Effects of Ascorbic Acid on Arenediazonium Salts Reactivity: Kinetics and Mechanism of the Reaction

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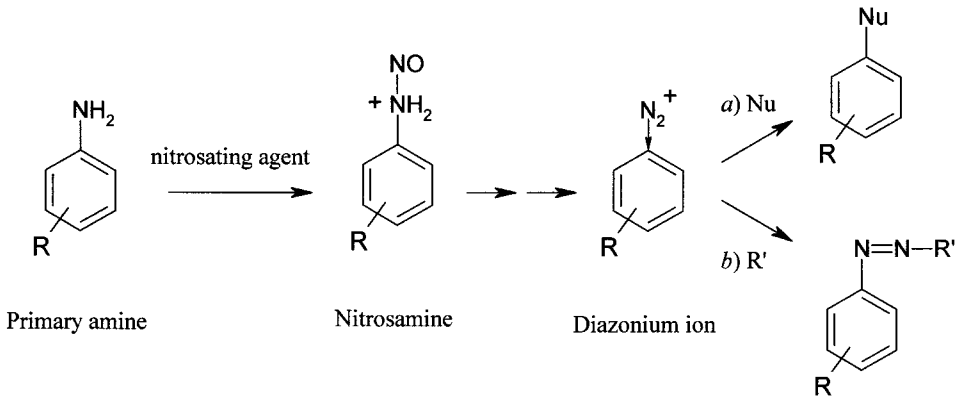
We have examined the kinetics and mechanism of dediazoniation of *o*-, *m*- and *p*-methylbenzenediazonium (ArN_2^+) tetrafluoroborate in the presence of ascorbic acid (H_2A) at different pHs by combining spectophotometric (VIS-UV), high performance liquid chromatography (HPLC), and polarographic measurements. Kinetic data show that, at low pH, observed rate constants increase linearly with increasing ascorbic acid concentration, but the saturation kinetics observed at higher pH suggest the formation of a transient diazo-ether complex preceding the slow step of the reaction. Experimental evidence for the formation of such a complex was obtained from a competitive coupling reaction with the Na salt of '2-naphthol-6-sulfonic acid' and by titration of ascorbic acid (H_2A) with the arenediazonium ions (electrochemical measurements). HPLC Analysis of dediazoniation products indicates that, in the absence of H_2A, only the heterolytic phenol derivative, ArOH, is formed quantitatively, in keeping with the predictions of the $D_N + A_N$ mechanism. In the pH 2–4 range and in the presence of H_2A, reduction products (ArH) are obtained in addition to heterolytic products (ArOH), corroborating that certain biological reducing agents like ascorbate (HA^-) are capable of inducing reductive fragmentation of ArN_2^+ into aryl radicals. All evidence is consistent with two competitive reaction pathways, the thermal decomposition of ArN_2^+, and a rate-limiting decomposition of the transient diazo ether 'complex', formed during the reaction of ArN_2^+ with HA^- in a rapid pre-equilibrium step.

1. Introduction. – *N*-Nitroso compounds may play a significant role in human carcinogenesis because the ubiquity of their precursor compounds leads to the ready formation of *N*-nitrosamines and other *N*-nitroso compounds in the human micro and macroenvironment [1][2]. *N*-Nitroso compounds can be classified in two broad categories, *N*-nitrosamine type and *N*-nitrosamide type [2]. Of these, *N*-nitrosamines, which can be considered amides of nitrous acid, are the most stable and are formally derived from the reaction of a secondary amine with nitrous acid. The *N*-nitrosamide-type substances have a carbonyl group attached to the N-atom bearing the NO group and include *N*-nitrosamides, *N*-nitrosocarbamates, and *N*-nitrosoureas. The instability of these *N*-nitrosamide-type compounds results from having two very electropositive functional groups (NNO and CO) joined and, under appropriate conditions, these compounds rearrange to give diazonium ion intermediates.

By far the best-known and most studied nitrosation reactions are the *N*-nitrosations of amines and related compounds [2]. Both aromatic and aliphatic amines react with a range of nitrosating agents to give, finally, products of deamination. Primary amines, *Scheme 1*, yield primary nitrosamines, which are not stable, and, in a series of rapid reactions that include proton transfer and loss of H_2O, yield diazonium ions that can eventually react further to give dediazoniation (*Scheme 1*,*a*) or nucleophilic addition

Scheme 1. *Simplified Representation for the Nitrosation of a Primary Amine To Yield an Arenediazonium Ion, and Further Decomposition* (*a*) dediazoniation; *b*) nucleophilic addition)



(*Scheme 1,b*) products. This behavior contrasts with that shown by the secondary amines, which yield stable nitrosamines, since there are no α-H-atoms available for the necessary proton transfer [2].

The carcinogenic properties of *N*-nitrosamines and other *N*-nitroso compounds have been known for over 30 years [1][3]. While compounds of the *N*-nitrosamide-type are known to be direct mutagenic agents requiring no biological activation, *N*-nitrosamines must be metabolized in order to elicit their mutagenic or carcinogenic properties [1][3]. Although the mode of carcinogenic biochemical activation is not known for all nitrosamines, it is believed that many of them are activated through the process of α-hydroxylation, resulting in formation of an unstable α-hydroxynitrosamine, which decomposes readily to a diazonium ion, which, in turn, is an aggressive alkylating agents due to their ability to generate aryl radicals [4][5].

The reactions of arenediazonium ions, ArN_2^+ (*Scheme 1*) have attracted considerable attention [6–8], from both synthetic and mechanistic points of view, because of their extraordinary sensitivity to environmental changes [9][10]. In spite of there being a substantial body of knowledge available about their reactions, some of the mechanisms are not completely understood. Electron-density analysis of a number of diazonium ions has shown that both aliphatic and aromatic diazonium ions are best thought of as carbenium ions closely associated with an internally polarized N_2 molecule [11], which implies a dative C–N bond (N → C σ donation and C → N π back-donation, designated with an arrow in all schemes). Among others, arenediazonium ions are currently being employed as chemical probes to determine interfacial concentrations in micellar systems [12–16], to study topologies and orientations of aggregate-bound polypeptides [17], as aryl radical sources for synthetic precursors [18], and their role in DNA arylations [19][20] and DNA deaminations [21] is being explored.

Arenediazonium compounds, ArN_2^+, are strong oxidizing agents that undergo homolytic fragmentation to produce aryl radicals upon reacting with certain electron donors [10][22], and there is good evidence [23–26] that the ability of arenediazonium

ions to generate radicals may be responsible, to some extent, for the mutagenic and carcinogenic properties of aromatic diazonium compounds [4][5][23–27]. To prevent nitrosation, a number of nitrosating scavengers are currently employed in the food [28] and cosmetic [29] industries. Among them, natural antioxidants like ascorbic acid (H_2A), α-tocopherol, butylated hydroxytoluene, sodium bisulfite, *etc.* are in common usage [1][28]. Although these nitrosamine inhibition reactions are relatively well-known, little attention has been paid to the reactions of those natural antioxidants with arenediazonium ions [9][10]. A number of studies concerning the effects of H_2A on dediazoniations have been reported [5][22][30][31], and there is some controversy about its effect on the mechanism of the reaction.

