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Diazonium ion chemistry: replacement of H by alkyl at the central carbon accelerates an S_N2 substitution reaction[†,‡]

Tara E. Agnew, Hyun-Joong Kim and James C. Fishbein*

Department of Chemistry and Biochemistry, University of Maryland, Baltimore County, 1000 Hilltop Circle, Baltimore, Maryland 21250, USA

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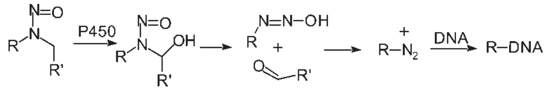
ABSTRACT: The rate constants for hydrolysis of diazomethane, diazoethane and 1-diazopropane in aqueous 5% acetonitrile at 25 °C and ionic strength 1 M ($NaClO_4$) were measured by stopped-flow spectrophotometry. The pH-rate profile for diazomethane hydrolysis exhibits a pH-independent section in the lower pH range, 8–10, with a downward break at higher pH, as has been reported for slightly different reaction conditions. In the case of diazoethane and 1-diazopropane, the reaction remains pH independent up to pH > 13. General acid catalysis of the hydrolysis reactions of diazomethane and diazoethane were examined in the pH-independent regions. For a limited number of catalysts, the value of Brønsted α was 0.58 for both diazoalkanes. The downward break in the pH rate profile for diazomethane hydrolysis is consistent with what was previously concluded, rate-limiting protonation by H_2O in the pH-independent region changing to rate-limiting attack of water on the diazonium ion in the pH-dependent region, the decrease in rate constant with increasing pH being attributed to deprotonation of the diazonium ion by hydroxide ion. The lack of a downward break in the pH–rate profiles for hydrolysis of the diazoethane and 1-diazopropane is attributed specifically to the increase, relative to the methyldiazonium ion, in the rate constant for water attack on the ethyl- and 1-propyldiazonium ions, perhaps by as much as $>10^3$-fold. Copyright © 2004 John Wiley & Sons, Ltd.

KEYWORDS: diazonium ion; hydrolysis; alkyl substitution; S_N2 reaction; rate acceleration

INTRODUCTION

The chemistry of diazonium ions is of fundamental importance in understanding the basis of the carcinogenicity and mutagenicity of nitrosamines.[1–3] In general, nitrosamines exert their biological effects as a result of metabolic activation by P450 enzymes to unstable α-hydroxynitrosamines. These decompose with the generation of diazoic acids, the precursors to diazonium ions that mediate the alkylation of DNA bases, as in Eqn (1):



(1)

Mechanisms and selectivity in diazonium ion substitutions are of importance because, at least for simple methylating and ethylating nitrosamines, exocyclic oxygen atom alkylation of guanine, cytosine and thymine appear to be especially promutagenic lesions.[1–4]

In 1991, Brosch and Kirmse reported that chiral 1-butylamine undergoes nitrous acid-catalyzed deamination in acetic acid or water with >98% inversion.[5] This result, combined with the detectable nucleophilic selectivities measured for methyl- and ethyldiazonium ion substitutions observed in DNA nucleoside alkylation and with other nucleophiles, $s = 0.42$ and 0.26, respectively,[6] requires the conclusion that the substitution reactions on simple primary alkyl diazonium ions occur by a concerted S_N2 process. This reaction is in competition with concurrent concerted hydride migration and probably elimination reaction as indicated by process a, b and c, respectively, in the mechanism of Eqn (2).[5] These latter reactions account for the balance of the products observed in diazonium ion decompositions. The report of Brosch and Kirmse rectified an erroneous, and widely cited, report which posited the involvement of primary carbocations in nucleophilic media and disoriented a generation of thinking about diazonium ion substitution mechanisms.[7] The selectivity of nucleophilic substitution at primary diazonium ions stands in contrast to that observed in the substitution of secondary and substituted-benzyl diazonium ions which are manifestly unselective, in the absence of powerful resonance

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**Correspondence to:* J. C. Fishbein, Department of Chemistry and Biochemistry, University of Maryland, Baltimore County, 1000 Hilltop Circle, Baltimore, Maryland 21250, USA.
E-mail: jfishbei@umbc.edu

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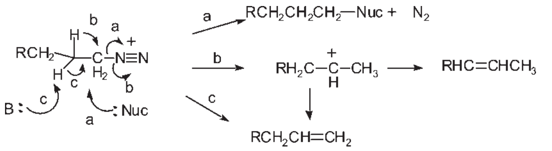
[†] This paper is dedicated to Dr William P. Jencks, indisputably among the most insightful thinkers concerning organic reaction chemistry of the last century. He has been an outstanding mentor, both exacting and tireless, and remains a powerful inspiration to all who have worked with him or encountered his prolific contributions.

