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Solvolyses of 4-methylbenzenediazonium ions in trifluoroethanol/water mixtures: Effects of [TFE], acidity and temperature on the kinetics and mechanism of the reaction[†]

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We studied the solvolyses of 4-methylbenzenediazonium (4MBD) ions in 2,2,2-trifluoroethanol (TFE) – water mixtures by employing a combination of spectrometric (UV–VIS) and chromatographic (high performance liquid chromatography (HPLC)) techniques. HPLC analyses of the reaction mixtures show that very small amounts (<8%) of the reduction product toluene, ArH, are obtained, suggesting that the reaction occurs primarily through a heterolytic mechanism. Kinetic results show that k_{obs} values do not change significantly on changing solvent composition, which means that nucleophilic attack by solvent is not involved in the rate-limiting step of the reaction. On lowering the acidity, both k_{obs} values and product distributions remained basically unchanged, suggesting that diazo ethers do not form in TFE, in contrast with the behaviour found in alcohols such as MeOH, EtOH or BuOH. In these reactions, the results support the formation of diazo ethers, Ar—N═N—O—R. To obtain additional evidence for the ionic mechanism, we determined the effect of temperature on k_{obs} at different acidities and calculated the corresponding activation parameters. $\Delta H^{\ddagger}$ values are high compared to those of bimolecular and radical reactions, and $\Delta S^{\ddagger}$ values are small, but positive. The results are consistent with the traditional heterolytic $D_N + A_N$ dediazoniation with a rate-determining formation of a highly reactive aryl cation that traps any nucleophile available in its solvation shell. Copyright © 2010 John Wiley & Sons, Ltd.

Keywords: arenediazonium; solvolyses

INTRODUCTION

Reactions of arenediazonium, ArN_2^+, ions are both synthetically useful and mechanistically interesting. They are exploited industrially in the manufacture of pharmaceuticals and dyestuffs among others. New applications are emerging: they are currently widely used as initiators to modify carbon surfaces, to probe the interfacial compositions of colloidal systems and their role in carcinogenic and mutagenic processes is being explored.[1–3] Reaction mechanism of arenediazonium ions has been studied by a wide variety of techniques for over a century. New applications continue to be found in contemporary organic synthesis;[4–11] however, few kinetics studies accompany by product analyses. Consequently, mechanistic understanding of the relationships between molecular structure of reactant, solvent and reaction conditions is less than complete.

Dediazoniations have been studied in a number of solvents,[4,12,13] and two main mechanisms are reported, heterolytic (1A) and homolytic (1B) (Scheme 1). Literature reports[4] indicate that, in the absence of electron donors and depending on experimental conditions, both homolytic and heterolytic mechanisms occur in a variety of solvents. Until recently,[3] the initiation step of the homolytic dediazoniation pathway was hypothesized to be an electron transfer from the solvent, but the absence of evidence for or against, this hypothesis means that the nature of the initiation step remains a matter of debate.[4]

Based on recent solvolytic studies in our laboratory,[14,15] we concluded that the initiation step is the formation of *Z*-diazo ether adducts, Ar—N═N—O—R, and not an electron transfer. These kinetically controlled products undergo isomerization to the stable *E* isomer or homolytic bond rupture initiating a radical process (Scheme 2) leading to the formation of reduction products. The evidence for this mechanism is based on the observed sigmoidal variation in both k_{obs} and product yields with acidity for a number of arenediazonium ions. Product distribution analyses of the reaction mixtures indicate that at relatively high acidities ($-\log[HCl] = 2$), only heterolytic products are formed, but upon decreasing the acidity, the reduction products become predominant at the expense of the heterolytic ones, suggesting a change in the reaction mechanism. In addition, sigmoideal variations of k_{obs} with acidity are usually observed in reactions of acid–base pairs where both forms are attainable and show different reactivities.[16] However, under our experimental conditions, the solvent ionization is negligible and a potential reaction between ArN_2^+ and OH^- ions is unlikely,[14,15,17] therefore, the formation of an O-adduct (the diazo ether) that initiates a radical process.