Ascorbate ion (HA^-) has been used to promote dediazoniation of ArN_2^+ in the presence of intentionally added metal ions like Cu^{+2} [32]. In these studies [22] the decomposition of ArN_2^+ was attributed to its reduction by the Fe^{+2} or the Cu^{+1} generated from the action of HA^- on the Fe^{+3} or Cu^{+2} metal ions, but the possibility that HA^- can directly reduce ArN_2^+ was not considered. *Doyle et al.* reported that H_2A reacts with 4-$X-C_6H_4-N_2^+$ ($X = NO_2$, Cl, or NHC_6H_5) to yield stable compounds whose structures have been spectroscopically identified as 3-*O*-arenediazoascorbic acids (diazo ethers) [31]. In contrast, *Reszka et al.*, have recently found that the reaction of 4-$X-C_6H_4-N_2^+$ ($X = NO_2$, Cl, Br, OMe, or $N(Et)_2$) with H_2A under similar conditions ($pH = 7$) generates aryl radicals [5].

In recent work, we have reported a novel method to determine H_2A in freshly prepared natural orange juices [33]. The method is based on the accelerating effect of H_2A on the dediazoniation of 3-methylbenzenediazonium ion, but the mechanism of such a reaction was not depicted. To expand our knowledge regarding the effects of H_2A on dediazoniations, we carried out a kinetic study of the reaction between ascorbic acid and *o*-, *m*-, and *p*-methylbenzenediazonium ions (OMBD, MMBD, and PMBD respectively) within the pH range 1–4, of interest to the food industry. In addition to the kinetics and mechanism of the reaction, the study may be pertinent to the food industry because of the extensive use of H_2A as a natural antioxidant. It can be also of interest to biochemists due to the ready ability of aryl radicals to add to DNA bases and to react with important physiologically relevant electron donors.

2. Results. – 2.1. *Effects of Citric Acid and* Britton-Robinson *Buffer on the Observed Rate Constant and Product Yields in the Absence of H_2A*. The effects of citric acid (CA) and acidity (HCl or *Britton-Robinson* (BR) buffer) on the thermal decomposition of OMBD, MMBD, and PMBD in the absence of H_2A were studied by spectrophotometric, polarographic, and chromatographic techniques. The protocols employed allowed measurement of rate constants for ArN_2^+ decomposition and of product formation and distribution at different acidities (see *Exper. Part*). *Fig. 1* shows the data obtained for OMBD, chosen as representative. *Fig. 1,a* shows the evolution of the first polarographic peak (−50 mV) of OMBD with time and the corresponding first-order plot depicting OMBD loss that yields an observed rate-constant k_{obs} of $10.2 \times 10^{-4}\ s^{-1}$, in agreement with published data [34][35]. A very similar value was obtained by spectrophotometrically monitoring the disappearance of OMBD absorbance at $\lambda = 314$ nm.

Rate constants for dediazoniation product formation were obtained by chromatography. Preliminary experiments show that only one dediazoniation product, *o*-

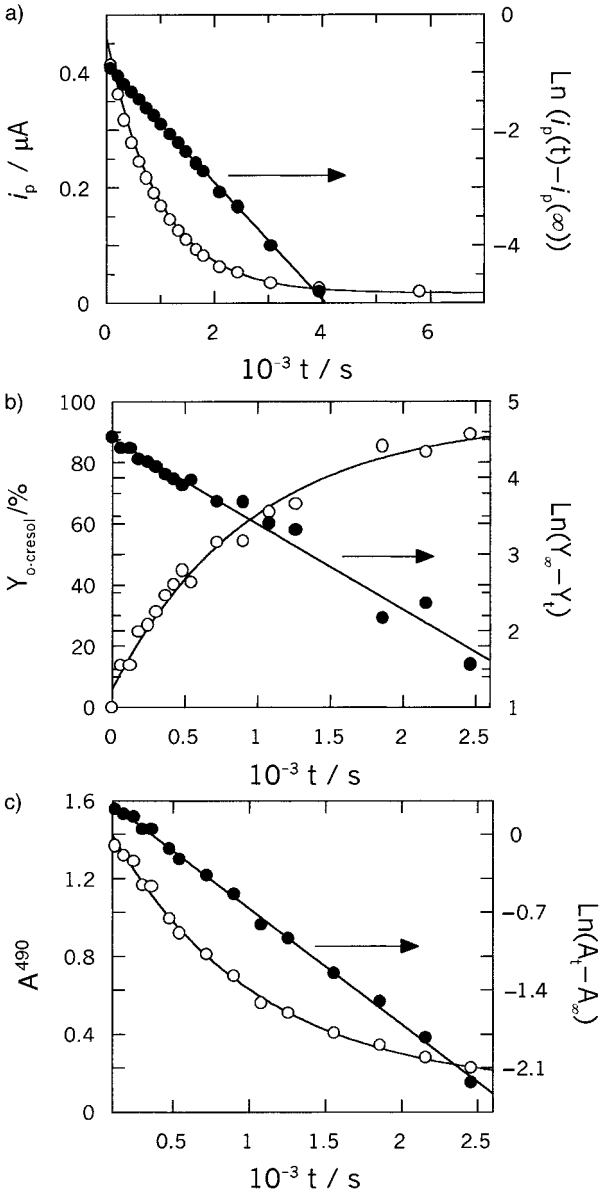


Fig. 1. *Representative kinetic plots for the decomposition at 35° of OMBD* (*ca.* 2.00×10^{-4} M) *in the absence of* H_2A. *a*) Evolution of the first polarographic peak (−50 mV), *b*) variation in the yield of *o*-cresol, and *c*) variation in the formation of the azo dye ($\lambda = 490$ nm) with time (○) and first-order plot (●).

cresol, is formed in significant yields. *Fig. 1, b* shows the variation in the yield of *o*-cresol with time and the corresponding first-order plot, yielding a k_{obs} of 10.5×10^{-4} s^{-1}. The protocol employed (see *Exper. Part*) also allowed us to determine indirectly the k_{obs} for

OMBD disappearance by measuring the change in the absorbance of the azo dye with time. A k_{obs} of 10.4×10^{-4} s^{-1} can be obtained from *Fig. 1,c*, chosen as representative, in agreement with the previously obtained values. *Table 1* shows the k_{obs} values obtained under the different experimental conditions employed, and, as observed, the effects of acidity, electrolytes and CA on k_{obs} are negligible, consistent with results reported for dediazoniations in aqueous systems [34].

