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On the Electron Transfer from Ascorbic Acid to Various Phenothiazine Radicals[1]

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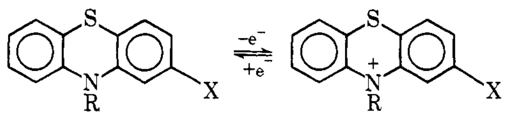
Abstract: The reaction of electron transfer from ascorbic acid to *N*-alkylphenothiazine radical cations was studied in the pH range 0–7.2. The radical cations were produced by oxidation with Br_2^- or Cl_2^- using the pulse radiolysis technique. The radical cations are reduced by the deprotonated form of ascorbic acid in the pH range 2.2–7.2. The product of this reaction has a spectrum which is identical with that of the ascorbate radical. It is concluded that, if a charge-transfer complex is formed upon the reaction of ascorbic acid with the phenothiazine radical cations, its lifetime is shorter than 7×10^{-8} s. It is suggested that even at high acidities no long lived complex is formed and it is proposed that at very low pH the thermodynamically stable species in this reaction is the phenothiazine radical cation rather than the ascorbic acid radical. It is shown experimentally that at 1 M HCl the ascorbic acid radical oxidizes *N*-alkylphenothiazine to give the radical cation of the latter in reverse to the direction of the electron transfer at higher pH.

There is currently considerable interest in the thermal and photoinduced electron transfer reactions of *N*-alkylphenothiazines and their radical cations.



	R	X
phenothiazine	H	H
N-methylphenothiazine	CH_3	H
promazine (PMZ)	$(CH_2)_3N(CH_3)_2$	H
chlorpromazine (ClPMZ)	$(CH_2)_3N(CH_3)_2$	Cl
promethazine (PMTZ)	$CH_2CH(CH_3)N(CH_3)_2$	H

The intensive interest in this group of compounds stems primarily from three different aspects, all related to their low ionization potentials.[3] (a) The effective use of *N*-alkyl derivatives in psychiatric therapy[4] (especially ClPMZ) is often attributed to their redox reactivity. Furthermore, much of the interest in the photochemical redox behavior of some of these tranquilizer drugs is stimulated by the observation that treatment with, e.g., ClPMZ causes photosensitization of skin and eye tissues.[7] (b) Due to the ease of their one-electron oxidation, the possible use of some phenothiazine derivatives (often phenothiazine or *N*-methylphenothiazine) as photo redox sensitizers is considered in solar energy conversion systems.[5] Furthermore, the diamino derivative of phenothiazine-thionine, in conjunction with Fe(II), constitutes one of the most studied systems for photogalvanic effects.[6] (c) The one-electron oxidation of the *N*-alkyl derivatives by various metal inorganic complexes is often a simple outer sphere electron transfer process. This fact was recently utilized to evaluate the parameters involved in the electron transfer between $Fe_{aq}{}^{3/2+}$, $Fe(CN)_6{}^{3/4-}$, and $Np^{6/5+}$ and several *N*-alkylphenothiazine derivatives, as well as the electron exchange between these derivatives,[8] in light of the Marcus theory for electron-transfer reactions.

In spite of this simple behavior of outer sphere electron-transfer processes, electron donor-acceptor complexes between phenothiazines and various acceptors have been observed in several cases. Thus, spectral evidence for EDA complexes between phenothiazine or ClPMZ and tetracyanobenzene, tetracyanoethylene, trinitrobenzene, and several quinone derivatives was presented by Dwivedi et al.[9] Charge-transfer complexes between acetylcholine or serotonin or hydroxydopamine with ClPMZ or its radical cation were reported.[10] The reduction of the chlorpromazine radical cation by ascorbic acid in 0.25–1.00 M HCl was recently studied by Klein and Toppen.[11] In this system again kinetic evidence was suggested to indicate the formation of an EDA complex between the radical cation and the ascorbate anion prior to the electron-transfer act. On the other hand, the reduction of many inorganic complexes by ascorbic acid was recently shown to follow the Marcus theory correlations of outer sphere electron-transfer reaction.[12]

In the present study we utilize the pulse radiolysis technique to investigate the electron transfer reaction between ascorbic acid (H_2A) and several *N*-alkylphenothiazine radicals over a wide range of pH. Over much of this range (pH 2.5–7.2) the rate of reaction is too rapid to be followed by the previously used stopped-flow technique. In view of the results of Klein and Toppen,[11] we hoped to observe the absorption spectrum of the EDA complex. However, this expectation did not materialize. Furthermore, evidence will be presented that at high acidity the phenothiazines are oxidized by ascorbic acid radicals.

