A Study of Electronic Effects on the Kinetics of Thermal Deamination of *N*-Nitrosoamides

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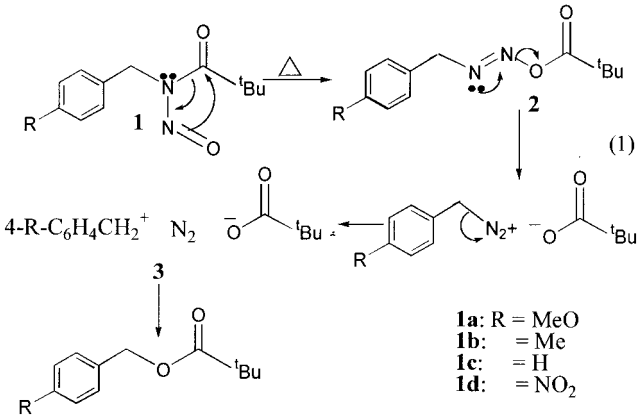
N-4-R-Benzyl-*N*-nitrosopivalamides (**1a**−**d**; R = MeO, Me, H, NO_2) were allowed to decompose at 18 °C in C_6D_{12}, $CDCl_3$, CD_3CN, and d_6-DMSO, and the rates of decomposition were followed by ^1H NMR spectroscopy. The half-lives of the nitrosoamides were found to vary in a systematic way with the nature of the R group on the aromatic nucleus. Electron-releasing groups were found to decrease the stability of the starting nitrosoamide, whereas electron-withdrawing ones increased the nitrosoamides' thermal stability. A Hammett-type plot of log(rate constants of deamination) vs σ_p was linear ($R^2 = 0.986$) with a ρ-type value of −0.90 indicating development of significant positive charge at the benzylic position in the transition state of the rate-determining step. The thermal stability of the nitrosoamides was also found to be systematically affected by the polarity of the solvent: as the solvent polarity increased, so did the lability of the nitrosoamides. This observation of intra- and intermolecular electronic perturbations of the kinetics of nitrosoamide decomposition appears to be novel. A closer look at the rate-determining step of nitrosoamide thermolysis is made, and a mechanistic framework is proposed that accounts for both steric and electronic modulation of nitrosoamide stability as well as the greater thermal stabilities of the related *N*-nitrocarboxamides and *N*-nitrosotosylamides.

Introduction

N-Nitrosoamides are labile compounds of significant interest in medicine,[1a,b] biochemistry,[1c] industry,[1d] and organic chemistry.[1e−i] For example, they have been implicated in mutagenesis[1a] and carcinogenesis[1b] but have also been successfully employed in enzyme inhibition and active site mapping,[1c] as novel initiators of addition polymerization,[1d] in unique synthetic methods,[1e,f,g] and as probes for the elucidation of reaction mechanisms.[1h−j]

N-4-R-Benzyl-*N*-nitrosopivalamides (**1a**−**d**), thermolyze unimolecularly[2] to generate very short-lived *n*itrogenous *e*ntity-separated *i*on-*p*airs[1k] (NESIPs;[1k] **3**) containing reactive 4-R-benzyl cations and pivalate ion (eq 1).[1d−i,2,3] Since the benzyl cation is incapable of rearrangements, fragmentations, and proton loss, S_N1-type reaction with the counterion (to yield ester) and any sufficiently nucleophilic solvent (to yield solvent-derived products = SDPs) is its only fate. When the solvent is nonnucleophilic to the carbocation under consideration, e.g., the 4-R-benzyl cations with $CDCl_3$,[3a] then the only product of significance (usually >99%) is the ester.[3a,4a]



(1)

Almost half a century ago, the kinetics of *N*-alkyl-*N*-nitrosoamide thermolyses were found to depend on steric factors.[2] Thus, as the alkyl and acyl portions of the nitrosoamide become bulkier, the nitrosoamides become less stable (e.g., the half-life of *N*-benzyl-*N*-nitrosoacetamide at 25 °C in benzene is ∼1 month, but that of the

