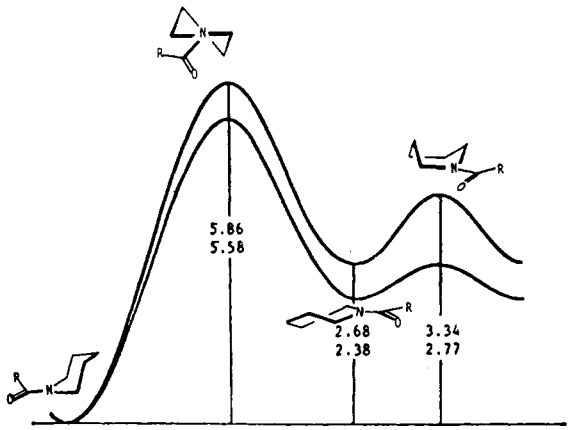


Figure 3. A representation of a portion of the calculated energy profile for ring inversion for *N*-formylpiperidine (**7**) and *N*-acetylpiperidine (**8**). The top curve and upper set of numbers are for **7** and the bottom curve and lower set of number are for **8**. The numbers are the calculated energies for the forms shown and their units are kilocalories/mole.

stituent on nitrogen in **7** and **8** renders them unsymmetrical, and thus there are more variations to consider; therefore, in order to find the lowest energy inversion pathway, steric energy calculations were performed for 19 possible energy maximum and minimum conformations—chair, boat, twist-boat, half-chair, and sofa—for each of the piperidine derivatives [reached by rotating (at 5-deg intervals via the dihedral driver) the C–N–C–C torsional angle in the ring of the chair conformation and minimizing the steric energies with each rotation]. The energy profile obtained is shown in Figure 3 for both **7** and **8**. The highest barriers to ring inversion for these compounds are located between the chair and twist-boat, and the energies of the barriers are 5.86 and 5.58 kcal/mol, respectively. These energies are near the average values for methylenecyclohexane and cyclohexanone. Additionally, there is a small energy barrier between the twist-boat and its mirror image. The boat conformation appears as a maximum. Rotation of the ring torsional angle N–C–C–C, in an attempt to examine another potential ring inversion path, generates a barrier exactly the same as that found above, although the path itself is clearly different. Clearly, there are various routes to reach one transition-state conformation from another (which may be the mirror image of the first) since the steric energies of the several boat and twist-boat conformations are similar (within 1.2 kcal/mol of each other).

Further, the steric energies of the various ring conformations of **7** and **8** are little influenced by the geometries of the respective acyl groups, and (as shown in Figure 3) (a) relative energies of **7** are generally higher than those of **8** for each similar conformation (which is directly comparable to the observation that the barrier in **3** is higher than that in **6** as shown earlier); (b) the conformations having energy maxima and minima are similar in both piperidine derivatives (despite the absolute differences in the amounts of energies); and, (c) as with the carbocycles to which comparison is made, the most stable conformers for both **7** and **8** are the chair forms with the relative energies of the twist-boat forms of both amides somewhat similar to cyclohexanone but substantially lower than cyclohexane and methylenecyclohexane.

Conclusion

We have extended MM2 to molecules containing the amide group and, in doing so, have successfully developed a set of parameters which reproduce, with reasonable accuracy, experimentally available data. The parameters developed for simple amides have been extended to more complicated systems, and predictions have been made. Among these the most striking may be that in dialkyl-substituted amides, the nitrogen atom deviates from the plane of the three carbon atoms to which it is attached.

Formation and Characterization of 3-*O*-Arenediazoascorbic Acids. New Stable Diazo Ethers

Michael P. Doyle,* Carey L. Nesloney, Michael S. Shanklin, Carol A. Marsh, and Kathlynn C. Brown

Department of Chemistry, Trinity University, San Antonio, Texas 78284

Received February 7, 1989

Ascorbic acid reacts with arenediazonium salts to form stable compounds whose structures have been spectroscopically identified as 3-*O*-arenediazoascorbic acids. The pK_a values of the *p*-nitro- and *p*-chlorobenzenediazo derivatives are 10.2 and 10.1, respectively, which also correspond to arenediazonium ion attachment at the 3-hydroxyl position of ascorbic acid. These diazo ethers are stable in the pH range of 3 to 11, and they are resistant to nucleophilic displacement and electron-transfer reactions that commonly occur with the unassociated diazonium ions. Reaction rates for diazo ether formation are first order in ascorbic acid and arenediazonium ion concentrations, and they exhibit inverse first-order dependence on the hydrogen ion concentration over the pH range of 6.0–8.0.