Experimental Section

Materials and Procedure. The *N*-alkylphenothiazines (denoted collectively as PTZ) were obtained from Rhone-Poulenc and their purity was checked as previously described.[8a] The ascorbic acid (Sigma) was purified by recrystallization. All other materials were

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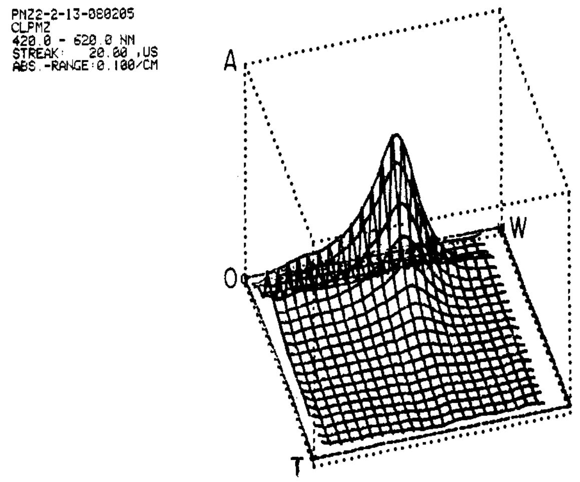

Figure 1. (a) Three-dimensional display of the streak camera for pulse irradiated 10^{-3} M ClPMZ + 2 × 10^{-4} M H_2A + 0.1 M NaBr, N_2O-saturated solution at pH 5.9. O-A is the absorbance axis (0.1 full scale); O-W is the wavelength axis centered at 520 nm (200 nm full scale); O-T is the time axis (20 μs full streak). Note the absence of any absorption at the end of the streak.

Table I. Kinetic, Thermodynamic, and Spectral Parameters for *N*-Alkylphenothiazines

pheno- thiazine	$k_4 \times 10^{-9}$, $M^{-1}s^{-1}$ [a]	$k_7 \times 10^{-9}$, $M^{-1}s^{-1}$ [b]	λ_{max}, nm	$\epsilon_{max} \times 10^{-4}$, $M^{-1}cm^{-1}$	$E°$,[c] V
PMZ	4.3	0.49	515	(0.98 ± 0.05)	0.71
ClPMZ	5.0	1.4	525	(1.07 ± 0.05)	0.78
PMTZ	3.0 (4[d])	1.3	517	(0.93 ± 0.05)	0.86
H_2A	1.6		360	(0.37 ± 0.03)	~0.95[e]

[a] Rate constant for the reaction of Br_2^- with PTZ measured at μ = 0.1 and pH 5.9 by following the decay of Br_2^- at 360 nm and formation of $PTZ^{+}\cdot$ at 520 nm. [b] Rate constant for $PTZ^{+}\cdot + HA^-$ at μ = 0.1 measured as above. [c] For $PTZ^{+}\cdot/PTZ$ taken from reference 8a. [d] Reference 18. [e] Calculated in reference 12 for $HA^{\cdot}/HA^-$. See also reference 17.

of the highest purity commercially available and were used as obtained. Water was triply distilled. Addition of the ascorbic acid to the solutions was done only after deaeration and saturation with N_2O which was bubbled through the solutions for at least 10 min. Ultrapure N_2O (Liquid Carbonic) was used throughout this study. Perchloric acid, acetate, or phosphate buffers (1-10 mM of the buffer) were used to adjust the pH. Unless otherwise stated, ionic strength of 0.1 was maintained by using NaBr. Dosimetry was performed with 10^{-2} M KSCN in N_2O-saturated neutral solutions by assuming $G(SCN)_2^-$ = 6.0 molecules/100 eV and its ϵ_{478} = 7600 M^{-1} cm^{-1}. The small yield of hydrogen atoms was ignored. This is justified since in 10^{-4} M solutions of PMZ at pH 3 and containing 0.1 M *tert*-butyl alcohol (the only radicals left at the end of the pulse under such conditions are H and the unreactive *tert*-butyl alcohol radicals), no formation of the promazine radical cation could be observed. The radiolytic in situ preparations of the radical cations are described below.

Instrumentation. The pulse radiolysis facilities of both the Notre Dame Radiation Laboratory and Argonne National Laboratory were used in this study. Many of the experiments were duplicated in the two laboratories to yield a very good agreement between the results.

Spectral search for the transient absorptions was done at ANL by using the streak camera technique[13a] (cf. Figure 1). More detailed kinetic and spectral analyses were performed in both NDRL and ANL by using the monochromator-photomultiplier combination[13b,c] (cf. Figure 2). In typical experiments, the total concentration of radicals produced by the electron pulse was 1-2 μM.