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(1) (a) Lee, K.; Gold, B.; Mirvish, S. *Mutat. Res.* **1977**, *48*, 131. (b) Preussman, R.; Stewart, B. W. *Chemical Carcinogenesis;* Searle, C., Ed., ACS Monograph No. 182, American Chemical Society, Washington, DC, 1984; p 643. (c) White, E. H.; Jelinski, L. W.; Politzer, I. R.; Branchini, B. R.; Roswell, D. R. *J. Am. Chem. Soc.* **1981**, *103*, 4231. (d) Darbeau, R. W.; Delaney, M. S.; Ramelow, U.; James, K. R. *Org. Lett.* **1999**, *1* (*5*) 796. (e) White, E. H.; De Pinto, J. T.; Polito, A. J.; Bauer, I.; Roswell, D. F. *J. Am. Chem. Soc.* **1988**, *110*, 3708. (f) Darbeau, R. W.; White, E. H. *J. Org. Chem.* **1997**, *62*, 8091. (g) Darbeau, R. W.; White, E. H.; Nunez, N.; Coit, B.; Daigle, M. *J. Org. Chem.* **2000**, *65*, 1115. (h) White, E. H.; Darbeau, R. W.; Chen, Y.; Chen, D.; Chen, S. *J. Org. Chem.* **1996**, *61*, 7986. (i) Darbeau, R. W.; White, E. H. *J. Org. Chem.* **2000**, *65*, 1121. (j) M.S. Thesis by Rebekah E. Gibble, 2001, McNeese State University, Lake Charles, LA. (k) Previously referred to as nitrogenous molecule-separated ion-pairs and inert molecule-separated ion-pairs (NSIPs and IMSIPs, respectively).[1d,f,g−i]

(2) (a) Huisgen, R.; Ruchardt, C. *Justus Liebigs Ann. Chem.* **1956**, *601*, 1. (b) White, E. H.; Dolak, L. A. *J. Am. Chem. Soc.* **1966**, *88*, 3790.

(3) (a) Darbeau, R. W.; White, E. H.; Song, F.; Darbeau, N. R.; Chou, J. C. *J. Org. Chem.* **1999**, *64*, 4 (*16*), 5966. (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) Song, F.; Darbeau, R. W.; White, E. H. *J. Org. Chem.* **2000**, *65*, 1825.

(4) (a) A minor reaction accompanying thermolysis is denitrosation. For nitrosopivalamides this pathway is not competitive.[4f] (b) Ph.D. Thesis by Ron W. Darbeau, 1996, The Johns Hopkins University, Baltimore, Maryland. (c) Darbeau, R. W.; Gibble, R. E.; Pease, R. S. *J. Chem. Soc., Perkin Trans. 2,* in press. (d) Darbeau, R. W.; Gibble, R. E.; Pease, R. S. *J. Chem. Soc., Perkin Trans. 2,* in press. (e) Darbeau, R. W.; Song, F.; Gallo, A., manuscript in preparation. (f) Darbeau, R. W.; Perez, E. V.; Rose, W. A.; Sobieski, J. I.; Yates, M. C.; Boese, B. J.; Darbeau, N. R. *J. Org. Chem.,* accepted. (g) A semilog plot of k vs σ_p was also linear ($R^2 = 0.999$).

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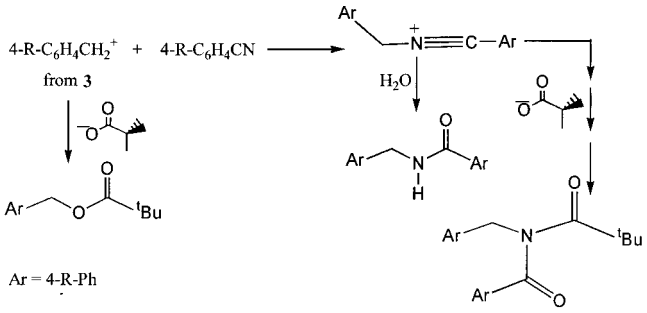
Scheme 1. Reaction Pathways for Deaminatively Generated 4-R-Benzyl Cations in Benzonitriles[4c,d]

