Methanolysis of 4-bromobenzenediazonium ions. Effects of acidity, [MeOH] and temperature on the formation and decomposition of diazo ethers that initiate homolytic dediazoniation

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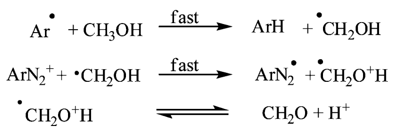
We have investigated the effects of solvent composition, acidity and temperature on the dediazoniation of 4-bromobenzenediazonium (4BrBD) ions in MeOH–H_2O mixtures by employing a combination of spectrometric and chromatographic techniques. The kinetic behaviour is quite complex; in the absence of MeOH, dediazoniations follow first-order kinetics with a half-life $t_{1/2} \approx 3000$ min ($T = 45$ °C), but addition of small concentrations of MeOH lead to more rapid but non-first-order kinetics, suggestive of a radical mechanism, with $t_{1/2} \approx 125$ min at 25% MeOH. Further increases in the MeOH concentration slow down the rate of dediazoniation and reactions progressively revert to first-order behaviour, and at percentages of MeOH higher than 90%, $t_{1/2} \approx 1080$ min. Analyses of reaction mixtures by HPLC indicate that three main dediazoniation products are formed depending on the particular experimental conditions. These are 4-bromophenol (ArOH), 4-bromoanisole (ArOMe), and bromobenzene (ArH). At acidities (defined as –log[HCl]) < 2, the main dediazoniation products are the substitution products ArOH and ArOMe but, upon decreasing the acidity, the reduction product ArH becomes predominant at the expense of ArOH and ArOMe, indicating that a turnover in the reaction mechanism takes place under acidic conditions. At any given MeOH content, the plot of k_{obs} or $t_{1/2}$ values against acidity is S-shaped, the inflexion point depending upon the MeOH concentration and the temperature. Similar S-shaped variations are found when plotting the dediazoniation product distribution against the acidity. The acid-dependence of the switch between the homolytic and heterolytic mechanisms suggests the homolytic dediazoniation proceeds *via* transient diazo ethers. The complex kinetic behaviour can be rationalized by assuming two competitive mechanisms: (i) the spontaneous heterolytic dediazoniation of 4BrBD, and (ii) an O-coupling mechanism in which the MeOH molecules capture ArN_2^+ to yield a highly unstable *Z*-adduct which undergoes homolytic fragmentation initiating a radical process. Analyses of the effects of temperature on the equilibrium constant for the formation of the diazo ether and on the rate of splitting of the diazo ether allowed, for the first time, estimation of relevant thermodynamic parameters for the formation of diazo ethers under acidic conditions.

Introduction

In 1977, Bunnett published two papers[1,2] focused on the thermolysis of arenediazonium ions, ArN_2^+, in acidic methanol seeking evidence to establish whether or not homolytic and heterolytic dediazoniations proceed *via* a common intermediate.[3] The phenomenon of interest was first described by DeTar and Kosuge,[4] who showed that substituted benzenediazonium ions such as 4-bromobenzenediazonium, 4BrBD, and 4-methoxybenzenediazonium ions decompose in acidic MeOH under a N_2 atmosphere yielding reduction products (mainly bromobenzene and anisole, respectively), but in the presence of O_2 they decompose yielding the corresponding solvolytic products (4-bromoanisole and 1,4-dimethoxybenzene, respectively).

On the basis of kinetic and product distribution measurements, Bunnett and co-workers[1,2] concluded that, in acidic methanol, dediazoniations take place through competing ionic and radical mechanisms, a conclusion substantiated in subsequent investigations by other researchers.[5–8] They assumed that the radical pathway followed the propagation sequence postulated by DeTar and Turetzky,[9] Scheme 1, but could not find convincing evidence for the nature of the initiation step and hypothesized a direct electron transfer from the methanol to the arenediazonium ion, step 1 in Scheme 1. The lack of convincing evidence for or against the postulated initiation mechanism made the topic remain a matter of debate for a long time because in such homolytic dediazoniations no obvious reductants are employed.



Scheme 1 Solvolytic dediazoniation mechanism proposed by Bunnett's group[1,2] showing the initiation step 1, which was assumed to be an electron transfer from the solvent to the arenediazonium ion, and the subsequent propagation steps.