Table 1. *Observed Rate Constants* (k_{obs}) *for Thermal Decomposition of Methylbenzenediazonium Ions* (OMBD, MMBD, and PMBD; at 2.0×10^{-4} M) *in the Absence of H_2A under Different Experimental Conditions at* 35°

$[H_3O^+]$/M	OMBD $10^4\ k_{obs}$ /s^{-1}	MMBD $10^4\ k_{obs}$ /s^{-1}	PMBD $10^4\ k_{obs}$ /s^{-1}
0.0011[a])	9.60	8.16	0.23
0.001[b])	10.0	8.23	0.21
0.004[c])	10.3	–	0.22
0.019[a])	9.6	9.10	–
0.019[d])	10.2	8.45	0.25
0.01[e])	9.5	8.36	0.21
0.1[f])	10.5	8.27	–
0.1[g])	10.4	8.51	0.24
0.16[a])	9.6	8.41	–
1.12[a])	9.9	8.23	–

[a]) UV-VIS, $\lambda = 314$ nm, HCl, monitoring ArN_2^+ loss. [b]) UV-VIS, $\lambda = 314$ nm, BR buffer, monitoring ArN_2^+ loss. [c]) UV-VIS, $\lambda = 314$ nm, HCl, $[CA] = 6.25 \times 10^{-3}$ M, monitoring ArN_2^+ loss. [d]) Polarography, HCl, ArN_2^+ loss. [e]) Polarography, $[CA] = 0.025$M, ArN_2^+ loss. [f]) HPLC, $\lambda = 210$ nm, HCl, monitoring formation of ArOH. [g]) UV-VIS, HCl, monitoring azo dye formation.

2.2. *Kinetic Effects of Ascorbic Acid on Dediazoniation*. The effects of H_2A on the dediazoniation of OMBD, MMBD, and PMBD were studied spectrophotometrically and chromatographically at different pHs by employing sufficient amounts of HCl or BR buffer to maintain the desired pH. Clean first-order behavior was obtained in all runs for at least three half-lives. *Fig. 2* shows the variation in k_{obs} with $[H_2A]$ at pH 1–3 for OMBD (*Fig. 2,a*), MMBD (*Fig. 2,b*), and PMBD (*Fig. 2,b*). It was not possible to study the effect of H_2A at higher pH because dediazoniations were too fast to be measured at relatively high H_2A concentrations.

Two different behaviors were observed. At low pH, relatively modest linear increases in k_{obs} with increasing $[H_2A]$ were obtained for all arenediazonium ions. From such linear relationships, the slope and intercept values shown in *Table 2* were obtained. Intercept values represent the k_{obs} values in the absence of H_2A and are in agreement with those previously obtained (*Table 1*).

In contrast, at higher pH, saturation kinetics patterns were obtained, the turnover pH being dependent on the position of the substituents in the aromatic ring. The finding of saturation kinetics patterns may suggest a mechanism involving rate-determining decomposition of a transient intermediate produced during a rapid preequilibrium step.

Observed rate constants for the formation of dediazoniation products were obtained by HPLC. *Fig. 3* shows a typical kinetic plot for formation of *o*-cresol at constant $[H_2A]$ and at pH 1.9, and the corresponding linear plot. The slope of this linear

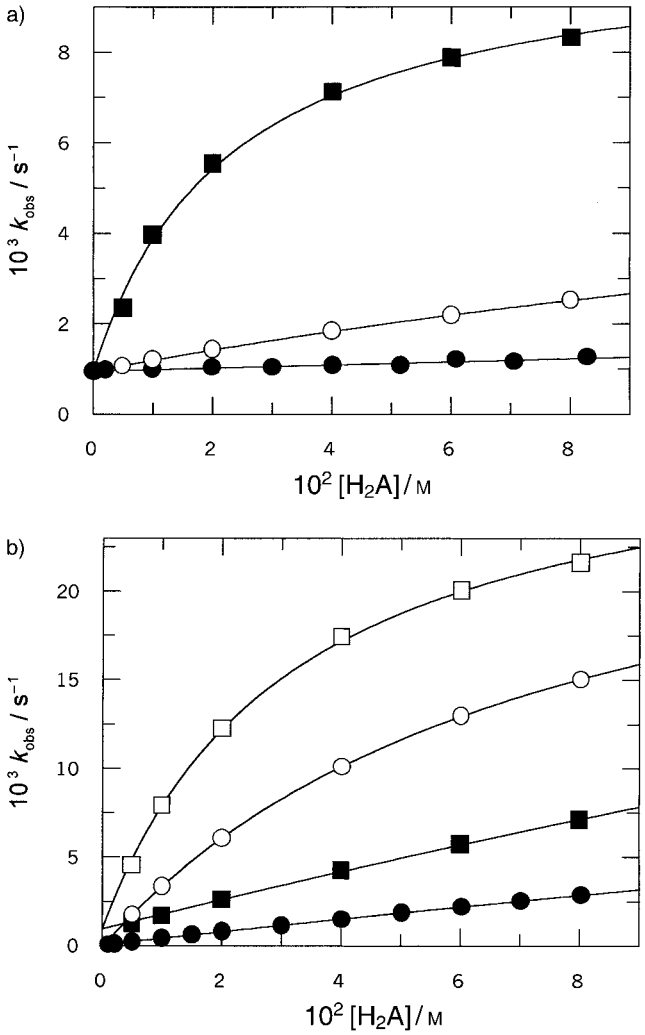


Fig. 2. *Effects of pH on dediazoniation of* ArN_2^+ (*ca.* 2.00×10^{-4} M) *at 35° as a function of* $[H_2A]$. *a*) OMBD: ●, pH 1.0; ○, pH 1.9; ■, pH 3.0. *b*) MMBD: ■, pH 1; □, pH 2; PMBD: ●, pH 1; ○, pH 2.

plot yields $k_{obs} = 12.4 \times 10^{-4}\,s^{-1}$, in agreement with the value obtained spectrophotometrically under the same experimental conditions.

It is worth noting that the total yields at pH 1.9 are much lower than 100% despite the first-order kinetics of the reaction. This low yield was unexpected and in contrast to that obtained in the absence of H_2A at the same pH. Chromatograms showed no extra peaks other than the *o*-cresol and toluene (<2% at infinite time) peaks, and the void-volume peak, which contains the electrolytes and H_2A, so the unknown product probably elutes in the void volume. In addition, it was not possible to obtain k_{obs} for disappearance of OMBD by measuring the absorbance of the azo dye because,

Table 2. *Equilibrium Constants* (K) *for the Formation of the Transient Diazo Ether DE and Rate Constants for its Decomposition According to* Scheme 3) *for OMBD, MMBD, and PMBD*

	10^4 a[a])	10^2 b[a])	Bk_{H_2A}	B	$10^2\ k_{H_2A}$	K
OMBD (pH 3)	–	–	0.46 ± 0.03[b])	44 ± 4[b])	1.0 ± 0.2[b])	741[c])
OMBD (pH 1.9)	–	–	0.029 ± 0.001[b])	3.6 ± 0.4[b])	0.8 ± 0.1[b])	722[c])
OMBD (pH 1)	9.53	0.34 ± 0.04	0.04 ± 0.01[d])	0.45 ± 0.04[c])	–	–
MMBD (pH 2)	–	–	0.95 ± 0.03[b])	32 ± 1[b])	3.0 ± 0.2[b])	5104[c])
MMBD (pH 1)	9.56	8.0 ± 0.1	0.09 ± 0.01[d])	3.2 ± 0.1[c])	–	–
PMBD (pH 2)	–	–	0.389 ± 0.005[b])	13.3 ± 0.3[b])	3.0 ± 0.2[b])	2121[c])
PMBD (pH 1)	0.25	3.5 ± 0.1	0.039 ± 0.003[d])	1.33 ± 0.03[c])	–	–

[a]) By linear regression analysis of data in *Fig. 2*. [b]) Calculated with *Eqn. 6*. [c]) Calculated with *Eqn. 5* and the corresponding $[H_3O^+]$. [d]) From B (see *Eqn. 5*) multiplied by the average k_{H_2A}.