Oxidation–reduction reactions of hydroquinone (H_2Q) and ascorbic acid (H_2A) are formally equivalent. Both substrates undergo one-electron-transfer processes through semidione intermediates. Their redox potentials, whose values are pH dependent,[1-4] converge with differences of as little as 15 mV at pH 13.5 and 50 mV at pH 0.[5] Rate constants for outer-sphere electron transfer with metal ions are only 2 to 3 orders of magnitude lower for H_2A than for H_2Q when compared under identical conditions,[6-8] al-

(1) Pelizzetti, E.; Mentasti, E.; Pramauro, E. *J. Chem. Soc., Perkin Trans. 2* **1978**, 620.
(2) Mentasti, E.; Pelizzetti, E.; Baiocchi, C. *J. Chem. Soc., Dalton Trans.* **1977**, 132.
(3) Pelizzetti, E.; Mentasti, E.; Pramauro, E. *Inorg. Chem.* **1976**, *15*, 2898.
(4) Pelizzetti, E.; Mentasti, E. *J. Chem. Soc., Dalton Trans.* **1976**, 2222.
(5) Steenken, S.; Neta, P. *J. Phys. Chem.* **1979**, *83*, 1134.

0022-3263/89/1954-3785$01.50/0

Table I. ^{13}C NMR Chemical Shifts for H_2A, Me-AH, and 1

position[b]	chemical shift, ppm[a]						
	H_2A[c]	Me-AH[c]	1a	1b	1c	H_2A/NaOAc[d]	1a/NaOAc[d]
C-6	63.4	63.3	70.7	70.8	70.8	65.1	72.2
C-5	70.4	70.2	70.9	70.9	70.9	72.0	74.8
C-4	76.1	76.1	77.0	77.1	77.1	80.6	75.6
C-3	152.6	151.8	159.2	159.5	159.6	171.0	156.3
C-2	119.6	120.4	(112.5)[e]	115.9	118.2	117.6	115.3
C-1	171.4	171.7	170.6	170.8	170.9	178.6	179.6

[a] Relative to TMS. Unless specified otherwise, solvent was CD_3CN. Values in acetone-d_6 were ±0.2 ppm from those reported. [b] Assignments were confirmed by HETCOR and DEPT experiments. [c] Spectra taken in acetone-d_6. Spectrum for H_2A corresponds to that previously reported: Ogawa, T.; Uzawa, J.; Matsui, M. *Carbohydr. Res.* **1977**, *59*, C32. [d] Spectra taken in 2:1 D_2O/CD_3CN saturated with sodium acetate. [e] Estimated value; overlap with ortho aromatic carbon absorption.

though rates for oxidation of HA^- are faster than those for oxidation of H_2Q. Self-exchange rate constants for $HA^-/HA^\bullet$ and $H_2Q/H_2Q^\bullet$ differ by only 2 orders of magnitude,[7] with the difference presumably due to the more extensive bond reorganization required for $HA^\bullet$ formation.

We have recently reported that hydroquinone is oxidized to *p*-benzoquinone by arenediazonium salts in aqueous solution.[9] The rate law exhibited inverse first-order dependence on the hydrogen ion concentration over a pH range of 1.0–9.5. Through application of Marcus theory, using electron-transfer self-exchange rate constants previously obtained for arenediazonium ions[10] and the absence of observable diazo ether formation, we were able to conclude that electron transfer to the hydroquinone monoanion occurred by an outer-sphere mechanism. Anticipating that ascorbic acid or its monoanion would undergo a similar redox reaction with arenediazonium salts, we undertook the present investigation to further evaluate their oxidative characteristics.

Results and Discussion

Formation and Characterization of 3-*O*-Arenediazoascorbic Acids. Treatment of ascorbic acid with *p*-nitrobenzenediazonium tetrafluoroborate in aqueous phosphate buffered solution at pH 7.0 did not result in the anticipated electron transfer that would have been visibly characterized by evolution of dinitrogen, nor did this transformation occur at pH values up to 11 where diazotate formation becomes prohibitively competitive.[11] Instead, rapid formation of an associated complex between ascorbic acid and *p*-nitrobenzenediazonium tetrafluoroborate occurs (eq 1). Titration of ascorbic acid at pH 4.7 (λ_{max} 266 nm)

$$H_2A + ArN_2^+BF_4^- \rightarrow HAN{=}NAr + HBF_4 \quad (1)$$

with *p*-nitrobenzenediazonium tetrafluoroborate (λ_{max} 262 nm) showed the appearance of a new compound (Figure 1) with a λ_{max} of 358 nm.