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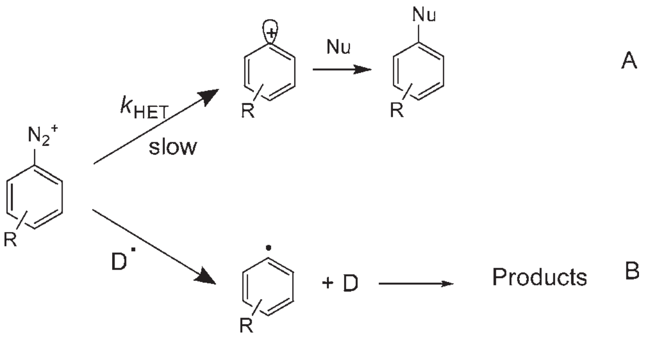


Scheme 1. Simplified dediazoniation mechanisms. (A) Heterolytic; (B) homolytic.

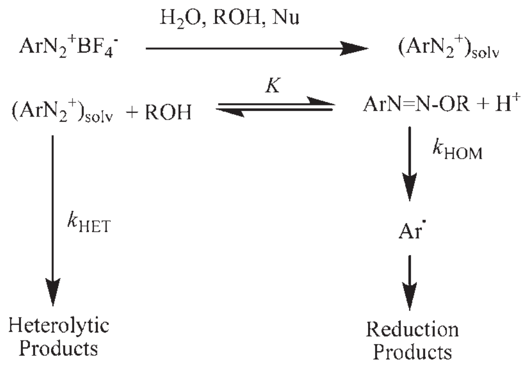
The results of our solvolytic studies[14,15,17] permit the demonstration of the identification of the dual role of ROH molecules as nucleophiles that either (i) solvate the diazonium ions (allowing them to undergo thermal heterolytic decomposition, i.e. decomposing through an ionic mechanism) or (ii) react directly with arenediazonium ions to yield O-coupling adducts in a highly unstable *Z* configuration, i.e. *Z*-diazo ethers. The *Z*-diazo ethers then undergo homolytic fragmentation initiating radical processes. The kinetics of methanolysis of **4**-NO_2- and **4**-Br-benzenediazonium ions under acidic conditions provides an excellent example of the influence of solvent composition and temperature on the change from a heterolytic mechanism to a homolytic one.[15,17] For these compounds, the formation of the diazo ethers is favoured on increasing [ROH] by the mass action effect but is inhibited by the medium effect on the equilibrium constant for the formation of the diazo ether, which decreases upon increasing [ROH].[15,17]

Here we expand our solvolytic studies with a kinetic study of the solvolysis of **4**-methylbenzenediazonium (**4**MBD) ions in **2**,**2**,**2**-trifluoroethanol (TFE)—water mixtures. The purpose is to obtain evidence for or against the formation of diazo ethers in TFE, by measuring the effects of solvent composition, acidity and temperature on the observed rate constants, k_{obs}, and on the product distributions.

EXPERIMENTAL SECTION

Instrumentation

UV–VIS spectra and some kinetic experiments were followed on an Agilent 8453 spectrophotometer equipped with a cell carrier thermostatted by Julabo F12-ED bath and attached to a computer for data storage. Product analysis was carried out on a WATERS HPLC system which included a model W600 pump, a W717 automatic injector, a W2487 dual wavelength detector and a computer for control and data storage. Products were analysed on a Nova Pak (Waters) reverse phase column (150 mm length, 3.9 mm internal diameter and 4 μm particle size) using a mobile phase of 50/50 v/v MeOH/H_2O containing 10^{-4} M HCl. The injection volume was 25 μl in all runs and the UV detector was set at 220 and 280 nm.



Scheme 2. Proposed competitive heterolytic (HET) and radical mechanisms (HOM) for the reaction of arenediazonium ions with alcohols under acidic conditions.

Materials

4MBD tetrafluoroborate was prepared by an anhydrous method,[18] purified three times from CH_3CN/cold ether, stored in the dark at low temperatures to minimize its decomposition and recrystallized periodically. **4**-Cresol (ArOH), **4**-chlorotoluene (ArCl) and toluene (ArH) were purchased from Sigma-Aldrich and TFE was purchased from Acros Organics; they were used without further purification. Other reagents were of maximum available purity from Panreac or Riedel de Häen. Solution composition was expressed as %TFE by volume. Molar concentrations were calculated by ignoring the small excess volume of mixed solvents.[19] All aqueous solutions were prepared by using Milli-Q grade water.