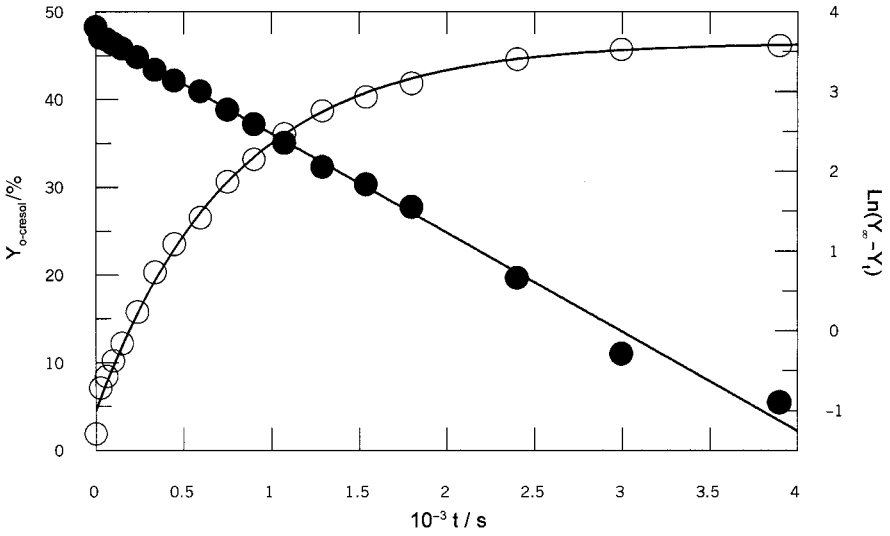


Fig. 3. *Formation of* o-*cresol with time* (○) *and first-order plot* (●) *at 35° and pH 1.9* ($[H_2A]_0 = 1.01 \times 10^{-2}$ M, $[OMBD]_0 = 2.08 \times 10^{-4}$ M)

surprisingly, it was not formed. Note that, although the reaction between H_2A and OMBD takes place at pH 1.9, the pH was modified to pH 8 upon the addition of an aliquot of the '2-naphthol-6-sulfonic acid' (2N6S) quenching solution to favor the coupling reaction (see *Exper. Part*). The pK_a of ascorbic acid has been reported to be 4.25, thus ascorbic acid is completely deprotonated at pH 8. Therefore, the clean first-order behavior observed together with the significantly lower yields obtained and the negligible formation of the azo dye may be explained by assuming a competitive reaction between ascorbate ion and the arenediazonium ion. This hypothesis will be discussed later.

2.3. *Effects of Ascorbic Acid on Dediazoniation Product Yields.* To further investigate the effects of H_2A on dediazoniation products, a number of reactions at different H_2A concentrations and pHs were allowed to proceed to completion and

analyzed chromatographically. *Fig. 4* shows that, for OMBD, chosen as representative, only two main dediazoniation products are obtained, ArOH and ArH. No extraneous peaks other than those associated with ArOH and ArH and the void-volume peak were

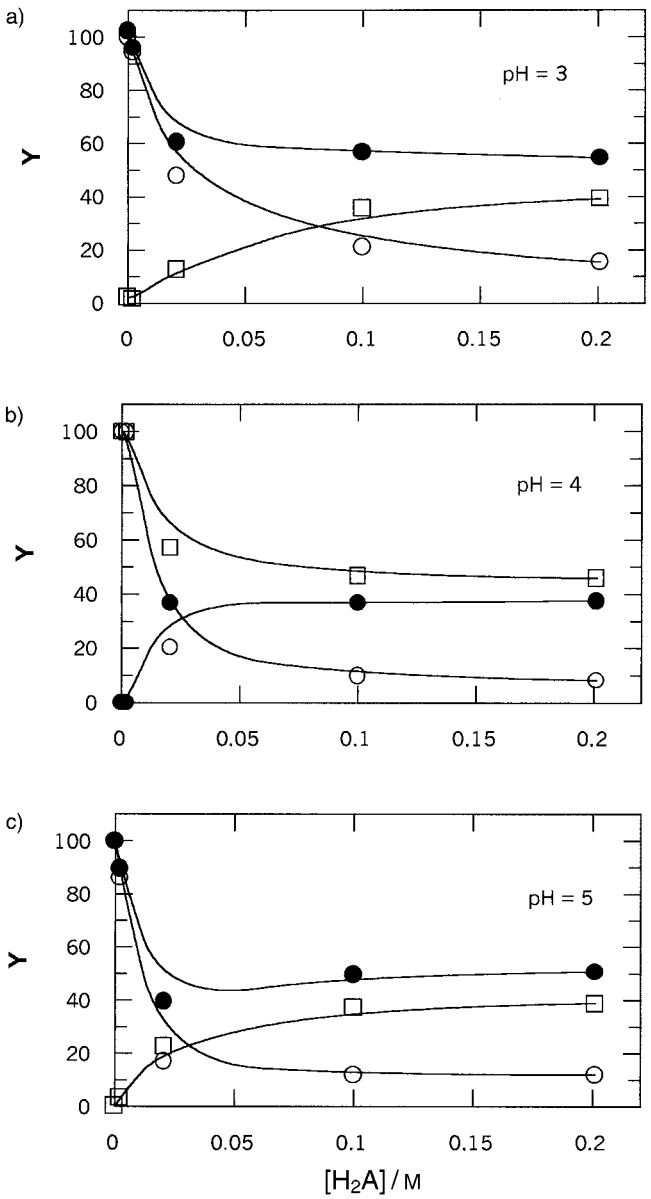


Fig. 4. *Effects of pH on product distribution for OMBD dediazoniation as a function of [H_2A]. a*) pH 3.0, *b*) pH 4.0, and *c*) pH 5.0; ○: ArOH; ●: Total; □: ArH. Reactions were allowed to proceed at 35° for more than eight half-lives.

obtained. At a given pH, ArOH yields decrease and ArH yields increase with increasing H_2A concentration and total yields are close to 50%. At pH 4 and 5, ArOH yields decrease very rapidly to only 20% when $[H_2A] \approx 2.5 \times 10^{-2}$ M and then more slowly, in contrast with the smooth ArH formation. Total yields ($Y_{ArOH} + Y_{ArH}$) are close to 50% at high $[H_2A]$, independently of the pH of the reaction mixture.