On a preparative scale, treatment of a pale yellow aqueous solution of *p*-nitrobenzenediazonium tetrafluoroborate with an equivalent molar amount of H_2A resulted in an immediate color change to intense yellow; extraction with ether and crystallization yielded a yellow solid whose ^1H NMR spectrum suggested diazo ether formation. The ^{13}C NMR spectrum of this complex further confirms the diazo ether formulation and supports the oxygen binding site on ascorbic acid as that of C-3 (1).

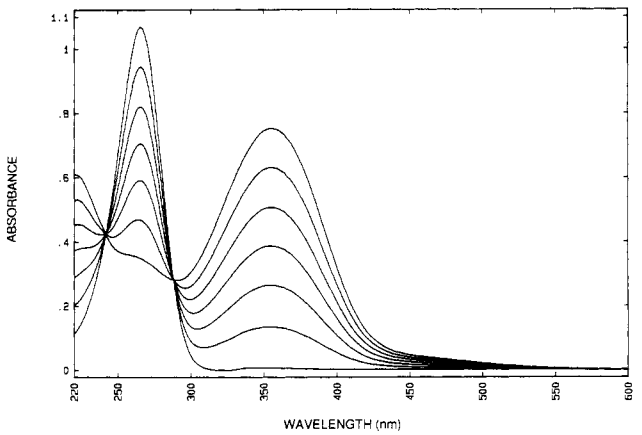
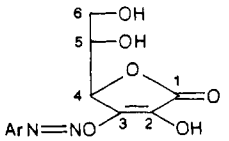


Figure 1. Titration of ascorbic acid (7.46×10^{-5} M) with 0.15 equiv aliquots of *p*-nitrobenzene-diazonium tetrafluoroborate (final concentration = 6.72×10^{-5} M) at pH 4.7. Isosbestic points are observed at 241 and 290 nm.



1a: Ar = *p*-$NO_2C_6H_4$
1b: Ar = *p*-ClC_6H_4
1c: Ar = *p*-$C_6H_5NHC_6H_4$

Similar analyses of ascorbic acid complexes formed with *p*-chlorobenzenediazonium tetrafluoroborate and *p*-anilinobenzenediazonium hydrogen sulfate (Variamine Blue RT) were obtained, and their comparative ascorbate ^{13}C NMR spectral characteristics are listed in Table I. An alternative structure, derived from attack by the diazonium ion at C-2 of ascorbic acid, is inconsistent with this spectral data and (vide infra) the acidity of the isolated product.

Ascorbic acid is diprotic with pK_a values of 4.25 and 11.79 for hydron[12] dissociation from the 3-hydroxyl and 2-hydroxyl groups, respectively.[6,13,14] Thus, if association with arenediazonium ions occurred at the 3-position, the presence of bases only moderately stronger than HA^- should leave 1 unaffected. Confirmation of this prediction was obtained from the ^{13}C NMR spectra of H_2A and 1a in the presence of sodium acetate. With H_2A, conversion

(6) Amjad, Z.; Brodovitch, J.-C.; McAuley, A. *Can. J. Chem.* **1977**, *55*, 3581.
(7) McAuley, A.; Oswald, T.; Haines, R. I. *Can. J. Chem.* **1983**, *61*, 1120.
(8) McAuley, A.; Spencer, L.; West, P. R. *Can. J. Chem.* **1985**, *63*, 1198.
(9) Brown, K. C.; Doyle, M. P. *J. Org. Chem.* **1988**, *53*, 3255.
(10) Doyle, M. P.; Guy, J. K.; Brown, K. C.; Mahapatro, S. N.; VanZyl, C. M.; Pladziewicz, J. R. *J. Am. Chem. Soc.* **1987**, *109*, 1536.
(11) Hegarty, A. F. In *The Chemistry of Diazonium and Diazo Groups*; Patai, S., Ed.; Wiley: New York, 1978; Part 2, Chapter 12.
(12) Recommended general name for H^+, to be used without regard to its nuclear mass: Bunnett, J. F.; Jones, R. A. Y. *Pure Appl. Chem.* **1988**, *60*, 1115.
(13) Mehrotra, U. S.; Agrawal, M. C.; Mushran, M. P. *J. Phys. Chem.* **1969**, *73*, 1996.
(14) Taqui-Khan, M. M.; Martell, A. E. *J. Am. Chem. Soc.* **1967**, *89*, 4176.