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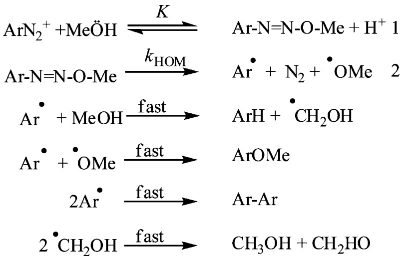
In recent solvolytic dediazoniation work under acidic conditions,[10,11] we proposed an initiation mechanism based on the formation of a transient O-diazo ether in a rapid pre-equilibrium step followed by a homolytic bond cleavage that initiates a radical mechanism, steps 1 and 2 in Scheme 2. The experimental basis for our proposal was the finding of S-shaped variations in both k_{obs} and product formation with acidity for toluenediazonium[10] and 4-nitrobenzenediazonium, 4NBD, ions[11] and the results allowed identification of the dual role played by the ROH molecules as nucleophiles that (i) simply solvate the diazonium ions (allowing them to undergo thermal heterolytic decomposition), and (ii) react directly with arenediazonium ions to yield O-coupling adducts in a highly unstable *Z* configuration, *i.e.* *Z*-diazo ethers. In the second route, the *Z*-diazo-ethers then undergo homolytic fragmentation initiating radical processes.[5,6,8,10,12–14] Moreover, the kinetic investigation of the methanolysis of 4NBD under acidic conditions provided an excellent example of the influence of solvent composition on the change from a heterolytic mechanism to a homolytic one.[11]



$$ArN_2^+ + Me\ddot{O}H \overset{K}{\rightleftharpoons} Ar\text{-}N{=}N\text{-}O\text{-}Me + H^+ \quad 1$$

$$Ar\text{-}N{=}N\text{-}O\text{-}Me \xrightarrow{k_{HOM}} Ar^{\bullet} + N_2 + {}^{\bullet}OMe \quad 2$$

$$Ar^{\bullet} + MeOH \xrightarrow{fast} ArH + {}^{\bullet}CH_2OH$$

$$Ar^{\bullet} + {}^{\bullet}OMe \xrightarrow{fast} ArOMe$$

$$2Ar^{\bullet} \xrightarrow{fast} Ar\text{-}Ar$$

$$2\,{}^{\bullet}CH_2OH \xrightarrow{fast} CH_3OH + CH_2HO$$

Scheme 2 Newly proposed solvolytic dediazoniation mechanism showing an initiation step comprising the formation of a highly unstable diazo ether in a rapid pre-equilibrium step that subsequently decomposes homolytically initiating a radical process. The spontaneous decomposition of ArN_2^+, which takes place through the rate-determining formation of an aryl cation that further reacts with available nucleophiles (D_N + A_N mechanism) is not shown for the sake of clarity.

Here we report an extension to our solvolytic studies by investigating the methanolysis of *p*-bromobenzenediazonium ions (4BrBD) over the whole MeOH–H_2O composition range at different acidities and temperatures. Our aim is to confirm the proposed initiation mechanism and to gain insights into the energetics of diazo ether formation and decomposition. For this purpose, a combination of spectrometric and chromatographic techniques was employed.

4BrBD was chosen as a model arenediazonium ion for several reasons; the most relevant are: I) 4BrBD is one of the ArN_2^+ ions employed in previous studies by DeTar *et al.*[4] and Bunnett and co-workers[1,2] and II) because it is well recognized that substituents in the aromatic ring of diazonium ions have important mechanistic effects.[5,6,15] For instance, electron-withdrawing substituents in the 4-position destabilize the aryl cation by induction more than they destabilize the parent arenediazonium ions, and therefore its spontaneous decomposition reaction is much slower than that of the parent, or of arenediazonium ions bearing electron-releasing groups such as Me.[7,16] A Br- group in the 4 position (like 4-MeO-) withdraws electrons by induction through the σ bonds but has an electron donating capability through resonance, which contrasts with other electronegative groups such as 4-NO_2, which has no electron donating capability. Electron-withdrawing substituents (as opposed to methyl, for example) in the aromatic ring make the arenediazonium ions prone to decompose through homolytic pathways. For example, transient O-diazo ether derivatives were detected in dediazoniation of 4NBD ions in the presence of β-cyclodextrin[17,18] or ascorbic acid;[19] for both nucleophiles, the adducts were detected experimentally and, in some instances, isolated.[20]

As we shall show, the results obtained for the methanolysis of 4BrBD provide further support for a radical initiation mechanism *via* formation of a transient diazo ether, Ar–N=N–OMe, which undergoes homolytic fragmentation yielding a bromophenyl radical ($Ar^{\bullet}$) and the methoxy radical (${}^{\bullet}MeO$). Formation of the O-adduct is dependent on the acidity, the MeOH concentration and the temperature. At a given temperature and $-\log[HCl] > 2$, competitive homolytic and heterolytic mechanisms are observed and the aryl radicals are able to abstract a hydrogen atom from MeOH within the solvent cage leading to the formation of the reduction product, bromobenzene. The formation of the O-coupling adduct is exothermic, but the large negative entropic term makes the Gibbs free energy for the equilibrium formation of the diazo ether small but positive at normal temperatures. An increase in the temperature does not favor diazo ether formation even in reaction mixtures with a high MeOH content.

