

# Acid-Base Properties of Radical Anions of Cis and Trans Isomers. I. Fumarates and Maleates

E. Hayon\* and M. Simic

*Contribution from the Pioneering Research Laboratory,  
U. S. Army Natick Laboratories, Natick, Massachusetts,  
and the Zoology Department, University of Texas, Austin, Texas.  
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**Abstract:** The radical anions of dimethyl fumarate (DMF) and dimethyl maleate (DMM) have been produced in aqueous solutions directly by reaction with solvated electrons, *e.g.*,  $e_{aq}^- + DMF \rightarrow \cdot DMF^-$ , or by electron transfer from an organic free radical, *e.g.*,  $(CH_3)_2\dot{C}OH + DMF \rightarrow \cdot DMF^- + CH_3COCH_3 + H^+$ . The  $\cdot DMF^-$  and  $\cdot DMM^-$  radicals have absorption maxima at 335 and 350 nm, extinction coefficients  $2.2 \times 10^4$  and  $1.45 \times 10^4 M^{-1} cm^{-1}$ , and decay constants  $2k = 2.9 \times 10^8$  and  $2.5 \times 10^8 M^{-1} sec^{-1}$ , respectively. The spectral characteristics of the radical anions are compared with those of the parent compounds in the ground state. In acidic solutions, the transient optical spectra are blue-shifted, producing the characteristic spectral shift of the protonated radicals  $\cdot DMF^- - H^+$  and  $\cdot DMM^- - H^+$ , with maxima at 320 and 342 nm and extinction coefficients of  $2.0 \times 10^4$  and  $1.25 \times 10^4 M^{-1} cm^{-1}$ , respectively. The acid-base properties of these radicals were studied, and a  $pK_a$  of  $2.8 \pm 0.1$  for the trans radical compared with  $4.8 \pm 0.1$  for the cis radical was observed. The strong resonance of these radicals leading to various hybrid structures is somewhat reduced in monomethyl fumarate (MMF), giving a  $pK_a = 11.5 \pm 0.2$  for the dissociation of  $\cdot MMF^- - H^+$  ( $\lambda_{max}$  335 nm,  $\epsilon$   $1.5 \times 10^4 M^{-1} cm^{-1}$ ) to the radical anion  $\cdot MMF^-$  ( $\lambda_{max}$  345 nm,  $\epsilon$   $1.4 \times 10^4 M^{-1} cm^{-1}$ ). The radical anions of fumaric (FH<sub>2</sub>) and maleic (MH<sub>2</sub>) acids have different absorption spectra and dissociation constants which are also dependent on the state of protonation of the carboxyl groups. For the dianion F<sup>2-</sup>, the radical  $\cdot F^{2-} - H^+$  ( $\lambda_{max}$  333 nm,  $\epsilon$   $2.7 \times 10^4 M^{-1} cm^{-1}$ ) has a  $pK_a \sim 10.9$  forming the anion  $\cdot F^{3-}$  ( $\lambda_{max}$  340 nm and  $\epsilon$   $2.6 \times 10^4 M^{-1} cm^{-1}$ ). For M<sup>2-</sup>, the radical  $\cdot M^{2-} - H^+$  has a maximum at 348 nm and  $\epsilon$   $1.7 \times 10^4 M^{-1} cm^{-1}$ , but no acid-base dissociation could be observed up to pH  $\sim 13.5$ . These results are discussed and possible implications to electron transfer reactions and cis-trans isomerization of biological systems are presented.

The nature of chemical reactions, chemical equilibria, and the rates of reaction of geometrical isomers are known<sup>1</sup> to be affected by spatial relationships. Differences in the physical properties<sup>1,2</sup> of cis and trans isomers of olefinic compounds, such as dipole moments, acid strengths, ultraviolet spectra, thermochemical and thermodynamic stability, have been observed. The interconversion of geometrical isomers can be brought about by heating, by acid- and base-catalyzed reactions, by radical addition, by photoinduced and radiation-induced isomerization, and by other methods. The energy levels of the excited states of cis and trans isomers have also been shown to be different in a number of cases.<sup>3</sup>

One property of the geometrical isomers of olefins and conjugated dienes which has received little attention is the nature and the rate constants of their reaction with free radicals, with solvated electrons, and with compounds which function as electron donors. This is probably of considerable importance biologically since many biomolecules have unsaturated linkages and undergo reactions with electron donors and electron acceptors, *e.g.*, the biochemistry of visual processes<sup>4</sup> and the isomerization of unsaturated fatty acids.<sup>2b</sup> In this work, the transient optical absorption spectra of the radical anions of cis and trans isomers of unsaturated

compounds were observed using the technique of pulse radiolysis, and the acid-base properties of these intermediates were examined. The radical anions were produced by reaction with hydrated electrons as well as by electron transfer from some organic radicals. Dimethyl fumarate, fumaric acid, and maleic acid were chosen in this first study since these are simple molecules and are commercially available in pure form.

The absorption spectra at 77°K of the electron adducts of some cis and trans isomers have been reported<sup>5</sup> using the matrix isolation method. Under these conditions the radical anions are long lived. The spectra of the electron adducts of dimethyl fumarate and dimethyl maleate have been obtained<sup>6</sup> in 2-methyltetrahydrofuran glasses at 77°K, and spectral shifts of  $\sim 10$ – $15$  nm were observed between the two isomers. Similar spectral differences have been observed<sup>6,7</sup> between *cis*- and *trans*-stilbene. On illumination of the radical anions with uv light, *cis*  $\rightarrow$  *trans* isomerization of the radicals takes place,<sup>6,7</sup> contrasting the predominant *trans*  $\rightarrow$  *cis* photoisomerization of the parent compounds.<sup>2</sup> The esr spectra of some cis and trans electron adducts have also been observed,<sup>6,8,9</sup> giving an insight into the distribution of the excess negative charge. Most of these experiments were conducted in aprotic solvents and consequently very little informa-

(1) See, for example, J. Hine, "Physical Organic Chemistry," 3rd ed, McGraw-Hill, New York, N. Y., 1971; E. S. Gould, Ed., "Mechanism and Structure in Organic Chemistry," Holt, Rinehart and Winston, New York, N. Y., 1959.

(2) (a) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962; (b) S. Seltzer, in "The Enzymes," Vol. VI, P. D. Boyer, Ed., Academic Press, New York, N. Y., 1972, p 381.

(3) R. B. Cundall, *Progr. React. Kinet.*, **2**, 165 (1964).

(4) C. D. B. Bridges, *Compr. Biochem.*, **27**, 31 (1967).

(5) W. H. Hamill, "Radical Ions," E. T. Kaiser and L. Kevan, Ed., Interscience, New York, N. Y., 1968.

(6) A. Torikai, T. Suzuki, T. Miyazaki, K. Fueki, and Z. Kuri, *J. Phys. Chem.*, **75**, 482 (1971).

