

Article

Effects of Electrolytes on the Dediazonation of Aryldiazonium Ions in Acidic MeOH/H₂O Mixtures

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Abstract: Aryldiazonium, ArN₂⁺, ions decompose spontaneously through the formation of highly reactive aryl cations that undergo preferential solvation by water, showing a low selectivity towards the nucleophiles present in their solvation shell. In this work, we investigate the effects of electrolytes (NaCl, LiCl, and LiClO₄) on the dediazonation of 2-, 3-, and 4-methylbenzenediazonium ions in acidic MeOH/H₂O mixtures. In the absence of electrolytes, the rates of dediazonation, *k*_{obs}, increase modestly upon increasing the MeOH content of the reaction mixture. At any solvent composition, the rate of ArN₂⁺ loss is the same as that for product formation. The main dediazonation products are cresols (ArOH) and methyl phenyl ethers (ArOMe). Only small amounts (less than 5%) of the reduction product toluene (ArH), which are detected at high percentages of MeOH. Quantitative yields of are obtained at any solvent composition. The addition of LiCl or NaCl ([MCl] = 0–1.5 M) to the reaction mixtures has a negligible effect on *k*_{obs} but leads to the formation, in low yields (<10%), of the ArCl derivative. The addition of LiClO₄ (0–1.5 M) to 20% MeOH/H₂O mixtures has a negligible effect on both *k*_{obs} and on the product distribution. However, at 99.5% MeOH, the addition of the same amounts of LiClO₄ leads to a modest decrease in *k*_{obs} but to a significant decrease in the yields of ArOMe. Results are interpreted in terms of the preferential solvation of perchlorate ions by the aryl cations, removing MeOH molecules from the solvation shell.

Keywords: solvolysis; aryldiazonium ions; perchlorate anions



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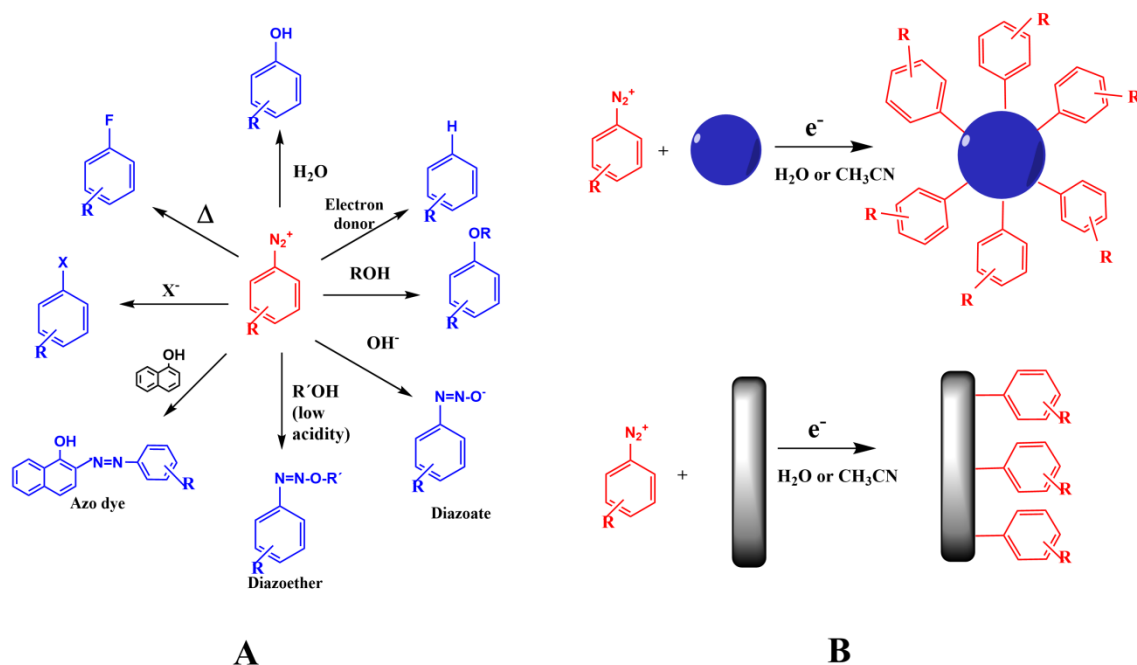
1. Introduction

Aryldiazonium, ArN₂⁺, salts have been profusely employed in organic chemistry for years [1–3]. The chemistry of these compounds has been originally carried out in aqueous solutions [4], but chemists went further and developed new synthetic methods that use reactions of diazonium salts in organic solvents [5–8]. In recent years, their chemistry has been exploited in the synthesis of unnatural amino acids [5], in palladium-catalyzed cross-coupling reactions [7,9,10] and, for example, as nitrogen-based Lewis acids [6,11].

Aryldiazonium ions are inherently reactive molecules that undergo a wide variety of chemical transformations that can be carried out under milder conditions, often at ambient temperature and pH levels [1,2,5,12–14]. Their reactivity is frequently dominated by the loss of the N₂ moiety, leading to the formation of heterolytic products, such as phenols, haloderivatives, and ethers. Scheme 1 shows some of the most common reactions of aryldiazonium ions, including the formation of diazoethers (O-coupling), azo dye (C-coupling) reactions, and their attachments to surfaces and nanoparticles.

In the last decades, after the pioneering work by J. Pinson et al. [15], the reductive properties of aryldiazonium salts have been exploited as a very potent method for surface functionalization [16–20]. The method is relatively simple, easy to process, is fast, and can be employed to functionalize massive surfaces that are either flat, or are nanomaterials of various shapes and sizes [17]. The formed surfaces are robust and resistant to heat, chemical degradation, ultrasonication, and, most importantly, the grafting of surfaces is a useful and practical approach that can be applied to a variety of conducting and insulating substrates.

Briefly, the grafting procedure comprises the formation of highly reactive aryl radicals that attack the surface and that are generated, for example, through the electrochemical reduction of ArN_2^+ . Variations of the method include the reaction of generated radicals with already-grafted aryl species, leading to the formation of multilayer films [17,20]. Scheme 1B illustrates the use of ArN_2^+ for the grafting of both spherical nanoparticles and flat surfaces.