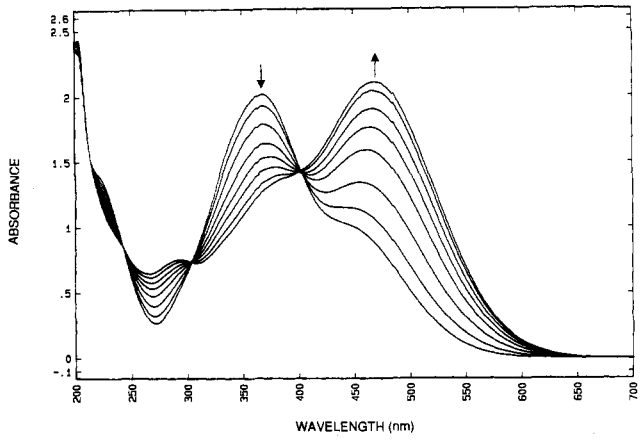


Figure 2. Titration of **1a** (2.54×10^{-4} M) with sodium hydroxide. The initial solution pH was 3.6, which, following addition of base, increased to 7.4, 9.6, 9.9, 10.1, 10.3, 10.4, and 10.5 sequentially. Isosbestic points are observed at 236, 311, and 400 nm.

by acetate to its monoanion resulted in the expected chemical shift for C-3 from 153 ppm to 171 ppm, which closely approaches the chemical shift for C-1 of 179 ppm. In contrast, the chemical shift difference between C-3 and C-1 with **1a** in the presence of sodium acetate was nearly the same as that in its absence (Table I). For reference, the ^{13}C NMR spectrum of the 3-methyl ether derivative of H_2A (Me-AH), formed by treatment of H_2A with an equivalent amount of diazomethane,[15] is also reported.

Further confirmation of the position for attachment of arenediazonium ions to H_2A was obtained from the pK_a values for the associated complexes. If attachment is at position 3, the pK_a value of 1 is expected to be approximately that for hydron transfer from the 2-hydroxyl group of H_2A, whereas if attachment is at position 2, a low pK_a value corresponding to that for hydron transfer from the 3-hydroxyl group of H_2A is expected. This is not a moot question since, although acylation of H_2A with acetic anhydride initially forms 3-O-acetylascorbic acid, intramolecular O → O acyl migration occurs readily between pH 4 and 7 to form the presumably more stable 2-O-acetylascorbic acid.[16]

The UV/vis spectrum of **1a** responds in the fashion of an indicator to base. Sequential addition of 0.75 equiv portions of sodium hydroxide to **1a**, prepared according to eq 1, produced the spectral changes shown in Figure 2. Addition of acid returned the spectrum of this complex to its original display, indicating that only hydron transfer occurs upon treatment of **1a** with base. For comparison, treatment of H_2A with base resulted in the bleaching of its absorbance at 266 nm, and treatment of *p*-nitrobenzenediazonium tetrafluoroborate with base forms the corresponding diazotate[11] with disappearance of the absorption at λ_{max} 262 nm and appearance of an intense absorption at λ_{max} 334 nm. When the absorbance of **1a** was followed at 358 nm as a function of pH, the titration curve of Figure 3 was obtained from which, with multiple determinations, a pK_a value of 10.2 ± 0.3 was obtained. Similar experiments with **1b** provided its pK_a value as 10.1 ± 0.4.

The high pK_a values obtained for **1a** and **1b** are in accord with the structure assignment of 1 as 3-O-arenediazoascorbic acid. However, these pK_a values are much higher than those reported for other 3-O derivatives of

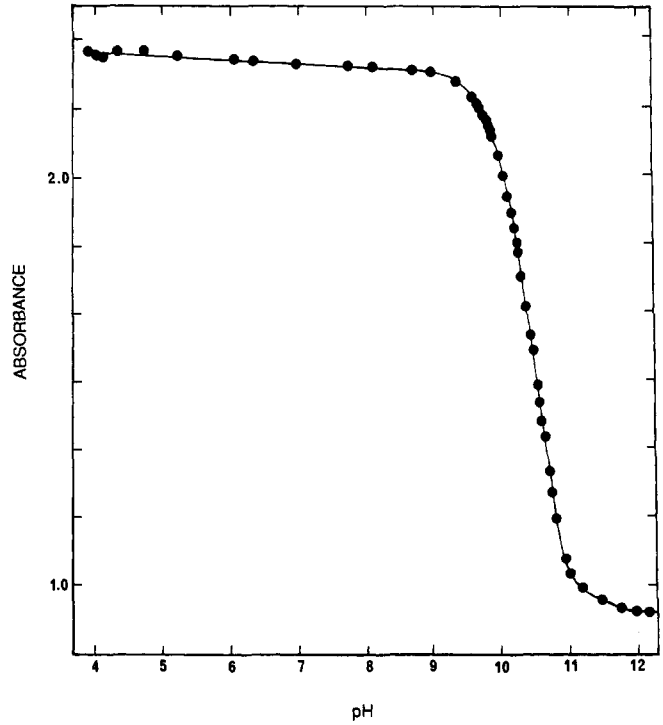


Figure 3. Absorbance at 358 nm versus pH for **1a** (2.0×10^{-4} M). The calculated pK_a value is 10.3.

