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Isotope Effects, Dynamics, and the Mechanism of Solvolysis of Aryldiazonium Cations in Water

Bryson R. Ussing and Daniel A. Singleton*

Contribution from the Department of Chemistry, Texas A&M University, P.O. Box 30012, College Station, Texas 77842

Received October 6, 2004; E-mail: singleton@mail.chem.tamu.edu

Abstract: The mechanism of the heterolytic solvolysis of *p*-tolyldiazonium cation in water was studied by a combination of kinetic isotope effects, theoretical calculations, and dynamics trajectories. Significant ^{13}C kinetic isotope effects were observed at the ipso ($k_{12}C/k_{13}C = 1.024$), ortho (1.017), and meta (1.013) carbons, indicative of substantial weakening of the C_2-C_3 and C_5-C_6 bonds at the transition state. This is qualitatively consistent with a transition state forming an aryl cation, but on a quantitative basis, simple S_N1 heterolysis does not account best for the isotope effects. Theoretical S_N2Ar transition structures for concerted displacement of N_2 by a single water molecule lead to poor predictions of the experimental isotope effects. The best predictions of the ^{13}C isotope effects arose from transition structures for the heterolytic process solvated by clusters of water molecules. These structures, formally saddle points for concerted displacements on the potential energy surface, may be described as transition structures for solvent reorganization around the aryl cation. Quasiclassical dynamics trajectories starting from these transition structures afforded products very slowly, compared to a similar S_N2 displacement, and the trajectories often afforded long-lived aryl cation intermediates. Critical prior evidence for aryl cation intermediates is reconsidered with the aid of DFT calculations. Overall, the nucleophilic displacement process for aryldiazonium ions in water is at the boundary between S_N2Ar and S_N1 mechanisms, and an accurate view of the reaction mechanism requires consideration of dynamic effects.

Introduction

The thermal decomposition of aryl diazonium cations in water affords phenols by an overall nucleophilic substitution process (eq 1). This amazing basic reaction figuratively pits the "immovable object" against the "irresistible force". Simple aryl groups are exceptionally resistant to nucleophilic substitution in the absence of powerful nucleophiles. However, N_2 is an exceptionally reactive leaving group, tremendously more so than a triflate anion in these reactions. N_2 is in fact the only effective leaving group for aryl solvolyses in water, outside of specially activated systems.[1]
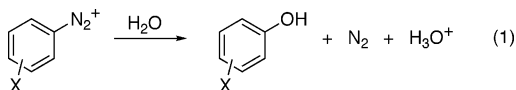

The difficulty of this process may be understood with reference to the usual S_N2 (A_ND_N), S_N1 ($D_N + A_N$), and S_NAr ($A_N + D_N$) mechanisms for nucleophilic substitution. The backside attack associated with a standard S_N2 displacement is sterically precluded. An S_NAr mechanism would normally require a strong nucleophile and electron-withdrawing groups

to stabilize a transient anionic complex. Within classical physical organic chemistry, one is left to choose between an S_N1 mechanism, involving an aryl cation (Scheme 1, path a) and a concerted *front-side* displacement (Scheme 1, path b, described here as S_N2Ar). Neither is savory. Aryl cations are highly unstable, and attempts to observe them directly by time-resolved spectroscopy and in magic acid have failed.[2,3] Only recently has evidence been presented for the observation of phenyl cation in an argon matrix at 8 K.[4] Despite the dearth of direct evidence, the stepwise S_N1 process via aryl cations has long been the favored mechanism.[5,6] Some observations have been interpreted as favoring the concerted S_N2Ar displacement, in particular Lewis's observation that the concentration of nucleophile can influence the rate,[7] but the bulk of solvent, substituent, and 15N and 2H isotope effect observations have been interpreted as favoring the intermediacy of an aryl cation.[8-10] At the least, the kinetic behavior of these reactions approximates that expected for a rate-limiting heterolytic cleavage to afford an aryl cation.

(1) (a) Laali, K.; Szele, I.; Yoshida, K. *Helv. Chim. Acta* **1983**, *66*, 1710–1720. (b) Subramanian, L. R.; Hanack, M.; Chang, L. W. K.; Imhoff, M. A.; Schleyer, P. v. R.; Effenberger, F.; Kurtz, W.; Stang, P. J.; Dueber, T. E. *J. Org. Chem.* **1976**, *41*, 4099–4103. (c) For solvolyses employing *ortho*-trimethylsilyl or *tert*-butyl groups, see: Himeshima, Y.; Kobayashi, H.; Sonoda, T. *J. Am. Chem. Soc.* **1985**, *107*, 5286–5288.

(2) (a) Laali, K.; Szele, I.; Zollinger, H. *Helv. Chim. Acta* **1983**, *66*, 1737–1747. (b) Butcher, V.; Costa, M. L.; Dyke, J. M.; Ellis, A. R.; Morris, A. *Chem. Phys.* **1987**, *115*, 261–267.

(3) Steenken, S.; Ashokkumar, M.; Maruthamuthu, P.; McClelland, R. A. *J. Am. Chem. Soc.* **1998**, *120*, 11925–11931.

(4) Winkler, M.; Sander, W. *Angew. Chem., Int. Ed.* **2000**, *39*, 2014–2016.

(5) Zollinger, H. *Diazo Chemistry I*; VCH: New York, 1994; Chapters 6–10.

(6) Waters, W. A. *J. Chem. Soc.* **1942**, 266–270.

(7) (a) Lewis, E. S.; Hinds, W. H. *J. Am. Chem. Soc.* **1952**, *74*, 304–308. (b) Lewis, E. S.; Hartung, L. D.; McKay, B. M. *J. Am. Chem. Soc.* **1969**, *91*, 419–425. (c) Pietra, F. *Q. Rev., Chem. Soc.* **1969**, *23*, 504–521.

Scheme 1
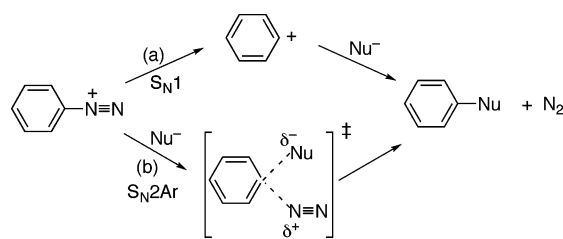
Scheme 2
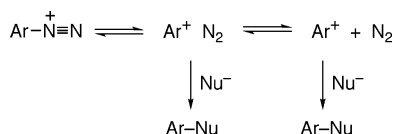
The most compelling evidence for the intermediacy of aryl cations has come from studies of isotopically labeled diazonium ions. In 1963, Lewis observed isotopic interchange between the proximal (α) and distal (β) nitrogen positions over the course of the solvolysis in water (eq 2).[11] The rate of this automerization process was 1.4% of the rate of the overall solvolysis. It is of course conceivable that the isotopic exchange occurs independently of the nucleophilic substitution. However, the simplest explanation is that the two processes are interrelated by a common heterolytic cleavage that is sufficiently reversible to afford small amounts of the isotopically scrambled diazonium ion.


(2)
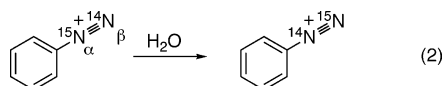
This evidence was strengthened further by Zollinger's observation that *external* N_2 was incorporated into recovered diazonium ion for reactions in trifluoroethanol and hexafluoro-2-propanol.[12-14] Zollinger's kinetic observations required a long-lived intermediate in these solvents, presumed to be an aryl cation. It was proposed that the loss of N_2 from aryl diazonium cations is reversible and can involve both ion–molecule pairs and free ions as intermediates (Scheme 2).[13] The effect of nucleophiles on reaction rate could then be understood by their decreasing the reversibility of aryl cation formation[15] or by nucleophilic solvation of the aryl cation.[16]

Aryl cations are structurally intriguing. From theoretical studies, the parent phenyl cation, in its singlet ground state, is quite distorted from the D_{6h} structure of benzene.[17-19] Gas-phase

(8) Swain, C. G.; Sheats, J. E.; Harbison, K. G. *J. Am. Chem. Soc.* **1975**, *97*, 783−790.
(9) Swain, C. G.; Sheats, J. E.; Harbison, K. G. *J. Am. Chem. Soc.* **1975**, *97*, 796−798.
(10) Swain, C. G.; Sheats, J. E.; Gorenstein, D. G.; Harbison, K. G. *J. Am. Chem. Soc.* **1975**, *97*, 791−795.
(11) Insole, J. M.; Lewis, E. S. *J. Am. Chem. Soc.* **1963**, *85*, 122.
(12) (a) Bergstrom, R. G.; Wahl, G. H., Jr.; Zollinger, H. *Tetrahedron Lett.* **1974**, 2975−2978. (b) Bergstrom, R. G.; Landells, R. G. M.; Wahl, G. H., Jr.; Zollinger, H. *J. Am. Chem. Soc.* **1976**, *98*, 3301−3305.
(13) Zollinger, H. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 141−150.
(14) (a) Szele, I.; Zollinger, H. *J. Am. Chem. Soc.* **1978**, *100*, 2811−2815. (b) Hashida, Y.; Landells, R. G. M.; Lewis, G. E.; Szele, I.; Zollinger, H. *J. Am. Chem. Soc.* **1978**, *100*, 2816−2823.
(15) It may be noted that the amount of reversibility based on $^{15}N-^{14}N$ isotopic scrambling is not sufficient to account for the changes in rate with nucleophiles (see ref 7b), unless there is some barrier to the scrambling.
(16) Richard, J. P.; Toteva, M. M.; Amyes, T. L. *Org. Lett.* **2001**, *3*, 2225−2228.
(17) Dill, J. D.; Schleyer, P. v. R.; Binkley, J. S.; Seeger, R.; Pople, J. A.; Haselbach, E. *J. Am. Chem. Soc.* **1976**, *98*, 5428−5431.