(7) T. Shida and W. H. Hamill, *J. Chem. Phys.*, **44**, 4372 (1966).

(8) N. H. Anderson, A. J. Dobbs, D. J. Edge, R. O. C. Norman, and P. R. West, *J. Chem. Soc. B*, 1004 (1971).

(9) A. R. Buick, T. J. Kemp, and T. J. Stone, *J. Phys. Chem.*, **74**, 3439 (1970).

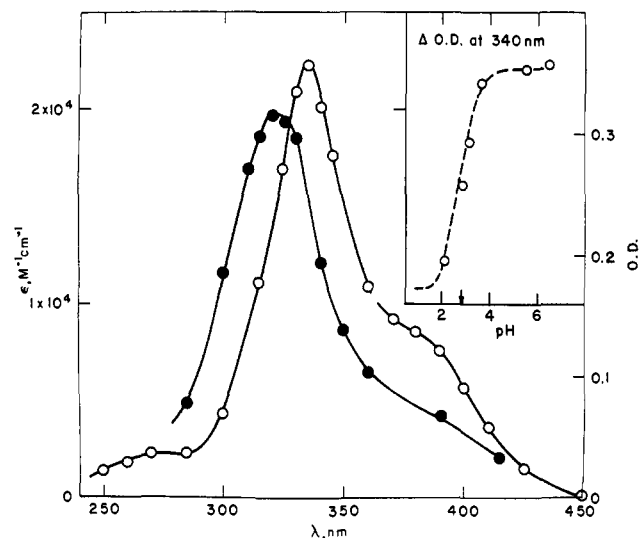


Figure 1. Transient absorption spectra of the radical anion of dimethyl fumarate,  $\cdot\text{DMF}^-$  (O), and its protonated form,  $\cdot\text{DMF}^- - \text{H}^+$  (●). Insert: change in absorbance at 340 nm with pH. Spectra obtained from the reaction of  $e_{\text{aq}}^-$  with  $10^{-3} M$  DMF,  $1.0 M$  *tert*-BuOH, pH 6.2 and  $10^{-2} M$  DMF,  $1.5 M$  *tert*-BuOH at pH 2.1. OD corrected for competition between DMF and  $\text{H}_3\text{O}^+$  for  $e_{\text{aq}}^-$ . Dose  $\sim 2.7$  krad/pulse.

tion is available concerning the acid-base properties of the radical anions.

### Experimental Section

The pulse radiolysis technique used has already been described.<sup>10,11</sup> In order to minimize the photoisomerization of the fumarates and maleates studied in aqueous solution by the monitoring light from a pulsed 450-W xenon lamp, a synchronized shutter was used which opened for  $\sim 5$ – $10$  msec only. In addition, appropriate glass filters were used.

Optical cells with a light path of 2 cm were used, and the absorbance of the transient species formed was measured at  $\sim 0.2$   $\mu\text{sec}$  after the 30 nsec electron pulse. Solutions were buffered using perchloric acid, potassium hydroxide, phosphates (1–3 mM), and tetraborate (1–2 mM). The pH was adjusted just previous to carrying out the pulse radiolysis experiment.

The chemicals used were supplied by Eastman (dimethyl fumarate and maleic acid), Baker (dimethyl maleate), Aldrich (fumaric acid), and K and K (monomethyl fumarate).

Dosimetry was carried out<sup>10</sup> using a KCNS solution. The extinction coefficients presented here were calculated based on  $G(e_{\text{aq}}^-) = G(\text{OH}) = 2.8$  and  $G(\text{H}) = 0.55$ , produced from the radiolysis of water,  $\text{H}_2\text{O} \xrightarrow{\text{radiolysis}} e_{\text{aq}}^-, \text{OH}, \text{H}, \text{H}_2, \text{and } \text{H}_2\text{O}_2$ .

### Results

In order to achieve optimal conditions for the formation of the radical anions of the fumarates and maleates and derive correct extinction coefficients, the rates of the reaction of hydrated electrons with the *cis* and *trans* derivatives were determined. This was obtained by following the decay kinetics of  $e_{\text{aq}}^-$  at 700 nm in the presence of different concentrations of the isomers. From the pseudo-first-order rates, the values of  $k(e_{\text{aq}}^- + \text{S})$  were derived. These rates are given in Table I. Because of the relatively low  $pK_a$  values of fumaric acid, maleic acid, and the monoanion of fumaric acid the rates of  $e_{\text{aq}}^-$  with these compounds could not be determined due to the competition with the reaction  $e_{\text{aq}}^- + \text{H}^+ \rightarrow \text{H}$  in acidic solutions.

The transient spectra of the radical anions and of the

(10) M. Simic, P. Neta, and E. Hayon, *J. Phys. Chem.*, **73**, 3794 (1969).

(11) J. P. Keene, E. D. Black, and E. Hayon, *Rev. Sci. Instrum.*, **40**, 1199 (1969).

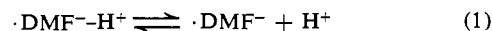
Table I. Absolute Rate Constants for the Reaction of  $e_{\text{aq}}^-$  and H Atoms with Fumaric and Maleic Acids and Their Methyl Esters in Aqueous Solution

Solute	$k(e_{\text{aq}}^- + \text{S}), M^{-1} \text{sec}^{-1}$ <sup>a</sup>	$k(\text{H} + \text{S}), M^{-1} \text{sec}^{-1}$ <sup>d</sup>
Fumaric acid, $\text{FH}_2$		$7.0 \times 10^9$
Fumaric acid dianion, $\text{F}_2^-$	$7.5 \times 10^9$ <sup>b</sup>	
Dimethyl fumarate, DMF	$3.3 \times 10^{10}$	$9.0 \times 10^9$
Maleic acid monoanion, $\text{MH}^-$	$1.8 \times 10^{10}$ <sup>c</sup>	
Maleic acid dianion, $\text{M}^{2-}$	$1.6 \times 10^9$	
Monomethyl fumarate $\text{MMF}^-$	$1.3 \times 10^{10}$	
Dimethyl maleate, DMM	$3.2 \times 10^{10}$	
Maleic acid, $\text{MH}_2$		$8.0 \times 10^9$

<sup>a</sup> Determined in the presence of  $\sim 0.5 M$  *tert*-BuOH; values good to  $\pm 10\%$ . <sup>b</sup> From ref 12. <sup>c</sup> Calculated from the experimental value of  $1.45 \times 10^{10} M^{-1} \text{sec}^{-1}$  determined at pH 5.77. <sup>d</sup> Determined in the presence of  $\sim 1.0 M$  *tert*-BuOH at pH 0.7.

