# Boundary Conditions on the Partitioning of Deaminatively Generated Benzyl Cations

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Nitrogenous entity-separated ion pairs (NESIPs) containing benzyl cations, nitrogen gas, and pivalate anions were generated via thermal deamination of *N*-benzyl-*N*-nitrosopivalamide. Some decompositions were performed in methanolic solutions saturated with selected nucleophiles: acetate, azide, or cyanide ions. Trace amounts of benzyl cyanide and tolunitriles were observed; no corresponding products were detected in the acetate and azide cases. Other decompositions were performed in the absence of traditional solvent but in the presence of the nucleophilic salts; again only poor cyanide interception of the cation was observed. The poor showing of the nucleophilic ions, when present, is discussed in the context of the lifetime of the cation, effective nucleophilicity, and cage effects in deamination.

#### Introduction

The ability of nucleophilic solvents such as benzene/ toluene mixtures,<sup>1a,b</sup> pyrrole,<sup>1c</sup> acetonitrile,<sup>1d</sup> styrene,<sup>1e</sup> and acetone<sup>1f</sup> to intercept deaminatively generated carbocations as probes of reaction mechanisms<sup>1a-c</sup> and to form novel and useful products in variable yields (7%<sup>1a,b</sup> to 78%<sup>1c</sup>) has been recently explored. These carbocations, formed via unimolecular<sup>1g,h</sup> thermolysis of N-alkyl-Nnitrosoamides as part of a nitrogenous-entity separated ion-pair (NESIP; Figure 1), are very reactive.<sup>1,2</sup> Their enhanced reactivity is due, in part, to the low activation energy required for the loss of the nitrogenous molecule from the alkyldiazonium precursor thus allowing the cation to be formed with minimal solvent participation.<sup>1,2</sup> Additionally, the temporary screening of the cation from its counterion by the sheer physical presence of the nitrogenous entity results in the maximal positive charge at the electron-deficient center.<sup>1,2</sup>

The alkyl cation is believed to be the active electrophile because (1) predominant *retention* of configuration observed in the ester from deamination of phenylethyl-*N*-



**Figure 1.** Initial structure of a NESIP containing alkyl and carboxylate ions.

nitrosonaphthamide<sup>2b</sup> (and its 2-butyl analogue<sup>2b</sup>) and <sup>18</sup>O-studies of "intramolecular inversion"<sup>2b</sup> require the finite existence of a carbocation. Additionally, (2) deamination of bridgehead amines leads to solvent-derived product (SDP),<sup>2c,e</sup> which is impossible if the diazonium ion were the alkylating agent.

The absence of a free-radical pathway is indicated by the nondetection of monodeuteriomethylbenzene or hexachloroethane from the decomposition of *N*-benzyl-*N*-nitrosobenzamide in 10:1 benzene/CDCl<sub>3</sub> at 80 °C.<sup>2d</sup> Since no D-abstraction from CDCl<sub>3</sub> occurred at a modestly high temperature in a fairly nonpolar medium, then a free-radical pathway is apparently not competitive with the cationic pathway. Further, the similarity among  $k_{\rm T}/k_{\rm B}$  and isomer distribution values from nitrosoamide decompositions in equimolar benzene-toluene at 80, 40, and 25 °C<sup>1b,2d</sup> also indicate the absence of a competitive radical pathway.

The high reactivity of these carbocations has been demonstrated by the interception of methylene chloride by the deaminatively generated 1-norbornyl cation with the eventual formation of 1-chloronorbornane as the major product.<sup>2c</sup> Additionally, the observations of significantly lower  $k_{\rm T}/k_{\rm B}$  values ( $\sim 2.5$  vs  $\sim 6$ ) and significantly higher yields of the meta isomer ( $\sim 18\%$  vs  $\sim 6\%$ ) from nitrosoamide thermolyses in equimolar benzene–toluene<sup>1a</sup>