Methods

Beer's law plots (not shown) of **4**MBD aqueous solutions up to 2.00×10^{-4} M were linear (cc. ≥ 0.999). Kinetic data were obtained spectrometrically by monitoring the disappearance of the absorbance of ArN_2^+ at an appropriate wavelength. Observed rate constants, k_{obs}, were obtained by fitting the absorbance-time data to the integrated first-order Eqn (1) using a nonlinear least squares method. All runs followed first-order kinetics for at least three half-lives

$$\ln\left(\frac{A_t - A_\infty}{A_0 - A_\infty}\right) = -k_{obs}t \qquad (1)$$

where A_t, A_o and A_∞ are the absorbances at any time, at $t = 0$ and when the reaction is finished (i.e. infinite time). Reactions were initiated by adding an aliquot (<100 μl) of the ArN_2^+ stock solution to the previously thermostated reaction mixture. Duplicate or triplicate experiments gave average deviations less than 10%.

Product yields were obtained by HPLC after dediazoniation was complete. Preliminary HPLC experiments showed that up to four dediazoniation products may be formed: **4**-cresol, ArOH, **4**-fluorotoluene, ArF, aryl trifluorotheyl ether, $ArOCH_2CF_3$, and toluene, ArH. Linear (cc. > 0.999) calibration curves for converting chromatographic peak areas, *A*, into concentrations were obtained for ArOH, and ArH by employing commercial samples dissolved in MeOH. $ArOCH_2CF_3$ is not a commercial product, it was not synthesized and its yield was not determined. Yields of ArF were determined either because the product was not available in our laboratory. The absence of these products' yields produces a systematic error in the total yields. However, this error does not affect the kinetic results because dediazoniation products are formed competitively. These variations in the yields of the ArOH or ArH do not affect the main mechanistic conclusions, that is the reaction with trifluoroethanol goes by a heterolytic pathway unlike aliphatic alcohols, that can be ruled out from the experimental data.[15,17,20]

Yields of a dediazoniation product, *Y*, were obtained from the product concentration, $[\text{Analyte}]_{\infty}$, and the initial arenediazonium salt concentration, $[\text{ArN}_2^+]_o$, estimated by weight, i.e. $Y = 100[\text{Analyte}]_{\infty}/[\text{ArN}_2^+]_o$, as described elsewhere.[4,7,21]

RESULTS

Effects of %TFE on the observed rate constant, k_{obs}, and on the product distribution

The effects of solvent composition on k_{obs} were determined by changing the %TFE in the reaction mixture at a fixed acidity ($-\log[\text{HCl}] = 2$). In the absence of TFE, $k_{obs} \sim 8 \times 10^{-4}\,\text{s}^{-1}$ at $T = 60\,^{\circ}\text{C}$, consistent with literature values.[20,22] Values of k_{obs} increase by a factor of almost 3 as %TFE increases from 0 to 98%. At 98% TFE, $k_{obs} = 16 \times 10^{-4}\,\text{s}^{-1}$, close to a previously reported value[23] (Figure 1).

At this high acidity ($-\log[\text{HCl}] = 2$), the size of the observed rate enhancement is similar to that obtained in solvents such as MeOH or EtOH,[20] but the linear increase in k_{obs} with TFE contrasts with the nonlinear variation found in those solvents where exponential variation of k_{obs} with [ROH] was found.

The effect of %TFE on the product distribution was determined by HPLC analysis of the reaction mixture at the end of the reaction, that is, at infinite time. Figure 2 shows that, in the absence of TFE, the major dediazoniation product is ArOH, in keeping with previous results. As expected, ArOH yields decrease upon increasing the percentage of TFE in the reaction mixture and only small amounts of the reduction product ArH were detected in reaction mixtures with TFE content higher than 80% (%ArH < 10%). The ArOH yields at 58 and 85% TFE are very close to those reported in the literature, which have been reported as 65 and 34% ArOH, respectively.[5]

Effects of acidity on k_{obs} and on the product distribution

Solution acidity has a major effect on the formation and decomposition of diazo ethers intermediates in previous solvolytic studies in MeOH and EtOH.[17,20] To investigate possible formation of diazo ethers in TFE solutions, we studied the effect of acid strength on k_{obs} and the product distributions at two TFE/H_2O compositions (35 and 70% TFE). The results in Table 1 show that, at both percentages of TFE, the k_{obs} values increased gradually with increase in the acidity ($0.1 < -\log[\text{HCl}] < 6$). The average k_{obs} values, $k_{obs} = (11.9 \pm 0.9) \times 10^{-4}\,\text{s}^{-1}$ (35% TFE) and $k_{obs} = (13.8 \pm 0.5) \times 10^{-4}\,\text{s}^{-1}$ (70% TFE), are the same as the k_{obs} values at the same %TFE (Fig. 2).