L-ascorbic acid. For example, 3-O-methyl-L-ascorbic acid has a pK_a value of 7.8,[17] while for 3-O-acetylascorbic acid the pK_a value is reported to be 3.6.[18] In addition, isopropylideneascorbic acids consistently show pK_a values greater than 4, but less than 7, for phosphorus esters formed at the 3-position and pK_a values less than 4 for those at the 2-position.[19] The reason for these differences is unclear but, as with the 4 order-of-magnitude difference in acidity between 3-O-methyl- and 3-O-acetylascorbic acids, the pK_a values for **1a** and **1b** may merely be reflections of their stability.

Rate Law and pH Dependence. Reactions between *p*-anilinobenzenediazonium hydrogen sulfate (VB) and ascorbic acid were conducted at pH 7.0 and 25.0 °C under nitrogen in aqueous 0.050 M phosphate-buffered solutions. Ascorbic acid was used in amounts ranging from 10-fold to 100-fold molar excess over the diazonium salt. Rates were followed by monitoring the decrease in absorbance at 377 nm. First-order kinetic dependence on the concentration of VB, normally extending through more than 3 half-lives, was established under these conditions. The kinetic dependence on ascorbic acid, obtained from the linear relationship between the experimental pseudo-first-order rate constant and the concentration of ascorbic acid at constant diazonium ion concentration, was also first order. Thus this transformation is second order overall, first order in the concentration of VB and first order in the concentration of AH_2, with a rate constant of 3.43 M^{-1} s^{-1}. As seen from the spectral time course for this reaction (Figure 4), conversion to **1c** is the only detectable process. The decrease in the absorbance at λ_{max} 377 nm due to VB and the shift in the λ_{max} of ascorbic acid to that of **1c** at 268 nm are accompanied by isosbestic points at 232, 274, and 322 nm.

(15) Reichstein, T.; Grussner, A.; Oppenauer, R. *Helv. Chem. Acta* **1934**, *17*, 510.
(16) Paulssen, R. B.; Chatterji, D.; Higuchi, T.; Pitman, I. H. *J. Pharm. Sci.* **1975**, *64*, 1300.
(17) Radford, T.; Sweeny, J.; Iacobucci, G. *J. Org. Chem.* **1979**, *44*, 658.
(18) Paulssen, R. B.; Chatterji, D.; Higuchi, T.; Pitman, I. H. *J. Pharm. Sci.* **1975**, *64*, 1300.
(19) (a) Cabral, J.; Haake, P. *J. Org. Chem.* **1988**, *53*, 5742. (b) Jernow, J.; Blount, J.; Oliveto, E.; Perrota, A.; Rosen, P.; Toome, V. *Tetrahedron* **1979**, *35*, 1483.

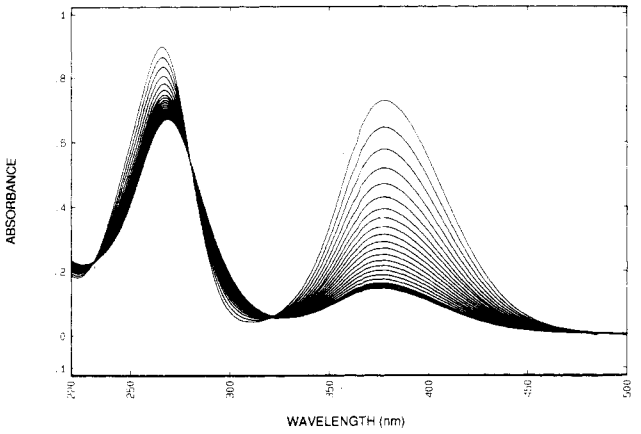


Figure 4. Time course for the reaction between *p*-anilinobenzenediazonium hydrogen sulfate (2.45×10^{-5} M) and ascorbic acid (4.93×10^{-5} M) at pH 6.9 and 25.0 °C in 0.050 M phosphate-buffered aqueous solution. Individual spectra were taken at 8-min intervals.