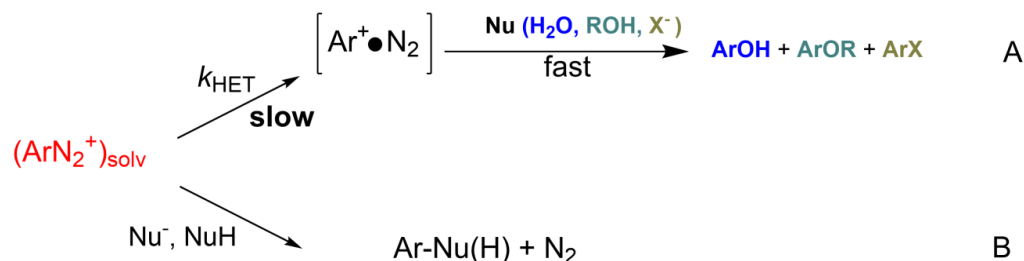
Scheme 1. (A) Some common reactions of aryldiazonium ions in solution. (B) Illustrative examples of the use of aryldiazonium ions as reagents to functionalize surfaces.

Aryldiazonium ions can be easily prepared from their anilines both in situ and in the solid state [1,21], and most of them can be easily handled under ambient conditions. Nevertheless, the stability of ArN_2^+ depends strongly on the nature of substituents R and counterions X^- . For example, aryldiazonium chlorides are highly unstable and can be explosive above 0 °C, as well as aryldiazonium perchlorates [12]. Nowadays, most synthetically prepared aryldiazonium salts are formulated as tetrafluoroborates because of the high stability and availability of the BF_4^- anion [3,12].

In an aqueous solution, in the dark, and in the absence of reducing species, ArN_2^+ undergoes a rich chemistry, comprising aromatic *ipso*-substitutions, *N*-terminal addition reactions, and O-coupling reactions, among others. However, the fate of the reactions strongly depends on the acidity of the solution. For instance, we showed, in previous dediazonation studies [2,14,22–24] that, in an aqueous acid solution and in mixed alcohol–water solvents ($[\text{H}_3\text{O}^+] > 10^{-2}$ M), in the dark and in the absence of reductants, the spontaneous decomposition of aryldiazonium ArN_2^+ salts proceeds through a $\text{S}_{\text{N}}1$ -type heterolytic mechanism, where a highly reactive aryl cation is formed, reacting with nucleophiles present in their solvation shell (dissociation + addition mechanism, $\text{D}_{\text{N}} + \text{A}_{\text{N}}$, Scheme 2). Recent dediazonation research suggests, however, that ArN_2^+ may decompose heterolytically through borderline $\text{S}_{\text{N}}1$ – $\text{S}_{\text{N}}2$ mechanisms. Surprisingly, upon moderately decreasing the acidity, reactions involving the formation of diazohydroxides, ArN_2OH , diazoethers, ArN_2OR , and diazoates, ArN_2O^- , become competitive and may even constitute the main decomposition pathway [2].

In this work, we analyze the effects of the solvent composition and of added electrolytes (NaCl, LiCl, and LiClO_4) on the esolvolytic dediazonation of 2-, 3-, and 4-methylbenzenediazonium ions (2MBD, 3MBD, and 4MBD, respectively) in acidic MeOH/ H_2O mixtures (20% and 99.5%). The aim of the manuscript is two-fold: (1) to complement previous kinetic studies that were focused on the effects of electrolytes on short-lived

carbocations, particularly on the effects of the solvent composition on the solvation shell of the *ipso* carbon of aryldiazonium ions, and (2) to investigate if the addition of electrolytes may modify the composition of the solvation shell of aryl carbocations.



Scheme 2. Illustrative representations of the (A) ionic or heterolytic $\text{S}_{\text{N}}1$ ($\text{D}_{\text{N}} + \text{A}_{\text{N}}$) dediazonation mechanism in the presence of various nucleophiles comprising the formation of an ion–molecule pair that traps (with very low selectivity) nucleophiles present in its solvation shell. (B) $\text{S}_{\text{N}}2$ dediazonation mechanism. In both cases, heterolytic products are formed.

For this purpose, we determined the dediazonation rate constants for ArN_2^+ loss and for product formation, as well as the product distribution at various solvent compositions. Reported thermodynamic and kinetic data, obtained upon the solvolysis of ArN_2^+ in a number of alcohol–water mixtures (MeOH, EtOH, 2,2,2-trifluoroethanol, BuOH), are consistent with the $\text{S}_{\text{N}}1$ mechanism; that is, the rate-determining formation of a highly reactive aryl cation that traps the nucleophiles in its solvation shell [14,22–29]. The major dediazonation products are the corresponding methylphenyl ethers and cresols, and the equal amounts of products that are produced at water molar fractions of 0.34–0.36, suggesting that the aryldiazonium ions undergo preferential solvation by water, and that the preferential solvation around the *ipso* carbon reflects the experimental product yield obtained [2,14,22].

The rates of the reactions of stable carbocations and aryldiazonium ions with water, alcohols, and anions have been described in terms of the Ritchie’s equation $\log(k/k_0) = N_+$, based on the assumption that the relative reactivities of two nucleophiles are controlled by the differences in their N_+ values, which are considered independent of the electrophilicities of the reaction partners. Later, Mayr et al. [30–32] demonstrated that the rates of these reactions can be described in terms of their electrophilicity and nucleophilicity parameters, $\log(k) = s(E + N)$, where s is a nucleophile-specific parameter. A theoretical interpretation of the physical meaning of s has been published and a comprehensive list of N and E parameters can be found elsewhere [33]. The development of nucleophilicity scales has intrigued chemists for years, and Grunwald and Winstein proposed a relationship for the solvolyses of $\text{S}_{\text{N}}1$ reactions on the basis of the solvent-ionizing power Y and a substrate-specific parameter m whose value was one for *t*-butyl chloride [34–36], $\log(k/k_{\text{W}}) = mY$. This equation holds for $\text{S}_{\text{N}}1$ reactions, where the nucleophilic participation of the solvent in the rate-determining step is negligible [2,35].