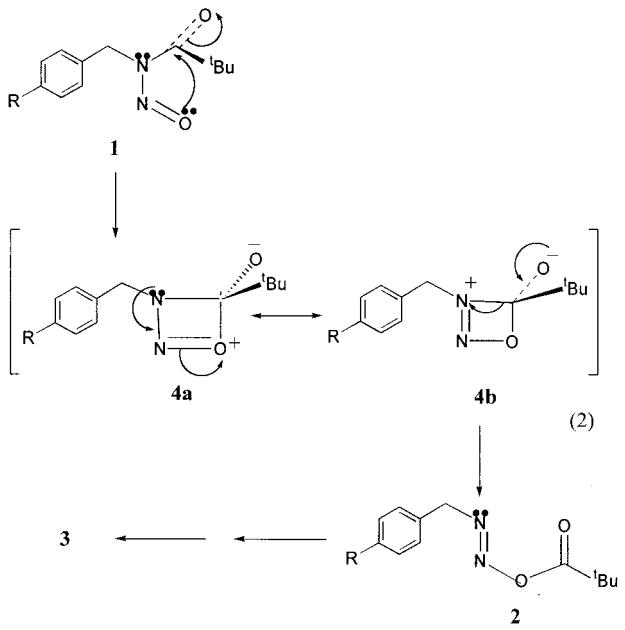


corresponding pivalamide (= trimethylacetamide) under the same conditions is ~2 h).[4b] The explanation of this observation ostensibly lay in the relief of steric strain between the alkyl and acyl groups as the nitrosoamide moiety rearranges into the labile *trans*-diazotate ester (**2**) during the rate-determining first step of nitrosoamide thermolysis (eq 1).[3a,b]

We have recently studied the formation of mixed diacylamines from the deamination of *N*-4-R-benzyl-*N*-nitrosopivalamides in 4-R-benzonitriles (Scheme 1).[1j,4c,d] Those investigations indicated that the nature of the R-group on the aromatic nucleus derived from the nitrosoamide significantly and systematically affected the interception of the nitrilium ion by the available nucleophiles.[1j,4c,d] Electron-releasing groups (ERGs) decreased the nitrilium ion's reactivity, whereas electron-withdrawing groups (EWGs) appeared to enhance the susceptibility of the onium ion to nucleophilic attack.[1j,4c,d]

These results are interesting in the context that *para*-substituents are able to modulate the electrophilicity of the carbon atom seven positions away and separated by an sp^3-hybridized site so that simple conjugation is not possible. It may be argued though that the polarizability of the aromatic nucleus and the paucity of electron density at the benzylic carbon due to its attachments to the aromatic ring and to a positively charged sp-hybridized nitrilium N may facilitate transmission of the electronic "information" between the *para*-substituent and the nitrilium C.[4e]

The rate-determining step (RDS) of the thermal rearrangement of nitrosoamides e.g., *N*-4-R-benzyl-*N*-nitrosoamides is believed to be the first step that results in the formation of the *trans*-diazotate ester (**2**; eq 1).[1c−i,2,3] Very little has been published concerning the details of this transformation, however.[5a] It is conceivable that it proceeds via a four-membered, oxadiazetyl-type entity (**4**, eq 2)[5a,b] in which the benzyl carbon is adjacent to a hypervalent, positively charged nitrogen atom[5b] similar to that in the nitrilium ion from the deaminations in benzonitriles.[1j,4c,d] It would appear therefore that if 4-R-groups could affect the kinetics of the nitrilium ion then they may effect a similar mediation of the stability of the postulated TS of the purported RDS of nitrosoamide thermolysis.



The present study was aimed at testing the validity of this hypothesis. It involved spectroscopic determinations of the rates of decompositions of a series of *N*-4-R-benzyl-*N*-nitrosopivalamides in various solvents at constant temperature. Nitrosopivalamides **1a**−**d** were used as the source of the 4-R-benzyl cations in this study because of their convenient rates of decomposition,[1g,4c,d] the absence of side reactions,[3,4a,f] and because variation of the R-group allowed systematic examination of any operating intramolecular electronic effects.