[‡] Selected paper part of a special issue entitled 'Biological Applications of Physical Organic Chemistry'.

electron donating substituents attached to the reactive center. Such reactions occur through preassociation mechanisms in which the carbocation intermediates react with even weak nucleophiles in the cation's primary solvation sphere, faster than diffusion.[8–13]



(2)

Still, some uncertainties about structure and reactivity of diazonium ions remain. Reports investigating DNA alkylation by methyldiazonium ion and its higher normal homologues indicate that the latter give lower yields of alkyated DNA bases.[14,15] At least part of the explanation lies in the lower nucleophilic selectivity of the latter compounds compared to the methyldiazonium ions (see above). An alternative explanation, invoking the formation of primary carbocations,[14] is inconsistent with the facts outlined above, and has otherwise been discounted.[16] The nature of the differences in selectivity and the intrinsic differences in reactivity of simple diazonium ions are uncertain. The rate constant for nucleophilic displacement by solvent, $k = 2.6\,\mathrm{s}^{-1}$, has been reported for the methyldiazonium ion in 60% aqueous tetrahydrofuran,[17] but there are no other experimental data bearing on the reactivity of the simple higher homologues. Glaser's group has carried out an *ab initio* investigation on the structure and stability of methyl- and ethyldiazonium ions and the energetics of their nitrogen dissociation reactions.[18] These results suggest the ethyl compound might be intrinsically less stable, but the implications for the energetics of S_N2 substitution in polar media are unclear. Reported here is a study of the hydrolysis of diazomethane, diazoethane and 1-diazopropane in aqueous media. The differing pH dependence of these reactions leads us to the conclusion summarized in the title of this paper.

RESULTS

The kinetics of hydrolysis of diazoalkanes were monitored at 235 or 240 nm by stopped-flow spectrophotometry at 25 °C and ionic strength 1 M (NaClO$_4$) in aqueous 5% acetonitrile. The decay of absorbance obeyed excellent first-order kinetics over the 4–7 half-lives during which it was monitored. Experiments were carried out in media buffered (up to a buffer concentration of 0.1 M) with various alkylammonium ion buffers or without buffer in sodium hydroxide solutions. Under these conditions the value of k_{obsd} varied according to the equation

$$k_{\mathrm{obsd}} = k_0 + k_{\mathrm{b}}[\mathrm{Buffer}]_{\mathrm{total}} \tag{2}$$

The constant k_0 represents the first-order rate constant for the buffer-independent reaction, derived from the y-intercepts of plots of k_{obsd} against total buffer concentration. The constant k_{b} is the observed second-order rate constant for the contribution from buffer components, and is taken as the slopes of such buffer dilution plots.

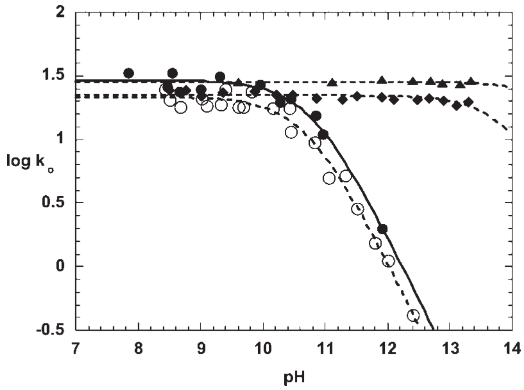


Figure 1. Plot of log k_0, the buffer-independent rate constant for diazolkane hydrolysis at 25 °C, in aqueous 5% acetonitrile, against pH for diazomethane (○), 0.2 M ionic strength (NaClO$_4$),[17] and diazomethane (●), diazoethane (◆) and 1-diazopropane (▲), 1 M ionic strength (NaClO$_4$)

The values of k_0 in some cases varied as a function of pH. It was possible to determine the value of k_0 in the range of pH from ~8 to 13 for diazomethane and diazoethane, and a more limited range was examined for 1-diazopropane. At values of pH below ~7.7, the buffer catalysis was so strong that accurate extrapolation to the y-intercept was not feasible. Values of log k_0 as a function of pH are presented in Fig. 1 for diazomethane (filled circles), diazoethane (diamonds) and 1-diazopropane (triangles) along with data previously published for diazomethane at 25 °C and ionic strength 0.2 M (NaClO$_4$) in aqueous 5% acetonitrile (open circles).