In this work, we are particularly interested in analyzing the effects of ClO_4^- ions on solvolytic dediazoniations. Aryldiazonium perchlorates are particularly effective for the Heck palladium-catalyzed arylation of olefins when reactions are carried out in alcohol–water mixtures because of the high yields obtained and because they are cheaper reagents than those with other counterions [37]. However, cautions must be taken, because some aryl diazonium perchlorates have been reported to be explosive when prepared in the solid state [38,39]. Conversely, they can be conveniently generated in situ [37]. Perchlorate is a commercially available anion that forms salts with many cations (NH_4^+ , Li^+ , Na^+ , K^+ , etc.). Probably the most common form of perchlorate includes ammonium perchlorate (frequently used as a solid rocket oxidant and as ignition source in fireworks) and potassium perchlorate (used in road flares and in air bag inflation systems). Other commercial perchlorate counterions include H^+ , Li^+ , Na^+ , K^+ , NH_4^+ , Al^{3+} , and N_2H_5^+ . Perchlorate is also formed in laboratory waste as a byproduct of perchloric acid. It is a very poor complexing

agent, similar to other weak anions, such as tetrafluoroborate or trifluoromethanesulfonates (triflate, CF_3SO_3^-), making it very useful in metal cation chemistry [40]. The high solubility in both aqueous and non-aqueous media, together with the highly delocalized monovalent charge over the four oxygen atoms and its large volume, allows it to be widely used to adjust ionic strength in kinetic experiments. From the thermodynamic point of view, perchlorates are expected to be powerful oxidizers ($E^0 = -1.229 \text{ V}$), but the stability of ClO_4^- in solution is governed by kinetics and not thermodynamics, and, therefore, they do not easily oxidize [40,41].

2. Materials and Methods

2.1. Materials

The aryldiazonium 2-, 3-, and 4-methylbenzenediazonium (2MBD, 3MBD, and 4MBD, respectively) were prepared as tetrafluoroborate salts under nonaqueous conditions, as described elsewhere [42,43]. The reagents used in their preparation were from Sigma-Aldrich (Taufkirchen, Germany). They were stored in the dark at low temperatures ($T < 5 \text{ }^\circ\text{C}$) to minimize their decomposition and were recrystallized periodically. All chemicals were of the maximum purity available and were used without further purification. methyl phenyl ethers, ArOMe, cresols, ArOH, chlorotoluenes, ArCl, and toluene were from Sigma-Aldrich (Germany). The coupling agent, sodium 2-Naphthol-6-sulfonate ((2N6S), was from Pfaltz & Bauer (USA). The salts NaCl, LiCl, and LiClO_4 were from Sigma-Aldrich (Germany) and other materials employed were from Panreac (Barcelona, Spain). All solutions were prepared by using deionized water (resistivity $> 18 \text{ M}\Omega\cdot\text{cm}$).

Hereafter, solution compositions are given by their percent of MeOH (by volume). Molar concentrations were calculated by ignoring the small excess volume of mixed solvents [44].

2.2. Instrumentation

UV-VIS spectra, and some kinetic experiments, were followed on a Beckman DU-640 UV-VIS or on an Agilent HP-6456 diode array spectrophotometer, both equipped with cell carriers thermostated with water from a refrigerated/heating circulator, Julabo F1 2-ED, and were attached to computers for data storage. A product analysis was carried out with the aid of a WATERS HPLC system, equipped with a model 2487 dual- λ absorbance detector, a model 717 automatic injector, a model 600 quaternary pump, and a computer for data storage. The dediazonation products were separated with a reverse phase column (Microsorb-MV C-18 (Rainin, 25 cm length, 4.6 mm internal diameter, and $5 \mu\text{m}$ particle size) using an acidic 70/30 (*v/v*) MeOH/ H_2O mobile phase, containing 10^{-4} M HCl . The injection volume was set at $25 \mu\text{L}$ in all runs and the UV detector was set at 220 nm. Details on the method can be found elsewhere [42,45].

2.3. Methods

Kinetic data were obtained both chromatographically and spectrophotometrically. Observed rate constants, k_{obs} , were obtained by fitting the percentage of yield-time or absorbance-time data to the integrated first order Equation (1), where X stands for the experimental measured UV-VIS absorbance or product yields. Runs were done at $T = 35 \pm 0.1 \text{ }^\circ\text{C}$ (2MBD and 3MBD) and at $T = 60 \pm 0.1 \text{ }^\circ\text{C}$ (4MBD) with aryldiazonium ions, ArN_2^+ , as the limiting reagents. The reported k_{obs} values are the average of duplicate or triplicate experiments, with deviations lower than 7%.

$$\ln\left(\frac{X_t - X_\infty}{X_0 - X_\infty}\right) = -k_{\text{obs}}t \quad (1)$$

Spectrophotometric kinetic data were obtained by monitoring ArN_2^+ loss at a suitable wavelength to minimize interferences with other components of the solution (dediazonation products) as much as possible. Linear variations (not shown) in the absorbance of ArN_2^+ in aqueous and MeOH solutions up to $[\text{ArN}_2^+] = 2.0 \times 10^{-4} \text{ M}$ (cc. ≥ 0.999) were

found, keeping with the predictions of Beer's law. ArN_2^+ solutions were prepared by dissolving the corresponding aryldiazonium salt in the appropriate acidic (HCl) MeOH/H₂O mixtures to diminish diazotate formation [2]. Final concentrations were approximately 1.0×10^{-4} M and $[\text{HCl}] = 0.01$ M. The stock ArN_2^+ solutions were kept in the dark at low temperatures ($T < 5$ °C) to minimize their photochemical and/or spontaneous decomposition (Zollinger, 1994) and were used immediately or within a time period of less than 60 min.