Figure 3 shows the variation of the product distribution with [HCl]. As shown, the percentage of both the heterolytic product ArOH and the reducted product ArH remain virtually constant from 1 to 10^{-7} M HCl. The constant k_{obs} values and product distributions over a wide range of acidities suggest that diazo ether formation is not important and the reaction mechanism remains unchanged. By contrast in EtOH–H_2O solutions, rate enhancements of 320-fold and stoichiometric amounts of the reduced product were found.

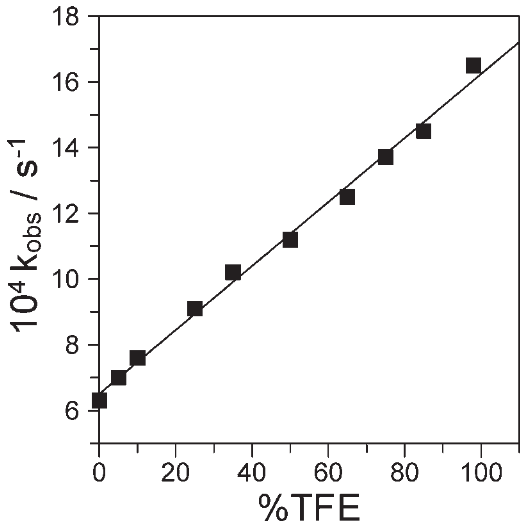


Figure 1. Influence of % TFE on k_{obs} for dediazoniation of **4**MBD. $[\mathbf{4}\text{MBD}] = 1.8 \times 10^{-4}$ M, $-\log[\text{HCl}] = 2$, $T = 50\,^{\circ}\text{C}$

Effect of temperature on k_{obs} for dediazoniation of *4*MBD in TFE–H_2O mixtures

The temperature effect on k_{obs} was studied at different acidities in two binary mixtures (35 and 70% TFE) at 50 and 60 °C (Fig. 4). Very similar variations in k_{obs} with acidity were obtained independent of the percentage of TFE in the reaction mixture.

The activation parameters of the reaction were estimated by using the Arrhenius equation and the theory of absolute rates, Eqn (2), where k_B and h stand for the Boltzmann and Plank constants, respectively. The results are in Table 2.

$$\ln\left(\frac{hk_{obs}}{k_B T}\right) = \frac{\Delta S^{\ddagger}}{R} - \frac{\Delta H^{\ddagger}}{RT} \qquad (2)$$

DISCUSSION

All runs obeyed first-order kinetics for more than three half-lives at any solvent composition. Upon increasing [TFE], k_{obs} increases modestly (Fig. 1) and no significant changes in k_{obs} with acidity

Table 1. Influence of [HCl] on k_{obs} for the decomposition of **4**MBD in two selected TFE/H_2O reaction mixtures. $[\mathbf{4}\text{MBD}] = 1.2 \times 10^{-4}$ M, $T = 50\,^{\circ}\text{C}$

$-\log[\text{HCl}]$	$10^4\,k_{obs}$ (s^{-1}) (35% TFE)	$10^4\,k_{obs}$ (s^{-1}) (70% TFE)
0.1	11.2 ± 0.2	12.8 ± 0.2
0.3	11.5 ± 0.2	
0.5	11.2 ± 0.2	13.4 ± 0.2
0.7	11.3 ± 0.2	13.9 ± 0.2
0.9	11.1 ± 0.2	13.5 ± 0.2
1.3	11.8 ± 0.3	13.4 ± 0.2
1.7	11.7 ± 0.3	13.3 ± 0.2
2.0	12.4 ± 0.4	13.2 ± 0.3
2.7	12.1 ± 0.5	14.0 ± 0.3
3.3	11.5 ± 0.5	14.7 ± 0.3
4.2	12.8 ± 0.5	14.5 ± 0.3
5.1	12.8 ± 0.6	15.4 ± 0.5