These low yields, together with finding patterns suggestive of saturation-kinetics at high pH (*Fig. 2*), prompted us to investigate the possibility of formation of a relatively stable transient intermediate between our arenediazonium probes and HA^-. *Doyle et al.* reported that reduction of some arenediazonium ions by H_2A at pH 7 does not proceed with the expected electron transfer but forms stable compounds, which have been identified as 3-*O*-arenediazoascorbic acids.

2.4. *Experimental Evidence for Complex Formation Between Arenediazonium Ions and Ascorbate Ion*. Evidence of formation of transient intermediates of the type Ar–N=N–R, where R is a reductant, were obtained primarily by UV-VIS spectroscopy in some dediazoniations [36]. However, under our experimental conditions, the absorption band of H_2A or that of HA^- masks those of reactants and products, especially at high $[H_2A]$, thus no new absorption bands beyond those attributable to the reactants were detected.

The first direct evidence for the formation of such complexes was obtained with the competitive coupling reaction employed to quench dediazoniations. As noted before, we were not able to obtain a k_{obs} for arenediazonium ion loss by monitoring the change in absorbance due to azo dye formation at pH 1.9. Auxiliary experiments demonstrated that, upon addition of OMBD to a mixture containing HCl, H_2A, 2N6S, and *Tris* so that final pH and concentrations were the same as those in the dediazoniation experiment at pH 1.9 after addition of the quenching solution, the azo dye is formed. Changes in the $[H_2A]$ did not result in changes in the amount of azo dye formed. Thus, under these experimental conditions, the formation of the azo dye is independent of $[H_2A]$, and the coupling reaction between 2N6S and OMBD at pH 8 is much faster than the hypothetical reaction between OMBD and the ascorbate ion. However, upon addition of an aliquot of the 2N6S quenching solution to an aqueous mixture containing HCl (10^{-2} M), OMBD, and different amounts of H_2A (with $[H_2A] < [OMBD]$, final pH 8), the azo dye is formed, but the amount of azo dye formed depends on $[H_2A]$ (*Fig. 5*). Note that when $[H_2A] = [OMBD]$, the amount of azo dye formed is negligible, consistent with the results obtained at pH 1.9. Similar conduct was observed for MMBD and PMBD. In consequence, by employing this competitive coupling reaction, we were able to obtain direct experimental evidence that the arenediazonium ions are being trapped by ascorbate ion, yielding a 'complex'. On the basis of the nature of the reactants and on literature reports [10][31], one would expect such a complex to contain the –N=N– entity, *i.e.*, presumably corresponding to a diazo ether compound.

Further evidence for the formation of diazo ether 'complex' between ascorbate and the arenediazonium ions was obtained from polarographic measurements. As noted in the *Exper. Part*, arenediazonium salts show two well-defined diffusion-controlled peaks, which appear at *ca.* –50 mV and –450 mV, while H_2A shows one polarographic peak at +180 mV *vs.* Ag/AgCl.

Polarograms of mixtures of OMBD, MMBD, or PMBD with H_2A at 6° show the almost immediate disappearance of the peaks associated with the arenediazonium ions

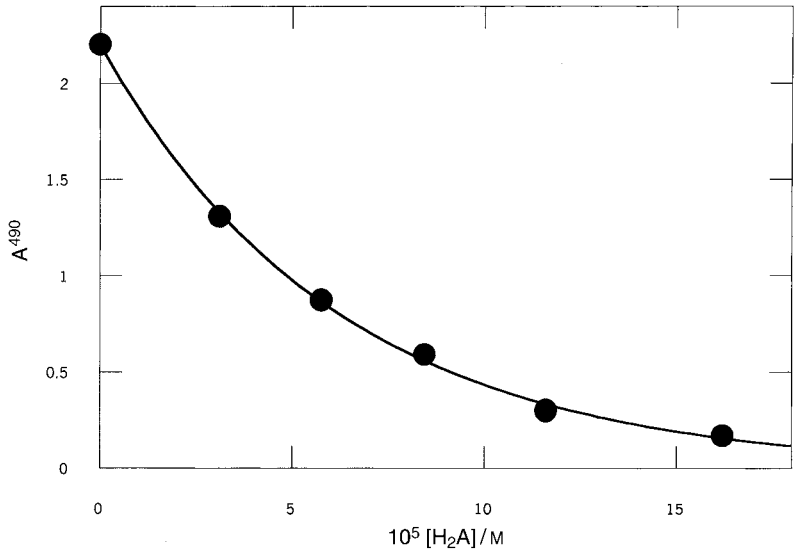


Fig. 5. *Absorbance* ($\lambda = 490$ nm) *of the azo dye formed between OMBD and 2N6S as a function of increasing amounts of added* H_2A *at pH 8 and 25°*

and the presence of two new polarographic peaks not observed before. Titration of ascorbic acid with aliquots of PMBD, *Fig. 6*, shows a linear decrease in the intensity of the H_2A peak with a concomitant increase in the intensity of the new peaks located at -1060 and -1200 mV (*Fig. 6*, inset).

Preliminary experiments indicate that the intensity of those new peaks is not constant with time even at 6°. Thus, such complexes are not stable under our experimental conditions and, apparently, the MMBD 'complex' is less stable than the analogs formed with OMBD and PMBD. The electrochemical characterization and kinetic studies concerning the stability of such complexes are in progress and will be part of a future communication.

3. Discussion. – Kinetic data in the absence of H_2A indicate that k_{obs} for ArN_2^+ loss is the same as that for product formation, and that it is essentially independent of acidity or added electrolyte concentration. Chromatograms in the absence of H_2A indicate that only one dediazoniation product, ArOH, is obtained and that quantitative conversion is achieved. No extraneous peaks that might be attributed to reduction products formed in radical pathways, like biphenyls (Ar–Ar) or toluene (Ar–H), *etc.*, were observed. The absence of reduced or isomerized products is consistent with the heterolytic mechanism. Consequently, all these results are consistent with a $D_N + A_N$ mechanism, *i.e.*, rate-limiting formation of a highly reactive aryl cation intermediate with very low selectivity towards different nucleophiles (*Scheme 2*).