Results and Discussion

Decomposition of *N*-4-R-Benzyl-*N*-Nitrosopivalamides (1a−d) in $CDCl_3$. Compounds **1a**−**d** were allowed to decompose in chloroform-*d* ($\epsilon = 4.80$, $\pi^* = 0.58$),[6] at 18 °C and the decompositions were followed by ^1H NMR spectroscopy (Table 1).[7] Decompositions of **1a** were also performed in cyclohexane ($\epsilon = 2.0$, $\pi^* = -0.04$),[6] acetonitrile ($\epsilon = 35.9$, $\pi^* = 0.75$),[6] and DMSO ($\epsilon = 46.5$, $\pi^* = 1.00$),[6] to probe the effects, if any, of external electronic (substrate−solvent) interactions (Table 2).[7]

(5) (a) Huisgen (Huisgen et. al. *Liebigs Ann. 562*, 137 and Huisgen et. al. *Liebigs Ann. 574*, 157) investigated the thermolyses of *N*-nitroso-*N*-4-R-acetanilides in which 4-R-aryl (not benzyl) groups were present. He believed that in these thermolyses, fragmentation of the diazotate ester resulted in acyl rather than aryl cations. Since Huisgen's work, extensive studies (e.g., Ruchardt, C.; Tan, C. C.; Freudenberg, B. *Tetrahedron Lett.* **1968**, *37*, 4019., Hassmann, V.; Ruchardt, C.; Tan, C. C. *Tetrahedron Lett.* **1971**, *42*, 3885, and Ruchardt, C.; Tan, C. C. *Angew. Chem., Int. Ed.* **1970** *9* (7), 522) have demonstrated that aryl diazoacetates also ionize into diazonium cations and acetate ions. In the aryl case, however, the products generated from this ion-pair are formed by homolytic pathways. Compared to the current study, these reactions showed remarkably little sensitivity (~15%) to the nature of the R group and to the polarity of the solvent. Huisgen suggested the presence of a resonance-stabilized oxadiazetyl species as the TS in the nitrosoamide → diazotate ester isomerization. This postulation was apparently not based solely upon the modulation of the reaction kinetics by solvents or substituents since such modulation was small. (b) The resonance forms **4a** and **4b** are likely to be of similar energy so the structure of true **4**, intermediate or activated complex, is probably one with charge delocalization and partial deposition of positive charge on both the oxadiazetyl O and the N more proximal to the benzylic carbon. (c) The entity **6** is likely to be unstable because of ring strain and charge separation as is **4** but also because two of the three resonance forms shown possess tremendous electronic instability because of the proximity of the positive charges. Thus **6** is both sterically and electronically activated.

(6) (a) The π^*_{azo} value is a general dipolarity/polarizability index that gauges the ability of a solvent to stabilize an ionic or polar species by means of its dielectric effect. Values of π^* are based upon the solvochromatic parameters of azomerocyanine dyes.[6b,c] (b) Kamlet, M. J.; Aboud, J.-L. M.; Abraham, M. H.; Taft, R. W. *J. Org. Chem.* **1983**, *48*, 2877. (c) Buncel, E.; Rajagopal, S. *Acc. Chem. Res.* **1990**, *23*, 226 and references therein.

(7) See "Supplemental Information" for more support data and plots.

Table 1. Kinetic Data from the Decomposition of *N*-4-R-Benzyl-*N*-nitrosopivalamides in Chloroform-*d*[a] at 18 °C[7]

R	rate constant ($\times 10^{-3}$ s^{-1})	half-life (min)	σ_p
MeO	8.56	81	−0.27
Me	7.39	94	−0.14
H	6.43	108	0.00
NO_2	1.05	660	0.78

[a] [Nitrosoamide] ~ 0.045 M.

Table 2. Kinetic Data from the Decomposition of *N*-4-Methoxybenzyl-*N*-nitrosopivalamide in Various Solvents[a] at 18 °C[7]

solvent[b]	ϵ[c]	π^*[d]	rate constant ($\times 10^{-3}$ s^{-1})	half-life (min)
cyclohexane	2.00	−0.04	2.54	273
chloroform	4.80	0.58	8.56	81
acetonitrile	35.9	0.75	20.6	34
DMSO	46.5	1.00	34.6	20

[a] [Nitrosoamide] ~ 0.045 M. [b] Deuterated solvents used. [c] Values from ref 6c. [d] Values from refs 6b,c.