calculations predict that the $C_2-C_1-C_6$ angle is expanded to 147−149°, making C_1 more sp in character. The cation thus has a large molecular effect on the structure that is not well represented by hexagonal localized Lewis structures. Our expectation was that this distortion would give rise to substantial ^{13}C kinetic isotope effects (KIEs) throughout the ring, allowing the ^{13}C KIEs to in turn serve as a detailed structural probe of the transition state.
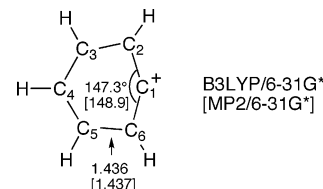
Theoretical studies of the dediazotization mechanism have gone against the conventional stepwise S_N1 process.[20,21] Using gas-phase RHF/6-31+G* geometry optimizations along with single-point calculations at the MP2/6-31+G* level employing an IPCM continuum solvent model, Cuccovia and co-workers have explored the decomposition of phenyldiazonium cation and its reaction with water and methanesulfonate nucleophiles.[20] Several transition structures were located for concerted S_N2Ar processes, including structure **1**, which was lowest-energy for displacement by water. No saddle point was present for either the loss of N_2 or nucleophilic attack on a phenyl cation. Cuccovia argued that many experimental observations were equally consistent with S_N1 and S_N2Ar mechanisms, and concluded that the S_N2Ar mechanism was operative.

1
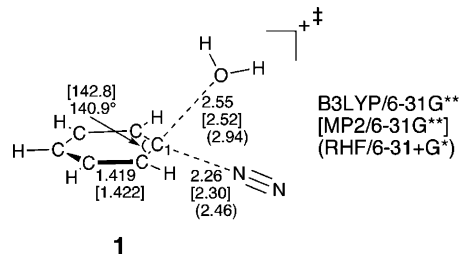
Using MP2 and B3LYP geometry optimizations and QCISD(T) single-point energies, Glaser very recently reported results similar to those of Cuccovia, and he reached a similar conclusion.[21] The out-of-plane transition structure **1** for a concerted displacement was deemed the best model for the physical reaction. Structure **1** was described as "rather loose" but there is a significant component of C_1-O bond formation accompanying C_1-N bond breakage, and the structure of the phenyl cation moiety does not correspond to that of a free phenyl cation.

Notably, the S_N2Ar displacement was concluded to be favored over the unimolecular S_N1 despite the fact that the latter was favored in Gibbs free energy (at standard state) by 6.7 kcal/mol. It was argued "there is no opportunity for a phenyl cation to exist ever in a water cage" because "the affinity of a water toward an incipient cation will always greatly exceed the affinity

(18) Nicolaides, A.; Smith, D. M.; Jensen, F.; Radom, L. *J. Am. Chem. Soc.* **1997**, *119*, 8083−8088.
(19) Hrusak, J.; Schroder, D.; Iwata, S. *J. Chem. Phys.* **1997**, *106*, 7541−7549.
(20) Cuccovia, I. M.; da Silva, M. A.; Ferraz, H. M. C.; Pliego, J. R., Jr.; Riveros, J. M.; Chaimovich, H. *J. Chem. Soc., Perkin Trans. 2* **2000**, 1896−1907.
(21) Wu, Z.; Glaser, R. *J. Am. Chem. Soc.* **2004**, *126*, 10632−10639.

of one water to any number of water molecules."[21] In a similar argument, Cuccovia had contended that a true S_N1 could only occur in nonnucleophilic solvents.[20] These conclusions appear inconsistent with Zollinger's kinetic observations.

Our view is that the argument requiring concert is nonphysical. If it were correct, identical arguments would seemingly exclude many well-accepted carbocation intermediates. The problem is that the argument ignores entropic barriers to reactions. The absence of an enthalpic barrier for a reaction with solvent does not require an instantaneous reaction. Because of entropic barriers, a great many enthalpically barrierless reactions occur with rate constants that would allow long-lived intermediates even in high-concentration solution chemistry.[22–27] This does not mean that the S_N2Ar mechanism is incorrect, but only that more detailed theoretical consideration and experimental evidence is required. Because of the similarity of energies for the concerted and two-step processes, as well as the critical question of the applicability of the calculations to the real reaction in bulk solution, it would seem impossible to arrive at any firm conclusion from single-water model calculations alone.

We describe here a study of the decomposition of p-tolyldiazonium cation in water using a combination of experimental isotope effects, theoretical calculations, and dynamics trajectories. The observed KIEs do not support the accuracy of very simple concerted transition structures such as **1**. However, the KIEs also do not fit best with the conventional two-step mechanism, and additional results provide new explanations for evidence that had ostensibly demanded the intermediacy of aryl cations. The ultimate picture that arises is a mechanism at the S_N2Ar/S_N1 boundary, with a consideration of dynamics necessary to understand the displacement process.

Results and Discussion

Experimental Isotope Effects. The decomposition of p-tolyldiazonium cation (**2**) was chosen for study because the methyl group provides an "internal standard" for determination of isotope effects. The reaction conditions employed were similar to common synthetic conditions, using sodium nitrite/sulfuric acid to diazotize p-toluidine at 0−5 °C, and decomposing 0.3 M solutions of the resulting **2** in water at ~55 °C to afford the product p-cresol (**3**). Under these conditions, the reaction affords >95% of **3**. The formation of p-cresyl sulfate under these conditions appeared negligible, as expected from studies of phenyldiazonium decomposition in the presence of sulfate anion.[28]
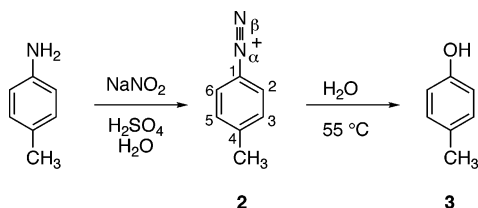

The ^{13}C KIEs for this reaction were measured at natural abundance by NMR methodology.[29] In usual form, this methodology requires comparison of recovered starting material from reactions taken to partial conversion with samples of starting
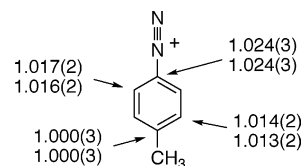
Figure 1. ^{13}C kinetic isotope effects ($k_{12}C/k_{13}C$) for the decomposition of **2** in water at 55 °C. The 95% confidence limits for the last digit are shown in parentheses.

material that have not been subjected to isotopic fractionation. Here, however, it is impractical to carry out NMR studies on **2**. Instead, reactions of **2** taken to 66 or 71% conversion were cooled and treated with sodium azide to convert the unreacted **2** into p-tolyl azide (**4**). This conversion is quantitative and has the virtue that the formation of **4** does not involve C−N bond cleavage.[5] The samples of recovered **4** were analyzed by ^{13}C NMR along with standard samples of **4** prepared by direct treatment of unheated **2** with sodium azide at 0−5 °C. The changes in isotopic composition in the aromatic carbons were determined assuming that the isotopic composition of the p-methyl group is unchanged between samples and standards. From the changes in isotopic composition, the ^{13}C KIEs were calculated as previously described.[29]
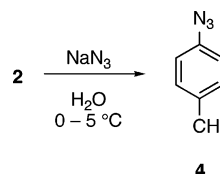
The results are summarized in Figure 1. The most striking observation is that substantial ^{13}C KIEs were observed not only at the ipso (C$_1$) carbon undergoing substitution but also in the ortho (C$_2$/C$_6$) and meta (C$_3$/C$_5$) positions. The magnitude of these KIEs is within a range normally associated with *primary* ^{13}C isotope effects; that is, the KIEs are typical of carbons undergoing discrete bond formation and breakage in the rate-limiting step. Since the ortho and meta positions are unchanged in the overall reaction, these KIEs appear quite peculiar. However, we have previously found that the presence of greatly weakened bonds in reactive intermediates can give rise to ^{13}C KIEs that mimic primary isotope effects.[30] This would be the simplest explanation for the unusual KIEs in the current example. Thus, the isotope effects suggest a substantial weakening of the C$_2$−C$_3$ and C$_5$−C$_6$ bonds at the reaction's transitions state, relative to the starting **2**.

(22) (a) Shustov, G. V.; Liu, M. T. H.; Houk, K. N. *Can. J. Chem.* **1999**, *77*, 540−549. (b) Morgan, S.; Jackson, J. E.; Platz, M. S. *J. Am. Chem. Soc.* **1991**, *113*, 2782−2783. (c) Moss, R. A.; Ho, G.-J. *J. Am. Chem. Soc.* **1990**, *112*, 5642−5644.