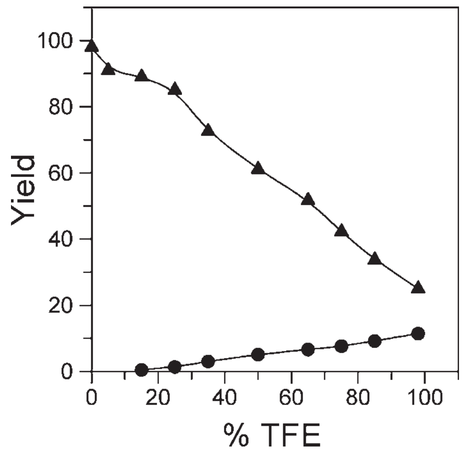


Figure 2. Influence of %TFE on the product distribution of **4**MBD. [**4**MBD] = 1.2×10^{-4} M, T = 50 °C and −log[HCl] = 2

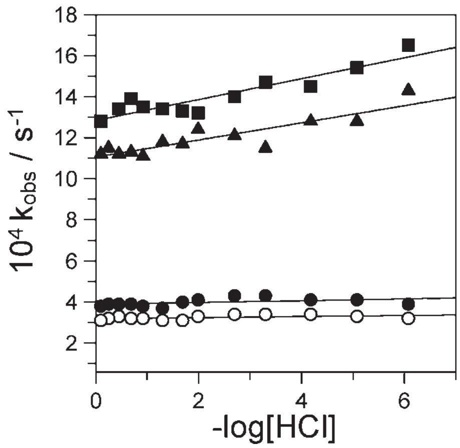


Figure 4. Influence of acidity on k_{obs} at two selected temperatures for the solvolyses of **4**MBD in TFE–H_2O binary mixtures. ○35% TFE, $T = 50$ °C, ● 70% TFE, $T = 50$ °C, ▲ 35% TFE, $T = 60$ °C, ■ 70% TFE, $T = 60$ °C. [**4**MBD] = 1.2×10^{-4} M

were detected, in contrast with results of solvolytic dediazoniations in more nucleophilic solvents, such as MeOH or EtOH, where S-shaped variations of k_{obs} with acidity were found,[14,15,17] indicating that the formation of diazo ethers of the type Ar—N═N—O—CH_2—CF_3 does not seem to be important. The low sensitivity of k_{obs} to changes in %TFE is related to its properties as solvent, which combines a lower nucleophilicity, basicity but a higher ionizing power compared to alcohols such as MeOH or EtOH, which makes TFE an excellent solvent to probe nucleophilic solvent assistance and, in general, for solvolytic dediazoniation studies.[5–7,24,25]

Further evidence supporting the hypothesis comes from the product analyses. Only heterolytic dediazoniation products are obtained in significant yields with increasing %TFE, temperature and acidity, and reduction products like ArH are in low yield. In contrast, large amounts of the reduction product ArH were obtained upon decreasing the acidity in solvolytic reactions carried out in MeOH or EtOH; for instance, stoichiometric amounts of ArH are found in the ethanolysis of **4**MBD at −log[HCl] = 5, meanwhile negligible amounts are found at −log[HCl] = 2.[15,26] Therefore, the absence of significant amounts of reduction products like ArH or biaryls, Ar–Ar, indicates that dediazonization is heterolytic mechanism (Scheme 3).

Rate-limiting nucleophilic attack of TFE on **4**MBD would lead to a strong dependence of k_{obs} on solvent composition, which is not observed (Fig. 1). The results are consistent with rate-determining formation of a highly reactive aryl cation that is trapped by available nucleophiles (Scheme 1). Aryl cations have not been isolated to date in aqueous systems because they are extremely short-lived intermediates (<0.5 ns[27]). However, Winkler and Sander[28] isolated them in a solid argon matrix and other reports indicate that photolyzed arenediazonium ions generate aryl cations that can be observed as addition products with aromatic compounds.[29]