H atom adducts to the compounds studied were obtained in the presence of  $1.0 M$  *tert*-butyl alcohol, which removes the OH radicals (produced from the radiolysis of water) and gives *tert*-butyl alcohol radicals which do not absorb<sup>10</sup> above  $\sim 280$  nm. Furthermore, *tert*-butyl alcohol radicals do not give rise to the transient optical absorptions observed. This was shown on saturation of the solution with  $\text{N}_2\text{O}$ , an effective  $e_{\text{aq}}^-$  scavenger [ $k(e_{\text{aq}}^- + \text{N}_2\text{O} \rightarrow \text{OH} + \text{N}_2 + \text{OH}^-) = 6.5 \times 10^9 M^{-1} \text{sec}^{-1}$ , ref 12], when the transient absorption of the radical anions disappeared.

The spectrum produced from the reaction of dimethyl fumarate (DMF) with  $e_{\text{aq}}^-$  is shown in Figure 1. The transient absorption was found to depend upon the pH of the solution. At lower pH values the electron adducts are protonated, with the rate of protonation increasing with increase in the  $[\text{H}^+]$ . On monitoring at a fixed wavelength the change in absorbance with pH, a "titration type" curve is obtained from which the dissociation constant of the equilibrium



was obtained,  $pK_a = 2.8 \pm 0.1$  (see also below). In this case, because of the low  $pK_a$  of the  $\cdot\text{DMF}^- - \text{H}^+$  radical, it was necessary to determine the spectrum of  $\cdot\text{DMF}^- - \text{H}^+$  at pH  $\sim 2.1$  where a considerable fraction of  $e_{\text{aq}}^-$  react with  $\text{H}^+$  to form H atoms



with  $k_2 = 2.3 \times 10^{10} M^{-1} \text{sec}^{-1}$ .<sup>12</sup> These in turn give H atom adducts



The extinction coefficient of the  $\cdot\text{DMF}^- - \text{H}^+$  radical was derived after correction for the competition between reactions 2 and 3



with  $k_3 = 3.3 \times 10^{10} M^{-1} \text{sec}^{-1}$ . The absorption maxima and extinction coefficients of  $\cdot\text{DMF}^-$  and  $\cdot\text{DMF}^- - \text{H}^+$  are given in Table II.

Organic free radicals were found<sup>13,14</sup> to react fast

(12) M. Anbar and P. Neta, *J. Appl. Radiat. Isotope*, **18**, 493 (1967).

(13) M. Simic and E. Hayon, *Int. J. Radiat. Biol.*, **20**, 589 (1971).

(14) E. Hayon and M. Simic, *Radiat. Res.*, **50**, 464 (1972)

**Table II.** Absorption Maxima, Extinction Coefficients, Decay Kinetics, and Dissociation Constants of the Electron Adducts to the Cis and Trans Isomers of Fumarate and Maleate

Solute	Radical anion				Radical				pK <sub>a</sub> <sup>S</sup>	pK <sub>a</sub> <sup>R</sup>
	Form	λ <sub>max</sub> , nm	ε, M <sup>-1</sup> cm <sup>-1</sup>	2k, M <sup>-1</sup> sec <sup>-1</sup>	Form	λ <sub>max</sub> , nm	ε, M <sup>-1</sup> cm <sup>-1</sup>	2k, M <sup>-1</sup> sec <sup>-1</sup>		
Dimethyl fumarate, DMF	·DMF <sup>-</sup>	335	2.2 × 10 <sup>4</sup>	2.9 × 10 <sup>8</sup>	·DMF <sup>-</sup> -H <sup>+</sup>	320	2.0 × 10 <sup>4</sup>	7.0 × 10 <sup>8</sup>	2.8	
Monomethyl fumarate, MMF <sup>-</sup>	·MMF <sup>2-</sup>	345	1.4 × 10 <sup>4</sup>		·MMF <sup>-</sup> -H <sup>+</sup>	335	1.5 × 10 <sup>4</sup>		11.5	
Dimethyl maleate, DMM	·DMM <sup>-</sup>	350	1.45 × 10 <sup>4</sup>	2.5 × 10 <sup>8</sup>	·DMM <sup>-</sup> -H <sup>+</sup>	342	1.25 × 10 <sup>4</sup>		4.8	
Fumaric acid, FH <sub>2</sub>	·FH <sub>2</sub> <sup>-</sup>	330	~2.6 × 10 <sup>4</sup>	~4 × 10 <sup>8</sup>	·FH <sub>2</sub> <sup>-</sup> -H <sup>+</sup>	320		~2 × 10 <sup>9</sup>	~3	
	·FH <sup>-</sup>	333	2.7 × 10 <sup>4</sup>		·FH <sup>-</sup> -H <sup>+</sup>	330	~2.6 × 10 <sup>4</sup>		3.02	
	·F <sup>2-</sup>	340	2.6 × 10 <sup>4</sup>	2.2 × 10 <sup>7</sup>	·F <sup>2-</sup> -H <sup>+</sup>	333	2.7 × 10 <sup>4</sup>		4.38	
Maleic acid, MH <sub>2</sub>	·MH <sub>2</sub> <sup>-</sup>	248	1.7 × 10 <sup>4</sup>		·MH <sub>2</sub> <sup>-</sup> -H <sup>+</sup>	342		~3 × 10 <sup>9</sup>	~4	
	·MH <sup>-</sup>	348	1.7 × 10 <sup>4</sup>		·MH <sup>-</sup> -H <sup>+</sup>	348	1.7 × 10 <sup>4</sup>	1.0 × 10 <sup>9</sup>	1.92	
	·M <sup>2-</sup>			~1.0 × 10 <sup>6</sup>	·M <sup>2-</sup> -H <sup>+</sup>	348	1.7 × 10 <sup>4</sup>	~1.0 × 10 <sup>6</sup>	6.23	
N-Ethylmaleamic acid <sup>a</sup> , NEMA <sup>-</sup>	·NEMA <sup>2-</sup>	360	1.5 × 10 <sup>4</sup>		·NEMA <sup>2-</sup> -H <sup>+</sup>	360	1.5 × 10 <sup>4</sup>	5.0 × 10 <sup>8</sup>	10.4	
N-Ethylmaleimide <sup>a</sup> , NEM	·NEM <sup>-</sup>	270	1.6 × 10 <sup>4</sup>	~3.0 × 10 <sup>9</sup>	·NEM <sup>-</sup> -H <sup>+</sup>				2.85	
		335	8 × 10 <sup>3</sup>							
		425	2.3 × 10 <sup>3</sup>							

<sup>a</sup> From ref 13 and 14.**Table III.** Efficiency and Rate Constants for Electron Transfer from ·CO<sub>2</sub><sup>-</sup> and (CH<sub>3</sub>)<sub>2</sub>ĊOH Radicals to Cis and Trans Isomers of Fumarate and Maleate