Further analysis of the buffer stimulated reaction indicates that the dominant component is the buffer acid, as has been previously reported in the case of diazomethane.[17,19,20] Plots of k_{b} as a function of the percentage of buffer acid in the buffer are presented in Fig. 2 in the reaction of diazomethane catalyzed by Tris

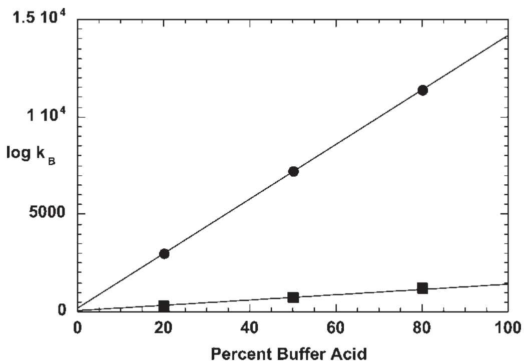


Figure 2. Plot of k_{b}, the apparent second-order rate constant for buffer catalysis of the hydrolysis of diazomethane by Tris buffer (●) and diazoethane by ethanolamine buffer (■), against percentage of buffer acid at 25 °C, in aqueous 5% acetonitrile, ionic strength 1 M (NaClO$_4$)

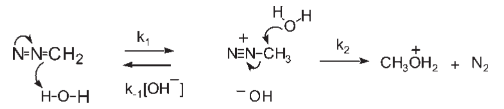
Table 1. Second-order rate constants for protonation of diazoalkanes by ammonium ion buffer acids at 25 °C ($\mu = 1$ M, $NaClO_4$, aqueous 5% by volume acetonitrile)

Buffer acid	k_{HA} for diazomethane ($M^{-1} s^{-1}$)	k_{HA} for diazoethane ($M^{-1} s^{-1}$)
Glycine ethyl ester-H^+	30 000	16 300
Tris-H^+	14 300	7400
Ethanolamine-H^+	2090	1480
Butylamine-H^+		320

buffer and diazoethane catalyzed by ethanolamine buffer. Within experimental error, the *y*-intercept value is not significantly different from zero, consistent with the buffer acid being the only active component at all compositions. The value of k_b at 100% buffer acid was taken as the value of k_{HA}, the specific second-order rate constant for ammonium ion-catalyzed decomposition. Values of the k_{HA} for the reactions of diazomethane and diazoethane with a few ammonium ions are summarized in Table 1.

DISCUSSION

The mechanism of hydrolysis of diazomethane has been previously analyzed in this laboratory, following, and in agreement with, the work of other groups under a variety of experimental conditions.[17,19–21] In mainly aqueous media from pH 7 to 12, the reaction exhibits a pH dependence, being independent of pH below pH 10 and exhibiting a downward break to a unit dependence on pH in the higher pH region, as exhibited by the open circles in Fig. 1 from a previous study. This dependence, in combination with solvent deuterium kinetic isotope effects on the buffer-independent reaction, analysis of solvent deuterium isotope incorporation into products and the observation of general acid catalysis that occurs with large solvent deuterium kinetic isotope effects was rationalized in terms of the mechanism of Eqn (3).[19]



(3)

The pH-independent reaction entails the rate-limiting protonation of diazomethane by water, k_1 (and general acids, k_{HA}, not pictured), while the rate-limiting step changes to k_2, attack of water on the diazonium ion, with increasing pH as the hydroxide ion-dependent k_{-1} step becomes increasingly competitive with, and ultimately faster than, k_2. The data previously published exhibit an excellent fit to the kinetic expression

$$k_{obsd} = k_1/\{(k_{-1}[OH^-]/k_2) + 1\} \tag{4}$$

for the mechanism of Eqn (3), seen in Eqn (4), as indicated by the dashed line through the open circles in Fig. 1.