Preliminary HPLC experiments showed that, in the absence of ClO_4^- , up to five decomposition products were detected to different extents. The most frequent were cresols, ArOH, and the methyl phenyl ethers (ArOMe), and, on occasion, depending on the particular experimental conditions, chlorotoluenes (when investigating Cl^- dependence), as well as the reduction product, toluene (ArH), that was detected in low yields when employing high percentages of MeOH in the solvent mixture. The calibration curves for all these products were obtained by employing authentic commercial samples. Linear (cc. > 0.999) calibration absorbance–concentration plots were obtained and employed for converting HPLC peak areas into concentrations. The following equation $\text{Yield} = 100 [\text{dediazonation product}]/[\text{ArN}_2^+ \text{T}]$ was employed to calculate the yields of the various dediazonation products.

When studying the effects of the perchlorate salts, a new chromatographic peak was found that was not observed in its absence, with a retention time lower than that of ArOH but higher than that of the front peak (see Figure S1, Supplementary Materials). The area of this new peak increased linearly upon the increasing $[\text{LiClO}_4]$. In dediazoniations, where sulfate ions were employed, the aryldiazonium sulfate anion, Ar-OSO_4^- was formed and could be isolated [46,47]. As the possibility of the formation of the aryldiazonium perchlorate derivative ArOCIO_3 exists, which is explosive in the solid state [3,38], we made no attempts in identifying nor isolating this new product. In spite of this, the failure in identifying this new derivative does not invalidate the main conclusions of the work because: (i) the peak area is proportional to the added $[\text{LiClO}_4]$ and (ii) dediazonation products are formed competitively and their rate of formation is the same as that of other dediazonation products (as determined from the variations in its peak areas with time), and equal to that of ArN_2^+ loss.

The rates of the formation of dediazonation products were obtained by employing a derivatization method, as described elsewhere [48]. To minimize side reactions that may occur upon the injection of ArN_2^+ in the HPLC system (metal parts, solvent, etc.), TRIS buffer ($[\text{TRIS}] = 0.05$ M) solutions of the coupling agent 2N6S, that allows for the rapid formation of a stable azo dye, were employed [48]. The dediazoniations were quenched at convenient times, as described elsewhere [42,48]. The derivatization reaction was carried out under pseudo-first order conditions ($[\text{2N6S}] > 20 [\text{ArN}_2^+]$). The final pH was adjusted to a pH of approximately 8, because naphthoxide ions are much more reactive than their protonated forms. It is not advisable to use lower acidities, because the competing reactions of aryldiazonium ions with OH^- , to form diazotates, becomes significant [2].

The experimental conditions were chosen so that the coupling reaction was essentially over by the time the reagents were mixed, i.e., azo dye formation is much faster than dediazoniations (at least 100 times faster) and ArN_2^+ is effectively quenched at any solvent composition. Figure 1 illustrates the determination of the rates of product formation (ArOMe, Figure 1A) and of ArN_2^+ loss by monitoring the decrease in the absorbance of the azo dye formed (Figure 1B).

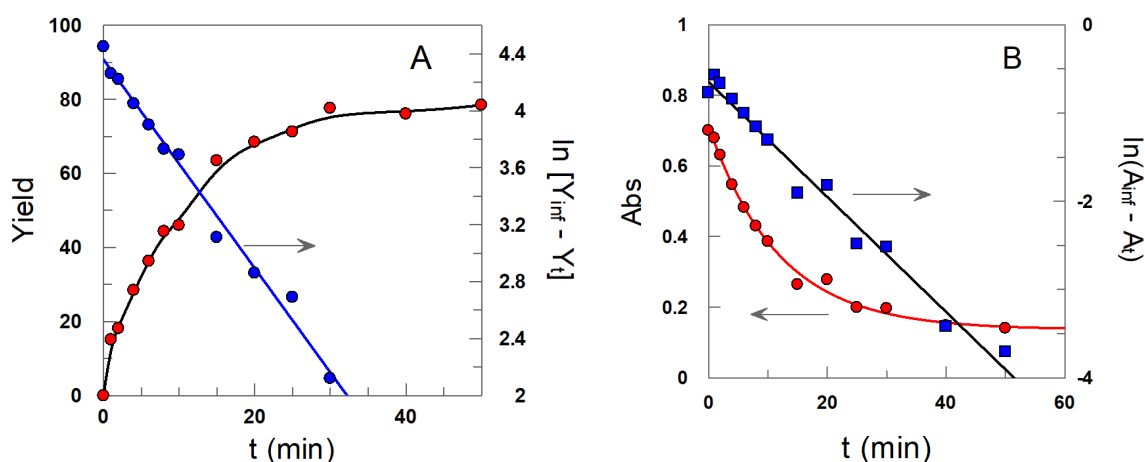


Figure 1. Illustrative examples of determination of the rate constant for product formation (ArOMe) by employing the chromatographic (A) and ArN_2^+ loss by monitoring the decrease in the absorbance of the azo dye formed in the derivatization method (B) under the same experimental conditions. The k_{obs} values obtained were similar ($\sim 12 \times 10^{-4} \text{ s}^{-1}$) with differences lower than 10%. Experimental conditions: 99.5% MeOH/ H_2O , $[\text{2MBD}] = 1 \times 10^{-4} \text{ M}$, $[\text{HCl}] = 0.01 \text{ M}$, $T = 35 \text{ }^\circ\text{C}$.