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<sup>(1) (</sup>a) White, E. H.; Darbeau, R. W.; Chen, Y.; Chen, D.; Chen, S. J. Org. Chem. **1996**, 61, 7986. (b) Darbeau, R. W.; White, E. H.; Song, F.; Darbeau, N. R.; Chou, J. C. J. Org. Chem. **1999**, 64(16), 5966. (c) Darbeau, R. W.; White, E. H. J. Org. Chem. **1997**, 62, 8091. (d) Darbeau, R. W.; White, E. H.; Nunez, N. P.; Coit, B. C.; Daigle, M. A. J. Org. Chem. **2000**, 65, 1115. (e) Darbeau, R. W.; Delaney, M. S.; Ramelow, U.; James, K. R. Org. Lett. **1999**, 1(5), 761. (f) Song, F.; Darbeau, R. W.; White, E. H. J. Org. Chem. **2000**, 65, 1825. (g) Huisgen, R.; Ruchardt, C. Justus Liebigs. Ann. Chem. **1956**, 601, 1. (h) Darbeau, R. W.; Pease, R. S. Gibble, R. E.; Perez, E.; Darbeau, N. R. J. Org. Chem., submitted.

<sup>(2) (</sup>a) White, E. H.; De Pinto, J. T.; Polito, A. J.; Bauer, I.; Roswell, D. F. J. Am. Chem. Soc. 1988, 110, 3708. (b) White, E. H.; Field, K. W.; Hendrickson, W. H.; Dzadzic, P.; Roswell, D. F.; Paik, S.; Mullen, P. W. J. Am. Chem. Soc. 1992, 114, 8023. (c) White, E. H.; McGirk, R. H.; Aufdermarsh, C. A.; Tiwari, H. P.; Todd, M. J. J. Am. Chem. Soc. 1973, 95(5), 8107. (d) Darbeau, R. W.; White, E. H. J. Org. Chem. 2000, 65, 1121. (e) Kirmse, W. J.; Moench, D. Chem. Ber. 1991, 124(1), 237.

(vs those data from standard Friedel–Crafts approaches) are further evidence of the enhanced reactivity of these cations.  $^{\rm 1a}$ 

The deaminative approach (especially via *N*-nitrosoamides) to carbenium ions is an excellent alternative to the standard carbocationation methods such as solvolyses and the acid-catalyzed Friedel–Crafts approaches because of the following variables: high reactivity of the electrophile, homogeneity of the reaction mixtures, straightforward chemistry, and excellent product balance.<sup>1b,2b,d</sup>

When the cation, e.g., benzyl cation, is stable and devoid of removable  $\beta$ -hydrogens, S<sub>N</sub>1-type reaction with available nucleophiles, e.g., the counterion and the solvent, is its only fate. Cation-solvent reactions must occur before diffusion of the nitrogenous molecule from between the ions in the solvent cage as the latter process leads to internal collapse of the ion pair to give the corresponding ester. Thus, the N<sub>2</sub> molecule is implicated in this context in the partitioning of the carbocation between its nascent counterion and the medium; the longer the  $N_2$  molecule remains in the pocket between the ions (prior to diffusion) the more opportunity is afforded the carbenium ion to interact with the medium. The yield of SDPs is increased by conditions that decrease the diffusion rate of the nitrogenous molecule.<sup>1b,3a</sup> Increased solvent yields are also achieved through use of large mole fractions of highly nucleophilic solvents, <sup>1b-d,f,2a,3a</sup> and employment of poorly nucleophilic counterions.<sup>1b-d,2a,3a</sup>

In this study, we attempted to answer the following questions regarding the  $S_{\rm N}\mathbf{1}$  reactions of deaminatively generated cations:

1. To what extent are nonsolvent nucleophiles external to the cage capable of competitive interception of deaminatively generated carbocations?

2. Does the solvent affect the ability of dissolved nucleophiles to intercept the cation?

3. How do reaction temperature and the nucleophilicity of the attacking species affect cation interception?

The source of the benzyl cation was deaminative since (1) the purpose of the study was to determine the vulnerability of deaminatively generated cations to attack by nucleophilic solute and (2) because cations generated in this manner probably represent the most reactive ones accessible in solution-phase chemistry under ambient conditions.<sup>1,2</sup> In the present study, some deaminations were performed in methanol (n = 0.0),<sup>4a</sup> whereas others were done solvent free (vide infra). The added nucleophiles were acetate (n = 4.3),<sup>4a</sup> azide (n = 5.8),<sup>4a</sup> and cyanide (n = 6.7).<sup>4a</sup>