(23) (a) Houk, K. N.; Rondan, N. G. *J. Am. Chem. Soc.* **1984**, *106*, 4293−4294. (b) Wong, P. C.; Griller, D.; Scaiano, J. L. *Chem. Phys. Lett.* **1981**, *83*, 69−72. (c) Turro, N. J.; Lehr, G. F.; Butcher, J. A., Jr.; Moss, R. A.; Guo, W. *J. Am. Chem. Soc.* **1982**, *104*, 1754−1756. (d) Moss, R. A.; Perez, L. A.; Turro, N. J.; Gould, I. R.; Hacker, N. P. *Tetrahedron Lett.* **1983**, *24*, 685−688.

(24) Mader, E. A.; Larsen, A. S.; Mayer, J. M. *J. Am. Chem. Soc.* **2004**, *126*, 8066−8067.

(25) de Sainte Claire, P.; Peslherbe, G. H.; Wang, H.; Hase, W. L. *J. Am. Chem. Soc.* **1997**, *119*, 5007−5012.

(26) Hase, W. L.; Wardlaw, D. M. In *Bimolecular Collsions*; Baggott, J. E., Ashfold, M. N., Eds.; Burlington House: London, 1989.

(27) Lei, W.; Zhang, R.; McGivern, W. S.; Derecskei-Kovacs, A.; North, S. W. *J. Phys. Chem. A* **2001**, *105*, 471−477.

(28) Lewis, E. S. *J. Am. Chem. Soc.* **1958**, *80*, 1371−1373.

(29) Singleton, D. A.; Thomas, A. A. *J. Am. Chem. Soc.* **1995**, *117*, 9357−9358.

(30) Singleton, D. A.; Merrigan, S. R. *J. Am. Chem. Soc.* **2000**, *122*, 11035−11036.

This is qualitatively consistent with a transition state that *resembles* an aryl cation. The theoretically predicted expansion of the $C_2-C_1-C_6$ angle for aryl cations may be described as increasing the overlap between the empty orbital at C_1 and the full in-plane C_2-C_3 and C_5-C_6 σ-orbitals (Figure 2).[17,18] Such hyperconjugative donation would weaken the C_2-C_3 and C_5-C_6 bonds, accounting for the KIEs. Supporting this idea, the predicted C_2-C_3/C_5-C_6 bond at B3LYP/6-31G* is lengthened to 1.435 Å.[18] The qualitative structural origin of the previously reported deuterium KIEs in these reactions is much less clear. Swain and co-workers had observed remarkable KIEs of 1.22 and 1.08 per deuterium for the ortho and meta positions, respectively,[10] and this was attributed to hyperconjugation with the C−H bonds. However, the structural distortion in an aryl cation has the effect of bending the ortho C−H bonds away from optimum for hyperconjugation. At B3LYP/6-31G*, the $H-C_2-C_1$ angle is increased to 131°.[18] Carbons C_2 and C_6 gain some sp character, and the C_2-H distance is slightly shortened relative to the corresponding diazonium ion. This does not fit with hyperconjugation, which would manifest as a weaker, lengthened bond. We will return to this issue and provide a much more detailed interpretation of the isotope effects after exploring the reaction of **2** theoretically.

Theoretical Calculations. A standard calculational exploration of the decomposition of aryldiazonium cations faces two fundamental problems. The first issue is whether any relatively simple theoretical model can adequately represent the potential energy surface in bulk water. The second issue is whether the potential energy surface is by itself sufficient for understanding the experimental reaction. Both problems ultimately plague the study of these reactions.

In gas-phase B3LYP calculations with a 6-31+G** basis set, loss of N_2 from **2** to afford the singlet *p*-tolyl cation (**6**) is uphill by 32.0 kcal/mol. (E + zpe. Similar results were obtained in B3LYP/6-31G* and mPW1PW91/6-31G* calculations; see Supporting Information.) Attack of water on **6** to afford **7** was downhill by 43.5 kcal/mol. Inclusion of a continuum solvent model (PCM, fully optimized with water as solvent) relatively stabilizes the localized charges in **6** and **7**. The predicted endothermicity for loss of N_2 from **2** is decreased to 29.1 kcal/mol, and the exothermicity for formation of **7** goes up to 50.3 kcal/mol. In agreement with the gas-phase results of Cuccovia,[20] neither process involves a well-defined transition structure; that is, there was no potential energy barrier for attack of N_2 or H_2O on **6** in either gas-phase or continuum solvent model (PCM, water) calculations.[31]

2 **5** **6** **7**
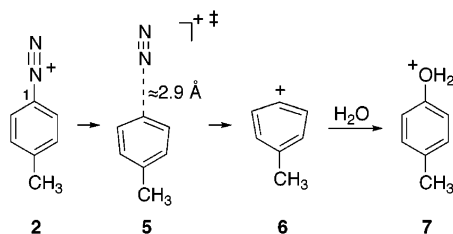
A search for an approximate canonical variational transition state for loss of N_2 from **2** was carried out by optimizing a

(31) In the Ar + N_2 or Ar + H_2O systems, it was possible to locate several very shallow potential energy saddle points at large (>3.5 Å) C_1-N or C_1-O separations. These were associated with either symmetry-breaking or interactions of N_2 or H_2O with aryl hydrogens and did not appear closely related to C_1-N or C_1-O bond breaking or formation.
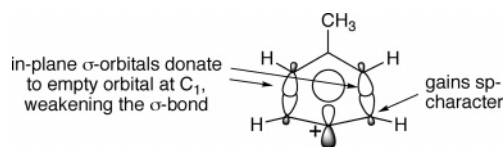

Figure 2. Hyperconjugation in *p*-tolyl cation.

series of structures with fixed elongated C_1-N distances, estimating entropy at 298 K for each structure from the unscaled harmonic frequencies. The free energy estimated in this way reaches a rough plateau as the C_1-N distance exceeds 2.6 Å, varying by less than 1.0 kcal/mol between 2.6 and 3.75 Å. A free energy maximum **5** was found at a C_1-N distance of 2.9 Å, corresponding to a dynamical bottleneck for dissociation of N_2 within the canonical approach. It may be noted for later discussion that treating entropy in gas-phase **5** as a model for entropy in solution is dubious, but **5** gives us a model for further consideration.
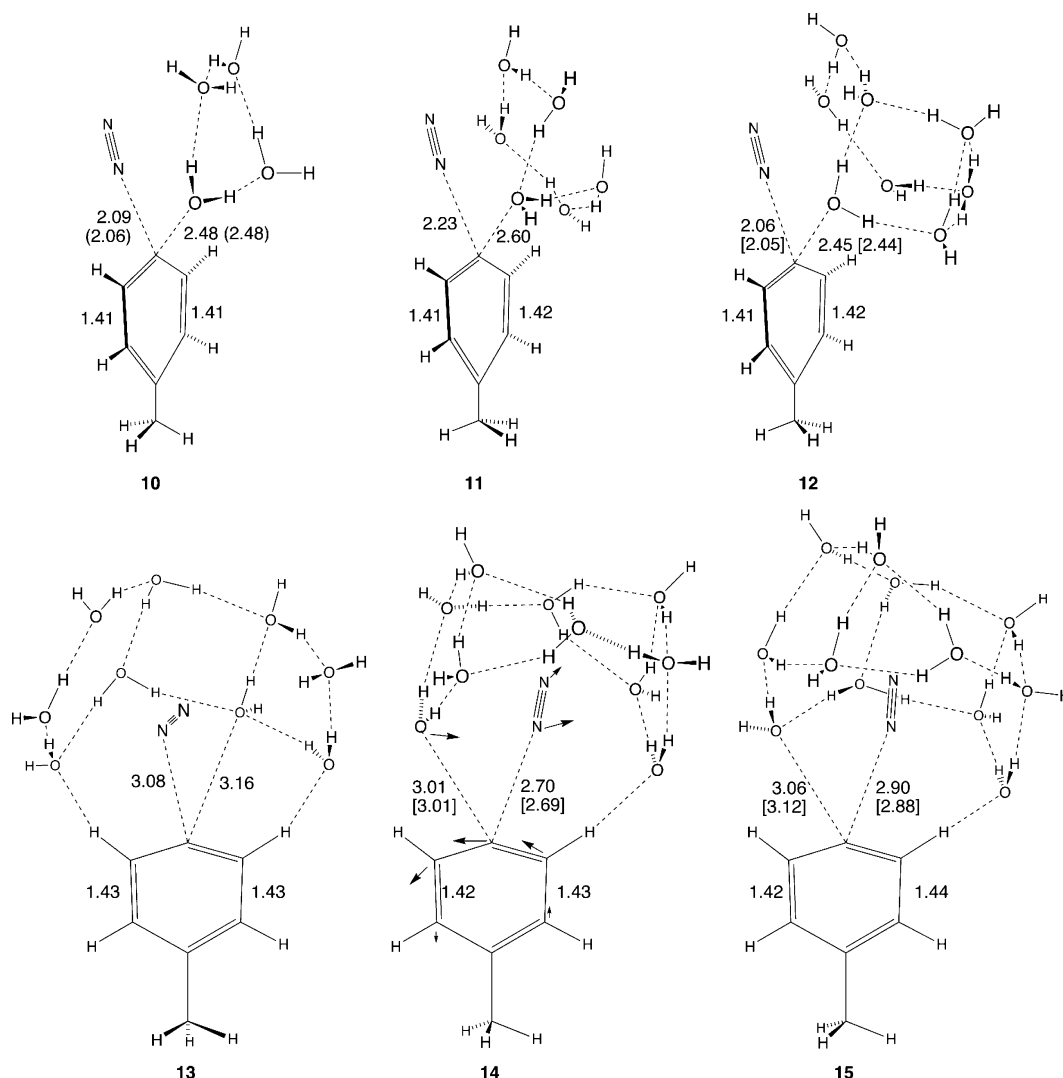
As found by Cuccovia and Glaser,[20,21] there are potential energy saddle points for loss of N_2 accompanied by attack of water. Transition structure **8** was located in the gas phase and in calculations employing a PCM solvent model (with full optimization). In either case, the displacement transition structure involves greater C−N bond breakage than C−O bond formation: the oxygen of the water is a distant 2.69 Å from C_1. Notably, participation by the water provides no more stabilization at the transition state than it did in the starting structure, as the reaction barrier is similar to that for loss of N_2 in the gas phase. Similar stabilization is alternatively provided by complexation of the water to one of the ortho hydrogens, as in **9**. Thus, in the presence of only one water molecule, loss of N_2 could occur without concerted attack by the water. However, the water molecule in **9** is, in effect, "hidden" within a shallow local potential energy well, shielded from the deep potential energy well associated with attacking the cation.
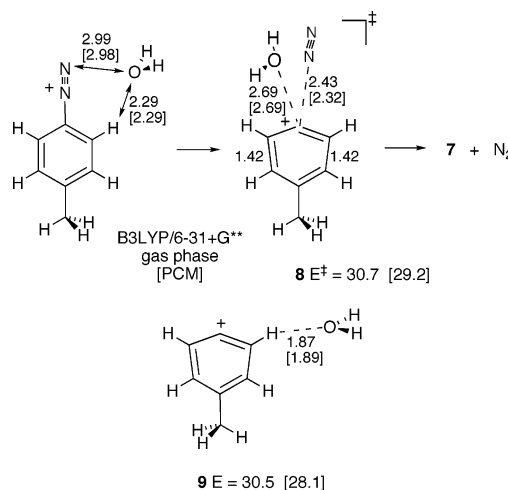
For the tolyl cation to be a minimum on the potential energy surface in bulk water, the entire primary solvation shell of water molecules surrounding the cation would have to be similarly tied up in local minima. We attempted to locate relevant structures for aryl cation−water clusters, but despite considerable effort, we were unable to locate any energy minima in which an aryl cation was solvated by more than two water