3. Results

3.1. Spontaneous Dediazonation of 2-, 3-, and 4-Methylbenzenediazonium Ions: Effects of Solvent (MeOH/ H_2O) Composition on the Observed Rate Constant, k_{obs}

The effects of the solvent composition on the observed rate constant k_{obs} for the spontaneous dediazonation of 2MBD, 3MBD, and 4MBD were explored by modifying the percentage of MeOH in the reaction mixture, as shown in Figure 2. Solvolytic rate constants k_{obs} increased smoothly at low percentages of MeOH, but more drastically at high percentages of methanol. The k_{obs} values at 0% MeOH, $k_{\text{obs}} = 6 \times 10^{-4} \text{ s}^{-1}$ (2MBD), $8 \times 10^{-4} \text{ s}^{-1}$ (3MBD), and $9.5 \times 10^{-4} \text{ s}^{-1}$ (4MBD) aligned with the reported values obtained by different techniques, including N_2 evolution [49] at pH = 1.6–1.8, as well as HPLC and VIS–UV spectrophotometry [14]. The increase in k_{obs} , upon changing the methanol content, was modest, less than two-fold, and much lower than those reported in other solvolytic reactions. It is, however, aligned with literature reports that indicate that the rates of heterolytic dediazonation of a number of arenediazonium ions vary by a factor of only 9 in 19 solvents [1].

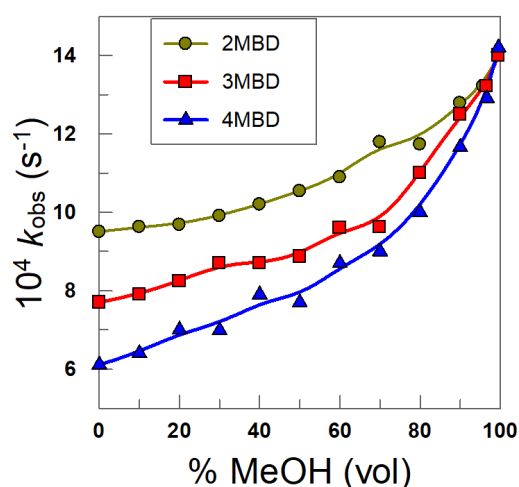


Figure 2. Effects of solvent composition on the solvolytic rate constants for the spontaneous decomposition of 2-, 3-, and 4-methylbenzenediazonium ions in acidic MeOH/ H_2O mixtures. Experimental conditions: $[\text{ArN}_2^+] = \sim 10^{-4} \text{ M}$, $[\text{HCl}] = 10^{-2} \text{ M}$, $T = 35 \text{ }^\circ\text{C}$ (2MBD, 3MBD), $T = 60 \text{ }^\circ\text{C}$ (4MBD).

3.2. Effects of Added Electrolytes on Dediazonation Rate Constants

The effects of electrolytes ($[\text{NaCl}] = 0\text{--}1\text{ M}$, $[\text{LiCl}] = 0\text{--}1\text{ M}$, and $[\text{LiClO}_4] = 0\text{--}1.5\text{ M}$) on k_{obs} were determined at two representative solvent compositions (20% and 99.5% MeOH), as seen in Figure 3. At 20% MeOH, k_{obs} values, in the absence of salt, were similar to those in Figure 1. The addition of NaCl, LiCl, or LiClO₄ did not have a significant effect on k_{obs} and the values remained essentially constant. However, when the percentage of MeOH increased to 99.5%, the addition of NaCl and LiCl (up to 1.5 M) did not significantly change k_{obs} , but, upon increasing $[\text{LiClO}_4]$, k_{obs} values decreased by approximately 40%. The observed decrease in k_{obs} values with the presence of ClO₄[−] ions, though somewhat modest, was unexpected and quite significant because no changes in k_{obs} were found in the presence of other salts and the decrease in k_{obs} was only detected at high percentages of MeOH. This is an important decrease that deserves further investigation, because we noted that k_{obs} values only had a two-fold change when going from 0 to 100% MeOH, as seen in Figure 3.

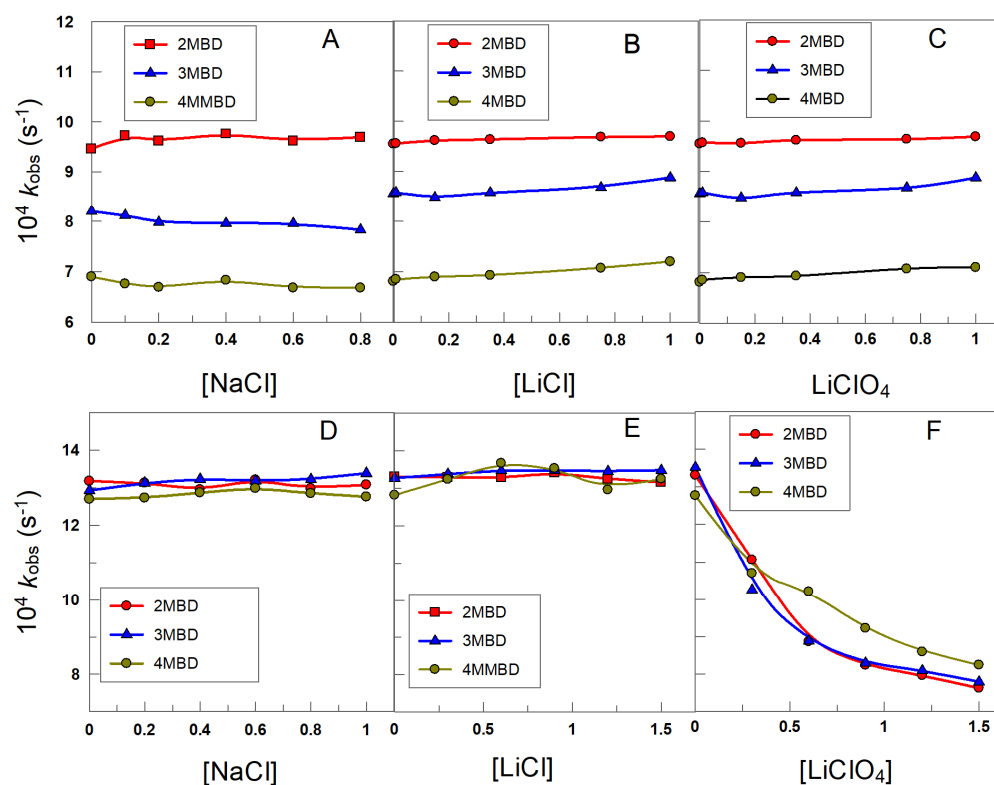


Figure 3. Effects of added electrolytes on k_{obs} for dediazonation of 2MBD, 3MBD, and 4MBD in 20% MeOH/H₂O (A–C) and in 99.5% MeOH/H₂O (D–F) mixtures. k_{obs} values were determined spectrophotometrically by monitoring ArN₂⁺ loss at $\lambda = 305\text{ nm}$ (2MBD) and $\lambda = 310\text{ nm}$ (3MBD, 4MBD). Experimental conditions: $[\text{ArN}_2^+] = 10^{-4}\text{ M}$, $[\text{HCl}] = 10^{-2}\text{ M}$, $T = 35\text{ }^\circ\text{C}$ (2MBD, 3MBD), $T = 60\text{ }^\circ\text{C}$ (4MBD).