Table 2. Rate constants and rate constant ratios derived for the kinetics, at 25 °C ($\mu = 1$ M, $NaClO_4$, aqueous 5% by volume acetonitrile), of diazoalkane hydrolysis according to the mechanism of Eqn (3)

Constant	Diazomethane	Diazoethane	Diazopropane
k_1 (s^{-1})	28	22	29
k_{-1}/k_2 (M^{-1})	950	<0.6	<0.1

As might be expected, a similar mechanism is operative for diazomethane under the slightly different conditions of increased ionic strength in the present study (1 M, $NaClO_4$) as is indicated by the pH dependence for the filled circles in Fig. 1. As with the original study,[19] there is some scatter in the values of k_0, particularly in the low range of pH, because the values of k_0 are obtained from extrapolation of buffer dilution plots and the reaction is strongly buffer catalyzed in this pH region. However, the number of experiments is sufficient to exhibit a good fit to Eqn (4), the solid line through the filled circles, and to so derive accurate values for the parameters k_1, and k_{-1}/k_2. These are included in Table 2. The value of k_1 under the present conditions is ~30% larger than observed previously at the lower ionic strength of 0.2 M ($NaClO_4$). The value of the ratio k_{-1}/k_2 is ~20% smaller than what was observed in the earlier study from this laboratory.

In contrast to diazomethane, the pH dependences of k_0 for the hydrolysis of diazoethane and diazopropane give no indication of a change in rate-limiting step with increasing pH. Figure 1 illustrates that the decomposition of these compounds occurs with rate constants that are similar to diazomethane in the lower pH range, but there is no indication of a downward break with increasing pH up to pH 13.3.

The general acid catalysis of the rate-limiting protonation reaction that was investigated in the case of diazomethane is similar in the case of diazoethane. The catalytic constants, summarized in Table 1, are within a factor of two of one another, the constant for the reaction of diazoethane being the smaller. Figure 3 illustrates the

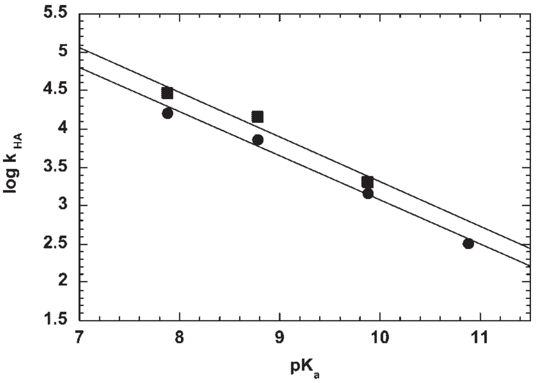


Figure 3. Brnsted plot for the general acid-catalyzed hydrolysis of diazomethane (■) and diazoethane (●) by ammonium ions at 25 °C, in aqueous 5% acetonitrile, ionic strength 1 M ($NaClO_4$)

dependence of the catalytic constants upon the acid ammonium ion pK_as. The Brønsted α values for these two reactions are both 0.58, suggesting a similar transition-state structure with respect to the degree of N—H bond cleavage.

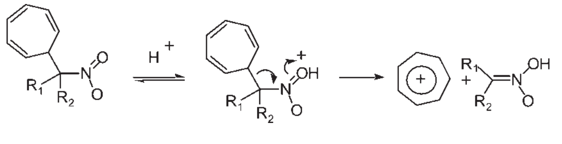
The conclusion above that, in contrast to diazomethane, protonation remains the rate-limiting step in substantially more basic media in the case of the higher normal homologues of diazomethane might have been anticipated from earlier studies, foremost in the methanolysis of diazobutane studied by Kirmse and Rinkler.[21] It was shown that in methanol containing $\geq$0.49 M sodium methoxide, the rate of methanolysis was roughly inversely proportional to methoxide ion concentration. This observation is consistent, as was pointed out, with a mechanism like that in Eqn (3), with MeOH and MeO^- replacing HOH and HO^-, in which k_2 is the rate-limiting step. The onset of a change to rate-limiting protonation by methanol in the least basic media in that study is indicated by experiments analyzing deuterium incorporation from solvent into product. At 0.49 M sodium methoxide, one-third of the 1-butyl methyl ether contains a single deuterium atom at the butyl carbon atom adjacent to oxygen and the balance of the product contained two atoms of deuterium. This observation suggests that at this methoxide ion concentration, methanol attack on the diazonium ion is just slightly slower than methoxide ion-catalyzed proton abstraction. Hence a further decrease in methoxide ion concentration, or a shift to less basic conditions such as those in the present study, would presumably result in a complete shift to rate-limiting protonation and the absence of a change in rate-limiting step for the higher homologues, as observed in the pH–rate profiles in Fig. 1. Similarly, it was later reported that the incorporation of deuterium, from D_2O, into C-1 of product 1-butanol during the decomposition of (*E*)-1-butanediazotate was pH dependent.[16] The intermediacy of diazonium ions in this reaction is well established. At pD = 10.50, 94% of the 1-butanol contains two H atoms and 6% contains one D atom. In 1 M NaOD, only 75% of the 1-butanol contains two H atoms, whereas 24% contains one D atom and 1% contains two D atoms. This clearly indicates that for 1-butyldiazonium ion in aqueous solutions, only at 1 M lyoxide ion does k_2 begin to become partly rate limiting, as k_{-1} becomes competitive with increasing lyoxide ion concentration.