Pre-association stepwise mechanisms (Scheme 3) in which the aryl cation has a short but finite lifetime have been used to describe product distribution in terms of ion–molecule or ion–nucleophile pairs.[22,30] Nucleophilic attack may occur on 'free' carbocations, contact ion–molecule pairs or contact ion–solvent pairs. Various research groups have proposed the formation of ion–molecule pairs involving ground state arenediazonium ions. Zollinger and coworkers[31] suggested the formation of ion–molecule pairs with N_2 at high N_2 pressures. More recently, transient coloured complexes between arenediazonium ions and aromatic hydrocarbons have been observed and characterized[32] and solid arenediazonium tetrachlorocuprate(II) complexes[33] have been isolated that decompose to give ArCl in high yields.[34]

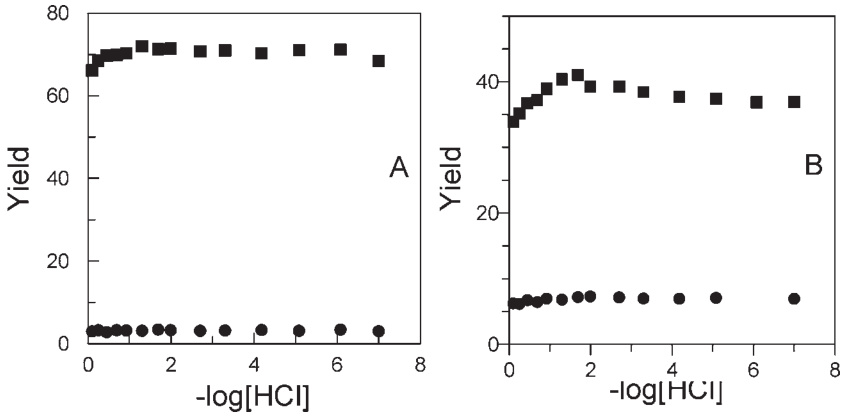


Figure 3. Influence of [HCl] on the product distribution for the decomposition of **4**MBD in (A) 35% TFE–H_2O, (B) 70% TFE–H_2O. ■ **4**MBOH, ● **4**MBH, [**4**MBD] = 1.7×10^{-4} M, $T = 50$ °C

Table 2. Estimated activation parameters for the solvolyses of **4**MBD in 35 and 70% TFE–H_2O reaction mixtures. For comparison, literature values in other solvents are included

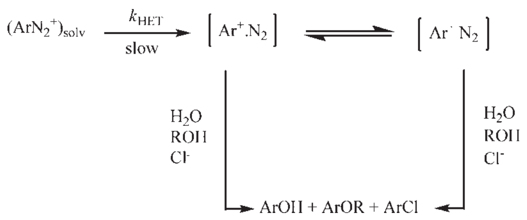
Solvent	*T* (°C)	−log[HCl]	$10^4\ k_{obs}$ (s^{-1}) ($T = 50$)	E_a (kJ mol^{-1})	$\Delta H^\ddagger$ (kJ mol^{-1})	$\Delta S^\ddagger$ (J mol^{-1}) K^{-1}	$T\Delta S^\ddagger$ (kJ mol^{-1})	$\Delta G^\ddagger$ (kJ mol^{-1})
35% TFE^a	50–60	1	3.2	119 ± 3	114 ± 2	41 ± 7	14	100
70% TFE^a	50–60	1	3.9					
H_2O^b	40–60	2	2.0	112.4	110	21.6	7	103
99.5% MeOH^b	40–65	2	3.5	114	109	25.6	9	100
98% EtOH^b	40–65	2	4.0	116	114	41	14	102

This work.
Data from Ref. [14].

Rate constants for nucleophilic attack on carbocations have been reported to be close to the diffusion control limit, $\sim 10^9$–10^{13} M^{-1} s^{-1}.[29] Aryl cations have lifetimes on the order of nanoseconds and they do not have much time to diffuse away reorganizing their nearest neighbour ions and molecules, similar to the behaviour of other extremely short-lived carbocations.[35] Thus, at a low concentration of other components, e.g. anions of salts, arenediazonium ions decompose primarily with solvent in the immediate vicinity of the aryl cation, that is, once the N_2 leaves, one nucleophile molecule in the first coordination shell will form its corresponding dediazoniation product. In other words, to obtain a specific dediazoniation product the precursor nucleophile must be in the solvation shell of the aryl cation prior to N_2 departing. Consistent with this interpretation (Scheme 3) the formation of the aryl cation does involve change transfer into the ring and only a small reorganization of the solvent shell is expected upon the formation of the corresponding aryl cation.[36,37]