Results

Effects of the percentage of MeOH on the rate of decomposition of 4BrBD

The effect of solvent composition on the observed rate constant, k_{obs}, was investigated by changing the percentage of MeOH in the reaction mixture at different acidities (HCl, $[H_3O^+]$ at least 10 times greater than initial concentrations of substrate). In the absence of MeOH, the thermal decomposition of 4BrBD in aqueous acid solution is extremely slow but the reactions appeared to follow first-order kinetics (results not shown) and a value of $t_{1/2} \approx 3000$ min was estimated at $T = 45\ ^{\circ}C$ (see Experimental section for details). This remarkable thermal stability is consistent with that of benzenediazonium ions bearing other electron-withdrawing groups in the aromatic ring compared with that of those bearing electron-donating groups.[6,16,21]

Addition of only small amounts of MeOH results in the UV absorbance against time plots becoming S-shaped, Fig. 1, which is clearly not compatible with simple first-order kinetics and suggests intrusion of a radical process. Careful purification of the diazonium salt (see Experimental section), and changes in the batches of the MeOH employed to prepare the reaction mixtures and of the MeOH supplier, did not result in significant changes in the observed kinetic behavior, indicating that the results obtained are not due to possible impurities in the MeOH.

Upon increasing further the percentage of MeOH, the reaction profiles gradually became first order again with $t_{1/2} \approx 1080$ min in 98% MeOH, *i.e.* $t_{1/2}$ is about 3 times higher in 98% MeOH than in pure water. All these observations are very similar to those found for the methanolysis of 4NBD ions.[10,11]

Because of the non-first-order behaviour obtained at intermediate MeOH percentages, but wishing to compare the effect of the percentage of MeOH on the rate of the reaction, we report half-lives, $t_{1/2}$ values of which are plotted instead of k_{obs} in Fig. 2.

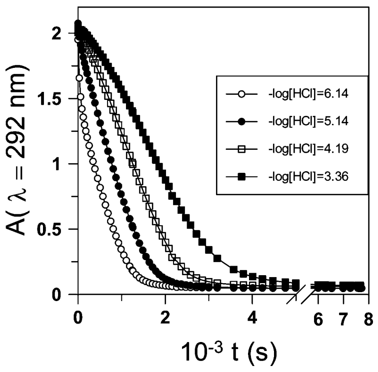


Fig. 1 Typical S-shaped kinetic plots obtained for the thermolysis of 4BrBD in a 25% (v : v) MeOH–H_2O binary mixture at different acidities. [4BrBD] ~ 1.3×10^{-4} M, $T = 45$ °C.

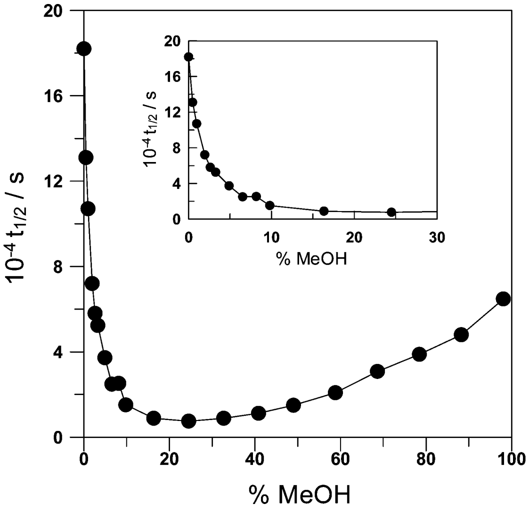


Fig. 2 Variation of $t_{1/2}$ with the percentage of MeOH for solvolyses of 4BrBD. [4BrBD] ~ 1.3×10^{-4} M, [HCl] = 0.01 M, $T = 45$ °C. The inset is a magnification of the 0–30% MeOH range.

As noted before, $t_{1/2} \approx 3000$ min ($T = 45$ °C) in the absence of MeOH, but addition of small amounts of MeOH speeds up the reaction appreciably with $t_{1/2}$ values decreasing to a minimum of about $t_{1/2} \approx 125$ min at 25% MeOH. Further addition of MeOH causes $t_{1/2}$ to increase smoothly up to about $t_{1/2} \approx 1100$ min at 98% MeOH. The inset in Fig. 2 is an expansion of the results obtained in the range 0–20% MeOH.

It may be worth noting that the ~ 24 fold decrease in $t_{1/2}$ found for 4BrBD, Fig. 2, is very similar to that observed for 4NBD, but a larger [MeOH] is required; for 4NBD the minimum in $t_{1/2}$ is reached at ~ 9% MeOH.[10,11]

Effect of acidity on $t_{1/2}$ and on the product distribution

The effects of acidity on $t_{1/2}$ were investigated at selected percentages of MeOH, Fig. 3. In both cases, S-shaped profiles were obtained, emphasizing the effect of acidity on the rate of the reaction. It was not possible, however, to obtain complete sigmoidal profiles at low percentages of MeOH because of the much higher HCl concentrations needed, Fig. 3, and because of the extremely low reactivity of 4BrBD (the thermal decomposition becomes competitive), but the data obtained are suggestive of S-shaped profiles.