The absence of a change in rate-limiting step with increasing pH in the hydrolysis of diazoethane and diazopropane indicates that the ratios k_{-1}/k_2 [Eqns (3) and (4)] are more than 1000 times smaller for these compounds compared with the case of diazomethane. Upper limits were estimated by allowing the data for diazoethane and diazopropane to be fit to Eqn (4), although there is no compelling evidence for a downward break in the plots of Fig. 1 for these compounds. The results of the fits are indicated by the dashed lines through the diamonds (diazoethane) and triangles (diazopropane). The upper limits for k_{-1}/k_2, and the much more certain values for k_1, are summarized in Table 2. The value of k_{-1}/k_2 is more than 1500 times and 9500 times smaller than for diazomethane in the cases of diazoethane and diazopropane, respectively. An alternative explanation to the differences in the pH–rate profiles, that hydroxide ion attack on primary alkyl- (but not methyl-) diazonium ions is faster than both k_{-1} and k_2 (water attack) so that k_1 is always rate limiting, is excluded by the pH-dependent deuterium incorporation into the 1-butyldiazonium ion in reactions in MeOD and D_2O, alluded to earlier.

It seems highly unlikely that much of the decrease in k_{-1}/k_2 can be ascribed merely to a decrease in the value of the rate constant k_{-1}. Methyl or ethyl group substitution for hydrogen, on changing from methyl- to ethyl- or 1-propyldiazonium ion, might be expected to be *acidifying* since the alkyl groups, relative to H, probably stabilize the carbon nitrogen double bonds in the diazoalkane bases. While it might therefore generally be expected that acidifying effects would increase, and not decrease, k_{-1}, a decrease in k_{-1} might be observed if these proton transfer reactions exhibit the same ‘anomaly’ as in the case of nitroalkanes.[22] Indeed, nitroethane and 2-nitropropane are more acidic than nitromethane by $\sim$1.6 and $\sim$2.4 units, respectively,[23,24] whereas the rate constants for proton abstraction by hydroxide ion, analogous to the k_{-1} process of Eqn (4), are in fact larger.[25,26] In the case of nitroethane, the second-order rate constant for reaction with hydroxide is smaller than for nitromethane, *but only by a factor of 5.2.*

The larger rate constant for the less acidic nitromethane arises as a result of the ‘nitroalkane anomaly’ in which there is a lag in the development of resonance and hyperconjugative stabilization in the transition state for proton abstraction so that the electropositive polar effects of the alkyl groups have more pronounced impact on the transition-state energy than in the ground states.[22,27] The analogy of nitroalkanes might be particularly appropriate here because the NO_2 group and the N_2^+ group are similarly acidifying, in spite of the much larger resonance electron-accepting ability of N_2^+ compared with NO_2 ($\sigma^- = 1.27$ for NO_2 and 3.43 for N_2^+).[28] For nitromethane, the aqueous p$K_a = 10.2$,[23,24] whereas p$K_a = 10 \pm 0.3$ in aqueous 60% tetrahydrofuran has been determined.[17]

However, there are factors that militate against presuming that proton transfer reactions of diazonium ions should be characterized by the strong imbalance that applies in the case of nitroalkanes. First, unlike nitroalkanes, alkyl for hydrogen substitution on the methyldiazonium ion will have significant intrinsic stabilization of the acid, the diazonium ion, in addition to the base, diazoalkane. This stabilization arises from the considerable positive charge on the carbon atom proximal to N_2 in the diazonium ion, as has been demonstrated by high-level *ab initio* calculations of Glaser’s group.[18] This stabilization will tend to mitigate imbalance by making the transition state for proton transfer more product-like with resonance delocalization more advanced. Second, there is evidence that enhanced resonance electron-accepting ability of a carbanion stabilizing substituent, as in the substitution of N_2^+ for NO_2 in comparing $CH_3N_2^+$ with CH_3NO_2, can alleviate transition state imbalance and result in a reversal of the 'nitroalkane anomaly'. Keefe and co-workers showed that in the loss of tropylium cation to form nitronic acids:



(5)

the substrate giving rise to the most stable nitronic acid ($R_1 = R_2 = CH_3$) is indeed the most reactive—the opposite what is observed in the proton loss to hydroxide of the corresponding nitroalkanes.[29] Hence the superior resonance accepting ability of the N_2^+ group compared with the NO_2 group (see above) diminishes the expectation that k_{-1} will decrease upon alkyl for hydrogen substitution on the diazonium ion in the reaction of Eqn (3).

To summarize the preceding discussion, both of the above considerations suggest that there may be relatively little imbalance in the proton transfer reactions of diazonium ions. This carries the implication that a decrease in the value of k_{-1} on changing from methyl- to ethyl- or 1-propyldiazonium ions might be slight to nil. In any case, the change will not be of a direction or magnitude sufficient to account for the more than 10^3-fold decrease in k_{-1}/k_2 indicated by the data in Fig. 1.

It is therefore concluded that much of the decrease in k_{-1}/k_2 in the change from the methyl- to the ethyl- and 1-propyldiazonium ions must be ascribed to an increase in the rate constant k_2, the reaction rate constant for S_N2 attack of water on the diazonium ions. This is opposite the tendency of the 'textbook' S_N2 substitution reaction, which is generally decelerated by alkyl-for-hydrogen substitution. An increase in k_2 upon alkyl-for-hydrogen substitutions may be anticipated for S_N2 substitution on alkyldiazonium ions on the basis of the aforementioned calculations of Glaser's group.[18] They ascribed the relative weakness of the C—N bond in the ethyl-compared with methyldiazonium ion to the dissipation, by the terminal methyl group in $CH_3CH_2N_2^+$, of positive charge on the central carbon that weakens the electrostatic attraction of the *negatively* charged internal nitrogen in the diazonium ion. An additional factor contributing to the relative instability of the ethyl- and 1-propyldiazonium ions may be the large amount of positive charge on the central carbon in the exploded transition states that typify S_N2 substitution reactions of diazonium ions. The energy of a carbocation-like transition state is expected to be greatly stabilized by substitution of an alkyl group for a hydrogen. These factors therefore appear to overcome the well-characterized tendency of alkyl-for-hydrogen substitutions to decelerate, through steric occlusion, the rates of more classical S_N2 substitutions.

EXPERIMENTAL

Inorganic and organic materials were obtained from commercial suppliers. Unless indicated otherwise, these were used as received. Amines, used for buffers, that were liquids at room temperature were purified by distillation under a nitrogen or an argon stream. Acetonitrile was distilled from, after reflux over, CaH. Water was distilled in glass.

Diazoalkanes were generated, from alkaline decomposition of the corresponding *N*-alkyl-*N'*-nitro-*N'*-nitrosoguanidines, as stock acetonitrile solutions for use within a single day. The nitrosoguanidines were decomposed in a commercially available (Sigma-Aldrich Fine Chemicals) 'diazomethane generator' by reaction of 50–100 mg of nitrosoguanidine with 40% by weight aqueous sodium hydroxide introduced to the solid dropwise by means of a syringe. The gaseous diazoalkanes were collected by diffusion into a 3–5 ml volume of stirred, initially dry, acetonitrile maintained at −30 °C by an ethanol–water–CO_2(s) bath. After complete addition (over ~10 min) of the sodium hydroxide solution to the solid, an additional 30 min were allowed for gaseous diffusion to proceed. The acetonitrile solution containing the diazoalkane was then diluted by addition of ~20 ml of dry acetonitrile. This solution was subsequently directly introduced into the stopped-flow spectophotometer by means of a syringe.