Solute	Form	·CO <sub>2</sub> <sup>-</sup>			(CH <sub>3</sub> ) <sub>2</sub> ĊOH		
		pH	%	k, M <sup>-1</sup> sec <sup>-1</sup>	pH	%	k, M <sup>-1</sup> sec <sup>-1</sup>
Dimethyl fumarate	DMF	7.0	>80	9.0 × 10 <sup>8</sup>	7.0	12	4.0 × 10 <sup>9</sup>
Fumaric acid	FH <sub>2</sub>				0.5	14	9.0 × 10 <sup>8</sup>
	FH <sup>-</sup>	4.0	>30	2.0 × 10 <sup>7</sup>			
	F <sup>2-</sup>	10.0	0		9.0	0	
Maleic acid	MH <sub>2</sub>				0.5	18	2.2 × 10 <sup>8</sup>
	MH <sup>-</sup>	5.2	≥65	1.1 × 10 <sup>8</sup>			
	M <sup>2-</sup>	10.5	0		10.0	0	

with *N*-ethylmaleimide (NEM) partly reducing it and producing the radical anion ·NEM<sup>-</sup>, and partly adding to the carbon-carbon double bond. The acetone ketyl radical (CH<sub>3</sub>)<sub>2</sub>ĊOH was used as a reducing agent for DMF, and was produced from the pulse radiolysis of 1.0 *M* aqueous isopropyl alcohol, in the absence of oxygen (Ar, 1 atm).



On reaction of the acetone ketyl radical with DMF, transient spectra were obtained (Figure 2) which were pH dependent and resembled the spectra produced from the reaction of e<sub>aq</sub><sup>-</sup> with DMF. A similar "titration curve" was obtained from which a pK<sub>a</sub> = 2.8 ± 0.1 was derived, in good agreement with the pK<sub>a</sub> value of ·DMF<sup>-</sup>-H<sup>+</sup> determined by reaction with e<sub>aq</sub><sup>-</sup>. Since the (CH<sub>3</sub>)<sub>2</sub>ĊOH radical also adds to the double bond of DMF (see Table III), the transient spectrum of the adduct is superimposed in Figure 2 on that of ·DMF<sup>-</sup> and ·DMF<sup>-</sup>-H<sup>+</sup>. The spectrum of the adduct is probably very similar (see below and ref 13 and 14) to that of the H atom adduct and therefore has a relatively very low extinction coefficient. The electron transfer reaction from (CH<sub>3</sub>)<sub>2</sub>ĊOH to DMF is only ~12% of the total free radical yield. Nevertheless, the ratio of reduction to addition is not expected to be different in the pH range 1-7, because both the radical and the parent compound do not undergo acid-base reactions, and the pK<sub>a</sub> value obtained in Figure 2 can be accepted with certain confidence.

The radical anion of dimethyl maleate (DMM) was

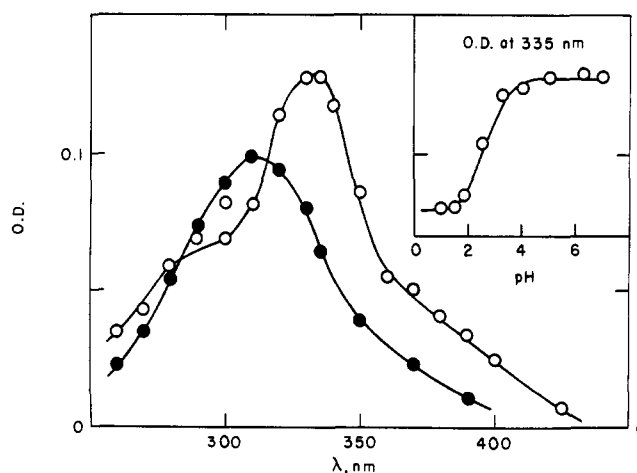


Figure 2. Transient absorption spectra produced from the reaction of (CH<sub>3</sub>)<sub>2</sub>ĊOH radicals with DMF at pH 6.7 (○) and pH 1.0 (●), in aqueous 1.0 *M* *i*-PrOH, 10<sup>-3</sup> *M* DMF and N<sub>2</sub>O (1 atm). Insert: change in absorbance at 335 nm with pH. Dose ~4.0 krad/pulse.

formed by reaction with e<sub>aq</sub><sup>-</sup>. The spectra of the ·DMM<sup>-</sup> and ·DMM<sup>-</sup>-H<sup>+</sup> radicals are shown in Figure 3 and the spectral characteristics given in Table II. A pK<sub>a</sub> = 4.8 ± 0.1 was obtained for the equilibrium



The spectra produced from the reaction of e<sub>aq</sub><sup>-</sup> with monomethyl fumarate (MMF) shown in Figure 4 were obtained at pH 4.7 and 12.0 and correspond to the rad-

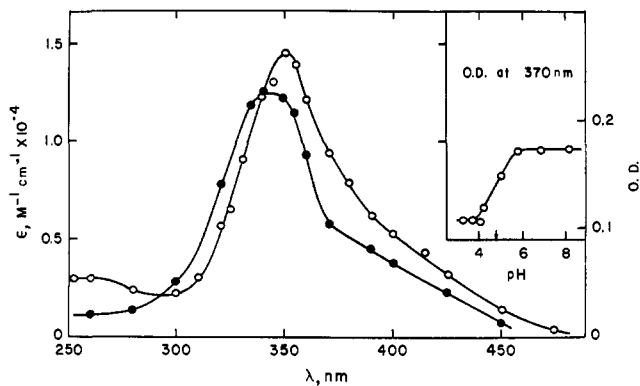


Figure 3. Transient absorption spectra of the radical anion of dimethyl maleate,  $\cdot\text{DMM}^-$  (○), and its protonated form,  $\cdot\text{DMM}^- - \text{H}^+$ . Insert: change in absorbance at 370 nm with pH. Spectra obtained from the reaction of  $e_{\text{aq}}^-$  with  $10^{-3} M$  DMM,  $1.0 M$  *tert*-BuOH, pH 7.4, and  $2 \times 10^{-3} M$  DMM,  $1.0 M$  *tert*-BuOH at pH 4.0. Dose  $\sim 3.2$  krad/pulse.

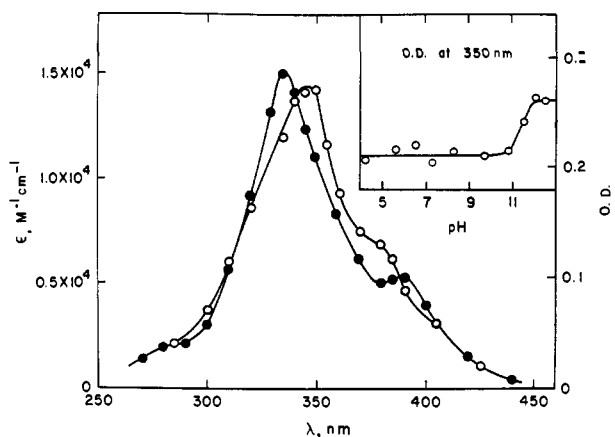
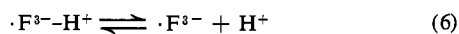


Figure 4. Transient absorption spectra of the radical anion of monomethyl fumarate,  $\cdot\text{MMF}^{2-}$  (○), and its protonated form,  $\cdot\text{MMF}^{2-} - \text{H}^+$  (●). Insert: change in absorbance at 350 nm with pH. Spectra obtained from the reaction of  $e_{\text{aq}}^-$  with  $10^{-3} M$  MMF,  $1.0 M$  *tert*-BuOH at pH 12.0 and 4.7. Dose  $\sim 3.4$  krad/pulse.