## **Results and Discussion**

**Deamination of N-Benzyl-N-nitrosopivalamide in Nucleophile-Saturated Methanol.** *N*-Benzyl-*N*-nitrosopivalamide (NBNNP, **1**) was decomposed (eq 1) in methanol saturated with the sodium salts of acetate and azide ions at 25 and 70 °C. To the detection limit of the



NMR spectrometer, no benzyl acetate or benzyl azide was observed (from nucleophilic attack at the benzyl carbon) and neither were the methylphenyl acetates or azido-toluenes (from nucleophilic attack on the aromatic nucleus).<sup>5</sup> When the decompositions were performed in the presence of NaCN, although no tolunitriles were detected, roughly 0.05% of benzyl cyanide was observed ( $\delta$  3.69) at 70 °C (none observed at 25 °C).

That benzyl nitrile is detectable only at elevated temperatures indicates a weak temperature dependence of the product distribution ostensibly related to the higher [CN<sup>-</sup>] at 70 °C.<sup>4d</sup> It should be borne in mind, though, that N<sub>2</sub> diffusion from between the ions is accelerated at elevated temperatures resulting in less opportunity for cation–medium interaction.<sup>1b</sup> Thus, the rise in temperature leads to two diametrically opposed effects on cation–cyanide interaction. An inescapable observation, however, is that even at the elevated temperatures the yields of cation–solute products are exceedingly low.<sup>5</sup>

Evidently, even in the presence of powerful nucleophiles such as azide (vide infra) and cyanide, no significant substitution of the deaminatively generated benzyl cation is observed. It is interesting that the presence of highly reactive cations and aggressive nucleophiles in the same reaction do not lead to appreciable yields of product from their interactions. There would appear to be two interpretations: (1) the benzyl cation is not the true active intermediate in these reactions or (2) factors conspire to prevent meaningful interactions between the cation and the added anions.

Given the considerable body of work<sup>1,2</sup> (vide supra) in support of carbocation intermediacy in nitrosoamide thermolyses, option 1 would appear to be unlikely. Jencks<sup>6a</sup> has argued that intermediates exist if and only if at least two significant barriers for collapse of the putative intermediate complex exist. In the case of the deaminatively generated benzyl cation, the reverse step, rediazoniation of the cation with molecular nitrogen, does not occur at ambient pressures.<sup>6b</sup> indicating a significant

<sup>(3) (</sup>a) The yield of SDP also rises with decreasing temperature and to a lesser extent as the nitrogenous molecule is changed from  $N_2$  to  $N_2O$ .<sup>1b</sup> (b) Although benzyl cyanide could conceivably arise from cyanide attack on NBNNP, the detection of products from nuclear attack by cyanide would require the formation of the discrete benzyl cation. Since the yields of benzyl cyanide and the tolunitriles appear to be of the same order of magnitude, and tolunitrile formation is impossible from NBNNP, it would appear reasonable that most, if not all, benzyl cyanide observed from these runs must have arisen from cyanide-cation interaction. Cyanide attack on the benzyl diazonium ion is also ruled out based on stereochemical and steric studies.<sup>2b</sup>

<sup>(4) (</sup>a) Swain, C. G.; Scott, C. B. J. Am. Chem. Soc. 1953, 75, 141.
(b) The reduction of ion nucleophilicity by solvation may not be true for the azide ion, since this ion is known<sup>4c</sup> to react at the diffusion limit with short-lived cations even in strongly solvating solvents. (c) Ritchie, C. D. Acc. Chem. Res. 1972, 5, 348. (d) In contrast, however, Henstock found the solubility of NaCN in MeOH to be depressed at the boiling point of the solvent (Henstock, H. J. Chem. Soc. 1934, 1340).

<sup>(5)</sup> Darbeau, R. W. Manuscript in preparation.

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barrier for this reverse step. The physical presence of the nitrogen molecule between the gegenions introduces a significant steric barrier to ion-pair collapse<sup>1,2</sup> as illustrated by the observations that solvent-derived product can predominate over ester.<sup>1c,2a,c</sup> The conclusion then is that benzyl cations can be reasonably assumed to be present along the reaction pathway as the active intermediates. To the extent that this is true then it would seem that under the present reaction conditions the benzyl cation is unable to interact to any significant extent with the added nucleophilic anions.