Results and Discussion

Preparation of the Radical Cations. Radiolytic one-electron oxidation of the PTZs was achieved by the use of Br_2^- radicals as oxidants. The following sequence of events is known to produce the Br_2^- radicals in irradiated aqueous bromide solutions saturated with N_2O:

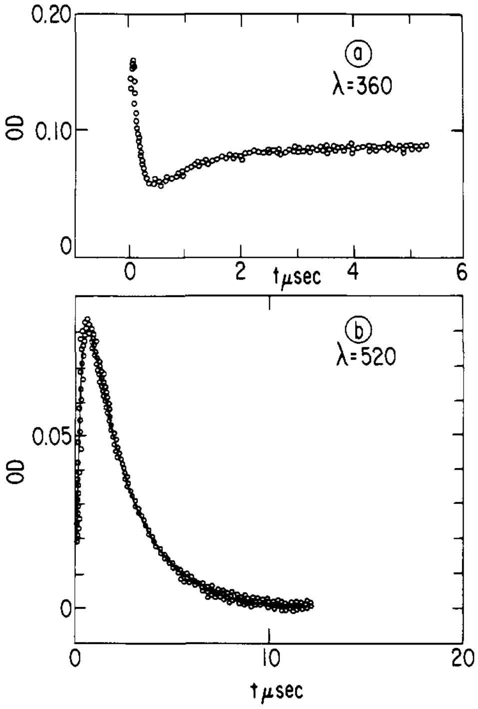

Figure 2. (a) Decay of Br_2^- on reaction with 10^{-3} M promethazine and subsequent formation of the ascorbate radical on oxidation of H_2A by $PMTZ^{+}\cdot$ radical cation, followed at 360 nm. $[H_2A] = 8 \times 10^{-4}$ M, pH 5.9, 0.1 M NaBr, N_2O saturated. (b) Formation of promazine radical cation by oxidation with Br_2^- and its decay by reaction with H_2A followed at 520 nm. [PMZ] = 10^{-3} M, $[H_2A] = 8 \times 10^{-4}$ M, pH 5.9, 0.1 M NaBr, N_2O saturated. Solid line is a least-squares fit to two consecutive exponentials of formation and decay.

$$H_2O \rightsquigarrow e_{aq}^-;\ OH;\ H;\ H_2O_2;\ H_2 \qquad (1)$$

$$e_{aq}^- + N_2O \xrightarrow{H^+} OH + N_2 \qquad (2)$$

$$OH + Br^- \xrightarrow{Br^-} Br_2^- + OH^- \qquad (3)$$

Thus, under the present experimental conditions ($[Br^-] > 10^{-2}$ M) practically all of the radiolytically produced radicals (with the exception of the small yield of H atoms) would be converted into Br_2^- at the end of the pulse.[14a,15] The latter then reacts with either PTZ or with ascorbic acid.[16] We chose Br_2^- as the primary oxidizing agent rather than OH radicals in order to ensure that electron transfer is the main pathway for the reaction with PTZ, free of addition reactions or hydrogen abstraction reactions which are common with OH radicals.[14b,c] The fact that Br_2^- indeed reacts by electron transfer without complications from side reactions has been previously shown for ascorbic acid[16] and is also evident from the spectral characteristics of the product radicals, as summarized in Table I. Both λ_{max} and ϵ_{max} are very similar to those obtained by chemical oxidation of PTZ.[8a] The concentrations of PTZ used (10^{-4} to 10^{-3} M) are sufficiently low that no OH radicals (or e_{aq}^-) react directly with PTZ and, on the other hand, practically all Br_2^- radicals react with it (or with H_2A). The rate constants for the oxidation of the various PTZ by Br_2^- are also summarized in Table I. Measurements for determination of these rate constants were done both at 360 nm and at 520 nm where the decay of Br_2^- and the formation of the $PTZ^{+}\cdot$, re-

Table II. Some Experimental Results on the Reaction of $PTZ^{+}\cdot$ with H_2A[a]