Figure 3. Transition structures for reaction of *p*-tolyl diazonium cation in the presence of clusters of water molecules. Numbers in parentheses are for optimizations including a PCM solvent model, and numbers in brackets are for optimizations including an Onsager solvent model. The arrows in structure **14** depict motion in the transition vector.

molecules. For comparison, we were able to locate minima for *tert*-butyl cation clustered with four water molecules and eight water molecules, but we were unable to do so with 12 water molecules in a cluster (see Supporting Information). In searching for aryl cation–water clusters, we surrounded a phenyl or tolyl cation with 4–14 water molecules, then minimized while constraining the system to prevent C_1–O bond formation (see Supporting Information for a series of structures explored). Invariably the systems would collapse to the product **7** when constraints were removed. Similar results were obtained in attempts to stabilize the aryl cation by incorporating two molecules of H_3O^+ into the solvent shell. Perhaps some unknown specific arrangement of water molecules allows the aryl cation to exist on the potential energy surface—this is impossible to rigorously exclude—but our explorations make it seem unlikely for typical solvation shells. From this, it seems fair to expect that potential energy saddle points for the loss of N_2 in the presence of multiple water molecules would also involve attack of water.

To explore this idea, and to provide us with structures suitable for the prediction of isotope effects, a series of transition structures were located for the loss of N_2 from **2** in the presence

of clusters of discrete water molecules. It is important to recognize upfront the difficulties and limitations of this approach. With increasing numbers of water molecules, the location of the global lowest-energy transition structure rapidly becomes impractical. The series of structures was generated by design to minimally model the hydrogen bonding patterns in bulk water, then fully optimized, but no effort was made to obtain globally optimized structures. Even if global optima were found, such calculated structures would, by themselves, be of uncertain relevance to bulk solution. Rather, our intent was to obtain a range of structures that could be used to structurally interpret the kinetic isotope effects.

A total of nine transition structures were located in the presence of 4, 6, 8, 9, 10, or 12 discrete water molecules (B3LYP/6-31G**). The diagrammatic structures **10**−**15** are shown as examples in Figure 3, and complete structures are given in Supporting Information. All of the structures are potential energy saddle points for displacement of the N_2 by a water molecule. The vague term "loose" might be used to describe any of these transition structures, as with **1** and **8**, but there is particularly little bonding of either N_2 or water to the aryl cation moiety in the transition structures located with 9,

Table 1. Predicted versus Experimental Kinetic Isotope Effects (k_{12C}/k_{13C}, k_H/k_D, k_{14N}/k_{15N}) for the Decomposition of *p*-Tolyldiazonium Cation in Water

	C_1	C_2/C_6	C_3/C_5	N_α	N_β	H_2/H_6[a]	H_3/H_6[a]	CH_3/CD_3
				Experimental				
	1.024	1.017	1.014	1.038[b]	1.011[b]	1.22[c]	1.08[c]	0.99[d]
	1.024	1.016	1.013					
Transition Structure				Predicted				
1 (1 H2O, MP2)[e]	1.032	1.012	1.009	1.039	1.010	1.13[e]	1.06[e]	N/A
8 (1 H2O)	1.031	1.014	1.010	1.037	1.009	1.16	1.07	0.95
8 (1 H2O/PCM)	1.036	1.014	1.009	1.037	1.009	1.21	1.07	0.96
10 (4 H2O)	1.041	1.009	1.007	1.037	1.011	1.11	1.04	0.96
10 (4 H2O/PCM)	1.044	1.008	1.006	1.037	1.011	1.13	1.04	0.97
11 (6 H2O)	1.038	1.012	1.008	1.034	1.009	1.16	1.05	0.96
6 H2O[f]	1.032	1.013	1.009	1.036	1.010	1.25	1.05	0.97
12 (8 H2O)	1.042	1.009	1.006	1.036	1.010	1.12	1.04	0.97
13 (9 H2O)	1.023	1.017	1.013	1.033	1.003	1.32[g]	1.08	0.97
14 (10 H2O)	1.027	1.016	1.012	1.034	1.003	1.25	1.07	0.97
10 H2O[f]	1.028	1.012	1.010	1.040	1.011	1.19	1.07	0.96
15 (12 H2O)	1.025	1.018	1.013	1.036	1.005	1.22/1.48[g]	1.08	0.97
15 (12 H2O/Onsager)	1.026	1.018	1.013	1.036	1.004	1.19/1.47[g]	1.08	0.96
12 H2O[f]	1.028	1.016	1.012	1.038	1.006	1.24	1.07	0.96
5	1.022	1.014	1.014	1.045	1.015	1.18	1.09	0.95
full formation of **6**[+] + N2/PCM	1.019	1.013	1.012	1.034	1.004	1.25	1.11	0.95
full formation of **9**[+] + N2/PCM	1.018	1.013	1.012	1.034	1.004	1.25	1.10	0.95

[a] Per deuterium. The H_2 and H_6 are not equivalent in the transition structures, but a geometric average KIE is given when the predictions for the two positions are similar. The H_2 and H_6 KIEs differ significantly only when hydrogen bonding with the water cluster is affecting one of the two. [b] See ref 9. Measurements and predictions are for 25 °C. [c] See ref 10. Measurements and predictions are for 25 °C. [d] See ref 38. [e] Structure **1** was taken from ref 21. The H_2/H_6 and H_3/H_5 KIEs predicted for **1** differ slightly from those in ref 21 because of scaling of the MP2 frequencies here. [f] Structure shown in Supporting Information. [g] Close hydrogen bonding with the water cluster is raising the predicted isotope effect for one or both of the H_2/H_6 positions.

10, or 12 water molecules. In fact, we would hesitate to describe structures **13**, **14**, and **15** as depicting nucleophilic displacements. The "incoming" water molecule is not directly approaching C_1 in the transition vector (see the arrows in structure **14**), and the qualitative appearance is that of the tolyl cation twisting from primary solvation by N_2 to primary solvation by a water molecule. A more detailed discussion of what is "happening" in these transition structures will be given with the consideration of dynamic issues below.