Two plausible scenarios for the poor showing of the anionic nucleophiles are as follows. (1) The concentrations of the nucleophiles were too low for the ions to enter into detectable bimolecular reaction with the benzyl cation ( $[CN^-]_{70^\circ C} = 2.2 \text{ M}; [^-OAc]_{70^\circ C} = 2.8 \text{ M}; [N_3^-]_{70^\circ C} = 1.1 \text{ M}$ ). This interpretation would be consistent with the high reactivity and short lifetimes<sup>2b</sup> (vide infra) of deaminatively generated carbocations, which are likely to react in an essentially statistical manner with available nucleophiles. (2) The effective nucleophilicity of the ions is reduced in the presence of the hydrogen-bonding MeOH<sup>4b,c</sup> to the point where their ability to significantly interact with the benzyl cation is severely compromised.

Deaminatively generated benzyl cations have been shown to be effective at capturing even weakly nucleophilic solvents (e.g., benzene),<sup>1a,b</sup> and hence, an investigation of the optimal conditions for their "interceptibility" by solute anions would require use of solvents that are inert to the nitrosoamide, cation, and the solute but that are sufficiently polar to dissolve appreciable amounts of salts.

Solvents such as  $SO_2$  or the sulfonyl halides, etc., are poor candidates because these media are inherently acidic and would catalyze the decomposition of the nitrosoamides, introducing an unwanted element in the reactions. Additionally, the sulfonyl halides and other traditional solvents such as methylene chloride and chloroform, etc., are also good enough electrophiles to react with cyanide and azide, etc. The question of solubility was also an issue. There is also sufficient precedent<sup>1d,f</sup> for the probability of the interception of the benzyl cation by the sulfonyl species.

Fortunately, because of the facility of dediazoniation, the deaminative approach to carbenium ions does not require solvents for ionization to occur,<sup>1,2</sup> and because the *N*-nitrosoamides are modestly polar liquids, they are capable of dissolving appreciable amounts of ionic compounds. In any event, the presence of diluents compromises the efficacy of the carbenium ion in trapping active nucleophilic solvent.<sup>1c</sup> Ostensibly then, the best opportunity to engineer the interception of external anionic nucleophiles would appear to be in the absence of solvents.<sup>7a</sup> Thus, the decompositions of *N*-benzyl-*N*nitrosoamides in the presence of added nucleophiles in the absence of solvents was investigated.<sup>7a</sup>

Solvent-Free Deamination of N-Benzyl-N-nitrosopivalamide in the Presence of Acetate and Azide **Ions.** NBNNP was separately saturated with sodium acetate and sodium azide and was allowed to decompose with stirring at 25 and 80 °C.<sup>7b</sup> After the reaction was complete, the filtered solution was analyzed by <sup>1</sup>H NMR. No interception of the benzyl cation by these salts occurred as evidenced by the absence of any benzyl signals (apart from that due to benzyl pivalate at  $\delta$  5.2<sup>8</sup>) in the region  $\delta$  3.5–6.0<sup>8</sup> or any acetyl signals (for benzyl acetate) at  $\delta \sim 2.4.^{8}$ 

Solvent-Free Deamination of *N*-Benzyl-*N*-nitrosopivalamide in the Presence of Cyanide. NBNNP was saturated with NaCN at 25 and 80 °C, and the suspension was vigorously stirred for 6 h and for 30 min, respectively. At the end of the reaction, the oil was filtered and the filtrate was analyzed by <sup>1</sup>H NMR. From the runs at 25 °C, benzyl pivalate ( $\delta$  5.2,<sup>8</sup> 1.27; 99.9%), benzyl cyanide ( $\delta$  3.69;<sup>8</sup> trace), *o*-tolunitrile ( $\delta$  2.39,<sup>8</sup> trace), and *p*-tolunitrile ( $\delta$  2.35,<sup>8</sup> trace) were observed. From the 80 °C runs the approximate product distribution was benzyl pivalate (99.7%), benzyl cyanide (~0.2%), *o*-tolunitrile (~0.07%), and *p*-tolunitrile (~0.03%). The presence of the nitriles (and the absence of *m*-tolunitrile) was confirmed by GC (vide infra).