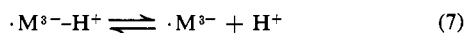
icals  $\cdot\text{MMF}^{2-} - \text{H}^+$  and  $\cdot\text{MMF}^{2-}$ , respectively. The dissociation constant for this species is  $\text{p}K_{\text{a}} = 11.5 \pm 0.2$ .



The radical anions and the protonated forms of the dianion of fumaric acid ( $\text{F}^{2-}$ ) and maleic acid ( $\text{M}^{2-}$ ) are shown in Figures 5 and 6. The acid-base equilib-



rium of reaction 6 gave a  $\text{p}K_{\text{a}} = 10.9 \pm 0.1$ . It was not possible experimentally to determine the  $\text{p}K_{\text{a}}$  of the maleate radical anion



since no significant difference was observed in the transient spectra determined in the pH range 5.0–13.8. The species  $\cdot\text{M}^{3-} - \text{H}^+$  and  $\cdot\text{M}^{3-}$  may have closely similar absorption spectra, or, more likely, the  $\cdot\text{M}^{3-} - \text{H}^+$  radical is a very weak acid with a  $\text{p}K_{\text{a}} > 13$ .

The intermediates produced from the reaction of  $(\text{CH}_3)_2\dot{\text{C}}\text{OH}$  radical with fumaric and maleic acids at pH 0.7 are shown in Figures 5 and 6. The ratio of reduction to addition of the acetone ketyl radical with these acids changes with pH, depending upon the state

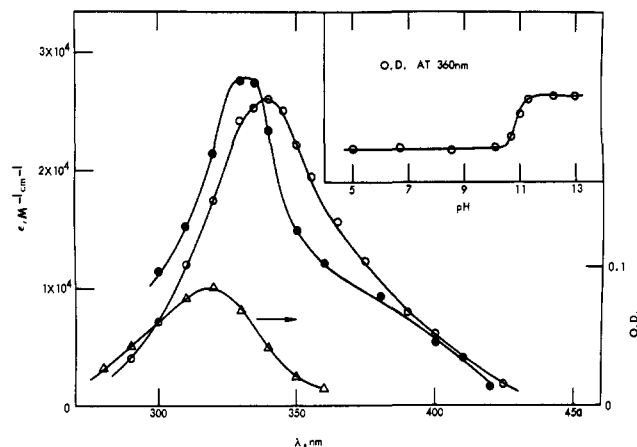


Figure 5. Transient absorption spectra of the electron adducts to fumaric acid. Spectra obtained from the reaction of  $e_{\text{aq}}^-$  with  $10^{-2} M$  fumaric acid,  $1.0 M$  *tert*-BuOH, at pH 12.3 (○)  $\text{F}^{3-}$ , and pH 9.0 (●)  $\text{FH}_2^-$ . The symbol  $\Delta$  is the spectrum obtained from the pulse radiolysis of  $10^{-3} M$  fumaric acid in aqueous  $1.0 M$  *i*-PrOH at pH 0.7. Dose  $\sim 1.5$  krad/pulse.

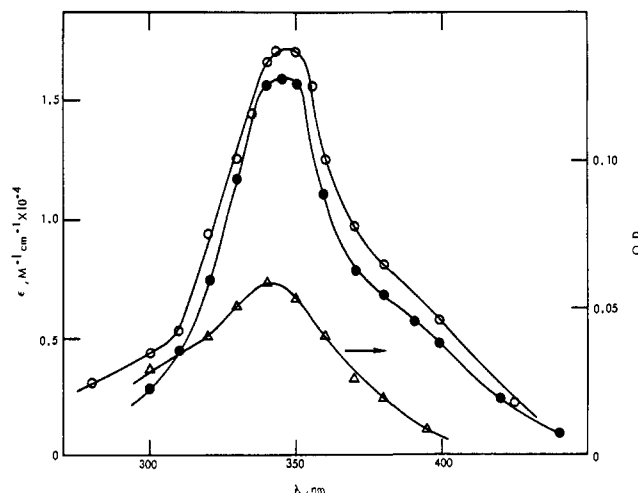


Figure 6. Transient absorption spectra of the electron adducts to maleic acid. Spectra obtained from the reaction of  $e_{\text{aq}}^-$  with  $10^{-2} M$  maleic acid,  $1.0 M$  *tert*-BuOH, at pH 13.8 (○)  $\text{M}^{3-}$  or  $\text{MH}_2^-$ , pH 9.0 (●)  $\text{MH}_2^-$  or  $\text{MH}^{2-}$ . The symbol  $\Delta$  is the spectrum obtained from the pulse radiolysis of  $10^{-3} M$  maleic acid in aqueous  $1.0 M$  *i*-PrOH at pH 0.7. Dose  $\sim 1.5$  krad/pulse.

of protonation of the carboxyl groups on these acids and the properties of these acids as electron acceptors. Some of these results are summarized in Table III. Only the fully protonated forms of fumaric ( $\text{FH}_2$ ) and maleic ( $\text{MH}_2$ ) acids react reasonably fast with the  $(\text{CH}_3)_2\dot{\text{C}}\text{OH}$  radical—the electron acceptor properties of the acids are now comparable to those of the corresponding methyl esters. The spectra of the intermediates produced from the reaction of  $(\text{CH}_3)_2\dot{\text{C}}\text{OH}$  with the fully protonated forms of fumaric and maleic acids were obtained (Figures 5 and 6) but the extinction coefficients could not be accurately determined.

The decay kinetics of the radical anions and their protonated forms did not always follow good first-order or second-order processes. Only the rates of those species where the kinetics was straightforward are given in Table II. The decay of the intermediates from fumaric and maleic acids was strictly second order and highly dependent upon pH and the ionic form of the radical. For example, the decay rates of  $\cdot\text{FH}_2^- - \text{H}^+$ ,

$\cdot\text{FH}_2^-$ , and  $\cdot\text{F}^{3-}$  (overall charge 0, 1, and 3, respectively) were  $2 \times 10^9$ ,  $4 \times 10^8$ , and  $2 \times 10^7 \text{ M}^{-1} \text{ sec}^{-1}$ , respectively.