The difference between **13**–**15** and the "tighter" transition structures is manifested in the carbocationic character of the tolyl cation. For example, the C_2–C_1–C_6 angles in **10**–**12** are 137.0°, 139.1°, and 136.4°, respectively, while the corresponding angles in **13**–**15** are 147.4°, 144.8°, and 146.0°. The calculated barriers for the four 10- and 12-water structures ranged from 25.4 to 32.0 kcal/mol, in the range of the gas-phase and PCM barriers. The experimental activation energy is 27.5 kcal/mol.[32]

Predicted Isotope Effects. The experimental KIEs reflect a complex ensemble of transition states and solvation shells. We would like to use isotope effect predictions to gauge which theoretical structures best model this ensemble, but no single model is likely to be completely adequate for this reaction. However, from the prediction of KIEs for diverse structures, we hope to establish a framework for the structural interpretation of the isotope effects in this system. In this way, the observed KIEs can ultimately delimit critical features of the experimental reaction, even in the absence of an ideal theoretical model.

Structures **1**, **8**, and **10**–**15** may be viewed as representing a spectrum of S$_N$2Ar mechanisms, with **13** and **15** at the "loosest end" of the spectrum. At the far end of this continuum, the N_2 could leave without any participation by H_2O. In this case, loss of N_2 could be rate-limiting, with a transition state resembling **5**, or at an extreme, the rate-limiting step could be solvent

reorganization or diffusional separation of N_2 after "complete" formation of the *p*-tolyl cation.

Isotope effects for all of these possibilities (including three additional structures shown in Supporting Information) were predicted from the scaled theoretical vibrational frequencies[33] using conventional transition state theory by the method of Bigeleisen and Mayer.[34] Tunneling corrections were applied using the one-dimensional infinite parabolic barrier model.[35] Such KIE predictions including a one-dimensional tunneling correction have proven highly accurate in reactions not involving hydrogen transfer, so long as the calculation accurately depicts the mechanism and transition state geometry.[36] Isotope effects for complete formation of *p*-tolyl cations **6** and **9** from **2** and **8** were based on calculated equilibrium isotope effects. The results are summarized in Table 1.

The ^{13}C KIEs appear highly sensitive to the carbocationic character of the transition structures. In line with the qualitative expectations described above, the C_2/C_6, and C_3/C_5 KIEs are associated with a weakening of the C_2–C_3 and C_5–C_6 bonds, as in each of the structures these bonds are elongated to 1.41–1.44 Å from 1.38 Å in the starting material. For the "tightest" transition structures **10** and **12** (having the shortest

(32) Crossley, M. L.; Kienle, R. H.; Benbrook, C. H. *J. Am. Chem. Soc.* **1940**, *62*, 1400–1404.

(33) The calculations used the program QUIVER (Saunders, M.; Laidig, K. E.; Wolfsberg, M. *J. Am. Chem. Soc.* **1989**, *111*, 8989–8994). Becke3LYP and MP2 frequencies were scaled by 0.9614 and 0.9427, respectively (Scott, A. P.; Radom, L. *J. Phys. Chem.* **1996**, *100*, 16502–16513). The exact choice of scaling factor makes little difference in the calculated KIE: varying the scaling factor from 0.94 to 0.98 changes the ^{13}C KIEs by less than 0.001.

(34) (a) Bigeleisen, J.; Mayer, M. G. *J. Chem. Phys.* **1947**, *15*, 261–267. (b) Wolfsberg, M. *Acc. Chem. Res.* **1972**, *5*, 225–233. (c) Bigeleisen, J. *J. Chem. Phys.* **1949**, *17*, 675–678.

(35) Bell, R. P. *The Tunnel Effect in Chemistry*; Chapman & Hall: London, 1980; pp 60–63.

(36) (a) Beno, B. R.; Houk, K. N.; Singleton, D. A. *J. Am. Chem. Soc.* **1996**, *118*, 9984–9985. (b) Meyer, M. P.; DelMonte, A. J.; Singleton, D. A. *J. Am. Chem. Soc.* **1999**, *121*, 10865–10874. (c) DelMonte, A. J.; Haller, J.; Houk, K. N.; Sharpless, K. B.; Singleton, D. A.; Strassner, T.; Thomas, A. A. *J. Am. Chem. Soc.* **1997**, *119*, 9907–9908. (d) Singleton, D. A.; Merrigan, S. R.; Liu, J.; Houk, K. N. *J. Am. Chem. Soc.* **1997**, *119*, 3385–3386.

C_1-N_α bond), the C_2-C_3 and C_5-C_6 bond lengths are least elongated and the KIEs in these positions are relatively low. At the opposite extreme, the loosest transition structures **13** and **15** have maximally elongated C_2-C_3 and C_5-C_6 bonds, leading to the largest C_2/C_6 and C_3/C_5 KIEs.

The C_1 KIE is different. Rather than reflecting a weakening of bonding to C_1, the C_1 KIE may be described as a measure of the "S_N2" character of the transition structure. The proximity of nucleophilic atoms to C_1 results in a reduction of the Cartesian force constants for in-plane and out-of-plane motion of C_1, reducing overall the zero point energy associated with motion of C_1. As a result, the greatest C_1 ^{13}C KIE occurs in the tightest substitution transition structures. This trend has precedent in observations of ^{13}C KIEs for S_N2 versus S_N1 reactions.[37]

The predicted ^{13}C KIEs at C_1 and C_2/C_6 for the S_N1 processes (via transition structure **5** or complete formation of **6** or **9**) are lower than those for the loosest saddle points **13**−**15**, and it is worthwhile to consider the structural origin of this difference. In **13**, **14**, and **15**, the transition vector at the saddle point involves a twisting of the aryl cation moiety away from solvation by the N_2 and toward solvation by a water nucleophile. (See the arrows on structure **14** of Figure 3.) Because of this twisting in the transition vector, ^{13}C isotopic substitution in the aryl group affects the imaginary frequency contribution to the isotope effect.[34b,c] This specific twisting in the concerted displacement process causes the predicted ^{13}C KIEs for the loosest transition structures to exceed the equilibrium isotope effects.

The H/D KIEs at H_2/H_6 and H_3/H_5 also appear sensitive to the carbocationic character of the transition structures. From an examination of the vibrational normal modes for the various structures, the H_2/H_6 and H_3/H_5 isotope effects are not the result of hyperconjugation with the $C-H$ bonds as proposed by Swain. The aromatic $C-H$ stretching frequencies in the transition structures are in fact similar to or greater than those in the starting diazonium cation. However, the in-plane and out-of-plane $C-H$ bending vibrational modes are greatly decreased versus starting material. This fits with the idea that the distortion of the aromatic ring to maximize hyperconjugation with the $C-C$ σ bonds leads to rehybridization of the ring carbons toward sp character (Figure 2). This rehybridization accounts for the H/D KIEs.

Unfortunately, the trend in the H/D KIEs at H_2/H_6 is complicated by a dependence on the detailed arrangement of water molecules in the structures. In **13** and **15**, weak hydrogen bonding of one or both of H_2/H_6 to proximal water molecules leads to increased H/D KIEs in these positions. This hydrogen bonding does not appear to be representative of the experimental reaction, because it leads to predicted H/D KIEs for the hydrogen-bonded positions that greatly exceed experiment.

In contrast to the ^{13}C and H/D KIEs, there is no apparent structural trend in the ^{15}N isotope effects. For example, the predicted ^{15}N KIEs for **5** and **13** are quite different, despite similar C_1-N distances. The variation in the ^{15}N KIEs appears mainly associated with the amount of motion of the departing N_2 molecule in the transition vector.

Having ascertained the trends the predicted isotope effects versus structure, the experimental KIEs may now be interpreted. The picture that emerges is of a transition state at the extreme loose end of the S_N2Ar spectrum. The KIEs do not support a simple, relatively tight S_N2Ar substitution, as such a process would lead to a larger C_1 KIE and smaller C_2/C_6, C_3/C_5, H_2/H_6, and H_3/H_5 KIEs than experimentally observed. Optimization including a PCM solvent model for **8** and **10** moves the predicted KIEs further from experiment. Structures **1**, **8**, **10**, **11**, and **12** would appear to be poor models for the solution chemistry.

On the other hand, the experimental ^{13}C KIEs at C_1 and C_2/C_6 are higher than those predicted or S_N1 processes (via transition structure **5** or complete formation of **6** or **9**). From the discussion above, this suggests that the aryl ring is twisting at the transition state from the solvation sphere of N_2 to the solvation by a water molecule. The predicted KIEs for transition structure **5** are sufficiently close to experiment that a transition state resembling this structure cannot be readily dismissed. However, the isotope effects best support an average transition state that resembles the loosest of the transition structures including 9, 10, or 12 water molecules.