	[PTZ], M	$[H_2A]$, M	λ 360 nm k_{obsd}, s^{-1}[b]	λ 360 nm D_{∞}[c]	λ 520 nm k_{obsd}, s^{-1}[d]	λ 520 nm D_0[e]
PMZ (pH 5.9)	10^{-3}			0.029		0.130
	10^{-3}	1×10^{-4}	5.6×10^{4}	0.056	5.1×10^{4}	
	10^{-3}	2×10^{-4}	1.4×10^{5}	0.057	1.0×10^{5}	0.129
	10^{-3}	4×10^{-4}	2.6×10^{5}	0.056	2.1×10^{5}	0.129
	10^{-3}	8×10^{-4}	4.2×10^{5}	0.069	4.5×10^{5}	0.115
	10^{-3}	8×10^{-4}			4.5×10^{5}	0.275[f]
	10^{-3}	2.2×10^{-3}	1.0×10^{6}	0.066	1.1×10^{6}	0.100
ClPMZ (pH 4.7)	2.3×10^{-5}	2.2×10^{-5}			2.5×10^{4}	
	4.7×10^{-5}	4.4×10^{-5}			5.1×10^{4}	
	9.0×10^{-5}	8.4×10^{-5}			9.3×10^{4}	
	1.6×10^{-4}	1.5×10^{-4}			1.7×10^{5}	
	3.1×10^{-4}	2.8×10^{-4}			3.3×10^{5}	
	5.7×10^{-4}	5.4×10^{-4}			5.6×10^{5}	
	1.1×10^{-3}	9.8×10^{-3}			1.0×10^{6}	
	1.7×10^{-3}	1.6×10^{-3}			1.6×10^{6}	
	1.6×10^{-3}	3.1×10^{-3}			3.1×10^{6}	
	1.5×10^{-3}	4.8×10^{-3}			4.5×10^{6}	
	4.9×10^{-3}	4.8×10^{-3}			4.5×10^{6}	
PMTZ (pH 5.9)	1×10^{-3}	1×10^{-4}	1.4×10^{5}	0.057	1.2×10^{5}	0.153
	1×10^{-3}	2×10^{-4}	2.9×10^{5}	0.068	2.7×10^{5}	0.142
	1×10^{-3}	4×10^{-4}	5.2×10^{5}	0.080	5.4×10^{5}	0.125
	2×10^{-3}	8×10^{-4}	1.1×10^{6}	0.085	1.1×10^{6}	0.120
	2×10^{-3}	2×10^{-3}	2.6×10^{6}	0.081	2.5×10^{6}	0.130

[a] All solutions are N_2O saturated containing 0.1 M NaBr. Unless otherwise stated, 4-ns pulse was used. [b] Rate constant for the formation of $A^{-}\cdot$. [c] Absorbance of $A^{-}\cdot$ at the end of the reaction. [d] Rate constant for disappearance of $PTZ^{+}\cdot$. [e] Absorbance at the beginning of the reaction. [f] 10-ns pulse.

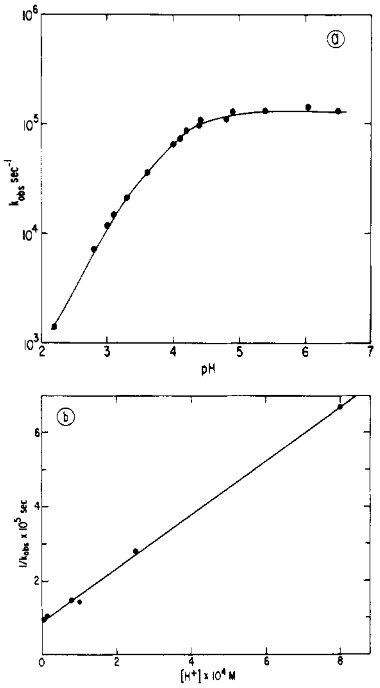

Figure 3. The dependence of k_{obsd} for the reaction of $ClPMZ^{+}\cdot + H_2A$ on pH. [ClPMZ] = 10^{-3} M; $[H_2A] = 10^{-4}$ M; N_2O-saturated solution containing 0.1 M NaBr (a), and the dependence of $1/k_{obsd}$ on $[H^+]$ in the region of the pK_a of H_2A (b).

spectively, could be followed (cf. Figure 2a,b).

$$PTZ + Br_2^{-} \rightarrow PTZ^{+}\cdot + 2Br^{-} \qquad (4)$$

$$HA^{-} \text{ (or } H_2A) + Br_2^{-} \rightarrow A^{-}\cdot + 2Br^{-} + H^{+} \qquad (5)$$

The $PTZ^{+}\cdot$ radicals are known to be rather stable. In the present systems, the cation radicals were found to undergo partial decay (in the absence of H_2A) with a half-life of a few milliseconds. This decay amounted to ≤10% of the initial absorption, while no changes in the spectra were observed during this decay. The exact nature of this process is not completely understood but it might be the result of a reaction of $PTZ^{+}\cdot$ with the small quantities of H atoms or H_2O_2 produced by the electron pulse. In order to avoid this complication, all reactions were studied at a rate which was at least three times faster than the rate of this small decay.

The Reaction of $PTZ^{+}\cdot$ with H_2A. When H_2A was present in the PTZ-containing solutions, concentrations were chosen such that most of the Br_2^{-} reacted with PTZ. In most cases the rate of reaction of $PTZ^{+}\cdot$ with HA^{-} (reaction 7) was well separated from its formation (reaction 4). When the concentration of H_2A was, however, increased some overlap of the two reactions (reactions 4 and 7) may occur. In such cases the experimental data were fitted to a two consecutive exponential formation and decay rate law (cf. Figure 2b).