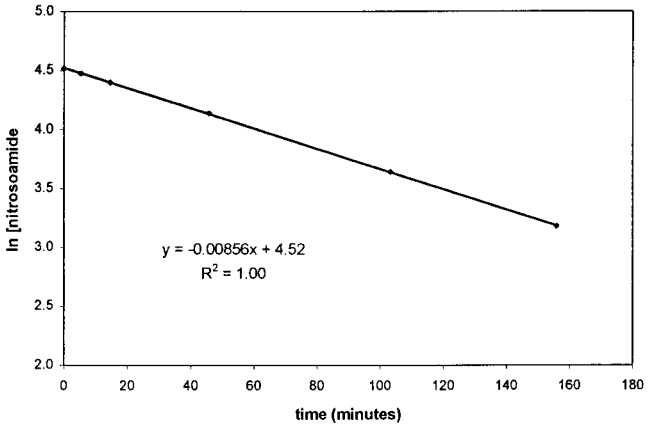


Figure 1. Plot of ln(% **1a**) vs time for decomposition of *N*-4-MeO-benzyl-*N*-nitrosopivalamide (**1a**) in chloroform-*d* at 18 °C.

For the decompositions in $CDCl_3$, the product distribution as a function of time was determined by ^{1}H NMR spectroscopy, looking specifically at the benzylic methylene protons of the product esters (~ δ 5.2) and the starting nitrosoamides (~ δ 4.9) (Table 1). Plots (e.g., Figure 1)[7] of the data (Table 1)[7] using ln(% nitrosoamide) vs time (min) yielded straight lines (R^2 values 0.997−1.000)[7] as would be expected of first-order kinetics.[2] From the rate constants for each decomposition, the half-lives were calculated and were found to vary systematically from 81 min for R = MeO, to 94 min for R = Me, to 108 min for R = H, and 660 min for R = NO_2 (Table 1). These data suggest that an intramolecular electronic component is present in nitrosoamide thermolyses to the extent that ERGs accelerate nitrosoamide thermolyses whereas EWGs stabilize the nitrosoamides.

A Hammet-type plot (Figure 2) of the log k (k = rate constants) for the thermolyses vs the σ_p values yields a straight line ($R^2 = 0.986$)[4g] with a "ρ" value of −0.90. The linearity of the plot confirms the existence of a correlation between electronic effects in the alkyl portion of the nitrosoamide and the latter's thermal stability. Further, the negative sign of "ρ" supports the notion of developing positive charge at the benzyl carbon in the transition state which would be the case during formation of the strained heterocylic moiety **4**.[5a,b] Ostensibly then, ERGs stabilize the developing +ve charge at the benzyl carbon in the TS thus facilitating the thermolysis; the converse is true of EWGs.

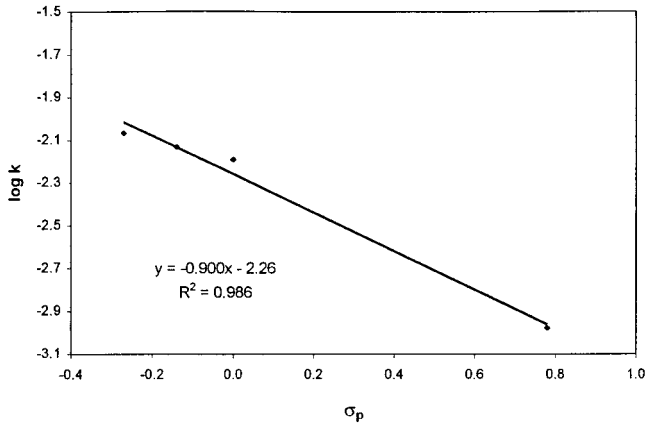


Figure 2. Hammett-type plot of log k vs σ_p for decomposition of *N*-4-R-benzyl-*N*-nitrosopivalamides (**1a**−**d**) in chloroform-*d* at 18 °C.