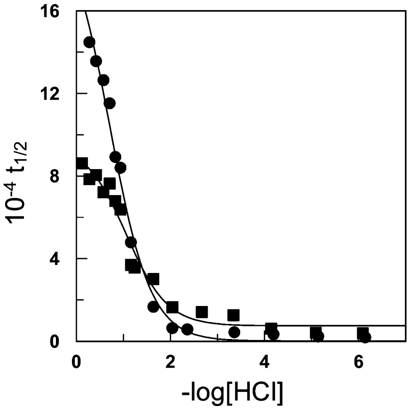


Fig. 3 Effects of acidity on the methanolysis of 4BrBD in a 25 : 75 (●) and in a 75 : 25 (■) MeOH/H_2O (v : v) binary mixtures. [4BrBD] ~ 1.3×10^{-4} M, $T = 45$ °C.

The finding of S-shaped kinetic profiles is in keeping with previous findings showing parallel variations of k_{obs} or $t_{1/2}$ with the acidity in the ethanolyses[10] and butanolyses[22] of toluenediazonium ions and in the methanolyses of 4NBD and attributed to the formation of transient diazo ether intermediates from the arenediazonium ions which then lead on to the reduction product ArH, Scheme 2. Note the large variation of $t_{1/2}$ in the –log[HCl] = 0–2 range compared to that in the 2–7 range, highlighting the crucial role of the acidity in the formation of the diazo ethers, whose formation seems to be important even under relatively high acidic conditions (–log([HCl] ~ 1–2).

HPLC analyses of the reaction mixtures indicate that three main dediazoniation products, ArH, ArOH, ArOMe were formed but total yields were less than 100% in all runs as in previous 4BrBD solvolytic dediazoniation works (see Experimental section). Fig. 4 shows the effects of acidity in the yields of the three main dediazoniation products, ArOH, ArH, and ArOMe, at two selected solvent compositions. Fig. 4A shows that, at low percentages of MeOH, the yield of ArOH drops very fast from ~70% at the highest acidity to only 8% at –log[HCl] = 2, with a concomitant increase in the yield of the reduction product (60% at –log[HCl] = 2). Thereafter, however, the yield of ArOH is remarkably constant on changing the acidity of the solution.

Fig. 4B displays the results at 75% MeOH showing the increase in the yield of the reduction product ArH at the expense of the substitution products ArOMe and ArOH. Note that the yield of ArH becomes constant at –log[HCl] > 3 and that the yields of ArOH and ArOMe are very similar in spite of the increase in [MeOH].

Effect of temperature on $t_{1/2}$ and on the product distribution

Fig. 5A and 5B show the effects of temperature on $t_{1/2}$ for the thermolysis of 4BrBD at different acidities in two selected MeOH : H_2O binary mixtures. Again, S-shaped kinetics are obtained at any temperature and, at a given temperature, the largest variations in $t_{1/2}$ are obtained in the –log([HCl] = 0–2 acidity range.

To determine the effect of the temperature on product distribution, the reaction mixtures at two solvent compositions and different acidities were chromatographed after the reaction was

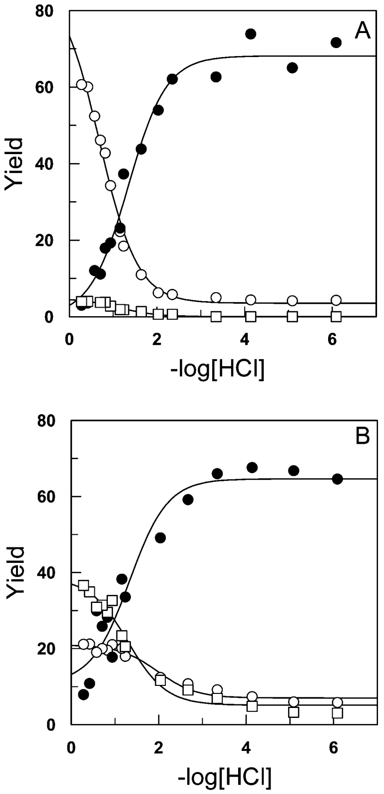


Fig. 4 Effects of acidity on the product distribution for the methanolysis of 4BrBD in 25 : 75 (A) and 75 : 25 (B) MeOH–H_2O binary mixtures. ○ ArOH □ ArOMe ● ArH. Experimental conditions as in Fig. 3.

complete, Fig. 6. At a given temperature, S-shaped variations in the yields are observed on increasing the acidity and at a given acidity temperature does not seem to have a major effect on the product distribution.