The rate of the reaction of PTZ^{+} with H_2A was measured under a wide variety of experimental conditions. The effect of the total amount of dose, pH, [PTZ], and $[H_2A]$ was checked for all three PTZ. Some typical results are given in Table II. Usually the rate was measured at 520 nm and at 360 nm (decay of PTZ^{+} and formation of $A^{-}\cdot$) and, as can be seen in Table II, both rates closely match one another. However, at pH <2.5 the rate of disappearance of PTZ^{+} is comparable to the lifetime of $A^{-}\cdot$ and its formation at 360 nm could not be followed. From these results it is concluded that the rate of reaction of $PTZ^{+}\cdot$ with H_2A under our experimental conditions is independent of the dose (i.e., of $[PTZ^{+}\cdot]$) and of [PTZ]. The pH dependence of the rate of the reaction of PTZ^{+} for ClPMZ with H_2A is shown in Figure 3. The leveling off of the pseudo-first-order rate constant at pH >5 seems to indicate that the reactive species toward PTZ^{+} is HA^{-}. The results are therefore analyzed in terms of reactions 6 and 7 and assuming that direct reaction of H_2A with PTZ^{+} has only a negligible contribution.

$$H_2A \overset{K_a}{\rightleftharpoons} HA^{-} + H^{+} \qquad (6)$$

$$HA^{-} + PTZ^{+}\cdot \rightarrow PTZ + A^{-}\cdot + H^{+} \qquad (7)$$

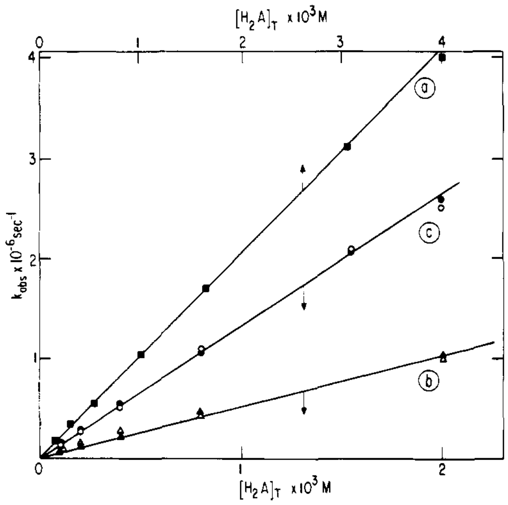

Figure 4. The dependence of k_{obsd} for the reaction of $PTZ^{+}\cdot + H_2A$ on $[H_2A]_T$. (a) $ClPMZ^{+}\cdot$, pH 3.25; (b) $PMZ^{+}\cdot$, pH 5.9; (c) $PMTZ^{+}\cdot$, pH 5.9; measured at 520 nm (■,●,▲) or at 360 nm (○,△). All other conditions as in Figure 2.

Such a mechanism would lead to the following dependence of the observed rate constant on $[H^+]$ and the total concentration of ascorbic acid $[H_2A]_t$:

$$k_{obsd} = \frac{k_7 K_a}{K_a + [H^+]}[H_2A]_t \tag{I}$$

In Figure 3b the expected linearity of $1/k_{obsd} = [(1/k_7[H_2A]_t) + ([H^+]/k_7 K_a[H_2A]_t)]$ is indeed obtained. The ratio of the intercept to the slope of the line in Figure 3b yields $pK_a = 4.0$ close to 4.1 recently obtained at $\mu = 0.1$.[12] Taking this value for pK_a we obtain $k_7 = 1.4 \times 10^9\ M^{-1}\ s^{-1}$ for $ClPMZ^{+}\cdot$ which agrees with the plateau value in Figure 3a.

The dependence of k_{obsd} on $[H_2A]_t$ is crucial to unraveling the mechanism of reaction 7. Many experiments were performed in order to determine whether k_{obsd} deviates from linearity on increasing $[H_2A]_t$. No such deviation could be observed on increasing $[H_2A]_t$ up to 10 mM by using ClPMZ or up to 2 mM by using PMZ or PMTZ (Figure 4). The values of k_7 are also summarized in Table I.

The primary salt effect on reaction 7 was checked for $ClPMZ^{+}\cdot$ at various concentrations of NaBr. The results are displayed in Figure 5. Similarly, the effect of salt on reaction 4 was also measured. Although the ionic strength effect was studied in rather high concentrations, several instructive conclusions can be derived from the results in Figure 5. Clearly these results indicate that both reactions are between a positively charged species and a negative one. This agrees with the assignment of HA^- as the reactive form of the ascorbic acid as previously deduced from the pH effect. The slopes of the lines in Figure 5 yield 1.08 for the reaction of Br_2^- with ClPMZ and 2.25 for the reaction of $ClPMZ^+$ with HA^-. Considering the fact that ClPMZ is already protonated at its amine site these values of the slopes are as expected. The reaction of $ClPMZ^{+}\cdot$ with HA^- seems to involve a doubly charged radical cation and will, therefore, indicate that no deprotonation of the amine site occurs upon one electron oxidation of ClPMZ in the pH range studied here. From the plots of Figure 5, one can derive for ClPMZ $k_4 = 7.8 \times 10^9$ and $k_7 = 3.8 \times 10^9\ M^{-1}\ s^{-1}$ at $\mu = 0$.