Kinetics of decay of the diazoalkanes were initiated by mixing 1 part of diazoalkane stock solution with 25 parts aqueous solutions that were of 1.05 M ionic strength ($NaClO_4$). The decay of diazoalkane absorbance was monitored at various wavelengths between 230 and 250 nm. The decay of absorbance exhibited good first-order kinetics when monitored from between four and seven half-lives of reaction. Values of the first-order rate constant k_{obsd} were determined from fits of data in this time range. Checks were carried out at multiple wavelengths where appropriate for a given set of reaction conditions that indicated that the values of k_{obsd} were independent of the wavelength monitored. Under other conditions, data from single wavelengths were used because background absorbance obviated monitoring at wavelengths around 230 nm where the diazo group absorbs most strongly. Plots of k_{obsd} against total buffer concentration were linear for amine buffers employed, and the slopes of these plots were taken as the second-order rate constant k_b. Extrapolation to zero buffer concentration gave the buffer independent rate constant k_0.

Acknowledgment

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REFERENCES

1. Lawley PD. In *Chemical Carcinogens*, vol. 1, Searle CE (ed.). ACS Symposium Series 182. American Chemical Society: Washington, DC, 1984; 325–484.
2. Lijinsky W. *Chemistry and Biolgy of N-Nitroso Compounds*. Cambridge University Press: Cambridge, 1992.
3. Loeppky RN, Michejda CJ. *Nitrosamines and Related N-Nitroso Compounds*. ACS Symposium Series 553. American Chemical Society: Washington, DC, 1994.
4. Loveless A. *Nature* 1969; **223**: 206–207.
5. Brosch D, Kirmse W. *J. Org. Chem.* 1991; **56**: 907–908.
6. Veleminsky J, Osterman-Golkar S, Ehrenberg L. *Mutat. Res.* 1970; **10**: 169.
7. Streitwieser A Jr, Schaeffer WD. *J. Am. Chem. Soc.* 1957; **79**: 2888.
8. Moss RA. *Acc. Chem. Res.* 1974; **7**: 421–427.
9. White EH, Field KW, Hendrickson WH, Dzadzic P, Roswell DF, Paik S, Mullen PW. *J. Am. Chem. Soc.* 1992; **114**: 8023–8031.
10. White EH, Ryan T, Field KW. *J. Am. Chem. Soc.* 1972; **94**: 1360–1361.
11. Finneman JI, Fishbein JC. *J. Am. Chem. Soc.* 1995; **117**: 4228–4239.
12. Pezacki JP, Shukla D, Lusztyk J, Warkentin J. *J. Am. Chem. Soc.* 1999; **121**: 6589–6598.
13. Glaser R, Farmer D. *Chem. Eur. J.* 1997; **3**: 1244.
14. Church KM, Gold B. *Chem. Res. Toxicol.* 1988; **1**: 269.
15. Gold B, Deshpande A, Linder W, Hines L. *J. Am. Chem. Soc.* 1984; **106**: 2072.
16. Ho J, Fishbein JC. *J. Am. Chem. Soc.* 1994; **116**: 6611–6621.
17. McGarrity JF, Smyth T. *J. Am. Chem. Soc.* 1980; **102**: 7303.
18. Glaser R, Choy GS, Hall MK. *J. Am. Chem. Soc.* 1991; **113**: 1109.
19. Hovinen J, Finneman JI, Satapathy SN, Ho J, Fishbein JC. *J. Am. Chem. Soc.* 1992; **114**: 10322–10328.
20. Kreevoy MM, Thomas SJ. *J. Org. Chem.* 1977; **42**: 3979.
21. Kirmse W, Rinkler HA. *Liebigs Ann. Chem.* 1967; **707**: 57–65.
22. Kresge AJ. *J. Am. Chem. Soc.* 1970; **92**: 3210–3211.
23. Wheland GW, Farr J. *J. Am. Chem. Soc.* 1943; **65**: 1433.
24. Turnbull D, Marion SH. *J. Am. Chem. Soc.* 1943; **65**: 212–218.
25. Bell RP, Goodall DM. *Proc. R. Soc. London* 1966; **294**: 273–297.
26. Goodall DM, Long FA. *J. Am. Chem. Soc.* 1968; **90**: 238–243.
27. Keefe JR, Gronert S, Colvin ME, Tran NL. *J. Am. Chem. Soc.* 2003; **125**: 11730–11745.
28. Hansch C, Leo A, Taft RW. *Chem. Rev.* 1991; **91**: 165–195.
29. Ihsan E, Keefe JR, Xu F-P, Zheng J-B. *J. Am. Chem. Soc.* 1993; **115**: 9834–9835.