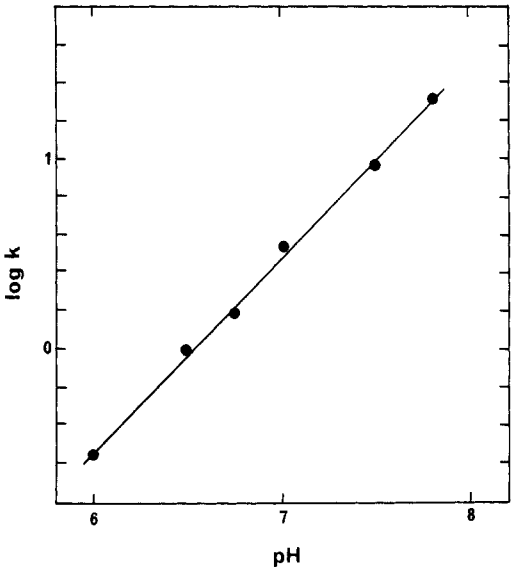


Figure 5. pH–rate profile for the reaction between ascorbic acid and *p*-anilinobenzenediazonium hydrogen sulfate (VB) at 25.0 °C in 0.050 M phosphate-buffered aqueous solution.

The dominant form of ascorbic acid at pH 7.0 is its monoanion, and AH^- is the anticipated reactive substrate. To ascertain the expected inverse first-order dependence on $[H^+]$, rate constants for the reaction between VB and ascorbic acid were obtained over the pH range of 6.0–8.0, and the resulting pH–rate profile is shown in Figure 5. The composite data establishes the mechanism for association of arenediazonium ions with ascorbic acid as that described in eq 2 and 3 with k_{HA^-} for VB equal to 1.92×10^3 M^{-1} s^{-1}. However, available data does not allow us to distinguish between syn and anti isomers[20] for ArN=NAH.

$$AH_2 \overset{K_a}{\rightleftharpoons} HA^- + H^+ \quad (2)$$

$$ArN_2^+ + HA^- \xrightarrow{k_{HA^-}} ArN{=}NAH \quad (3)$$

Stability of 1. Diazo ethers of the general structure ArN=NOR (R = alkyl, aryl) are rarely formed, as is **1**, as stable products. Bunnett has shown that treatment of *p*-nitrobenzenediazonium ion with methoxide results in the formation of the reduction product, nitrobenzene, often in high yield.[21] The anti form of the diazo methyl ether is produced in competition with nitrobenzene, presumably from the initially formed syn isomer, and has been isolated and characterized. However, the preferred method for the preparation of arenediazo methyl ethers is from the reaction of metallic diazotates with methyl iodide.[22,23] Phenolic ethers have also been prepared, often by indirect methods,[24-27] but they are relatively unstable. The diazo ether formally derived from 1-naphthol and the benzenediazonium ion[26] is sensitive to acid and base as well as to light, which cause its decomposition to the isomeric diazo coupling products. In contrast, **1** is formed in quantitative yield by the direct combination of arenediazonium salts with ascorbic acid and, perhaps because it possesses a built-in buffer, **1** is relatively stable to acid and base. For example, **1a** does not undergo dissociation to the *p*-nitrobenzenediazotate even at pH 11.2, although irreversible decomposition of the complex, which leaves the *p*-nitrobenzenediazo ether linkage intact, occurs slowly under these conditions. Similarly, **1a** is stable above pH 3 but undergoes dissociation to the *p*-nitrobenzenediazonium ion and ascorbic acid at higher acidities.

Ascorbic acid has been reported to promote the Sandmeyer reaction between arenediazonium salts and copper(II) halides,[28,29] and the promotion of this transformation was believed to be related to the reduction potential of H_2A.[30] More recently, the direct action of H_2A on arenediazonium chlorides to form aryl chlorides was found to lack the correlation observed from use of well-established electron-transfer agents (Cu^+, Fe^{2+}, Sn^{2+}), and a heterolytic mechanism was proposed for aryl chloride formation in the presence of ascorbic acid.[31] Given the stability of the complex formed between H_2A and arenediazonium ions that we have established in the present study, it is fair to say that H_2A plays only a protective role in electron-transfer reactions that normally occur with uncomplexed arenediazonium ions. Indeed, dediazoniation did not occur when **1a** was treated with large excesses of chloride or hydroxide and, in what is an even more critical test for the stability of **1**, no reaction occurred between **1a** and potassium ferrocyanide, although ferrocyanide is known to undergo electron transfer to the *p*-nitrobenzenediazonium ion with a reaction rate constant at 25 °C of 7×10^4 M^{-1} s^{-1}.[10]

The complete absence of electron transfer between arenediazonium ions and ascorbic acid, its monoanion, and its dianion was unexpected. Self-exchange rate constants for outer-sphere electron transfer between these substrates[7,10] indicated the feasibility of this process. However, in a recent evaluation of available electron-transfer data for ascorbic acid, Creutz suggested that the intrinsic barriers to electron transfer for ascorbic acid and its con-

(20) (a) Lewis, E. S.; Hanson, M. P. *J. Am. Chem. Soc.* **1967**, *89*, 6268. (b) Lewis, E. S.; Suhr, H. *Ber. Dtsch. Chem. Ges.* **1959**, *92*, 3031, 3043.

