
H		205–206	7a	4	5.0 ± 0.2	0.000
F	173–178	177–178	7c	4	5.4 ± 0.2	0.062 ± 0.02[f]
I	258–260	257–258	7c	5	10.6 ± 0.6	0.18 ± 0.01[g]
Cl	223–224	224.5–226	7c	5	10.1 ± 0.5	0.227 ± 0.02[f]
Br	216–218	218–220	7c	5	11.2 ± 0.8	0.232 ± 0.02[f]
COOH	270–272[a]	250–253[b]	7b	3	18.1 ± 0.7	0.406 ± 0.04[h]
COOMe	233–239	236–237	7b	2	24.7 ± 1.0	0.463 ± 0.02[h]
NO$_2$	241–242[a]	240–242[a]	7b	4	105 ± 5	0.778 ± 0.02[f]

[a] With decomposition. [b] It is believed that the earlier report may have been a typographical error since the methyl esters melt in the same general range. [c] Number of trials. [d] Range includes the standard deviation. [e] Para substituent constants. [f] Primary σ values (ref 11). [g] Secondary σ value (ref 11). [h] Secondary σ value: H. van Bekkum, P. E. Verkade, and B. M. Wepster, *Recl. Trav. Chim. Pays-Bas*, **78**, 815 (1959).

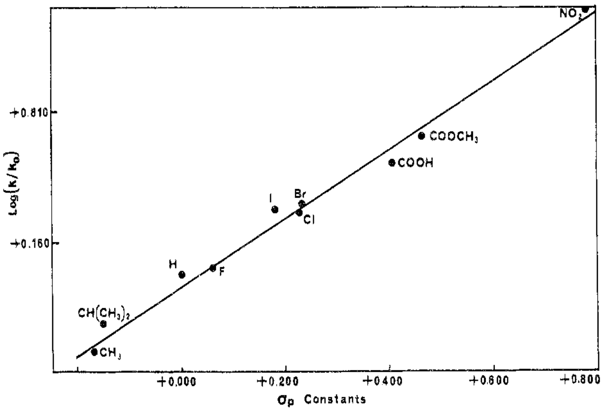


Figure 1.—Hammett plot of reaction rate data from Table I.

TABLE II

CONSTANTS AND STATISTICAL VALUES CALCULATED FOR THE HAMMETT PLOT

Calculated quantity	—Substituents considered— Primary only	All
ρ, reaction constant	1.74	1.69
Sρ, standard deviation of ρ	0.06	0.07
S, standard deviation from regression line	0.05	0.06
γ, correlation factor	0.997	0.994
Log k_0	0.650	0.650

The positive sign further substantiates the inverse electron demand character of the addition of styrene to the acridizinium ion, while the magnitude of the reaction constant implies that the addition is more ionic and less synchronous than in the conventional Diels–Alder reaction. Concerted reactions usually fail to give a significant Hammett plot and very few Diels–Alder reactions have been so represented. For most of this small group of additions, low and uncertain values of ρ have been recorded.[14]

The two-step mechanism proposed for the cycloaddition reaction gains additional support from the present work. The 9 position is not symmetrically located with respect to the 6 and 11 (meso) positions of the acridizinium ion, but is para to position 6 and meta to position 11. Significantly, the Hammett para substituent constants gave an excellent correlation, whereas the meta constants failed to give a significant plot. This would seem to imply that initially the 6 position is either the exclusive or principal bonding site, and if the reaction is in any way concerted it must be approaching the limiting case in which the cycloaddition occurs in two separate steps.[15]

Registry No.—**1** (R = Me), 27705-56-2; **1** [R = CH(Me)$_2$], 27705-57-3; **1** (R = H), 18507-95-4; **1** (R = F), 1695-36-9; **1** (R = I), 1695-42-7; **1** (R = Cl), 1695-37-0; **1** (R = Br), 1695-39-2; **1** (R = COOH) 27705-63-1; **1** (R = COOMe), 27705-64-2; **1** (R = NO$_2$), 27755-38-0; styrene, 100-42-5.

[14] P. R. Wells, *Chem. Rev.*, **63**, 171 (1963).

[15] The authors are indebted to Professor N. A. Porter for helpful discussions concerning this problem.