To obtain further insights into the dediazonation process, we employed the chromatographic technique, as illustrated in Figure 4, to determine k_{obs} for product formation, in the absence and in the presence of added electrolytes, at two selected solvent compositions (20% and 99.5% MeOH). The k_{obs} values for product formation were the same as those obtained spectrophotometrically for ArN₂⁺ loss, confirming that products are formed competitively, in keeping with the predictions of the D_N + A_N mechanism shown in Scheme 2A.

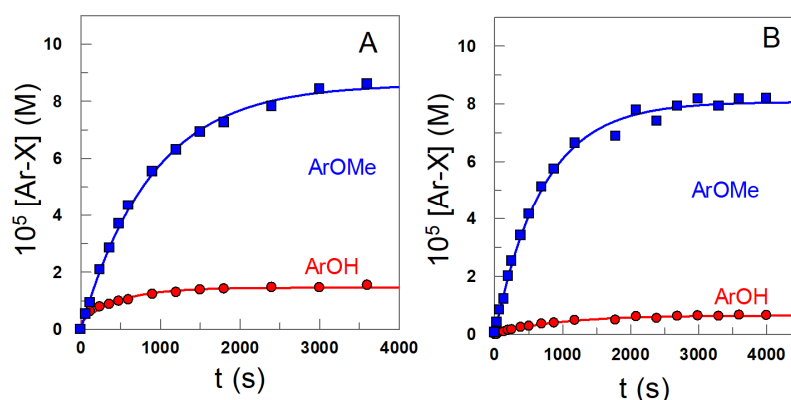


Figure 4. Illustrative determination of the rates of dediazonation product formation in 99.5% MeOH/H₂O mixture as determined by HPLC. Rates are determined by fitting the variation in the concentration of a particular dediazonation product with the time to a first order kinetic Equation (1). (A) 2MBD. (B) 4MBD. Experimental conditions: [2MBD]₀ = [4MBD]₀ = 10⁻⁴ M, [HCl] = 10⁻² M; T = 35 °C (2MBD), T = 60 °C (4MBD).

3.3. Effects of Added Electrolytes on Product Distribution

Figure 5 shows the effects of the solvent composition on the product distribution of 3- and 4MBD in the absence of added electrolytes. Only the heterolytic products (cresol and methyl phenyl ethers) were formed in significant yields, and the formation of the reduction product Ar-H was only detected in highly alcoholic solutions (4MBD) but its yield was very low when compared with those of heterolytic products; therefore, such a mechanism (homolytic) can be neglected. In all cases, the quantitative conversion to products was achieved in all composition ranges. The results are in agreement with published data [30,32,34].

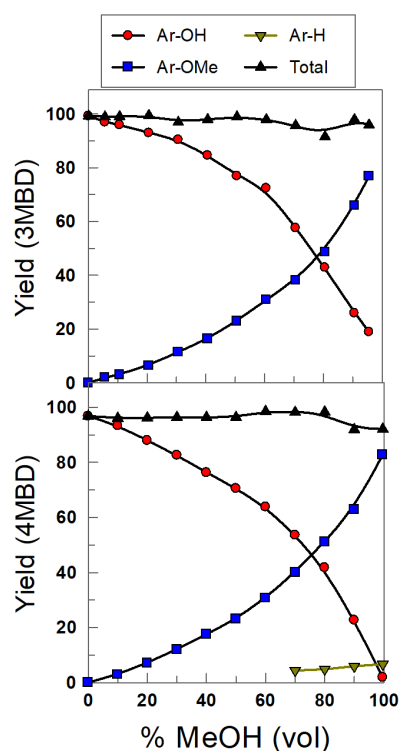


Figure 5. Variation of the percentage of solvolytic dediazonation products in MeOH/H₂O binary mixtures in the absence of electrolytes. Experimental conditions were the same as those in Figure 2.

To analyze the effects of added electrolytes, we selected two methanol compositions, 20% and 99.5% MeOH. At a low methanol content, the addition of salts (NaCl and LiClO₄)

up to 1.5 M had a negligible effect on the production distribution, as illustrated in Figure 6. However, this was not the case at high percentages of MeOH, Figure 7.

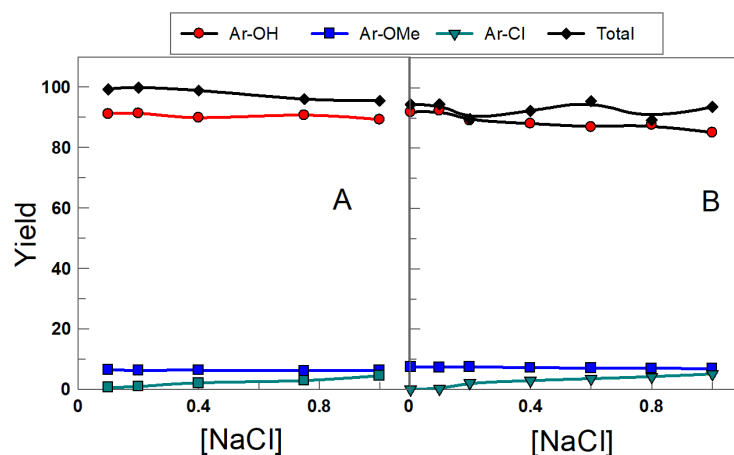


Figure 6. Effects of NaCl on dediazonation product distribution in 20% MeOH/H₂O mixtures as determined by HPLC. (A) 3MBD, (B) 4MBD. Experimental conditions: [3MBD₀] = [4MBD₀] = 10^{−4} M, [HCl] = 10^{−2} M, *T* = 35 °C (3MBD), *T* = 60 °C (4MBD).