Dynamics. Recent work in the literature has suggested that reactions that would be concerted based on their potential energy surface can nonetheless end up as stepwise processes. In theoretical calculations on the ionization of **16**, Yamataka, Aida, and Dupuis found that the loss of the water leaving group was accompanied by a concerted methyl-group rearrangement to afford the tertiary cation **18**, on the potential energy surface.[39] However, dynamics simulations found that most trajectories at 400 K afforded initially the secondary cation **19**. This cation is not "connected" to the starting material by a minimum-energy path, but can be formed readily by a process that simply breaks the $C-O$ bond without concurrent methyl rearrangement. A thermodynamic interpretation of this observation is that, in contrast to the potential energy surface, the canonical variational transition state on the free energy surface leads to the secondary cation. Entropy should favor the stepwise process in this case because it requires a less organized transition state.
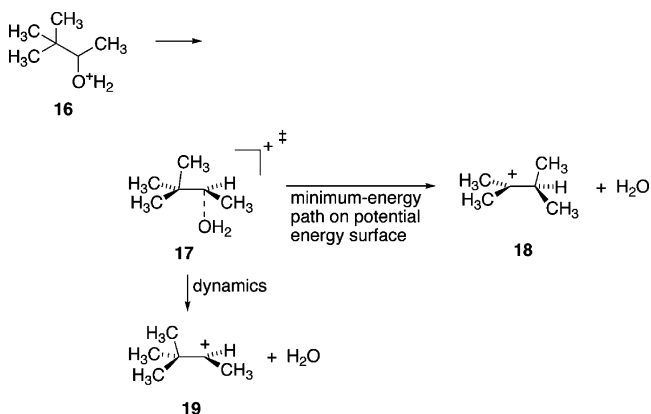
When we applied this idea to the decomposition of aryl-diazonium cations, it was important to determine if aryl cation formation can be favored on the free energy surface, even though

(37) (a) Lee, J. K.; Bain, A. D.; Berti, P. J. *J. Am. Chem. Soc.* **2004**, *126*, 3769−3776. (b) Lynn, K. R.; Yankwich, P. E. *J. Am. Chem. Soc.* **1961**, *83*, 3220−3223. (c) Stothers, J. B.; Bourns, A. N. *Can. J. Chem.* **1960**, *38*, 923−935. (d) Kresge, A. J.; Lichtin, N. N.; Rao, K. N.; Weston, R. E., Jr. *J. Am. Chem. Soc.* **1965**, *87*, 437−445.

(38) Lewis, E. S.; Kinsey, J. L.; Johnson, R. R. *J. Am. Chem. Soc.* **1956**, *78*, 4294−4296.

(39) Ammal, S. C.; Yamataka, H.; Aida, M.; Dupuis, M. *Science* **2003**, *299*, 1555−1557.

aryl cations do not appear to be minima on the potential energy surface. Our approach to this question was to examine the ionization dynamically.

Structures **13** and **14** were used as the starting points for quasiclassical direct dynamics trajectories on the B3LYP/6-31G** surface. Trajectories starting from structure **20**, the transition structure for an S_N2 displacement of the N_2 of ethyldiazonium cation by water, were also explored for comparison. The trajectories were initialized by giving each mode a random sign for its initial velocity, along with an initial energy based on a random Boltzmann sampling of vibrational levels appropriate for 328.15 K, including zero point energy. The starting atomic positions on the potential energy ridge in the area of the transition structures were randomized using a linear sampling of possible classical displacements for each normal mode. The mode associated with the imaginary frequency was treated as a translation and given a Boltzmann sampling of translational energy "forward" over the col. Employing a Verlet algorithm, we took 1-fs steps until either product or starting material was formed (as judged by a C–O or C–N distance <1.7 Å), with a maximum trajectory of 250 fs to minimize the effect of intramolecular vibrational energy redistribution (IVR).[40] Plots of the C_1- -O distance for the incipient C_1- -O bond versus time for some typical dynamics trajectories are shown in Figure 4.
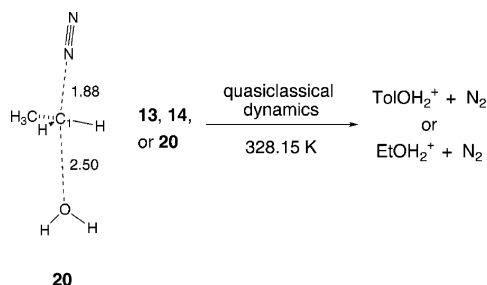
For 47 trajectories based on **20**, the product was formed rapidly. All of the trajectories were complete within 100 fs, and the median time was 57 fs. In a few of the trajectories the progress toward product formation was slowed by motion in an orthogonal mode that twists the orientation of the water moiety, but in all trajectories the water is clearly caught in the potential energy well leading to product.

Trajectories based on **13** and **14** appeared quite different. First of all, product formation was considerably slower. For 30 trajectories starting from **14** and 17 trajectories starting from **13**, the median times for product formation were 157 and 172 fs, respectively. Most notably, 11 of the trajectories did not form product at all within 250 fs (nor did they return to starting material). The lifetime of the longest-lived tolyl cation moieties cannot be well explored in a quasiclassical simulation because of IVR, but unlike with **20**, there is no obvious limitation on the time to product formation. In several of the trajectories, the water molecule that was "performing the displacement" in the potential energy saddle point was further from C_1 after 250 fs than another water molecule! It may thus be expected that in some cases the nucleophile for the formal S_N2Ar transition structure would not end up in the product. Regardless of the potential energy surface, such trajectories are not well described as "concerted."
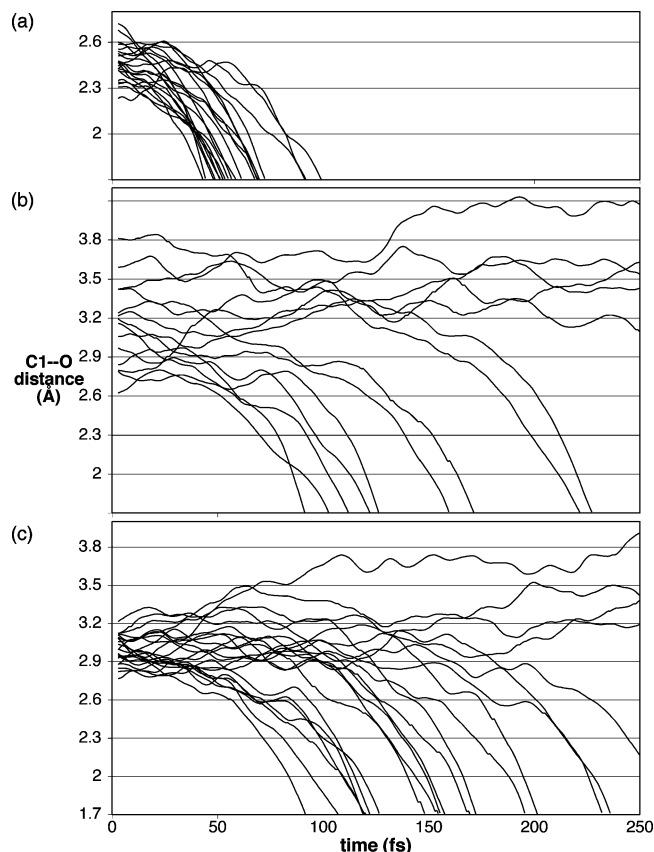
Figure 4. Plots of C_1- -O distance versus time for dynamics trajectories starting from (a) **20**, (b) **13**, and (c) **14**. Trajectories were stopped after 250 fs or when the C_1- -O distance dropped below 1.7 Å.

Expectations for Aryl Cation Lifetimes. Many nucleophilic substitution reactions occur by a true S_N1 mechanism in which a highly unstable carbocation intermediate, in water, has a discrete lifetime. How should an aryl cation in water compare to other carbocations? To address this issue, it is enlightening to compare the reactions of **6** and *tert*-butyl cation with water from a Marcus-type perspective.[41,42] To gauge the relative internal reorganization energy of the two cations, their energies were compared in B3LYP/6-31+G** calculations to hypothetical cations placed in the product geometry. That is, **7** and *tert*-butyl-OH_2^+ were optimized (including a PCM model), the water atoms were removed, and the single-point energies of the resulting cations were compared to the energies of optimized structures. By this process, the internal reorganization energy for the *tert*-butyl cation was 22.9 kcal/mol. The reorganization energy for the **6** was smaller, 17.1 kcal/mol, but still substantial. Because both cations are similarly localized, we will assume that the solvent reorganization energy in their reactions with water is similar. With such localized cations, the solvent reorganization energy should be relatively small since the location of the positive charge changes little (moving from the carbon to the incipiently adjacent oxygen) as the reaction proceeds. The final factor affecting the rate of reaction with water is its exothermicity. As mentioned above, the exothermicity for reaction of **6** to afford **7** is 50.3 kcal/mol (including

(40) Ben-Nun, M.; Levine, R. D. *J. Chem. Phys.* **1994**, *101*, 8768−8783.
(41) (a) Richard, J. P.; Toteva, M. M.; Crugeiras, J. *J. Am. Chem. Soc.* **2000**, *122*, 1664−1674. (b) Richard, J. P.; Amyes, T. L.; Toteva, M. M. *Acc. Chem. Res.* **2001**, *34*, 981−988.
(42) Toteva, M. M.; Richard, J. P. *J. Am. Chem. Soc.* **1996**, *118*, 11434−11445.

a PCM water solvent model). For comparison, the exothermicity of the reaction of water with *tert*-butyl cation, calculated analogously, is only 13.1 kcal/mol. From these considerations, it would be expected that the reaction of water with **6** would be faster that the reaction of water with *tert*-butyl cation.

The reaction of water with *tert*-butyl cation is itself incredibly fast. The rate constant for reaction of a *tert*-butyl cation in 1:1 trifluoroethanol/water has been estimated as 1.6×10^{12} s^{-1}.[42] From this, the half-life for a *tert*-butyl cation would only be about 400 fs. A moderately faster reaction for **6** would be consistent with the dynamics lifetimes.