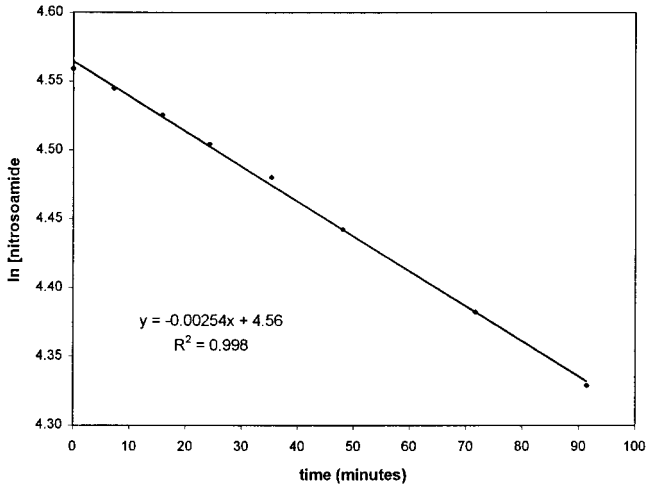


Figure 3. Plot of ln(% **1a**) vs time for decomposition of *N*-4-MeO-benzyl-*N*-nitrosopivalamide (**1a**) in cyclohexane-d_{12} at 18 °C.

Decomposition of *N*-4-Methoxybenzyl-*N*-Nitrosopivalamide (1a) in Solvents of Varying Polarity. The importance of the internal electronic perturbation of the stability of **4** to the kinetics of nitrosoamide thermolyses would suggest that similar modulation by external factors might occur. Since there is significant charge separation involved in going from **1** to **4**, then increasing the polarity of the medium would ostensibly preferentially stabilize **4** (regardless of whether it is an intermediate or an activated complex) leading to an enhancement in the rate of thermolysis.

To investigate this effect, the most labile of the nitrosoamides (**1a**) was allowed to decompose at 18 °C in solvents of varying polarity (cyclohexane, chloroform, acetonitrile, and DMSO; Table 2; e.g., Figure 3).[7] The data (Table 2) show that as the solvent polarity rises, the rate of decomposition also rises. Indeed, plots (Figure 4) of log k vs log ϵ and vs π^*[6] for decompositions of **1a** are linear ($R^2 = 0.939$ and 0.971, respectively) confirming the correlation between solvent polarity and the rate of nitrosoamide decomposition.

The observation of significant inter- and intramolecular electronic modulation of nitrosoamide stability to thermolysis appears to be novel[5a] *and complements the previously observed steric modulation of the reaction.*[2]

The Nature and Age of Species "4" and a Mechanistic Framework for Rationalization of Steric and

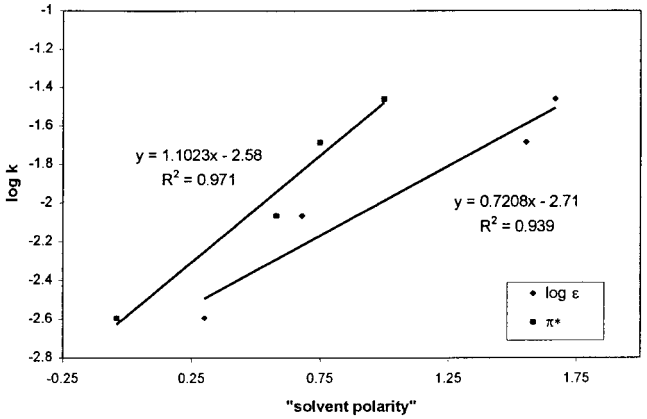


Figure 4. Overlay plot of log k for thermolyses of *N*-4-MeO-benzyl-*N*-nitrosopivalamide (**1a**) in various solvents vs solvent polarity terms (log ϵ and π^*[6]).

Electronic Effects in Nitrosoamide Thermolyses. The enhancement of nitrosoamide thermolyses by ERGs in the alkyl portion of the nitrosoamide and by polar solvents supports the presence of a charge-separated entity such as **4** along the reaction profile of the RDS. Whether species **4** represents the activated complex (AC) between the starting nitrosoamide and the diazotate ester (**2**) of the RDS, or whether it is a true (but high energy) intermediate between those two extreme minima is an interesting question.