(21) (a) Bunnett, J. F.; Takayama, H. *J. Org. Chem.* **1968**, *33*, 1924. (b) Boyle, W. J.; Broxton, T. J.; Bunnett, J. F. *J. Chem. Soc., Chem. Commun.* **1971**, 1469.

(22) Pechmann, V. H.; Frobenius, L. *Ber. Dtsch. Chem. Ges.* **1894**, *27*, 3412.

(23) Masoud, N. K.; Ishak, M. F. *J. Chem. Soc., Perkin Trans. 2* **1988**, 927.

(24) Dimroth, O.; Hartmann, M. *Ber. Dtsch. Chem. Ges.* **1908**, *41*, 4012.

(25) Kauffmann, T.; Friestad, H. O.; Henkler, H. *Justus Liebigs Ann. Chem.* **1960**, *634*, 65.

(26) Tezuka, T.; Ando, S.; Wada, T. *Chem. Lett.* **1986**, 1667.

(27) Tezuka, T.; Sasaki, K.; Ando, S. *Tetrahedron Lett.* **1987**, *28*, 4427.

(28) Galli, C. *Tetrahedron Lett.* **1980**, *21*, 4515.

(29) Galli, C. *J. Chem. Soc., Perkin Trans. 2* **1982**, 1139.

(30) Galli, C. *J. Chem. Soc., Perkin Trans. 2* **1981**, 1459.

(31) Galli, C. *J. Chem. Soc., Perkin Trans. 2* **1984**, 897.

jugate bases are greater than previously determined.[32] Since the intrinsic barriers for electron transfer to arenediazonium ions are also high,[10] the absence of outer-sphere electron transfer from ascorbic acid is consistent with the understanding provided by Creutz. Furthermore, as is demonstrated by the stability of **1**, homolytic decomposition of diazo ethers is not the spontaneous process that it is often described to be.[11]

Experimental Section

Materials and Methods. *p*-Chlorobenzenediazonium tetrafluoroborate salts were prepared from the corresponding *p*-chloroaniline by treatment with *tert*-butyl nitrite and boron trifluoride etherate[33] and recrystallized from acetone–ether. *p*-Nitrobenzenediazonium tetrafluoroborate and *p*-anilinobenzenediazonium hydrogen sulfate were commercially available. Reagent-grade ascorbic acid was stored under nitrogen. Stock solutions of the diazonium salts were prepared in acetonitrile and maintained under nitrogen. Concentrated solutions of L-ascorbic acid were prepared in deoxygeneated phosphate buffer (0.050 M) by using double-distilled water immediately before use. NMR spectra were taken on a Varian VXR-300 spectrometer using TMS as an internal standard. Electronic spectra were obtained with the HP 8145A diode array spectrophotometer. HPLC analyses were performed with the HP 1090 Series L liquid chromatograph with a diode array detector.

3-O-*p*-Nitrobenzenediazoascorbic Acid (1a). *p*-Nitrobenzenediazonium tetrafluoroborate (1.17 g, 5.00 mmol) was dissolved in 2.0 mL of degassed acetonitrile and diluted by using 15 mL of double-distilled water. To this pale yellow solution was added 0.881 g of L-ascorbic acid (5.00 mmol), and the solution immediately turned to a darker yellow color. After flushing with argon for 30 min, the aqueous solution was extracted by using three 20-mL portions of ether. The combined ether solution was then dried over anhydrous magnesium sulfate, and the ether was removed under reduced pressure to yield 1.62 g of a yellow solid characterized as **1a** (4.97 mmol, 99% yield). Recrystallization was performed with 2-butanone–dichloromethane. Although thermally unstable above 40 °C, this complex remains intact during HPLC analysis on a C-18 column using methanol as the eluent. ^{1}H NMR (CD_3COCD_3): δ 8.13 (d, J = 9.2 Hz, 2 H), 7.02 (d, J = 9.2 Hz, 2 H), 5.72 (d, J = 7.6 Hz, 4-CH), 4.88 (q, J = 7.6 Hz, 5-CH), 4.62 (dd, J = 7.6, 8.8 Hz, 1 H of 6-CH_2), and 4.19 (dd, J = 7.6, 8.8 Hz, 1 H of 6-CH_2).[34] ^{13}C NMR (CD_3CN): Table I and δ 154.4 (C-4), 141.1 (C-1), 126.4 (C-3, C-5), and 112.5 (C-2, C-6). λ_{max} at pH 5.0: 358 nm ($\epsilon = 1.05 \times 10^4$). Anal. Calcd for $C_{12}H_{11}N_3O_8$: C, 44.32; H, 3.41; N, 12.65. Found: C, 44.10; H, 3.49; N, 12.65.