The Products of the Reaction of HA^- with $PTZ^{+}\cdot$. The question of the products of reaction 7 is to be addressed now. The fact that k_{obsd} for all the three PTZ was found to be linear with $[H_2A]$ up to relatively high concentrations of H_2A excludes the possibility of an experimentally detectable equilibrium reaction between the products and the reactants at near neutral pH. The redox potential for the couple $HA\cdot/HA^-$ was estimated recently to be $E°_{HA\cdot/HA^-} \sim 0.9$ V.[12] Since under the present experimental conditions the ascorbate radical is deprotonated, the redox potential should drop to ~0.3 V at near neutral pH.[17] Reaction 7 therefore is expected to be shifted completely to the right. The possibility of a charge-transfer complex between $PTZ^{+}\cdot$ and A^{2-} has to be examined more carefully. If the mechanism proposed by Klein and Toppen[11] is operative at near neutral pH, then reaction 7 should lead exclusively to a charge-transfer complex which should slowly decompose to the ascorbic acid radical anion and PTZ (tens of milliseconds). To check this possibility the absorption spectrum at the end of the decay of $ClPMZ^{+}\cdot$ was recorded in the range of 320-600 nm. Results are displayed in Figures 1 and 6 and compared with the spectrum of $A^-\cdot$ obtained under similar conditions in the absence of ClPMZ. The spectra are practically indistinguishable. No other absorption bands could

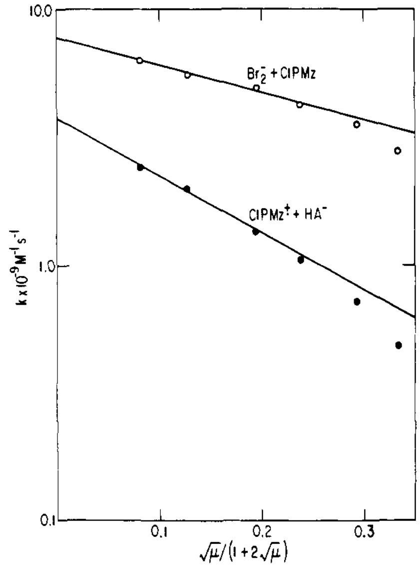

Figure 5. The effect of ionic strength on the rate constant of $ClPMZ^{+}\cdot + HA^-$ and on that of $Br_2^- + ClPMZ$. Measured at pH 5.9; $[ClPMZ] = 10^{-3}$ M; $[H_2A] = 10^{-4}$ M. Varying [NaBr].

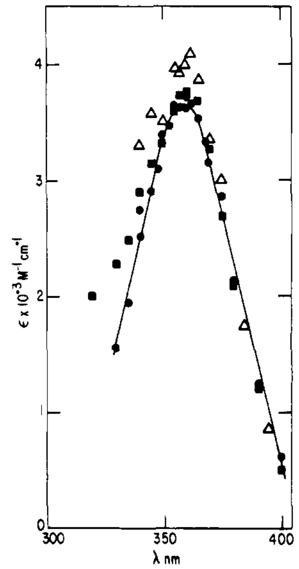

Figure 6. Absorption spectra of the product of the reaction of $ClPMZ^{+}\cdot$ with HA^-. (●) $[ClPMZ] = 1.7$ mM; $[H_2A]_T = 1.7$ mM. (△) $[ClPMZ] = 1.7$ mM; $[H_2A]_T = 5.4$ mM. (■) $[H_2A]_T = 2.3$ mM; all solutions contained 0.1 M NaBr, 0.01 M phosphate buffer at pH 6.3 and were N_2O saturated.

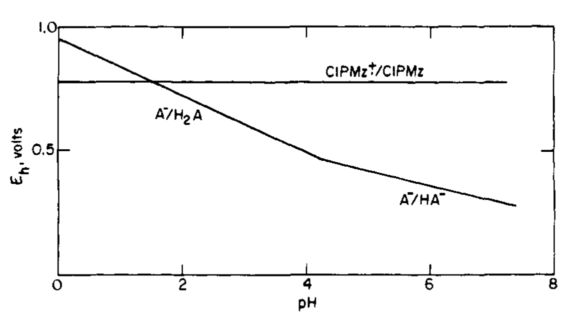

Figure 7. The dependence of the reduction potential of the systems ClPMZ$^{+}\cdot$/ClPMZ and $A^{-}\cdot/H_2A$ on pH. For H_2A, pK_1 = 4.1 and pK_2 = 11.5; for $HA\cdot$, pK_r = −0.45 and E_h at pH 11 of 0.085 V were assumed (Table IV in reference 17). For ClPMZ, the same states of protonation of the radical and the parent compound were assumed in the range pH 0–7 (reference 8a).