Discussion

S-shaped variations in k_{obs} (or $t_{1/2}$) with acidity such as those shown in Fig. 3–6 are usually observed in reactions of acid–base pairs where both forms are attainable and show different reactivities.[23] Only two specimens under our experimental conditions may undergo acid–base processes, the ArN_2^+ ions and MeOH. The pK_a of MeOH is ~ 15 and the pK_a value of 4BrBD has been reported to be ~ 11.1,[24] so it appears unlikely that ArN_2^+ ions react with MeO^- or with OH^- ions, as in alkaline medium,[1,2] under our experimental conditions. We propose the reaction mechanism shown in Scheme 2 which hypothesizes two competitive mechanisms: (i) the thermal decomposition of the solvated ArN_2^+ ions through the heterolytic $D_N + A_N$ mechanism (not shown), and (ii) the formation of an adduct between ArN_2^+ ions and MeOH in a rapid pre-equilibrium step followed by its rate-determining homolysis, initiating a radical process.

Similar mechanisms have been employed to interpret the reactivity of arenediazonium ions with a number of ascorbic acid derivatives where the formation of a diazo ether intermediate was detected experimentally by employing electrochemical methods[19,25] and for the ethanolysis of toluenediazonium ions[10] and methanolysis of 4-nitrobenzenediazonium ions.[11] The assumption of a rate-limiting decomposition of the diazo ether

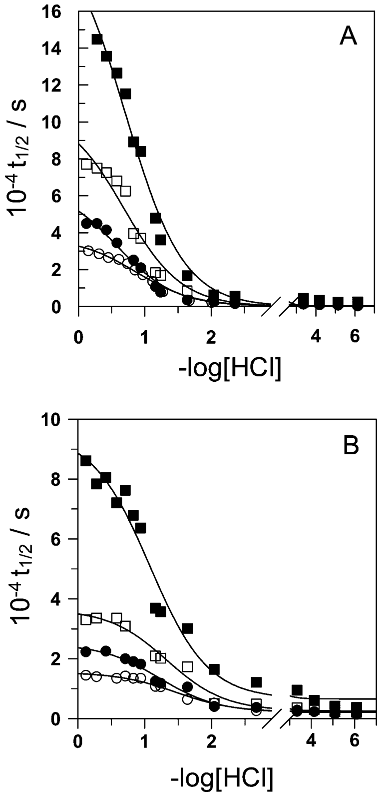


Fig. 5 Effects of temperature and acidity on $t_{1/2}$ for the methanolyses of 4BrBD in 25% (A) and 75% (B) MeOH–H_2O binary mixtures. ■ T = 45 °C □ T = 50 °C ● T = 55 °C ○ T = 60 °C. [4BrBD] = 1.37×10^{-4} M.

is also consistent with reported results for other O-coupling reactions,[12,14,26,27] and was probed experimentally in reactions of arenediazonium ions where geometric restrictions apply.[17,28]

From Scheme 2, eqn (1) can be derived where k_{HET} and k_{HOM} are the rate constants for the spontaneous thermal heterolytic decomposition of ArN_2^+ and the decomposition of the diazo ether, respectively, with K standing for the equilibrium constant for diazo ether formation shown in Scheme 2.

$$k_{obs} = \frac{k_{HET}[H^+] + k_{HOM}K[MeOH]}{K[MeOH] + [H^+]} \qquad (1)$$

This equation is typical of processes where an S-shaped dependence of k_{obs} with $-\log[H^+]$ is observed (where $[H^+]$ represents the concentration of protonated solvent molecules). From eqn (1), and by considering limits, we find that when $[H^+] >> K[MeOH]$, $k_{obs} \approx k_{HET}$, *i.e.*, the reaction proceeds wholly through the D_N + A_N mechanism and only heterolytic products are obtained. On the other hand, when $[H^+] << K[MeOH]$, $k_{obs} \approx k_{HOM}$, *i.e.* the reaction proceeds wholly through the O-diazo ether and formation of reduction products is favored. The solid lines in Fig. 3–6 were obtained by fitting the experimental data to eqn (1) by means of a non-linear least-squares method provided by the GraFit 5.0.5 computer program and the average K values obtained are listed in Table 1.