There are several notable features of these results: (1) solvated cyanide ions are capable of intercepting the benzyl cations; (2) such interception occurs principally at the benzylic position but minor attack occurs at both the ortho and para positions;<sup>3b,5</sup> (3) despite its high nucleophilicity, cyanide ions compete very poorly against the much less nucleophilic pivalate ions for the deaminatively generated benzyl cation; (4) minimal nuclear attack by cyanide ions on the benzyl cation occurs<sup>5</sup> even when these ions are generated in the absence of solvent; (5) the extent of nuclear attack rises with increasing temperature.<sup>5</sup>

Nucleophilic interception of the deaminatively generated benzyl cation at the aromatic nucleus is apparently a novel observation. Indeed, interception of the aromatic ring of benzyl and related cations by nucleophiles of any type appears to be a rare event.<sup>5</sup>

The poor showing of cyanide is discussed in the following sections in terms of cage and lifetime effects in the NESIP (vide infra). The dependence upon temperature is probably related to the enhanced solubility of sodium cyanide at elevated temperatures and to the availability of increased energy under these conditions for the more difficult reactions on the aromatic nucleus (vide supra).

Limitations on the "Freedom" of Deaminatively Generated Benzyl Cations: Cage Effects in Deamination. The solvent-free decomposition of *N*-nitrosoamides in the presence of nucleophilic salts was investigated with two goals in mind: (1) investigation of a novel synthetic approach to nucleophile-substituted toluenes and to synthesis of those toluenes that may be difficult to prepare via conventional aromatic substitutions and (2) for studying physical organic aspects of reactions of benzyl cations with nucleophiles with mini-

<sup>(6) (</sup>a) Jencks, W. P. Acc. Chem. Res. 1980, 13(6), 161. (b) Szele, I.;
Zollinger, H. Top. Curr. Chem. 1983, 112, 1. (c) Finneman, J. I.;
Fishbein, J. C. J. Am. Chem. Soc. 1995, 117, 4228. (d) Richard, J. P. Tetrahedron 1995, 51, 1535. (e) McClelland, R. A.; Chan, C.; Cozens, F.; Modro, A.; Steenken, S. Angew. Chem. Int. Ed. Engl. 1991, 30, 1337. (f) Pezacki, J. P.; Shukla, D.; Lusztyk, J.; Warkentin, J. J. Am. Chem. Soc. 1990, 121, 6589. (g) Amyes, T. L.; Richard, J. P. J. Am. Chem. Soc. 1990, 112, 9507.

<sup>(7) (</sup>a) There are several precedents for solvent-free organic chemistry (e.g., that employing microwave technology, or Friedel–Crafts reactions of liquid aromatics) when traditional solvents are either unnecessary or unwanted. Another example is the reaction of halide ions in molten tetrapentylammonium salts (Gordon, M.; Varughese, P. *Chem. Commun.* **1971**, 1160). (b) A previous study<sup>2d</sup> has shown the mechanism of deamination to be the same at 25 and 80 °C.

<sup>(8)</sup> Pouchert, C. J. *The Aldrich Library of NMR Spectra*; The Aldrich Chemical Co.: Milwaukee, WI, 1998; Vol. I.

Table 1.Solubility (M) of Selected Sodium Salts in<br/>Methanol at 25 and 70 °C

salt	solubility	
	25 °C	70 °C
NaCN	0.7	2.2
$NaN_3$	0.5	1.1
NaOAc	2.0	2.6

mal solvent perturbations. The observations, however, show that the deaminative approach is also unsuitable for generating appreciable yields of products from the interaction of benzyl cations and external, nonsolvent nucleophiles.