be observed at wavelengths higher than those presented in Figure 6 which would have an extinction coefficient higher than 400 M^{-1} cm^{-1}. In view of the close resemblance in the absorption spectra in Figure 6, we believe that reaction 7 is a simple electron transfer from HA^- to ClPMZ$^{+}\cdot$. From the match between the rate of decay of ClPMZ$^{+}\cdot$ at 520 nm and the rate of formation of the product at 360 nm at the highest [HA^-] used (Table II), we conclude that, if a complex is formed, its lifetime is shorter than 7×10^{-8} s at pH 5.9 and μ = 0.1. However, if such a complex is longer lived than the above mentioned lifetime, then its absorption spectrum is identical with that of $A^{-}\cdot$. Although the experimental conditions in the present study differ widely from those described by Klein and Toppen,[11] it is difficult to see a straightforward explanation for the different conclusions. The pH in the previous work was much lower than that in our study. However, since the pK_a of the amine group is above the highest pH used in this study, no change in the mechanism is expected to occur due to deprotonation of ClPMZ. On the other hand, the results in the preceding section indicate no deprotonation of the radical cation at near neutral pH either. The ascorbate anion was shown above to be the reactive species in the pH range 2.2–7.2, while it was previously[11] concluded that its acidic form is reactive at pH <1. However, the mechanism proposed by Klein and Toppen requires deprotonation of H_2A upon formation of the charge-transfer complex. It seems therefore unnecessary to assume a change in the mechanism when H_2A is already partially deprotonated at the higher pH. Furthermore, it is noted that extrapolation of our results (at μ = 0.1) to [H^+] = 1 M would yield $k_{obsd}/[H_2A]_T = 1.1 \times 10^5$ M^{-1} s^{-1} which is approximately two times larger than the results given in the previous study[11] at low $[H_2A]_T$ (and at μ = 1). This difference is entirely consistent with the ionic strength effect and would indicate no change in the mechanism of the electron-transfer stage. In an attempt to provide a unified explanation for the results over the whole pH range, we note that at the very high acidities the first pK_a of the $A^{-}\cdot$ radical is approached (pK_{a8} = −0.45[19])

$$HA\cdot \rightleftharpoons H^+ + A^{-}\cdot \qquad (8)$$

and the reduction potentials of PTZ$^{+}\cdot$ and HA are close to one another (Figure 7). Under such conditions reaction 9

$$PTZ^{+}\cdot + HA^- \rightleftharpoons HA\cdot + PTZ \qquad (9)$$

is not necessarily shifted completely to the right and might therefore afford the saturation dependence on $[H_2A]_T$ as observed by Klein and Toppen.[11] To show that this possibility should seriously be considered we reconstruct in Figure 7 the pH dependence of the redox potential of both couples PTZ$^{+}\cdot$/PTZ and $HA\cdot/H_2A$. The value of $E°_{PTZ^{+}\cdot/PTZ}$ was taken from ref 8a and, in accordance with the results obtained above, no deprotonation, of either PTZ or PTZ$^{+}\cdot$ in the pH range of interest, was assumed. For the couple $HA\cdot/H_2A$ the pulse radiolytic determination of Steenken and Neta[17] at pH 11 was adopted, along with the above mentioned pK_a values of H_2A and its radical. From Figure 7 it is clear that at pH <1 the thermodynamically stable radical among PTZ$^{+}\cdot$ and HA· is the former and the electron-transfer reaction should proceed in the reverse direction. The disappearance of PTZ$^{+}\cdot$ in this system when studied at high acidities is controlled then by a reaction that consumes the small amounts of $A^{-}\cdot$ and HA· that are produced in the equilibrium of reaction 9. The kinetic order of the disappearance of PTZ$^+$ would then be determined by the mode of draining of HA and $A^{-}\cdot$ from the system but a mechanism consisting of reactions 6, 8, and 9 and a disappearance reaction for HA (disproportionation, reaction with PTZ$^{+}\cdot$, or reaction with impurities) can account for most of the observations in both studies.

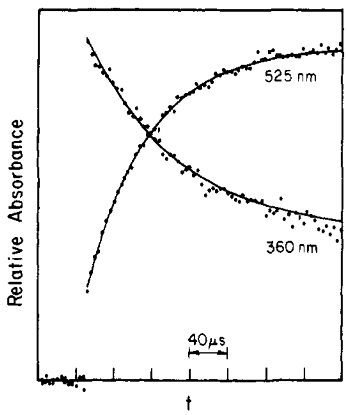

Figure 8. The kinetics of the oxidation of ClPMZ to its radical cation by the ascorbate radical at 1 M HCl. Note the increase in ClPMZ$^{+}\cdot$ absorption at 520 nm and the concomitant decrease in $A^{-}\cdot$ absorption at 360 nm. The relative absorbances were normalized to give the same height at the maximum point. Solutions were Ar saturated and contained 0.3 M 2-propanol; $[H_2A]_T = 10^{-2}$ M; [ClPMZ] = 2×10^{-4} M.