Looked at from this kinetic perspective, the displacement in aryl diazonium ions may be viewed as a two-step reaction in which the second step is incredibly fast, often so fast that no definable intermediate is involved, but occasionally the intermediate is long-lived. This is interesting from a fundamental perspective. The normal understanding of the competition between concerted and stepwise processes is that the preferred mechanism arises from a specific energy preference. If a reaction prefers a concerted mechanism over a two-step alternative, we expect some "energy of concert." In the loosest transition structures such as **13**, however, the stabilization of the transition state by the water nucleophile is a limited dipolar solvation effect. (Even in the one-water reaction via "tight" transition structure **8**, the water stabilizes the starting material more than the transition state.) "Concerted" displacement, when it occurs, arises simply from the speed of collapse of the solvation shell.

Reconsideration of Evidence for Aryl Cation Intermediates. As described in the Introduction, the automerization of α and β nitrogen atoms in aryl diazonium cations under reaction conditions in water, along with exchange with external nitrogen in less nucleophilic solvents such as trifluoroethanol, compose the strongest evidence for free aryl cation intermediates. We discuss here evidence for alternative interpretations of these observations.

One alternative explanation for α/β automerization of diazonium ions, not involving an aryl cation intermediate, is the intervention of a concerted automerization process in competition with solvolyses. The automerization transition state and nucleophilic substitution transition state would have to be "similar", as it has been observed that variation in reaction conditions results in little variation in the relative amount of automerization.[43]

Fitting this prescription, Glaser and Horan have reported the transition structures **21** and **22** for the α/β automerization of phenyldiazonium cation.[44] The in-plane structure **21** was predicted to be favored, with an energy 2.0 kcal/mol (QCISD-(T)/6-31G*//MP2(full)/6-31G* + zpe) below that of completely dissociated N$_2$/phenyl cation.[44] Using larger basis sets, we find that **21** becomes a third-order saddle point, out-of-plane **22** is favored,[45] and the N$_2$/phenyl cation attraction is reduced to 1.1 kcal/mol (QCISD(T)/6-311+G**//MP2/6-311++G** + zpe). However, it seems questionable to argue that these structures are relevant to the water reaction. Aside from the extremely weak nature of the N$_2$/phenyl cation interaction, the calculation ignores entropy and thermal energy. A free energy estimate using unscaled frequencies places **22** 6.3 kcal/mol above free N$_2$/phenyl cation (at standard state). Another issue is that the C$_1$−N distance in these structures is sufficiently long to allow a facile attack by water in solution. (Optimizing **22**

with the C$_1$- -N distances fixed in the presence of one water molecule affords PhOH$_2^+$.)
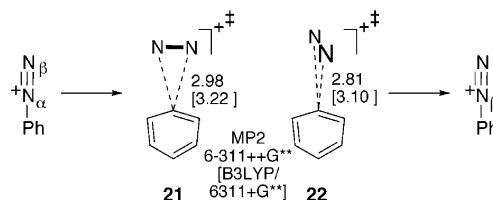
In the process of searching for transition structures for the loss of N$_2$ from **2** in the presence of 10 water molecules, we located by accident the α/β automerization transition structure **23**. In **23**, the automerization process is capped by a shell of water molecules, having the effect of forcing the N$_2$ closer to the aryl cation. The energy of **23** is 0.5 kcal/mol above **14** and a free energy estimate at 298 K places the structures within 0.8 kcal/mol. Most notably, the existence of **23** supports the idea that the automerization reaction can occur in the presence of water molecules. Key to this is that the N$_2$ positionally blocks nucleophilic attack by water, and thus the shortest C$_1$−O distance is 3.60 Å.
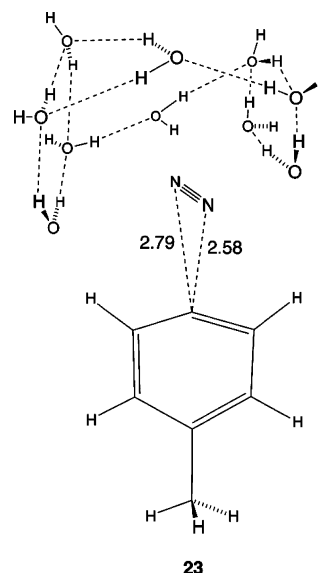

From the arguments of Cuccovia and Glaser,[20,21] any nucleophilic solvent should preclude the intermediacy of an aryl cation, but the nucleophilic substitution process is certainly not exclusively concerted in trifluoroethanol and hexafluoro-2-propanol. Zollinger observed extensive incorporation of external N$_2$ into recovered diazonium ion under these conditions, and for hindered diazonium ions, the molecular N$_2$ is almost as effective a nucleophile as the fluorinated alcohols.[12,14] This suggests a relatively long-lived but highly reactive and unselective intermediate. The particular observation of a rate decrease with increasing N$_2$ is not consistent with competitive concerted processes.[14b] If fact, after assuming an absence of concerted substitution or automerization, the kinetics appear to require two intermediates, as Zollinger proposed in Scheme 2.

(43) Lewis, E. S.; Holliday, R. E. *J. Am. Chem. Soc.* **1966**, *88*, 5043−5044.
(44) Glaser, R.; Horan, C. J. *J. Org. Chem.* **1995**, *60*, 7518−7528.
(45) B3LYP/6-311++G** calculations favor **21**, with **22** being a second-order saddle point (see Supporting Information), but QCISD(T) single-point energies slightly favor the MP2 description.

However, the kinetic observations are equally consistent with the operation of competitive concerted and stepwise processes, and no observation requires a *free* aryl cation. In contemplating alternatives, we were fascinated by the recent observation of Maskill and co-workers that aryl fluorides are formed in solvolyses of diazonium ions in trifluoroethanol (eq 3).[46] The nucleophilicity of the fluorine atoms of trifluoroethanol in product formation requires some consideration of their nucleophilic character as the C_1- -N2 bond is breaking.
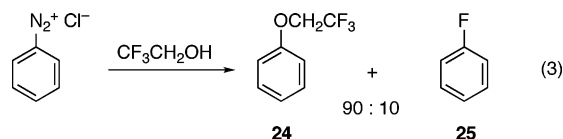

To explore this nucleophilic character, we located transition structures **26** and **27** for the loss in N_2 in the presence of trifluoroethanol. In **26**, the oxygen atom of trifluoroethanol is acting as a nucleophile in a concerted displacement that would ultimately afford the ether **24**. In **27**, a fluorine atom of trifluoroethanol is playing the role of nucleophile. The transfer of a fluoride anion from trifluoroethanol to phenyl cation in the gas phase is predicted to be exothermic by 8.6 kcal/mol (B3LYP/6-311++G**), so ultimately **27** can afford **25**. Interestingly, **27** is lower in energy than **26** in the gas phase; in such loose transition states it would appear that the nucleophilicity is dominated by dipolar interactions without regard to the ultimate stability of the product. Even in **26**, there appears to be some dipolar stabilization by a fluorine atom proximal to the developing charge at C_1.
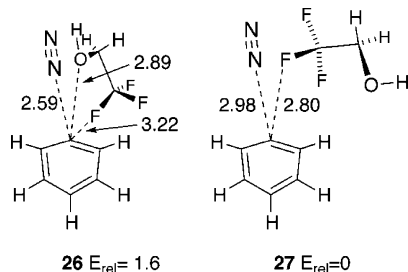
The strongest evidence for an intermediate has been seen in the decomposition of 2,4,6-trimethylbenzenediazonium salt **28** in trifluoroethanol.[14] The rate of this reaction is decreased by 11% under 300 atm of N_2 compared to 300 atm of argon, and 16.5% incorporation of external N_2 was observed in recovered diazonium ion after 70% conversion. Addition of thiocyanate anion, a good nucleophile, increases the rate by up to 27% under 300 atm of N_2. These observations require an intermediate. We have calculationally located the complex **29** from the interaction of the 2,4,6-trimethylphenyl cation with trifluoroethanol, and we propose that this complex accounts for the observations in this system. Complex **29** is predicted to lie 8.3 kcal/mol below separate molecules of aryl cation and trifluoroethanol (B3LYP/6-31+G(d′,p′) + zpe). This is an intriguing structure. The fluorine atom "bridge" in **29** is very unsymmetrical—unsurprisingly, since a symmetrical bridge would formally place the positive charge on the fluorine—but the C_1- - -F distance of only 2.06 Å is indicative of substantial bonding between the

aryl cation and the solvent molecule. Similar structures have been proposed to be intermediates in gas-phase reactions.[47]
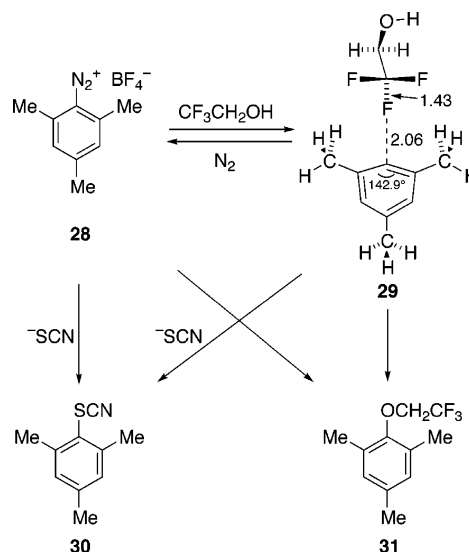
We propose that complexes of this type can account for the diverse observations in this system. In competition with a displacement to afford the ether product **31**, complex **29** could be formed. In the presence of large amounts of external N_2, **29** could revert to starting material, and it seems reasonable that N_2 could compete with solvent in attacking the hindered C_1 of **29**. A nucleophile such as thiocyanate would be expected to increase the rate in two ways—either via the loose direct displacement process or by inhibiting reversion of **29** to starting material—and the observed effects of thiocyanate14b appear consistent with this picture.[48]