It would appear that the carbenium ions generated by deamination, though essentially "uncomplexed" on formation,<sup>1,2</sup> are not "free" to pursue the theoretical range of reactions with all available nucleophiles. There appear to be only two species with significant opportunity to intercept these carbenium ions: (1) the counterion, which is trapped with it in the cage and which from a previous study<sup>1c</sup> leads to a minimum of 20% product, and (2) the solvent molecules that form the cage.<sup>1,2</sup> Even in solutions saturated with them, highly nucleophilic ions do not compete well against either of these favored nucleophiles. This behavior ostensibly arises due to the statistical limitations imposed on nonsolvent, external nucleophiles (= solutes) because of their finite solubilities in the solvent of choice (traditional or nitrosoamide). Thus, the highly reactive deaminatively generated carbocation essentially reacts in a statistical manner with the nucleophiles to which it is exposed during its brief insulation from its counterion. The preponderance of solvent molecules over other nucleophiles in the medium places a cap on the ability of the latter (no matter how high its nucleophilicity) to intercept the cation. There also appears to be threshold nucleophilicity/concentration below which solute-derived products are not observed. Thus, in the competition vs solvent (when present) and counterion, cyanide is probably favored over azide because of the larger concentration of its sodium salt at saturation and its inherently greater nucleophilicity. Interestingly, although [AcO<sup>-</sup>] is larger than [CN<sup>-</sup>] at saturation (Table 1), its lower nucleophilicity, which is likely even further compromised by extensive hydrogen bonding to MeOH or by strong ion-dipole bonds to the N-nitroso moiety (when NBNNP is solvent), must be responsible for its nonappearance in the benzyl products.

It should be pointed out, however, that if the added nucleophile is miscible with the solvent (e.g.,  $D_2O$  with  $CD_3CN^{1d}$ ) the yield of products due to this nucleophile is proportional to its mole fraction,<sup>1d</sup> indicative of the statistical nature of the reactions of these carbenium ions.

A Note on Lifetime-Imposed Limitations on Carbocation Selectivity. An impressive body of work exists on the lifetimes of deaminatively and solvolytically generated carbocations.<sup>6d-g</sup> These studies indicate that, whereas the methyl cation may react with nucleophiles from within an encounter complex without traversing an energy barrier, as substitution of the methyl cation by electron releasing groups occurs, true barriers arise.<sup>6d</sup> These barriers for carbocation–nucleophile combination reactions are much smaller for inductively stabilized ions than for resonance stabilized ones such as the benzyl cation.<sup>6e</sup> Further, a similarity in the reaction barriers for inductively stabilized cations results in a lack of selectivity of such cations to a variety of nucleophiles (solvent + solute).<sup>6f</sup> By contrast, the benzyl cation would be expected to show less selectivity between nucleophiles resulting in appreciable amounts of varied nucleophile-derived benzyl species when an assortment of nucleophiles compete for the benzyl cation.<sup>6e</sup>

That solute-derived products are virtually absent from the reaction in the present case is instructive and consistent with the cations' fleeting existence. Lifetimes of  $10^{-12}-10^{-14}$  s (i.e., around the time for a bond vibration) have been determined for substituted benzyl cations from solvolyses of substituted benzyl chlorides in watertrifluoroethanol mixtures;6g lifetimes of deaminatively generated 2-propyl, cyclobutonium, and 2-adamantyl and other (nonresonance stabilized) ions have been clocked at  $\sim 10^{-10} - 10^{-9}$  s in similar solvents.<sup>6f</sup> It is apparent, therefore, that the lifetime of the deaminatively generated carbocation is so short that it reacts with the more abundant and favorably positioned solvent molecules and nascent counterion before it can diffuse to encounter added solutes. Thus, the virtual specificity of the deaminatively generated benzyl cation for its nascent counterion and the solvent is a boundary condition imposed upon it by its short lifetime and ostensibly heightened by both the cage in which the cation is generated and the statistical limitation on the availability of solute ions.

Apart from the unlikely diffusion of the short-lived carbocation (or any intermediate preceding it) into the medium and chance collision with added solute, there remains one other option for cation-solute interaction. Ostensibly, ion-dipole interactions between the solute and the polar nitrosoamide may exist and persist during the nitrosoamide's decomposition. Hence, at the moment of formation of the cation, the solute ions are present in the solvent cage (originally housing the nitrosoamide and the adventitious solute) and so positioned for interaction with the cation. To the extent that these preassociation complexes are responsible for solute-derived products then low product yields would be obtained because the association constants for the formation of substrate-solute complex are likely to be small and the benzyl cation is not a "free" intermediate to the extent that its lifetime is too short to allow for diffusion through the medium.<sup>6a,c,g</sup>

A Final Note on Azide–Carbocation Noninteraction. A significant body of information on the nature and properties of carbocations in intimate- and solventseparated ion pairs has been obtained from studies in which carbocationation has occurred in the presence of dissolved azide ions.<sup>9</sup> These data were gleaned from studies determining the yield and stereochemistry of alkyl azides derived from azide–carbocation reaction. It is worth mentioning here that the use of azide or other nucleophilic salts in deaminative systems would evidently yield limited information because of the inability of the deaminative carbocations to interact with these ions in a meaningful fashion.