Previous solvolytic dediazoniations in TFE are line with the above conclusions. Maskill and coworkers[7] investigated the source of fluoride atoms in ArF, concluding that ArF was formed by fluorine abstraction by the presumed aryl cation, in part from the solvent and in part from the tetrafluoroborate counterion within an undissociated ion pair. They, however, could not identify the nature of the species remaining after fluoride abstraction from TFE or whether fluoride abstraction is concerted or stepwise.[6,7]

Analysis of the activation parameters (Table 2) shows that both $\Delta H^\ddagger$ and $\Delta S^\ddagger$ values are very similar to those found in water and in short chain alcohols such as MeOH or EtOH.[20] Solvolytic unimolecular reactions can show positive or negative $\Delta S^\ddagger$ values.[38,39] The positive $\Delta S^\ddagger$ values in Table 2 suggest that the transition state has a greater structural freedom than reactants, in line with the reported positive volumes of activation, $\Delta V^\ddagger$, for a number of dediazoniations in different solvents.[40–43] Scheme 3 shows that the parent arenediazonium ion and the aryl cation polarize the surrounding solvent molecules to a similar extent; thus, the gain of entropy due to the increase in molecular vibrations is not compensated by the loss of entropy due to the restricted motion of the solvating molecules. On the other hand, $\Delta H^\ddagger$ values are relatively high as in many unimolecular reactions,[44,45] unlike $\Delta H^\ddagger$ values usually found for bimolecular reactions. In typical S_{N_2} reactions,[45] activation enthalpies are substantially lower because the bond breaking of old bonds, which requires energy, and bond making, which releases energy, are highly concerted, usually synchronous and of similar energies. Thus, the relatively high $\Delta H^\ddagger$ values for **4**MBD in TFE/H_2O solutions suggest a transition state that has undergone substantial bond breaking with little compensating bond making. Positive $\Delta S^\ddagger$ values, as those found in this work, compensate the large enthalpy term making dediazoniations and $\Delta G^\ddagger$ is relatively small. Thus, dediazoniation is often faster than other unimolecular reactions, and consistent with results for a number of dediazoniations, that show a much lower solvent dependence than typical unimolecular reactions.[4,23,43,46]



Scheme 3. Proposed heterolytic (HET) $D_N + A_N$ dediazoniation mechanism for solvolyses of **4**MBD in TFE. Intimate $[Ar^+. N_2]$ and solvent separated $[Ar^+\ N_2]$ ion–molecule pairs trap any nucleophile available in their solvation shells.

Finally, it may be worth noting the change in the behaviour of **4**MBD ions compared with that of arenediazonium ions bearing electro-withdrawing substituents such as **4**-NO_2- or **4**-Br-benzenediazonium ions.[15,17] Substituent effects on the aromatic ring have a significant effect on the stability and reactivity of arene diazonium ions, but their effects cannot be accounted for in terms of the Hammet equation but a dual substituents parameter equation separating the resonance and inductive effects is needed.[4,47,48] It is well known that **4**-alkyl substituents in the aromatic ring make ArN_2^+ ions less prone to decomposition through homolytic pathways than those bearing electronwithdrawing substituents[4] and this is reflected in the lower values of the equilibrium constant *K* for the formation of diazo ether of **4**MBD compared with those for **4**-NO_2- and **4**-Br-benzenediazonium ions.[15,17]

In conclusion, the kinetic and product yield results are not consistent with the formation of diazo ethers which leads to reduction products in TFE. This is in keeping with previous solvolytic studies showing that heterolytic dediazoniations tend to occur in solvents of low nucleophilicity, such as H_2O, or fluorinated alcohols, such as TFE, but that both ionic and homolytic dediazoniations occur in non-fluorinated alcohols of higher nucleophilicity such as MeOH and EtOH or DMSO. Our results are completely consistent with the heterolytic $D_N + A_N$ mechanism shown in Scheme 3, that is rate-limiting formation of an extremely reactive aryl cation that is trapped by any nucleophile available in its immediate vicinity.

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