At a given temperature, the K values at 75% MeOH are lower than those at 25% MeOH in keeping with previous findings and confirming that increasing concentrations of MeOH have opposing effects upon the formation of the diazo ether in this

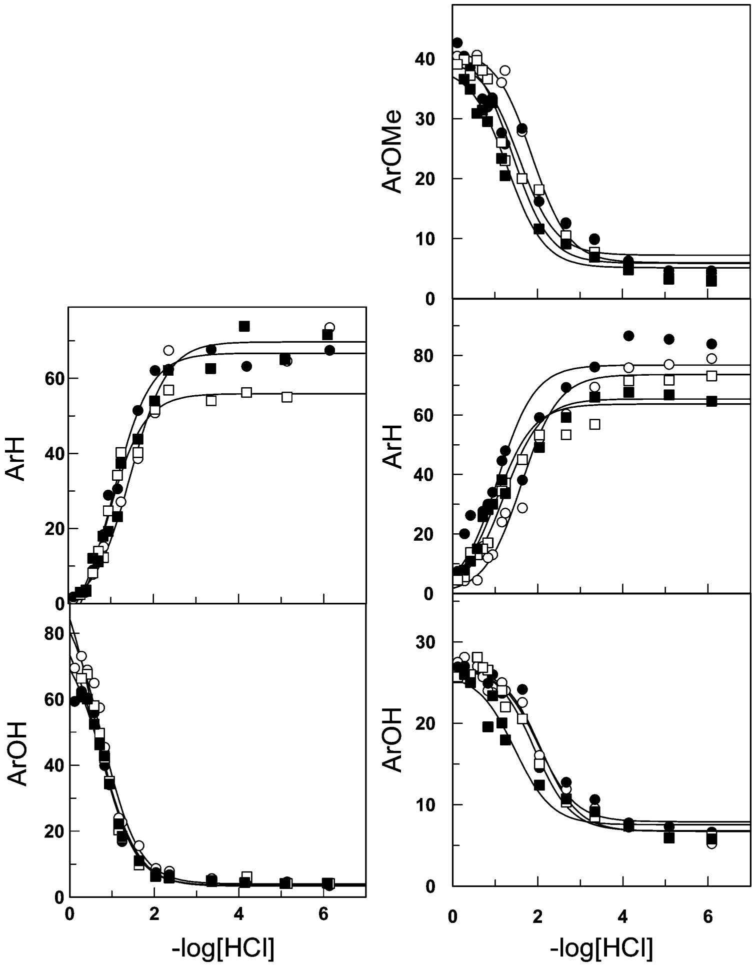


Fig. 6 Effects of T on product distribution for thermolysis of 4BrBD in a 25 : 75 (left) and in a 75 : 25 MeOH–H_2O (right) mixtures. In the 25 : 75 MeOH–H_2O mixture only traces of ArOMe were detected and for this reason the variation in its yield with acidity is not plotted. ■ $T = 45$ °C □ $T = 50$ °C ● $T = 55$ °C ○ $T = 60$ °C. Other conditions as in Fig. 5.

Table 1 Average values for the equilibrium constant K, determined by fitting the data in Fig. 3–6 to eqn (1), and values for the enthalpy and entropy of the formation of the diazo ether (step 1 in Scheme 2) determined by means of eqn (2), (3)

T/°C	45	50	55	60
MeOH : H_2O (v : v)	**25 : 75**			
10^2K	3.6	3.2	2.6	2.0
ΔH/kJ mol^{-1}	−35			
ΔS/J mol^{-1} K^{-1}	−137			
MeOH : H_2O (v : v)	**75 : 25**			
10^3K	3.4	2.1	1.7	0.9
ΔH/kJ mol^{-1}	−77			
ΔS/J mol^{-1} K^{-1}	−288			

concentration range: it is favored modestly by higher concentrations of MeOH through the mass action effect, but strongly opposed by the medium effect on the equilibrium constant. It is worth noting, however, that the variation of K with the percentage of MeOH seems to be smaller than that found for the methanolysis of 4NBD[11] but larger than that for the ethanolysis of toluenediazonium ions.[10] At low percentages of MeOH, an increase in the temperature does not seem to have a significant effect on K but the effect seems to be more noticeable on increasing the concentration of MeOH, and at 75% MeOH, an increase in K of 1.5 fold is obtained on increasing the temperature from $T = 40$ to 60 °C.

The analysis of the variation of the K values with the temperature allows one, for the first time, to gain insight into the energetics of diazo ether formation, step 1 in Scheme 2. Fig. 7

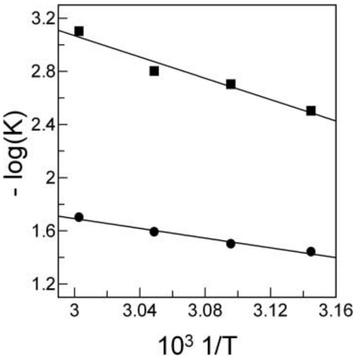


Fig. 7 van't Hoff plot according to eqn (2) for the equilibrium of formation of the diazo ether, step 2 in Scheme 2. ● 25 : 75, ■ 75 : 25 MeOH : H_2O (v : v). Data from Table 1.