### **Summary**

The present, novel observation of low yields of solutederived product from deaminatively generated carbocations and the previously observed statistical interception of  $D_2O$  are consistent with the short lifetimes of

<sup>(9) (</sup>a) Richard, J. P.; Rothenberg, M. E.; Jencks, W. P. J. Am. Chem. Soc. **1984**, 106, 1361. (b) Richard, J. P.; Jencks, W. P. J. Am. Chem. Soc. **1984**, 106, 1373. (c) Richard, J. P.; Jencks, W. P. J. Am. Chem. Soc. **1984**, 106, 1383.

NESIPs,<sup>1,2</sup> and the superior positioning of the native gegenion with respect to the deaminatively generated carbenium ion.<sup>1,2</sup> It would appear that the yields of products from these reactions are controlled by the short lifetime of these carbocations as well as cage effects in deamination. They do, however, force the reevaluation of the term "essentially free carbenium ions" that has been used<sup>1,2</sup> in connection with these ions since it is clear from the present study that the ions though relatively uncomplexed initially, are "fated" to appreciable reaction only with counterion and nucleophilic solvent and are thus not "free" in this regard.

Ostensibly, the carbocation enters into bimolecular reaction with solvent at a rate that is significantly larger than diffusional encounter with nucleophilic solute. Thus solute-cation adducts can only form by virtue of solutes present in a preassociation complex between the added solute and the starting nitrosoamide. These complexes are likely to be transient and present in small amounts and hence very small yields of solute-derived products are observed.

#### **Experimental Section**

Materials and Methods. All commercial reagents were reagent grade and were used without further purification. Spectra were recorded on 300 MHz FT-NMR, FT-IR, and UVvis spectrometers. GC data were obtained using an HP-5 crosslinked 5% Ph Me capillary column (30 m  $\times$  0.25 mm  $\times$  0.25  $\mu$ m) at 150 °C, 8.1 psi (carrier gas = He; FID detector).

Stability of the Precursors: Handling and Storage. N-Benzyl-N-nitrosopivalamide in addition to being photolabile and thermolabile is unstable in the presence of acids, bases, and moisture. As a result, the dry, neutral oil was stored in a desiccator in liquid N<sub>2</sub>. The compounds used in this study could be stored in this fashion indefinitely. The half-life of NBNNP is ~15 min at 25 °C in MeOH. All compounds were handled in the dark. Caution! N-Nitrosoamides should be handled with extreme care because of their possible mutagenicity<sup>10a</sup> and carcinogenicity (local and systemic).<sup>10b</sup> Efficient fume hoods and appropriate personal protection (chemical-resistant gloves, safety glasses, lab coat, etc.) are recommended when handling these compounds.

**N-Benzylpivalamide** was prepared from the method of Heyns and von Bebenburg:11a mp 81-82 °C (lit.11b mp 81-82 °C); IR (KBr) 3309, 1689, 1510, 1390, 1375 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ 1.27 (s, 9H), 4.44 (d, 2H, J = 7 Hz), 5.90 (bs, 1H), 7.26–7.32 (m, 5H); UV (ET<sub>2</sub>O)  $\lambda_{max} = 284$  nm ( $\epsilon = 209$ ).