The transient spectra produced from the addition of H atoms to DMF, DMM, MMFH,  $\text{FH}_2$ , and  $\text{MH}_2$  are shown in Figure 7. These were obtained at pH  $\sim 0.5$  in the presence of 1.0 M *tert*-BuOH. Identical absorption spectra and extinction coefficients,  $\lambda_{\text{max}} \sim 320$  nm and  $\epsilon \sim 600 \text{ M}^{-1} \text{ cm}^{-1}$ , were observed. These transients decay with  $2k = 1.2 \times 10^9 \text{ M}^{-1} \text{ sec}^{-1}$ ; the decay may, in part, involve the reaction of the H atom adducts with the *tert*-BuOH radical.

## Discussion

**Reactivity with  $e_{\text{aq}}^-$ .** In general, olefinic double bonds are neither very reactive toward solvated electrons [ $k(e_{\text{aq}}^- + \text{alkenes}) \leq 10^6 \text{ M}^{-1} \text{ sec}^{-1}$  (ref 12)] nor good oxidizing agents in free radical reactions. The presence of an electron-withdrawing substituent adjacent to a double bond, or any conjugation introduced into a molecule with a double bond, greatly increases the rate of reaction with  $e_{\text{aq}}^-$ . The rate of  $e_{\text{aq}}^-$  with the dianion of fumarate and maleate is  $> 10^9 \text{ M}^{-1} \text{ sec}^{-1}$ , indicating presumably that the added electron resonates between the carboxyl groups and the double bond (see Table I). This rate is further increased either on protonation of one of the carboxyl groups or on esterification, because of the increased electrophilic character of the  $-\text{COOR}$  group; e.g., the monoanion and the monomethyl ester of maleic acid have approximately the same reactivities (Table I). The reactivity toward  $e_{\text{aq}}^-$  of the dimethyl esters of fumaric and maleic acids are still higher,  $\sim 3 \times 10^{10} \text{ M}^{-1} \text{ sec}^{-1}$ , and comparable reactivities of the fully protonated acids could not be determined because of their low  $pK_a^1$  values. These rates are expected to be about the same as those of the diesters.

The significant difference in the rates of  $e_{\text{aq}}^-$  with the dianions of fumarate and maleate has been explained<sup>15</sup> on the basis of the strongly negative environment of the cis isomer (see more below).

**Spectra and Structure of Radical Species.** The optical spectra of  $\cdot\text{DMF}^-$  and  $\cdot\text{DMM}^-$  are different and have absorption maxima at 335 and 350 nm, respectively, in aqueous solutions. Recent observations<sup>6</sup> in MTHF glasses at 77°K produced similar spectra with  $\lambda_{\text{max}}$  at 335 and 345 nm, respectively. The extinction coefficient of  $\cdot\text{DMF}^-$  reported<sup>6</sup> is lower ( $\epsilon_{335} 1.5 \times 10^4 \text{ M}^{-1} \text{ cm}^{-1}$ ) than the value obtained in this work ( $\epsilon_{335} 2.2 \times 10^4 \text{ M}^{-1} \text{ cm}^{-1}$ , see Table II), due probably to the uncertainty in deriving the  $G(e_{\text{sol}^-})$  in MTHF at 77°K.

The spectral differences between the radical anions of DMF and DMM and the electronic spectra of the parent compounds should be noted. The electronic spectra of organic compounds are known<sup>2</sup> to be dependent on the stereostructure of the chromophores involved. The cis isomer in most cases has its absorption maximum at a slightly shorter wavelength and its extinction coefficient is usually smaller than that of the trans isomer. DMF and DMM have maxima<sup>16,17</sup> at

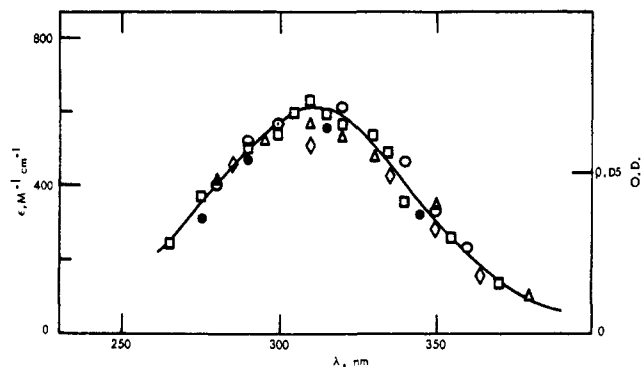
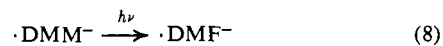


Figure 7. Transient absorption spectrum of the H atom adduct to dimethyl fumarate ( $\square$ ), dimethyl maleate ( $\Delta$ ), monomethyl fumaric acid ( $\circ$ ), fumaric acid ( $\bullet$ ) and maleic acid ( $\diamond$ ). Spectra obtained in 1.0 M *tert*-BuOH, pH 0.5, and  $10^{-3}$  M solute concentration. Dose  $\sim 17$  krad/pulse.

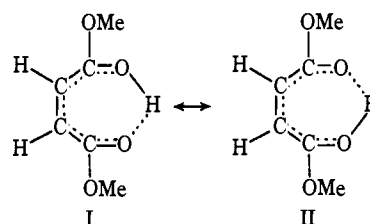
214 and 198 nm, respectively, and  $\epsilon_{\text{max}} 3.4 \times 10^4$  and  $2.6 \times 10^4 \text{ M}^{-1} \text{ cm}^{-1}$ . While the  $\epsilon$  of the radical anion of the cis isomer,  $\cdot\text{DMM}^-$ , is smaller than that of  $\cdot\text{DMF}^-$ , the reverse is the case for the absorption maxima of these radical anions, see Table II. No isomerization of the radical anions was taking place under the experimental conditions used, since optical absorption measurements were recorded at the very initial stage ( $\sim 0.1 \mu\text{sec}$ ) after the electron pulse. Photoisomerization can be achieved<sup>6</sup> on illumination with uv light, leading to the cis  $\rightarrow$  trans conversion



The activation energy and quantum yield of this reaction have not been established. No immediate explanation is available to explain the higher transition energy of  $\cdot\text{DMF}^-$  compared to  $\cdot\text{DMM}^-$ . However, similar results are obtained with the radical anions of fumaric and maleic acids (see Table II).

The spectra of the protonated radical anions, i.e.,  $\cdot\text{DMF}^- - \text{H}^+$  and  $\cdot\text{DMM}^- - \text{H}^+$ , have not been reported. These spectra (Figures 1 and 2, Table II) are blue shifted, as generally found for the protonated forms of radicals, and the maxima are at 320 and 342 nm, respectively. Again the trans radical absorbs at lower wavelength and has a higher  $\epsilon$  than the cis radical.