Conclusions

It would seem that even the strongest classical evidence for the intermediacy of aryl cations in nucleophilic solvents is ambiguous. In such difficult cases, theoretical calculations have certainly proven their power. However, the current case is particularly challenging for a purely theoretical approach for three reasons: (1) the energetic similarity of S_N1 and S_N2Ar pathways, (2) the difficulty of modeling a reaction of a charged species in bulk water, and (3) the large role of entropy in the competition between S_N1 and S_N2Ar mechanisms. We therefore turned to the combination of kinetic isotope effects and theoretical calculations as a powerful probe of the transition state geometry. Interestingly, in the end, a detailed knowledge of the transition state geometry may not be sufficient to characterize the mechanism because of a final complication: dynamic effects.

In their calculations, Cuccovia[20] and Glaser[21] each located a concerted transition structure for displacement of N_2 by a single water molecule, and they established that such a structure is energetically plausible. However, the predicted isotope effects for these structures do not fit well with the structurally

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(48) If thiocyanate is preventing reversion of **29** to starting material, a greater rate effect would be expected under 300 atm of N_2 versus 300 atm of argon. Reference 14b summarizes the effect of thiocyanate under N_2 versus argon as "similar", but at each of the four concentrations studied, the percentage rate increase under N_2 is greater.

significant isotope effects, in particular by overpredicting the C_1 KIE and underpredicting the remaining ^{13}C and H/D KIEs. The structural interpretation of the ^{13}C KIEs supports a much looser displacement process, if the water is involved at all, and we conclude that the previous relatively tight substitution transition structures are not good models for the solution chemistry. On the other hand, the observed ^{13}C KIEs do not approximate equilibrium isotope effects for tolyl cation formation. This weighs against a reversible dissociation of C_1–N bond.

Among the various KIEs measured in these reactions, the ^{13}C isotope effects appear to be most structurally significant. These isotope effects fit best with an extremely loose displacement process. In the model potential energy saddle points **13**–**15**, the leaving N_2 and the "incoming" water molecule are quite distant from the aryl cation, and the aryl cation is rotating from solvation by N_2 to solvation by water.

However, the misleading nature of these potential energy saddle points becomes apparent when dynamics trajectories based on these structures are compared with those from a true S_N2 displacement. Because there is only a weak interaction between the nucleophilic water molecule and the aryl cation, dynamic effects become significant. Some trajectories afford long-lived aryl cation intermediates, and in some the product from this cation may not contain the nucleophile involved at the transition state. This is far more complicated than the classical view of a concerted displacement.

Rate-limiting simple dissociation of N_2 from an aryl diazonium ion, as modeled in **5**, cannot be fully excluded on the basis of isotope effects. We are skeptical of **5** as a physical model because its derivation was based on gas-phase entropy effects, dubiously applicable to solution. For the reaction of a charged species in water, solvation entropy effects should be large and not entirely predictable. It is thus plausible that the entropy effects in **5** could approximate those in solution, if only by accident.

From dynamics considerations, however, the distinction between a unimolecular dissociation of N_2 as in **5** and an extremely loose, formally bimolecular displacement as in **13**–**15** is not necessarily meaningful. We cannot model well the unimolecular dissociation of N_2 in water, but it seems likely that such a process would often afford the product within 200 fs. On the other hand, a bimolecular displacement, as modeled by the dynamics of **13** and **14**, need not afford the product quickly and may well lead to a long-lived intermediate. The isotope effects show that the mechanism is near the boundary between S_N2Ar and S_N1 mechanisms and, when

dynamics are taken into account, there is no clear dividing line between the two mechanisms.

The impact of dynamic effects continues to challenge basic physical organic ideas. Products may be formed nonstatistically from reactions passing through intermediates.[49,51] Intermediates may be formed in reactions that should be concerted.[39] Kinetic selectivity in a reaction can be unrelated to reaction barriers[52,53] and involves a kinetically distinguishable step without an intermediate.[54] Here, it appears that transition structures for a reaction need not lead to the product of the reaction, and the very definition of what constitutes an intermediate and what constitutes a concerted reaction appears unclear. We are continuing to investigate the impact of these ideas and dynamic effects on ordinary organic reactions in solution.

Experimental Section

Solvolysis of 2 in Water. Example Procedure. A stirred mixture of 1125 mL of water, 150 mL of concentrated H_2SO_4, 2.4615 g of trimethylacetic acid (an internal standard for aliquots), and 53.33 g (480 mmol) of *p*-toluidine under N_2 was cooled to <5 °C in an ice–water bath. To this mixture was added dropwise over 1 h a mixture of 38.92 g (556 mmol) of $NaNO_2$ in 100 mL of water, and the resulting mixture was stirred for an additional 1 h. The reaction mixture was then heated rapidly to ~55 °C, with evolution of N_2 becoming apparent as the reaction temperature exceeded 50 °C. After 15 min at ~55 °C, the mixture was rapidly cooled to <5 °C, and a mixture of 16.4 g (252 mmol) of NaN_3 in 150 mL of water was added dropwise over 30 min. The mixture was then extracted with five 150-mL portions of CH_2Cl_2. The combined organic layers were dried ($MgSO_4$), and the solution was concentrated on a rotary evaporator. The residue was analyzed by ^1H NMR, and the percent solvolysis of the intermediate **3** was determined as 71 ± 3% based on the ratio of *p*-cresol to *p*-tolyl azide. From comparison with the internal standard, the mass balance was 103% (±~10%). No toluene (a likely product from radical-mediated reactions) was detectable in the mixture. The crude mixture of *p*-cresol and *p*-tolyl azide was chromatographed in portions on a 9″ × 2.25″ silica gel column using 9:1 hexane/diethyl ether as eluent. A sample of 3 g of *p*-tolyl azide obtained in this way was further purified for NMR analysis by vacuum distillation.

A standard sample of *p*-tolyl azide for NMR analysis was prepared by diazotization of *p*-toluidine (from the same bottle as that used in the previous experiment) at <5 °C under conditions analogous to those

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above, followed by direct treatment of the intermediate diazonium at <5 °C with NaN$_3$. After an extractive workup, the resulting *p*-tolyl azide was purified by vacuum distillation.

NMR Measurements. All samples were prepared using 0.40 g of *p*-tolyl azide in 0.47 g of d_6-DMSO in a 5-mm NMR tube. The ^{13}C spectra were recorded at 125.701 MHz using inverse gated decoupling, 80-s delays between calibrated $\pi/2$ pulses, and a 6-s acquisition time to collect 300 032 points. Integrations were determined numerically using a constant integration region for each peak. A zeroth-order baseline correction was generally applied, but in no case was a first-order (tilt) correction applied. Twelve spectra were obtained for each *p*-tolyl azide sample along with six spectra for the corresponding *p*-tolyl azide standards. The resulting ^{13}C integrations for these spectra are given in Supporting Information. From the ^{13}C integrations the KIEs and uncertainties were calculated as previously described.[29]

Computational Methods

All calculations of ground-state and transition structures were performed using Gaussian 98 or Gaussian 03 programs.[55] PCM calculations were carried out using Gaussian 03 with default parameters and water as solvent in each case. Density functional theory calculations employed the Becke3LYP hybrid HF-DFT method as implemented in Gaussian.[56] Calculations for structures **2**, **5**, **6**, **7**, **8**, **9**, **26**, and **27**, as well as simple structures related to *tert*-butyl cation, employed a 6-31+G** basis set. Calculations for structures **10**, **11**, **12**, **13**, **14**, **15**, **20**, and **23**, along with related structures and starting materials given in Supporting Information, employed a 6-31G** basis set. Attempts to optimize structures **13**, **14**, and **15** employing diffuse functions failed to converge. B3LYP and MP2 calculations for structures **21** and **22** used a 6-311++G** basis set. A 6-31+G(d′,p′) basis set was used for the fluorine-containing structure **29**. Optimizations of **14** and **15** employing an Onsager water model, as implemented in Gaussian 03, used radii of 5.23 and 5.67 Å, respectively.

The program used for dynamics was given and described in Supporting Information for a previous publication.[52] The latest version of this program may be obtained for free by e-mailing the corresponding author.

Supporting Information Available: Energies and full geometries of all calculated structures and NMR integration results for all reactions. This material is available free of charge via the Internet at http://pubs.acs.org.

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