N-Benzyl-N-nitrosopivalamide (1). A mixture of Nbenzylpivalamide (95.5 mg, 0.5 mmol), NaOAc (250 mg, 3.0 mmol), and Na<sub>2</sub>SO<sub>4</sub> (0.5 g) was dried at oil pump vacuum. Methylene chloride (3.0 mL), freshly distilled from P<sub>2</sub>O<sub>5</sub>, was added to the solid material (under  $N_{2})\!,$  and the suspension was cooled to -78 °C. A solution of N<sub>2</sub>O<sub>4(l)</sub> (0.2 mL, 3.1 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (1.0 mL) at -78 °C was then added to the stirred suspension at -78 °C, which was then allowed to warm to -25°C over 10 min. After a further 15 min at -25 °C, the suspension was evaporated in vacuo for  $\sim 15$  min until a lemon yellow color was observed. Ether at -20 °C was then added, and the suspension was washed in turn with saturated solutions of NaCl, Na<sub>2</sub>CO<sub>3</sub>, and NaCl at -5 °C. The organic phase was dried over  $Na_2SO_4$  at -30 °C and then evaporated in vacuo (at -30 °C) to yield 0.11 g (0.5 mmol, 100%) of a lemon yellow oil. The synthesis and isolation were performed in the dark: IR (neat) 1720, 1605, 1502, 1390, 1375 cm<sup>-1</sup>; <sup>1</sup>H NMR (CD<sub>3</sub>CN) & 1.45 (s, 9H), 4.97 (s, 2H), 7.05-7.40 (m, 5H); UV  $(CH_2Cl_2) \lambda_{max} 275 \text{ nm} (\epsilon = 500), 400 \text{ nm} (\epsilon = 63) 394 \text{ nm} (sh),$ 422 nm ( $\epsilon = 66$ ).

Decomposition of N-Benzyl-N-nitrosopivalamide (1): (a) In Saturated Methanolic Solution. In an Opticlear vial equipped with a stir bar was dissolved a calculated excess of the appropriate sodium salt (acetate, azide, or cyanide) in 500  $\mu$ L of methanol until solid remained. Approximately 50 mg of 1 was then added with stirring, and the vial was closed and incubated in the dark at the desired temperature until decomposition was complete (overnight at 25 °C or 4 h at 70 °C). The solution was then filtered and treated as described above. For the acetate and azide salts at both temperatures and for NaCN at 25 °C, the <sup>1</sup>H NMR spectra showed only benzyl pivalate and benzyl methyl ether in 1:3 ratio as above. However, for saturated methanolic NaCN, a new signal at  $\delta$ 3.69 was observed. The sample was spiked with commercial benzyl cyanide when selective growth of the  $\delta$  3.69 signal was observed. (b) In the Absence of Solvent. These runs were set up in the same fashion as just described except that  $\sim 250$ mg of **1** was used as solvent and reagent. At the end of the runs, the samples were filtered, an aliquot was dissolved in CDCl<sub>3</sub>, and <sup>1</sup>H NMR spectra were taken. For the acetate and azide salts at both temperatures, the <sup>1</sup>H NMR spectra showed only benzyl pivalate. However, for saturated NaCN, benzyl pivalate ( $\delta$  5.2,<sup>8</sup> 1.27; 99.9%), benzyl cyanide ( $\delta$  3.69,<sup>8</sup> trace), o-tolunitrile ( $\delta$  2.39,<sup>8</sup> trace), and p-tolunitrile ( $\delta$  2.35,<sup>8</sup> trace) were observed from the runs at 25 °C. From the 80 °C runs the product distribution was benzyl pivalate (99.7%), benzyl cyanide ( $\sim 0.2\%$ ), *o*-tolunitrile ( $\sim 0.07\%$ ), and *p*-tolunitrile (~0.03%).

Determination of Solubility of Sodium Salts in Methanol. Aliquots of a known excess mass of the appropriate anhydrous salt were added in portions with stirring to methanol (10 mL) in an Erlenmeyer flask in water baths at 25 and 70 °C. After saturation (as evidenced by the appearance of undissolved solid), a heated pasteur pipet with a cotton wool plug at the end was used to remove the methanolic solution, and the solvent volume was measured. The mass of the added salt was determined by the difference between that of the original excess and that of the final ("unadded") mass. The undissolved residue in the flask was weighed and its mass was used to correct that required for saturation. From the volume of methanolic solution and the corrected mass of added solute, the solubilities of the salts in g  $mL^{-1}$  were determined (Table 1).

Gas Chromatographic Detection of the Isomeric Tolunitriles and Benzyl Cyanide. Aliquots of product mixtures from the reactions in saturated NaCN were diluted in ether and determined by gas chromatography. Signals at  $t_{\rm R} = 5.0$ , 5.3, and 5.8 min corresponding to the retention times of the commercial *o/p*-tolunitriles and benzyl cyanide, respectively, were observed. No signal at  $t_{\rm R} = 5.2$ , for *m*-tolunitrile, was detected. The yields of the nitriles were very low, and no reproducible ratios could be determined (although the compounds were always detected above the baseline noise).

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