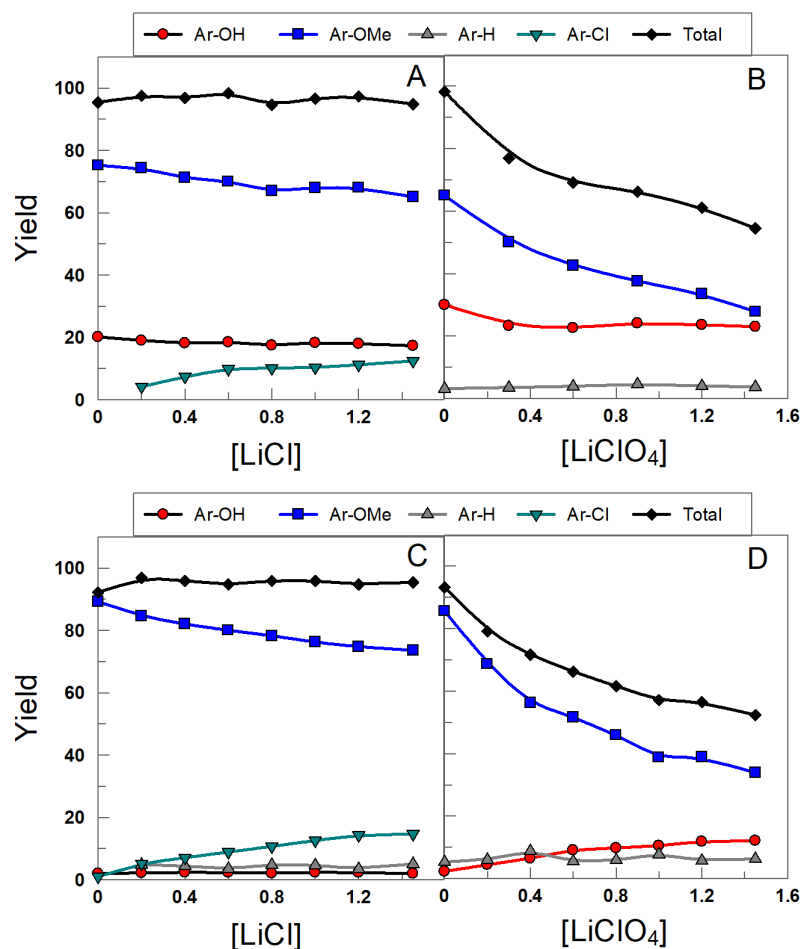


Figure 7. Effects of added electrolytes on the percentage of formation of dediazonation products in 99.5% MeOH/H₂O mixtures. (A,B) 3MBD (C,D) 4MBD. Note the formation of the ArCl derivative at the expense of ArOMe (A,C). In the presence of LiClO₄ the ArCl derivative is not formed but the yield of ArOMe decreases substantially upon increasing [LiClO₄] (B,D), attributed to the formation of the arylperchlorate derivative.

At 99.5% MeOH, in the presence of LiCl, the Ar-Cl derivative was detected, in addition to Ar-OH and Ar-OMe, and an increase in [LiCl] of up to 1.5 M had a negligible effect on the product distribution, as seen in Figure 7A,C, so that the quantitative conversion to products was obtained. As expected, when using LiClO₄ instead of LiCl, the Ar-Cl derivative was not detected but, surprisingly, a significant reduction in the yields of Ar-OMe was detected, as seen in Figure 7B,D. We note that the total yield decreases because of the presence of an unidentified dediazonation product, whose yield could not be computed because we made no attempts to fully identify the new product, mainly for safety reasons (see Section 2).

4. Discussion

Solvolytic dediazoniations have long been studied, and there is now a substantial body of knowledge on the reactions. For instance, the sensitivity of dediazoniations towards solvent polarity has been analyzed by employing the Winstein–Grunwald equation [26,27], yielding slopes for 2MBD, 3MBD, and 4MBD of $m = -0.026$, -0.018 , and -0.058 , respectively. These values are quite low and reflect the astonishing insensitivity of dediazoniations to the nature of the solvent [1]. The low values are interpreted on the grounds of similarities in the structure and the charge allocation between the parent aryldiazonium ion and the corresponding aryl cation [14,50,51].

The selectivity values for a number of aryldiazonium ions have also been obtained, assuming that the nucleophilic attack on the carbocation is under kinetic control. In aqueous solution, aryldiazonium ions have a small selectivity against reacting nucleophiles, compared to water, typically ranging from 0.4 to 6 [46], following the order $\text{Br}^- > \text{Cl}^- > \text{SO}_4^{2-} > \text{H}_2\text{O}$. Such values are orders of magnitude lower than those observed for nucleophiles competing with water in reactions with stabilized carbocations [14,52,53], and are essentially constant with solvent composition. Table 1 shows the selectivity values for 2-, 3-, and 4-MBD. Such low values are consistent the formation of highly reactive aryl cations and with the preassociation of the stepwise mechanism, as shown in Scheme 1A.

Table 1. Selectivity values for 2-, 3-, and 4MBD. Data from references [14,22,54].