The Reaction of Ascorbic Acid Radicals with PTZ. In the previous section it is suggested that at pH <1 the electron transfer from PTZ to $A^{-}\cdot$ (or HA·) should dominate over reaction 7; i.e., the equilibrium reaction 9 should be shifted to the left. This suggestion is now to be verified.

The sequence of reactions of the radiolytically produced radicals is somewhat different at high acidities than in the previously discussed higher pHs. The high [H^+] (1 M) is now the predominant scavenger of e_{aq}^- which will convert the latter to H· atoms.

$$e_{aq}^- + H^+ \rightarrow H\cdot \qquad (10)$$

The solutions in the following experiments were therefore deaerated by Ar saturation. The H· atoms are then rapidly converted to the less reactive 2-propanol radicals in the presence of 0.3 M 2-propanol ($k_{11} = 7.9 \times 10^7$ M^{-1} s^{-1})[20]

$$H\cdot + (CH_3)_2CHOH \rightarrow (CH_3)_2\dot{C}OH + H_2 \qquad (11)$$

Due to experimental difficulties of handling the bromide solutions at such high acidities we decided to use HCl. Thus the majority of the OH· radicals will be converted to the highly oxidizing Cl_2^- radicals

$$OH\cdot + Cl^- \xrightarrow{H^+,Cl^-} Cl_2^- + H_2O \qquad (12)$$

At the end of the pulse the only radicals left are therefore the 2-propanol radicals and Cl_2^-. The Cl_2^- radicals were shown to oxidize H_2A with a rate constant of 6.5×10^8 M^{-1} s^{-1}.[14c]

The rate constant for the oxidation of 2-propanol by Cl_2^- is much slower, about 10^5 M^{-1} s^{-1}.[14c] In Figure 8 we show the results obtained from a 1 M HCl, Ar-saturated solution containing 0.3 M 2-propanol, 10^{-2} M H_2A, and 2×10^{-4} M ClPMZ. Immediately following the pulse and the rapid decay of Cl_2^- the absorption of $A^-\cdot$ can be observed at 360 nm (and a small yield of $ClPMZ^+$ at 520 nm). $A^-\cdot$ can then be seen to decay, while $ClPMZ^{+}\cdot$ builds up (520 nm) with the same rate. The initial spectrum in the near-UV was found to closely match the spectrum of $A^-\cdot$ (cf. Figure 6), while the spectrum at the end of the reaction is identical with that of $ClPMZ^+$.

The only concern at this stage, with regard to the formation of $ClPMZ^{+}\cdot$, is the possibility that the 2-propanol radical rather than $A^-\cdot$ (or $HA\cdot$) is the species that oxidizes ClPMZ. This possibility is, however, easily dismissed since in the absence of H_2A only an immediate formation of $ClPMZ^{+}\cdot$ (by direct oxidation with Cl_2^-) was observed with no further formation on the time scale shown in Figure 8. We consider the results similar to those shown in Figure 8 as a convincing evidence for the reversal of the direction of electron transfer as discussed above.

The pseudo-first-order rate constant for the reaction (−9) was found to be linear with [ClPMZ] in the range of $2-9 \times 10^{-4}$ M under otherwise the same conditions as given under Figure 8. From this dependence we derive $k_{-9} = 5.0 \times 10^7$ M^{-1} s^{-1}. From the value $k_9 = 1.1 \times 10^5$ M^{-1} s^{-1} obtained in the previous section by extrapolation to 1 M HCl one derives $K_9 \sim 2 \times 10^{-3}$, in close agreement with the value expected from the difference in the redox potentials, ΔE_h, given in Figure 7.

Conclusions

Two of the main points that were experimentally verified in the present study are predictable on the basis of the presently available thermodynamic data. Thus from the estimate of $E^\circ_{HA\cdot/H_2A}$, which was based on the Marcus theory for outer sphere electron-transfer reactions[12] and was later verified experimentally,[17] a full E_h vs. pH curve could be reconstructed. From such a curve then one can deduce that the active reductant of the *N*-alkylphenothiazine radical cations at pH >2 will be the singly deprotonated form of ascorbic acid. On the other hand, one would predict that at pH <1 the phenothiazines are thermodynamically capable of reducing the ascorbate radical. Our failure to observe any intermediate in the products of the electron transfer from HA^- to $PTZ^{+}\cdot$, along with the match between the kinetic and thermodynamic data, seems to indicate that the reaction is an outer sphere electron transfer reaction. In that sense this reaction resembles that of the *N*-alkylphenothiazines with several metal cations[8] rather than that with aromatic strong electron acceptors.[9,10]

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References and Notes

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