All evidence and the composite data for rate dependence on $[H_2A]$ in the pH 1–3 range is consistent with two competitive reaction pathways (*Scheme 3*). The first one is the thermal $D_N + A_N$ dediazoniation mechanism, which is predominant in the absence

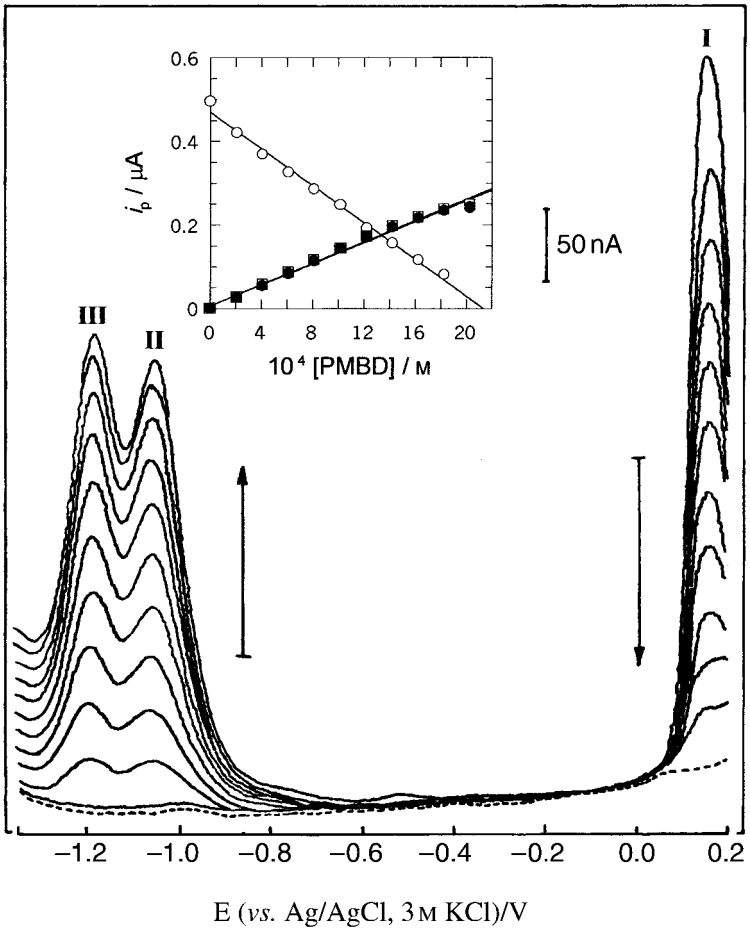
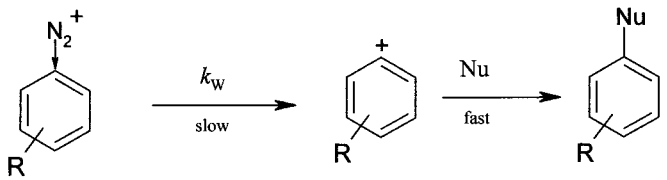


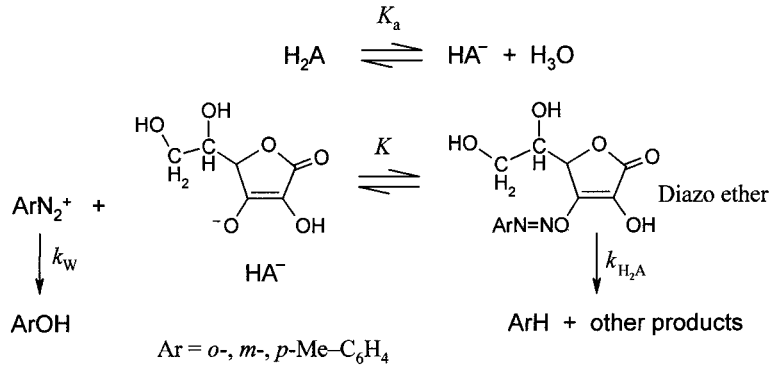
Fig. 6. *Polarographic titration of H_2A* (2.00×10^{-4} M) *with 10 µl aliquots of PMBD* (to a final concentration of 2×10^{-4} M) *at pH 4 and 6°*. Peak **I**: H_2A; peaks **II** and **III** were not observed in the absence of H_2A and are attributed to the transient diazo ether formed between PMBD and HA^-. Also note that the polarographic peaks of PMBD (at −50 and −450 mV) are not observed. *Inset:* Amplitude of the polarographic peaks of H_2A (**I**, ○), and the transient diazo ether peaks **II** (□) and **III** (●) as a function of [PMBD].

Scheme 2. *The Dediazoniation* ($D_N + A_N$) *Mechanism*



of H_2A. The second one is the rate-limiting decomposition of a diazoether complex that is formed in a rapid pre-equilibrium step from the interaction between the arenediazonium ion and the monobasic form of ascorbic acid. Since H_2A is a diprotic

Scheme 3. *Proposed Mechanism for the Reaction between Arenediazonium and Ascorbate Ions* (note the most probable structure of the transient diazo ether formed in the reaction)



acid with pK_a values of 4.25 and 11.79 for the C(3) and C(2) OH groups, respectively, the diazo ether complex is most likely linked *via* C(3), as shown in *Scheme 3*, in keeping with literature reports [31]. The assumed rate-limiting decomposition of the diazo ether is also consistent with reported results for other O-coupling reactions [10][37–39].

From *Scheme 3*, the generalized rate law given by *Eqn. 2* can be obtained:

$$v = \frac{-d[\mathrm{ArN_2^+}]}{dt} = k_w[\mathrm{ArN_2^+}]_\mathrm{F} + k_{\mathrm{H_2A}}[\mathrm{DE}] \tag{2}$$

where k_w and k_{H_2A} are the rate constants for the thermal decomposition of ArN_2^+ and for the cleavage of the diazo ether, and [DE] and $[ArN_2^+]_F$ represent the concentrations of complexed and 'free' arenediazonium ions, respectively. The [DE] is given by *Eqn. 3*,

$$[\mathrm{DE}] = K[\mathrm{ArN_2^+}]_\mathrm{F}[\mathrm{HA^-}] \tag{3}$$

where K is the equilibrium constant for complex formation and $[ArN_2^+]_F$ the concentration of 'free' arenediazonium ion. Substitution of *Eqn. 3* into *Eqn. 2*, and taking into consideration the corresponding mass balance for ArN_2^+, the first ionization equilibrium for H_2A and bearing in mind that we have worked under pseudo-first-order conditions, the observed rate constant is given by *Eqn. 4*,

$$k_\mathrm{obs} = \frac{k_w + k_{\mathrm{H_2A}}B[\mathrm{H_2A}]_\mathrm{T}}{1 + B[\mathrm{H_2A}]_\mathrm{T}} \tag{4}$$

where B is given by *Eqn. 5*

$$B = \frac{K_\mathrm{a}K}{K_\mathrm{a} + [\mathrm{H_3O^+}]} \tag{5}$$

If the thermal decomposition is negligible compared with the reaction through the complex, *i.e.* if $k_w \ll k_{H_2A}B[H_2A]_T$, *Eqn. 4* can be rearranged to *Eqn. 6*,

$$\frac{1}{k_\mathrm{obs}} = \frac{1}{k_{\mathrm{H_2A}}} + \frac{1}{Bk_{\mathrm{H_2A}}[\mathrm{H_2A}]_\mathrm{T}} \tag{6}$$

which predicts that a plot of $1/k_{obs}$ *vs.* $1/[H_2A]_T$ should be linear. *Fig. 7* shows such linear dependence for the three arenediazonium salts, from which one can obtain the values for the unimolecular decomposition of the diazo ether, k_{H_2A}, and the equilibrium constant for complex formation, K (*Table 2*).