The esr spectra of the radicals  $\cdot\text{DMF}^-$ ,<sup>6</sup>  $\cdot\text{DMM}^-$ ,<sup>6,18</sup>  $\cdot\text{DMM}^- - \text{H}^+$ ,<sup>8</sup> have been observed. From the equivalence of the splitting constants for the olefinic protons in  $\cdot\text{DMM}^- - \text{H}^+$ , it can be concluded that the odd electron is distributed between the carboxyl groups intramolecularly *via* hydrogen bonding, leading to the interconversion of the tautomers I and II; i.e., protonation



of the electron adduct takes place at the carbonyl group. Protonation of the double bond is ruled out, further-

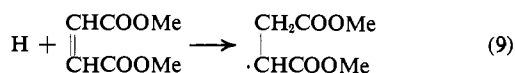
(18) S. F. Nelsen, *Tetrahedron Lett.*, 3795 (1967).

(15) E. J. Hart, S. Gordon, and J. K. Thomas, *J. Phys. Chem.*, **68**, 1271 (1964).

(16) Reference 2a, p 330.

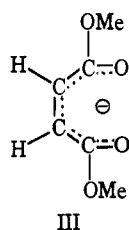
(17) A. Wasserman and A. Smakula, *Z. Phys. Chem., Abt. A*, **155**, 366 (1931).

more, since it would lead to a transient absorption similar to that obtained *via* addition of an H atom.



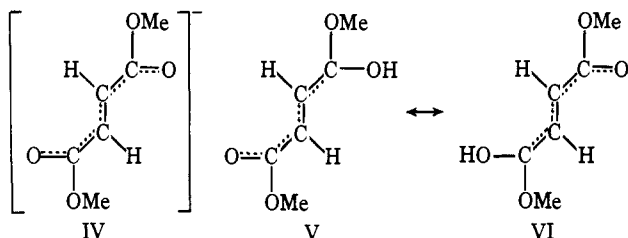
Similar conclusions concerning the site of protonation of the radical anion of *N*-ethylmaleimide were reached<sup>13,14</sup> (see Table II), a compound with a similar structure and electrophilic character.

With the  $\cdot\text{DMM}^-$  radical anion various resonance hybrid structures can be expressed based on III.



It is interesting to point out that although the resonance partly destroys the character of the double bond, it is still considerably strong to prevent isomerization of the radical anions. Apparently, a certain activation energy (*e.g.*, optical excitation) is required to bring about the isomerization of the radicals.

The corresponding structures IV-VI are suggested for the radicals  $\cdot\text{DMF}^-$  and  $\cdot\text{DMF}^--\text{H}^+$



**Acid-Base Properties.** The acid dissociation constants of the protonated radical anions of the *cis* and *trans* isomers were found to be significantly different, with  $pK_a$  values of 2.8 and 4.8 for  $\cdot\text{DMF}^--\text{H}^+$  and  $\cdot\text{DMM}^--\text{H}^+$ , respectively. This surprising difference is probably a consequence of the higher spatial density of the negative charge in structure III, compared to IV, making radical III a weaker acid. Similar explanations have been proposed<sup>1,2</sup> to account for the difference between the two dissociation constants of fumaric acid ( $pK_a^1 = 3.02$ ,  $pK_a^2 = 4.38$ ) and maleic acid ( $pK_a^1 = 1.92$  and  $pK_a^2 = 6.23$ ).

The  $pK_a$  value of the radical  $\cdot\text{MMF}^2--\text{H}^+$  of mono-methyl fumarate is  $\sim 11.5$ , considerably higher than the  $pK_a$  of the corresponding diester. This is probably due to appreciable decrease in conjugation. The  $pK_a$  value obtained is also close to the  $pK_a$  of electron adducts to some saturated esters.<sup>19</sup> Here again the protonation is expected to take place at the ester group, judging from the spectral similarities of the mono- and diester radicals (Figures 3 and 4). The  $pK_a$  value for protonation of the carboxyl group of the radical should be much lower, in the region<sup>20</sup> of the  $pK_a^1$  of the parent compound.

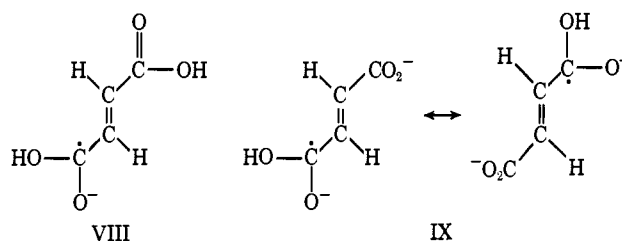
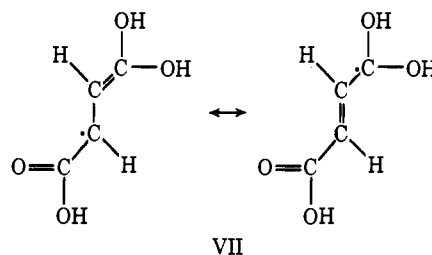
**Fumaric and Maleic Acids.** The absorption spectra of the electron adducts of fumaric acid in various states

(19) M. Simic and E. Hayon, *Radiat. Res.*, **48**, 244 (1971).

(20) P. Neta, M. Simic, and E. Hayon, *J. Phys. Chem.*, **73**, 4207 (1969).

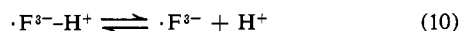
of protonation ( $\text{FH}_2$ ,  $\text{FH}^-$ , and  $\text{F}^{2-}$ ) are not too different from each other. The absorption maxima for  $\cdot\text{FH}_2^-$ ,  $\cdot\text{FH}_2^--\text{H}^+$ ,  $\cdot\text{F}^{3-}$ , and  $\cdot\text{F}^{3-}-\text{H}^+$  are 330, 320, 340, and 333 nm, respectively. The spectra are very close to those of  $\cdot\text{DMF}^-$  and  $\cdot\text{DMF}^--\text{H}^+$ , see Figures 1 and 5. The spectral shifts are even smaller for the electron adducts of maleic acid, see Table II.

The esr spectra of the electron adducts and their protonated forms of maleic and fumaric acids have been examined<sup>8,21,22</sup> in some detail. Structures VII-IX have been assigned to the radicals  $\cdot\text{FH}_2^--\text{H}^+$ ,

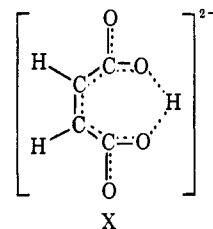


$\cdot\text{FH}_2^-$ , and  $\cdot\text{FH}_2^--\text{H}^+$ , respectively. The corresponding structures for maleic acid show considerable intramolecular hydrogen bonding. The assignment of the radicals given in Table II for fumaric and maleic acids was based on the reported esr data<sup>8,21,22</sup> and on the observed absorption spectral changes.