3-O-*p*-Chlorobenzenediazoascorbic acid (1b) was prepared by the same procedure as that for **1a**. ^{1}H NMR (CD_3COCD_3): δ 7.21 (d, J = 9.0 Hz, 2 H), 6.92 (d, J = 9.0 Hz, 2 H), 5.71 (d, J = 7.6 Hz, 4-CH), 4.86 (q, J = 7.5 Hz, 5-CH), 4.60 (dd, J = 7.5, 8.9 Hz, 1 H of 6-CH_2), and 4.18 (dd, J = 7.5, 8.9 Hz, 1 H of 6-CH_2). ^{13}C NMR (CD_3CN): Table I and δ 147.9 (C-1), 129.6 (C-3, C-5), 125.8 (C-4), and 115.6 (C-2, C-6). λ_{max} at pH 5.0: 238 nm ($\epsilon = 1.49 \times 10^4$) and 286 nm ($\epsilon = 2.50 \times 10^4$). Anal. Calcd for $C_{12}H_{11}ClN_2O_6$: C, 45.80; H, 3.52; Cl, 11.27. Found: C, 45.72; H, 3.49; Cl, 11.38.

3-O-*p*-Anilinobenzenediazoascorbic acid (1c) was prepared by the same procedure as that for **1a**. ^{1}H NMR (CD_3COCD_3): δ 9.51 (br s, NH), 7.2–6.7 (m, 9 H), 5.61 (d, J = 7.7 Hz, 4-CH), 4.75 (q, J = 7.7 Hz, 5-CH), 4.51 (dd, J = 7.6, 9.0 Hz, 1 H of 6-CH_2), and 4.06 (dd, J = 7.6, 9.0 Hz, 1 H of 6-CH_2). ^{13}C NMR (CD_3CN): Table I and δ 130.2, 130.1, 121.6, 121.3, 120.1, 118.4, 116.4, and 115.8. Attempts to isolate this compound as a pure crystalline compound resulted in its partial decomposition.

Determination of pK_a Values. Recrystallized **1a** or **1b** was dissolved in 100.0 mL of distilled water (1.0×10^{-4} to 2.0×10^{-3} M). An aliquot of this solution was drawn and its spectrum, from 200 to 700 nm for **1a** and from 200 to 400 nm for **1b**, was obtained. The pH of the solution was obtained, and then 0.050 mL of 0.100 M NaOH was added. The absorbance spectrum was obtained, and the solution pH was again recorded. This procedure was repeated up to pH 12. Absorbance readings for **1a** at 358 nm were plotted against pH, and absorbance readings for **1b** at 238 nm were similarly plotted against pH. A minimum of three separate experiments were performed for each pK_a determination.

Kinetic Determinations. Experiments were performed under nitrogen at 25.0 °C. Reactions were initiated by the injection of an aloquot of a concentrated stock solution of VB into a solution of ascorbic acid in 0.050 M phosphate buffer adjusted to the appropriate pH in the range of 6.0 to 8.0. The decrease in absorbance of VB at 377 nm was followed as a function of time. Pseudo-first-order conditions were maintained through the use of initial ascorbic acid concentrations (1.0×10^{-4} to 1.0×10^{-2} M) that were 10 to 100 times that of VB. The plot of ln $[(A_0-A_\infty)/(A_0-A_t)]$ versus time was linear through greater than 3 half-lives for each determination. Average second-order rate constants from a minimum of three separate determinations are reported with average deviations of ±4%.

Acknowledgment. Support for this research from the National Institutes of Health (Grant GM 37469) is gratefully acknowledged. The National Science Foundation and Keck Foundation provided partial support for the acquisition of the high-field NMR spectrometer. C. A. Marsh is a high school chemistry teacher whose support in this project was provided by the National Science Foundation (Grant TEI-8550235). C. L. Nesloney was an undergraduate research participant in a program sponsored by Merck Sharp & Dohme.

(32) Creutz, C. *Inorg. Chem.* **1981**, *20*, 4449.
(33) Doyle, M. P.; Bryker, W. J. *J. Org. Chem.* **1979**, *44*, 1572.
(34) Assignments made from COSY experiments.