Methylbenzenediazonium Ions	$S_w^{\text{Cl}^-}$	S_W^{MeOH}
2MBD	2.7	0.40
3MBD	2.6	0.60
4MBD	2.7	0.74

Figure 5 shows that, at about 80% MeOH/H₂O, the yields of ArOH and ArOMe are equal to each other. That is, equal yields of dediazonation products are obtained when the concentrations of nucleophiles in solution are approximately 8.3 M for [H₂O] and approximately 14.6 M for [MeOH], indicating that ArN₂⁺ ions show favored solvation with H₂O molecules. This preferential solvation is fully consistent with the moderate variation in k_{obs} on changing the MeOH content of the solvent, Figure 2. Moreover, barriers for the capture of carbocations by the solvent [55] are sufficiently small, so that the product distribution reflects the solvent distribution in the first solvation shell of the reactant, suggesting, therefore, that the solvation of the ground state ArN₂⁺ is essentially the same as that in the proximity of the transition state. Thus, at low MeOH content, the presumed aryl cations are mostly solvated by water molecules, and a relatively modest increase in the concentrations of NaCl, LiCl, or LiClO₄ (in comparison to that of water) does not have significant effects on both the dediazonation rate constants (Figure 3), and on product distributions (Figure 6).

The sensitivity of dediazoniations to changes in the solvent polarity can be illustrated by means of a Winstein–Grunwald plot, as shown in Figure 8, where a linear relationship between $\log(k/k_w)$ with the Y parameter is found, with slopes of $m = -0.032 \pm 0.001$ (2MBD), $m = -0.037 \pm 0.001$ (3MBD), and $m = -0.072 \pm 0.003$ (4MBD), consistent with the low selectivity of aryldiazonium ions to solvent effects [52,56]. This low sensitivity

can be attributed to the similarity in the structure and charge distribution of the parent aryldiazonium ion, compared to that of the corresponding aryl cation.

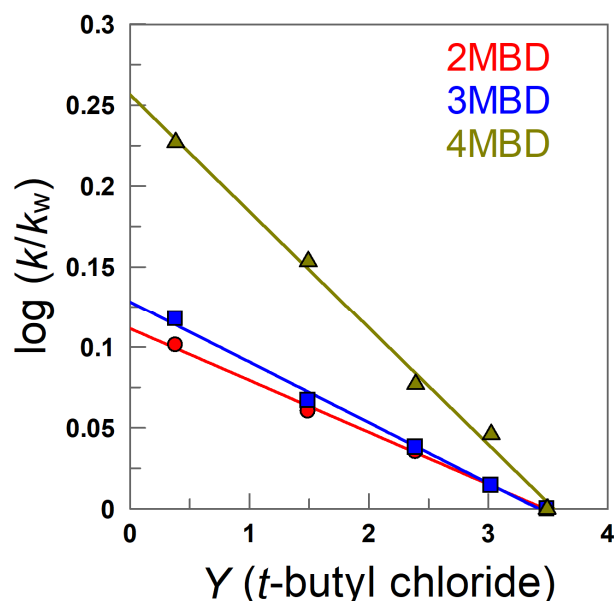


Figure 8. Winstein–Grunwald plots for 2MBD, 3MBD, and 4MBD. Y values were collected from Leffer et al. [57].

Surprisingly, when dediazoniations are carried out in solutions with high concentrations of MeOH, a different behavior is observed. The addition of NaCl or LiCl does not modify k_{obs} values, as seen in Figure 3D,E, and the analysis of the product distribution confirms the expected formation of the chlorobenzene derivatives. However, upon the addition of LiClO₄, both k_{obs} (Figure 3F) and the yields of the corresponding methyl phenyl ethers (ArOMe, Figure 7B,D) decrease. We note that chromatograms do not show the formation of the reduction products (toluenes, Ar-H) in a large extent and, thus, we can safely presume that the mechanism of the reaction does not change in the presence of LiClO₄. Thus, the variations in the yields of Ar-OMe can be attributed to the replacement of MeOH molecules in the solvation shell by ClO₄⁻ ions, presumably leading to the formation of the potentially explosive (in the solid state) aryldiazonium perchlorates.

Our hypothesis regarding perchlorate ions modifying the solvation shell of aryldiazonium ions seems to be supported by the results of Cruz et al. [58], who carried out a molecular dynamic study of dediazoniations and calculated the local concentrations of solvents around diazonium ions, concluding that, in the absence of salts, the local solvent composition varied linearly on the molar fraction of water in methanol/water mixtures, although they found non-linear variations for other solvent mixtures. The same authors also found that the calculated number of solvent molecules around the aryldiazonium cation can predict the product distribution when preferential solvation is considered. However, results must be taken with some caution because of the failure to identify the new product formed in the presence of LiClO₄.

The rates of dediazoniations with uncharged nucleophiles (such as MeOH or H₂O) are hardly affected by the nature of the solvent, as shown in Figure 2, because the electric charges are neither destroyed nor created in the rate-determining step. In fact, the rates of heterolytic dediazoniations have been reported to vary only by a factor of 9 when carried out in 19 solvents [1]. Thus, the low variation in k_{obs} with [MeOH] suggests that the solvation of the ground-state is similar to the proximity of the transition state; otherwise, unimolecular reactions, where the nucleophilic attack of the solvent is rate-determining, would lead to a strong dependence of k_{obs} on nucleophile concentration, which is not observed. The rates of the nucleophilic attack on aryl cations have been reported to be close

to the diffusion control limit ($\sim 10^9 \text{ M}^{-1} \cdot \text{s}^{-1}$) and the preassociation of the nucleophile with the aryl cation does not account for much of the trapping [1,2,46].

A different situation is found when charged nucleophiles are present in the solvation shell, as they may distort the charge distribution, compared to that of neutral nucleophiles. The Mayr's reactivity scale is certainly useful to predict whether an electrophile/nucleophile reaction can be expected to take place at room temperature, or to predict the selectivity of competing nucleophiles. The rate constants of electrophile–nucleophile combination reactions are mostly dependent on four factors: nucleophilicity, electrophilicity, temperature, and solvent. Strictly, it is not possible to separate these four factors, mainly because the values of the electrophilicity and nucleophilicity parameters are usually linked to the type of solvent, whose physical properties may change with changing temperatures. Nucleophilicity scales may also be affected by changes in temperature [33,59]. However, to our knowledge, an all-embracing theory of electrophile–nucleophile reactions is still not in sight, and further work on the effects of electrolytes on ionic reactions is needed.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/compounds2010005/s1>, Figure S1: The chromatogram in Figure 1.

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