The  $pK_a$  value for the equilibrium



was found to be 10.9, much higher than that of  $\cdot\text{DMF}^--\text{H}^+$  ( $pK_a = 2.8$ ). The increased charge on  $\cdot\text{F}^{3-}-\text{H}^+$  makes it a very weak acid. The reason for the difference between the dissociation constants of reactions 5 and 10 is not clear. The addition of an electron to the dianion of maleic acid produced a radical anion which is rapidly protonated. Presumably due to intramolecular hydrogen bonding, the  $pK_a$  of structure X



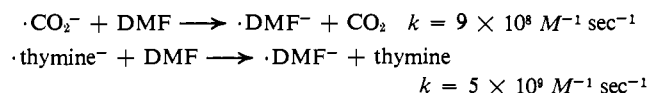
( $\cdot\text{M}^{3-}-\text{H}^+$ ) could not be observed and is probably above 13.

**Reactions with Other Free Radicals.** Organic free radicals do not appear to reduce DMF and DMM very efficiently because of preferential addition to the double bond. It is interesting to compare this phenomenon with some other solutes. In the case of NEM, a stronger oxidizing agent than the above compounds ( $\cdot\text{DMF}^-$  transfers an electron to NEM, see below), the  $(\text{CH}_3)_2-$

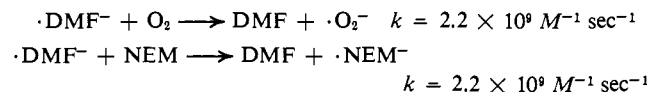
(21) P. Neta, *ibid.*, **75**, 2570 (1971).

(22) P. Neta and R. W. Fessenden, *ibid.*, **76**, 1957 (1972).

$\dot{\text{C}}\text{OH}$  radical has  $\sim 50\%$  reducing efficiency<sup>13,14</sup> compared to  $\sim 12\%$  for DMF. Increasing the redox potential of the compound seems to increase the efficiency for reduction (electron transfer) by organic radicals. Electron transfer from radical anions (e.g.,  $\cdot\text{CO}_2^-$  and  $\cdot\text{thymine}^-$ ) to DMF is more efficient



In the presence of stronger oxidizing agents such as NEM, quinones, and oxygen, the  $\cdot\text{DMF}^-$  radical loses its electron to these solutes, e.g.



These rates were determined by following the disappearance of  $\cdot\text{DMF}^-$  or the appearance of  $\cdot\text{NEM}^-$ .

The reactions of free radicals with fumaric and maleic acids are much more complex than those with the diesters. Just as found with  $e_{\text{aq}}^-$  (Table I), the reactivity of organic radicals is dependent upon the state of protonation of the unsaturated dicarboxylic acids. While the dianions of these acids react with  $e_{\text{aq}}^-$  at an appreciable rate, the radicals  $\cdot\text{CO}_2^-$  and  $(\text{CH}_3)_2\dot{\text{C}}\text{OH}$  do not transfer an electron to them ( $k < 10^6 \text{ M}^{-1} \text{ sec}^{-1}$ ). The rate increases for the monoanion form and becomes relatively fast for the fully protonated acids (see Table III). The preferential addition reactions of free radicals to the dianion of these acids have recently been used<sup>21</sup> as a means of trapping free radicals. Based on the above results, one can now explain why these acids are efficient in trapping radicals.

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### Thermodynamics of Acid-Base Equilibria. III. Ionization of Substituted Anilinium Ions

Charles L. Liotta,\*<sup>1a</sup> Edward M. Perdue,<sup>1a</sup> and Harry P. Hopkins, Jr.<sup>1b</sup>

*Contribution from the School of Chemistry, Georgia Institute of Technology, Atlanta, Georgia 30332, and the Department of Chemistry, Georgia State University, Atlanta, Georgia 30303. Received June 16, 1972*

**Abstract:** The standard enthalpies of ionization of 21 meta- and para-substituted anilinium ions have been determined calorimetrically in aqueous solution at 25°. Standard entropies of ionization have been calculated from the experimental enthalpies of ionization and the literature Gibbs free energies of ionization. Both the enthalpies and entropies of ionization show a good linear correlation with the Gibbs free energy of ionization. The experimental results have been analyzed in terms of Hepler's theory of substituent effects and have been compared to the predictions of electrostatic theory.

Because of the theoretical and practical interest in the ionization of organic acids in aqueous solution, numerous determinations of the thermodynamic functions of ionization for these acids have appeared in the literature. A recent review article by Larson and Hepler has summarized the available data.<sup>2</sup>

Reliable Gibbs free energies of ionization or  $\text{p}K_{\text{a}}$ 's have now been obtained in aqueous solution for a majority of the known organic acids. However, the enthalpies and entropies of ionization are needed if the details of the ionization process are to be fully understood. Hepler and coworkers<sup>2</sup> have shown that the variation in the  $\text{p}K_{\text{a}}$ 's of substituted phenols is almost entirely due to changes in the entropy of ionization. An analysis of the enthalpies and entropies of ionization of a wide variety of structurally different mono- and dicarboxylic acids by Christensen, Izatt, and Hansen<sup>3</sup> has shown that the Gibbs free energies of ionization

correlate extremely well with the entropies of ionization whereas neither the Gibbs free energies nor the entropies demonstrate a distinct correlation with the enthalpies of ionization. This lack of a good correlation between the enthalpies of ionization and the other thermodynamic functions is probably due to the inherent difficulty in making accurate determinations of the very small enthalpies of ionization of carboxylic acids.

Recently Bolton, Fleming, and Hall<sup>4</sup> have reported a spectrophotometric determination of the thermodynamic functions of ionization for a number of meta- and para-substituted benzoic acids. Excellent correlations were obtained not only between  $\Delta G^\circ$  and  $\Delta S^\circ$ , but also between  $\Delta G^\circ$  and  $\Delta H^\circ$ . If it is assumed that the experimental uncertainty is on the order of  $\pm 50 \text{ cal/mol}$  for  $\Delta H^\circ$ , then correlation between  $\Delta G^\circ$  and  $\Delta H^\circ$  may be considered fortuitous at best.

In ionogenic processes such as the ionization of phenols and carboxylic acids, it has been established that entropy differences are mainly responsible for relative acidities of these acids. The study of a system involving organic cation acids would determine the relative

(1) (a) School of Chemistry, Georgia Institute of Technology; (b) Department of Chemistry, Georgia State University.

(2) J. W. Larson and L. G. Hepler, "Solute-Solvent Interactions," J. F. Coetzee and C. D. Ritchie, Ed., Marcel Dekker, New York, N. Y., 1969.

(3) J. J. Christensen, R. M. Izatt, and L. D. Hansen, *J. Amer. Chem. Soc.*, **89**, 213 (1967).

(4) P. D. Bolton, K. A. Fleming, and F. M. Hall, *ibid.*, **94**, 1033 (1972).