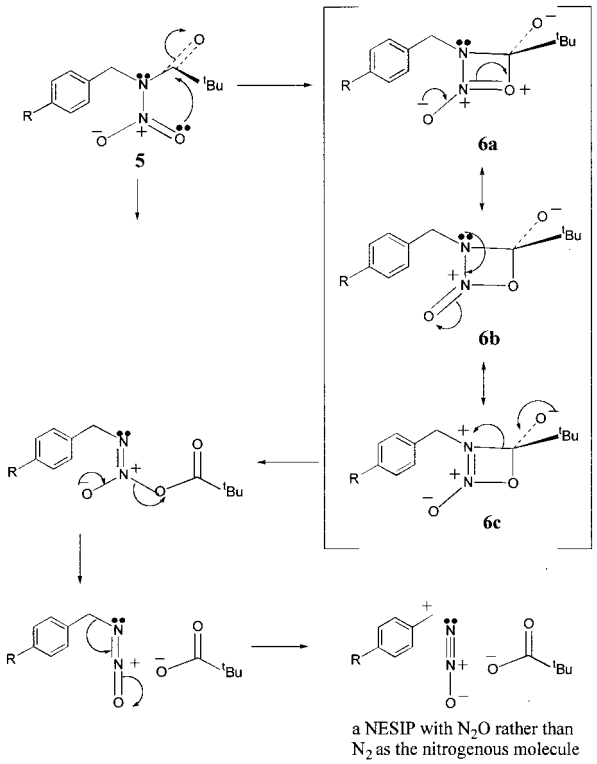
It is likely that the position (energy maximum or minimum) of **4** along the reaction profile between **1** and **2** that flank it will vary in degree depending upon the nature of R and the polarity of the solvent. Hence it is more likely to be atop the lone energy barrier between **1** and **2** when R = NO_2, but may slip into an energy well preceding the diazotate ester when R = MeO. Similarly, in nonpolar media that are unable to stabilize **4**, the entity is likely to crest the reaction profile but will occur later along it in polar solvents. If **4** is the activated complex of the lone step converting **1** → **2**, then its stabilization (by ERGs in polar media) would hasten nitrosoamide thermolyses as observed. If instead **4** is a high energy intermediate between **1** and **2**, then from the Hammond−Leffler postulate, stabilization of the activated complex preceding it (by ERGs in polar media) would have the same effect. Thus regardless of the nature of **4** (intermediate of activated complex) its stabilization produces the rate enhancements observed.

While the presence of **4** in the RDS accounts for the observed electronic effects,[5a] an interesting question arises, however. How does the steric acceleration of nitrosoamide thermolyses arise? Previously, relief of steric strain around the *N*-nitrosoamido moiety (O═N−N−C═O) was thought to be responsible for the observed rate enhancement.[2] This interpretation is consistent with the marked difference in spatial separation of the acyl and alkyl R groups in the nitrosoamide and in the diazotate (eq 2). For example, computer molecular modeling gives the shortest distance between the closest benzylic H-methyl H pair (of the pivalyl group) as being 3.54 Å for the nitrosoamide and 3.90 Å in the diazotate ester.

If, however, the charge-separated, strained entity **4** does feature in the RDS (as is required to account for the observed electronic effects), then no relief of steric strain occurs when it is formed from the nitrosoamide. This would be so because although the relative stereochemistry of R and R′ are very similar in both structures, the distance between the benzyl Hs and the pivaloyl Hs is only1.98 Å for the heterocyclic species **4.** Ostensibly, then the system should actually suffer an *increase* in steric strain (due to ring strain and van der Waals strain) on going from **1** → **4**. To the extent that this is true, how then does an increase in the steric bulk of R and R′ manifest an acceleration of thermolysis?

The answer appears to lay in the following argument. The nitrosoamide is acyclic and possesses a significant degree of flexibility. The presence of bulky groups around the nitrosoamido moiety, will introduce steric strain where little had existed. Such groups would be expected to cause a significant increase in the energy of the thermal ground state of the nitrosoamide. However, species **4** is inherently energetic by virtue of its strained oxadiaxetyl ring, endocyclic double bond, and charge separation. Thus, although the introduction of bulky groups at R and R′ will raise the energy of **4**, the effect is not as dramatic as in the nitrosoamide precursor. Hence bulking up the R groups raises the nitrosoamide energy *more* than it does that of **4** (or the activated complex leading to it, if **4** is really an intermediate). The effect then is one of preferential destabilization of the ground-state rather than the TS of the RDS resulting in a decrease of the activation energy of the RDS and the observed steric acceleration.