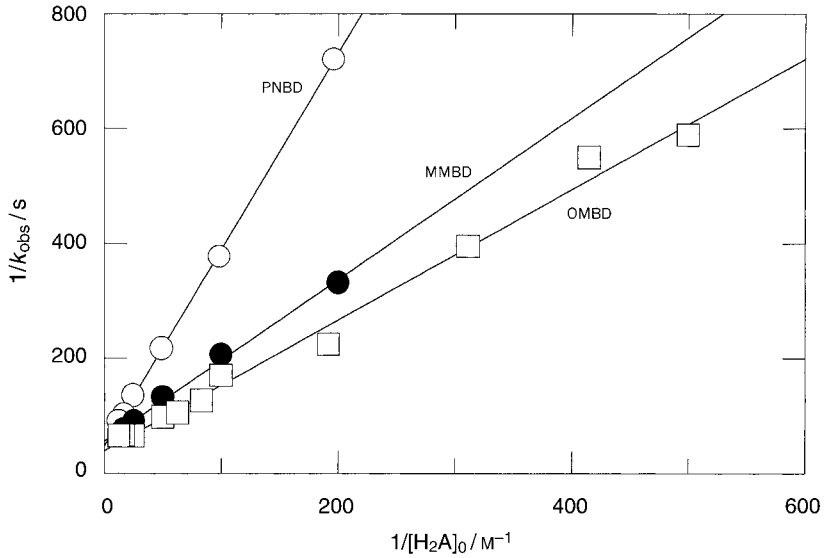


Fig. 7. *Double-reciprocal plot* ($1/k_{obs}$ *vs.* $1/[H_2A]_T$, according to *Eqn. 6*) *for the reaction of* H_2A *with OMBD* (□: pH 3), MMBD (●: pH 2), and PMBD (○: pH 1). Data as in *Fig. 2*.

As observed in *Table 2*, the equilibrium-constant values are strongly dependent on the substituent in the aromatic ring on the diazonium ion, indicating a significant orientational effect of the Me group. The k_{H_2A} values also seem to be dependent on the position of the substituent in the aromatic ring, and they are about 100 times higher than those for the thermal decomposition. Equilibrium-constant and rate-constant values for diazo ether formation have been published [10], but they were obtained with totally different substrates and under very different experimental conditions, thus comparison with published data isn't reliable.

According to the data indicated in *Table 2* for low pH, *Eqn. 4* predicts that $B[H_2A]_T \ll 1$ for those cases in which $K_a \ll [H_3O^+]$, *i.e.*, for those reactions at low pH. Therefore, k_{obs} is better given by *Eqn. 7*

$$k_{obs} = k_w + k_{H_2A} B [H_2A]_T \tag{7}$$

which predicts a linear increase in k_{obs} with $[H_2A]_T$, consistent with the observed behavior at low pH (*Fig. 2*). Comparison of the slopes of the linear plots with the Bk_{H_2A} values obtained from *Eqn. 7* indicate that they are equal within experimental error (*Table 2*), providing further support for the proposed mechanism.

Arenediazonium ions function as one-electron oxidizing agents, and, therefore, in reactions with suitable electron donors, free radicals are generated [4][5][10][36]. Two

particular mechanisms, outer and inner sphere, have been proposed for these reactions [9][10]. The outer-sphere mechanism assumes that a direct electron transfer from a reducing agent to ArN_2^+ takes place, yielding a radical from the reducing agent and an aryl diazenyl radical, $ArN_2^{\bullet}$, which subsequently decomposes spontaneously in aqueous solution to yield N_2 and the corresponding aryl radicals. An example of this mechanism has been provided by *Brown* and *Doyle*, who performed a kinetic study of the reaction of arenediazonium salts by hydroquinone, *p*-QH_2 (oxidation-reduction of hydroquinone and H_2A are formally equivalent) [36]. They showed that the reduction of arenediazonium ions involves a rate-limiting single electron transfer from a semiquinone intermediate to the diazonium ion, with a net stoichiometry ArN_2^+/*p*-QH_2 of 2 : 1. The lack of new absorption bands in the VIS-UV spectrum beyond those attributable to the added reducing agents support the proposed outer-sphere mechanism.

That this mechanism is unlikely in our experiments can be explained on the basis of the reduction potential of the diazonium ions to give the diazenyl radical. From a mechanistic standpoint, the simplest way of achieving an electron transfer to an arenediazonium ion is by reduction at the surface of an electrode. In aqueous solution, the reduction and the spontaneous dediazoniation of a number of C(4)-substituted benzenediazonium ions have been studied with a dropping mercury electrode (DME) [33][35][40][41]. Two polarographic waves were observed in potential regions of + 0.05– – 0.02 V (*vs.* Ag/AgCl) and – 0.97– – 1.03 V. Microcoulometry [42] at the DME shows that the first wave corresponds to the uptake of one electron, yielding a diazenyl radical. Therefore, if the outer mechanism operates, the diazenyl radical should be detected in the + 50– – 20 mV range, which is not the case (*Fig. 6*).

In the alternative inner-sphere mechanism, reduction of the arenediazonium ion is preceded by the formation of a transient complex, namely Ar–N=N–R, generated by reaction of ArN_2^+ with R^-, which then decomposes into $Ar^{\bullet}$ and $R^{\bullet}$ radicals and N_2. The finding of saturation kinetics together with the appearance of new polarographic peaks (*Fig. 6*) at potentials clearly different from those of $ArN_2^{\bullet}$ suggest that, for these arenediazonium ions, inner-sphere mechanisms operate.

Diazo ethers of the general structure ArN=NOR (with R = alkyl, aryl) are rarely formed as stable products [10][37][38][43]. For example, the diazo ether formally derived from naphth-1-ol and the benzenediazonium ion is sensitive to acid and base as well as light. Previous studies [10][37][38][43] concerning the reaction of arenediazonium ions with alkoxide or phenoxide compounds, which yield diazo ethers, further support the proposed mechanism but suggest that decomposition of the diazo ether complex may not be as simple as indicated in *Scheme 3*.

Basically, the reaction of arenediazonium ions with methoxide ion occurs in three phases. The first is the very rapid formation of (*Z*)-diazo methyl ether. In the second step, some of the (*Z*)-diazo ether decomposes to yield reduction products (usually hydro-dediazoniation), and the rest is converted to the (*E*)-diazoether. Investigations by *Broxton et al.* [44] confirmed that the initial reaction of the arenediazonium ions takes place in such a way that almost exclusively the (*Z*)-diazo ether is formed directly, and part of it is transformed to the (*E*)-isomer by an ionization-recombination mechanism. The low yields obtained in our experiments can be explained, tentatively, if the initial complex formed in our system is essentially the (*Z*)-isomer, which, in part, decomposes to give the reduction product ArH and, in part, is transformed to the (*E*)-

isomer, which is much more stable. This (*E*)-isomer is probably very soluble because of the presence of a substantial number of hydroxyl groups, and, therefore, it probably elutes with the void volume peak, which contains, among other compounds, the excess H_2A.