shows a typical van't Hoff plot, according to eqn (2), illustrating the linear variation found between –log K and $1/T$ at the two methanol percentages investigated and from which the enthalpy values shown in Table 1 were determined. Entropic terms, ΔS, determined by employing eqn (3), are also displayed in Table 1. Details on the assumptions and limitations on the use of eqn (2) and (3) can be found elsewhere.[29]

$$\Delta H = -2.3R\left[\frac{\partial(\log K)}{\partial(1/T)}\right]_P \tag{2}$$

$$T\Delta S = \Delta H - \Delta G \tag{3}$$

Data in Table 1 show that ΔH and ΔS are of the same sign, and so work in opposite directions. Formation of the diazo ether is exothermic yet has a positive standard free energy of formation at any of the temperatures investigated. The Gibbs free energy ΔG for the 75 : 25 mixture is higher than that for the 25 : 75 one, highlighting the opposing effects of [MeOH]. Because $\Delta G > 0$, $K = k_1/k_{-1} < 1$ and thus $k_1 < k_{-1}$. An increase in the temperature increases k_{HOM}, Fig. 8, and at any temperature k_{HOM} must be higher than k_{-1} since once the diazo ether is formed it splits homolytically according to the steps indicated in Scheme 2.

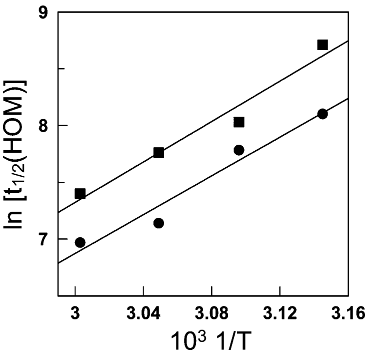


Fig. 8 Variation of ln[$t_{1/2}$(HOM)], which refers to the fitted value at low acidity, eqn (1), for the methanolysis of 4BrBD with the reciprocal of the temperature in a 25 : 75 (●) and a 75 : 25 (■) MeOH–H_2O mixture. [4BrBD] ~1.40×10^{-4} M, –log[HCl] = 4.1.

The analyses of the effects of temperature on k_{HET} (or $t_{1/2}$(HET)) and k_{HOM} (or $t_{1/2}$(HOM)) allowed us to estimate the values for the activation energy of the heterolytic and homolytic pathways, Fig. 8. The estimated value for the heterolytic process is in line with those reported in the literature,[30] $E_a \approx 100$ kJ mol^{-1} and those for the decomposition of the diazo ether in 25 : 75 (E_a = (71 ± 10) kJ mol^{-1}) and 75 : 25 MeOH/H_2O mixtures (E_a = (74 ± 10) kJ mol^{-1}) are very similar to each other but substantially lower than that for the heterolytic process.

Previous studies on the formation of diazo ethers under alkaline conditions suggest that diazo ethers are initially formed in a highly unstable, kinetically controlled, Z-configuration which then may undergo subsequent isomerization to the thermodynamically stable E-isomers, which be in some instances can isolated,[20] or eventually may give rise to homolytic rupture of the bonds providing the initiation of a radical process.[14,19,25,31] This bond-rotating mechanism to transform the Z- into the E-isomers has been recently described for Sandmeyer hydroxylations and chlorination reactions.[31] All kinetic and product distribution evidence suggests, therefore, that in the present case there is no conversion of the unstable Z-diazo ether to the much more stable E-isomer, which would eventually undergo acid catalyzed fragmentation,[12,14,32] as was found for the methanolysis of 4NBD.[11]

In conclusion, we have been able to show that the methanolysis of 4BrBD under acidic conditions takes place through two competitive mechanisms where a MeOH molecule may act as a nucleophile by simply solvating 4BrBD (allowing it to undergo thermal heterolytic decomposition) or react directly with 4BrBD to yield an O-coupling adduct which undergoes homolytic fragmentation. The formation of this adduct is favoured by decreasing the acidity but suppressed by increasing [MeOH] and the temperature.

Because large amounts of the reduction product ArH are formed under relatively mild conditions, the results obtained here also indicate a simple, effective and quick practical method for replacing an aromatic amino group by hydrogen, representing an improved alternative to the method proposed by Kornblum[33] using hypophosphorous acid as reducing agent or that proposed by Bravo-Díaz *et al.* using sodium dodecyl sulfate surfactants[34] or β-cyclodextrin.[17]

Formation of diazo ethers with neutral and anionic nucleophiles in the course of dediazoniations has been described.[17,19,20,25,35–37] In most instances analyzed, the nucleophile must possess a charge, such as OH^-, CN^-, RO^- or ascorbate ions, and experimental conditions are chosen so that substantial concentrations of the anionic form of the nucleophile are present.[14,19,25,31] However, our results suggest that the formation of Z-diazoethers with neutral nucleophiles is much more common than expected, and further investigations to elucidate the role of substituents in the aromatic ring and experimental conditions on the formation and decomposition of diazo ethers are warranted.