In conclusion, we have been able to demonstrate that H_2A can directly reduce arenediazonium ions, and we propose the reaction mechanism indicated in *Schemes 2* and *3*. All evidence is, therefore, consistent with competitive mechanisms, the unimolecular $D_N + A_N$ mechanism and a second mechanism in which the slow step is the decomposition of a transient diazo ether formed from the interaction between the arenediazonium ion and HA^- in a rapid pre-equilibrium step. On the basis of our results and literature reports, the decomposition of such a diazo ether yields the reduction product ArH and the more stable (*E*)-diazo ether. Our data provide mechanistic support for the observations pointed out by *Reszka et al.* [5], but we would like to stress that the formation of stable 3-O-arenediazoascorbic acids (diazo ethers) can not be completely ruled out because preliminary experiments strongly suggest that the stability depends on the position and probably on the nature of the substituents in the aromatic ring.

Experimental Part

Reagents were of maximum purity available and were used without further purification. Cresols, ArOH, chlorotoluenes, ArCl, toluene, ArH, H_2A, CA, and the reagents used in the preparation of diazonium salts (as tetrafluoroborates) and in the preparation of *Britton-Robinson* (BR) buffer were purchased from *Fluka* or *Aldrich*. The Na salt of 2-naphthol-6-sulfonic acid (2N6S) was purchased from *Pfaltz & Bauer*. Other materials employed were from *Riedel de Häen*. All solns. were prepared with *Milli-Q*-grade H_2O. Solns. employed in electrochemical measurements were bubbled with dry N_2 (99.999%) for at least 20 min and kept under N_2 during the measurements. Arenediazonium salts were prepared under nonaqueous conditions [45] and were stored in the dark at low temperature to minimize decomposition. The BR buffer was prepared by mixing the sufficient amounts of H_3BO_3, AcOH, and H_3PO_4 with a concentrated NaOH solution to obtain the desired pH. The final concentration of each electrolyte was 0.25M.

UV-VIS spectra and some kinetic experiments were followed on a *Beckman DU-640* UV-VIS spectrophotometer equipped with a thermostatted cell carrier and interfaced with a computer for data transfer. Product analysis was carried out on a *Waters* HPLC system, which included a model *560* pump, a model *717* automatic injector, a model *486* UV-VIS detector, and a computer for data collection. Products were separated on a *Microsorb-MV C-18* (*Rainin*) reverse-phase column (25 cm, 4.6 mm ID,, and 5 μm particle size) with a mobile phase of 65/35 *v/v* MeOH/H_2O containing 10^{-4} M HCl. The injection volume was 25 μl, and the UV detector was set at 210 nm to detect PMBD and at 220 nm for OMBD and MMBD. The pH was measured with a previously calibrated *Metrohm 713* pH meter equipped with temperature sensor. Differential pulse polarograms (DPP) were obtained on a *Metrohm Polarecord 506* equipped with a model *663 VA Stand* and a water-jacketed voltammetry cell. A three-electrode system, composed of a mercury multimode (DME, SMDE, or HMDE) working electrode, an Ag/AgCl reference electrode, and a glassy carbon rod (2×65 mm) auxiliary electrode, was employed. Polarograms were recorded at constant temperature ($35 \pm 0.1°$) except where otherwise indicated.

Kinetic data were obtained from spectrophotometric, chromatographic (HPLC), or electrochemical data by well-established methodologies [33][34][46–49]. The k_{obs} values were obtained by fitting the absorbance-time, percent yield-time or peak current-time data to the integrated first-order equation (*Eqn. 8*) with a non-linear least-squares method provided by a commercial computer program, where *M* is the measured magnitude.

$$\mathrm{LN}\left(\frac{M_t - M_\infty}{M_0 - M_\infty}\right) = k_{obs}t \tag{8}$$

Experiments were performed at $35 \pm 0.1°$ with arenediazonium salts as the limiting reagents except where otherwise indicated.

Spectrophotometric kinetic data were obtained by following the disappearance of diazonium salt at an appropriate wavelength. Chromatographic kinetic data for all dediazoniation products were obtained according to a well-established procedure [46][47] by quenching the dediazoniation reaction at convenient times with an aliquot of an aq. stock soln. of 2N6S with *Tris* buffer (0.05M) to give, after mixing, a final [2N6S] in *ca*. 20-fold excess over that of arenediazonium salts, and a final pH of *ca*. 8. Details of the method and the equations for converting HPLC peak areas (A) to concentration are reported elsewhere [46][48]. Percent yields, Y, of the dediazoniation products were obtained from the ratio of the concentration of dediazoniation product to the initial concentration of diazonium salt (estimated by weight).

Electrochemical behavior (DPP) of solns. containing 0.1M HCl and 1.11×10^{-4} M of one of the three arenediazonium salts showed two well-defined diffusion-controlled peaks, which appear about at -50 mV and -450 mV (*vs.* Ag/AgCl (3M KCl)) in agreement with literature data [33][40][50–53]. Polarograms (not shown) of HCl or buffered (*Britton-Robinson*) aq. solns. containing increasing amounts of diazonium salt show that the height of both peaks increases linearly ($r > 0.999$) with concentration up to 4×10^{-4} M (peak at -50 mV, slope = 2000 μA mol^{-1}) and up to 3×10^{-4} M (peak at -450 mV, slope = 40 μA mol^{-1}). Stronger adsorption phenomena were observed at higher ArN_2^+ concentrations. Consequently, electrochemical kinetic data were obtained by monitoring the evolution of the first peak with time (due to its higher sensitivity) and fitting the data to *Eqn. 8*.

Polarograms of H_2A in aq. soln. containing 0.01M HCl or buffered (BR, pH 3) at 35° show a single reduction peak at $+180$ mV *vs.* Ag/AgCl. H_2A is highly sensitive to various modes of degradation [28]. Among others, factors that can influence the degradative process include the temp., pH, O_2, and metal catalysts. To minimize degradation, aq. stock solns. of H_2A were freshly prepared daily by dissolving solid H_2A with the appropriate acid (HCl) or BR buffer and CA. Auxiliary spectrophotometric and polarographic experiments demonstrated the stability of H_2A under these conditions for at least 24 hours at 35°.

Upon dediazoniation of ArN_2^+ in the presence of H_2A, an unknown product was produced, especially under conditions of low acidity. The presence of unknown products in dediazoniations has already been reported for other dediazoniations [15][41][47] under different experimental conditions. We assume that, whatever the mechanism is for formation of the unknown product, it is a competitive reaction leading to a reduction in the total observed yields, which are calculated on the basis of the initial ArN_2^+ concentration. The results obtained support this assumption.

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