Experimental section

Instrumentation

UV-VIS spectra and some kinetics experiments were followed on an Agilent 8453 spectrophotometer equipped with a Julabo F12-ED thermostatted cell carrier 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 analyzed on a Microsorb-MV C-18 (Rainin) reverse phase column (150 mm length, 3.9 mm internal diameter, and 4 μm particle size) using a mobile phase of 45 : 55 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 225 nm.

Materials

4-Bromobenzenediazonium (4BrBD) tetrafluoroborate (Aldrich, 96%) was purified three times from CH_3CN–cold ether; it was stored in the dark at low temperatures to minimize its decomposition and was recrystallized periodically. 4-bromophenol (ArOH), 4-bromoanisole (ArOMe), bromobenzene (ArH), were from Across Organics and were used without further purification. Other reagents were of maximum available purity from Panreac or Riedel de Häen. Solution composition is expressed as percent MeOH by volume. Molar concentrations were calculated by ignoring the small excess volume of mixed solvents.[38] All aqueous solutions were prepared by using Milli-Q grade water.

Methods

Kinetic data were obtained spectrophotometrically and by HPLC. Observed rate constants were obtained by fitting the absorbance-time data for at least three half-lives to the integrated first-order eqn (4) using a non-linear least squares method in those cases where clean first-order kinetics were observed; otherwise, $t_{1/2}$ values are reported and defined as the time elapsed for the absorbance or concentration of the reactant to decrease to half its initial value, or for the yield of a product to increase to half its final value.

$$\ln\left(\frac{M_t - M_\infty}{M_0 - M_\infty}\right) = -k_{\text{obs}}t \qquad (4)$$

Duplicate or triplicate experiments gave average deviations less than 10%. Stock 4BrBD salt solutions were prepared by dissolving it in the appropriate acidic (HCl) mixture to minimize diazotate formation;[39] solutions of final concentrations about 1×10^{-3} M and [HCl] = 3.6×10^{-3} M were used generally immediately or within 90 min with storage in an ice bath to minimize spontaneous decomposition. Beer's law plots (not shown) in aqueous and methanolic solutions up to 2.00×10^{-4} M were linear (cc. ≥ 0.999). Spectrophotometric kinetic data were obtained by following the disappearance of the absorbance of ArN_2^+ at $\lambda = 292$ nm. Reactions were initiated by adding an aliquot (<100 μL) of the ArN_2^+ stock solution to the previously thermostatted reaction mixture.

Product analysis of reaction mixtures was by HPLC after dediazoniation was complete. Preliminary HPLC experiments showed that three main products are formed, ArOH, ArH, and ArOMe. Linear (cc. >0.999) calibration curves for converting HPLC peak areas, A, into concentrations were obtained for these products by employing commercial samples. Percentage of formation, Y, of dediazoniation products were obtained from the dediazoniation product concentration, [analyte], and the initial diazonium salt concentration, $[ArN_2^+]_o$, estimated by weight, *i.e.* $Y = 100[\text{analyte}]/[ArN_2^+]_o$, as described elsewhere.[1,14,15]

Inasmuch as total yields were less than 100%, careful purification and quantification of 4BrBD was done, and the MeOH employed in the kinetic experiments was HPLC grade from different suppliers and batches (and used as received), but the yields did not improve significantly. HPLC chromatograms showed no extraneous peaks that could be eventually associated to unidentified dediazoniation products. Large scale thermolysis reactions were carried out to provide substantial amounts of minor by-products for easy identification and quantification but all efforts were unsuccessful and no tangible amounts of other products were detected except traces of 4,4′-dibromobiphenyl at percentages of MeOH ranging 5–15%.

We found no easy explanation of the anomalous low total yields found, which contrasts to the quantitative yields found in other solvolytic dediazoniations under similar experimental conditions.[5,8,10,11] One might think the cause to be an erroneously low measurement of the initial amount of 4BrBD used. This is unlikely to be the case because, in addition to the careful purification of 4BrBD, different experiments and batches carried out in different days gave similar results.

Yields less than 100% were already reported for the thermolysis of 4BrBD in acidic MeOH in previous dediazoniation works[1,2,4,27,40] and no clear explanation was provided in spite of the numerous attempts to isolate minor products. Even in some of the most recent dediazoniation studies, where the yields of 4BrBD solvolytic reactions were determined by GC analyses,[41] the computed total yields are substantially less than 100% both in the presence and absence of radical trapping agents such as iodoacetic acid. Here we assumed, as Bunnett *et al.*[1,2] did in the past, that the low yields should be recognized as a systematic error on computing total yields, which does not affect the kinetic results (since dediazoniation products are formed competitively, see experimental results) nor the variation in the yield of a given dediazoniation product with acidity or temperature, thus not affecting the main mechanistic conclusions that can be ruled out from the experimental data.

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