The Relative Stabilities of *N*-Nitroso- and *N*-Nitroamides. *N*-Nitroamides, **5**, like their *N*-nitroso counterparts also undergo unimolecular thermolysis to generate a NESIP.[3a,8a] In this case, however, the nitrogenous molecule temporarily interspaced between the ion-pair is N_2O rather than N_2 as formed in the *N*-nitroso case (eqs 1, 3).[3a,8a] *N*-Nitroamide decomposition differs



(3)

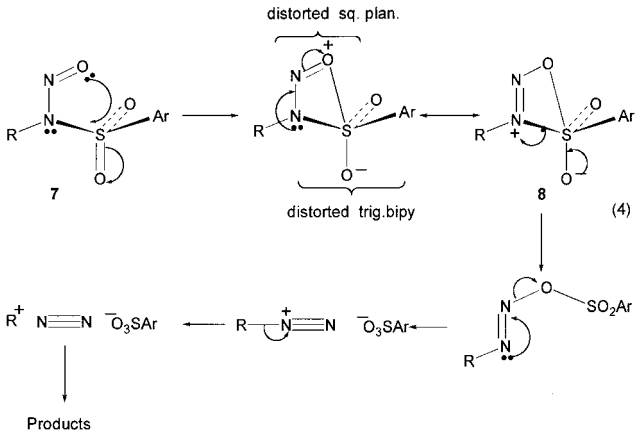
from nitrosoamide decomposition in two other principal ways: (1) the partitioning of the carbocation slightly

favors the solvent,[3a,4b] and (2) the *N*-nitroamides are less labile.[3a,4b,8a] The former difference may arise because of better shielding of the carbocation from its nascent counterion by the more massive and heavier N_2O (vs N_2)[8b] which allows the cation more opportunity to scavenge molecules in the solvent cage leading to enhanced yields of SDP.[3a]

A reasonable interpretation of the greater thermal stability of the *N*-nitroamides follows. It is likely that *N*-nitroamides, rearrange in a fashion similar to their nitroso analogues and that this rearrangement proceeds via a corresponding four-membered species, **6** (eq 3) that is analogous to species **4** (eq 2). In this case, however, **6** is a significantly unstable entity due to contributions from the resonance forms **6a** and **6c** in which positive charges reside on adjacent atoms connected via short N═X (X = N, O) bonds. Interestingly, while resonance form **6b** is analogous to species **4a**,**b**, there is no corresponding destabilizing resonance form of **4** that is analogous to **6a**,**c**.[5c]

Fundamentally, therefore, the energy gap between **5** and **6** is larger than that between **1** and **4** and, regardless of whether **4** and **6** are intermediates or transition states, the result would be that the **5** → **6** conversion would be less facile than the corresponding **1** → **4** reaction. Consequently, *N*-nitroamides are more thermally stable than *N*-nitrosoamides as observed.[3a,8a]

The Relative Stabilities of *N*-Nitrosocarboxamides and *N*-nitrosotosylamides. *N*-Nitrosotosylamides (**7**) are much less labile than their nitrosocarboxamide analogues.[4b] Assuming that the nitrosotosylamide to diazotate ester conversion traverses a pathway analogous to those above, then the thermostability of **7** would stem from preferential stabilization of **7** or destabilization of the corresponding TS/AC species, **8** (eq 4).



Species **8** (comparable to **4** and **6**, vide supra) would be expected to be highly energetic partly because of inherent ring strain but also because the rehybridization of the sulfur during the **7** → **8** conversion requires its change from a tetrahedral geometry to a severely distorted trigonal bipyramid. Indeed, **8** is likely to be very unstable (relative to **7**) because the thiaoxadiazetyl ring is a distorted square planar and the S is at the center of a severely distorted trigonal bipyramid (eq 4).

Summary

Novel evidence for the existence of an electronic modulation of the stability on *N*-alkyl-*N*-nitrosoamides have been presented. Electron-releasing groups and polar solvents accelerate *N*-nitrosoamide thermolysis whereas electron-withdrawing groups and nonpolar media enhance the thermal stability of the nitrosoamides. The identification of this electronic effect in *N*-nitrosoamide thermolysis complements the steric effects in the reaction observed almost a half century ago. Further, it allows workers in deamination chemistry to rationally and more efficiently exploit the decomposition of nitrosoamides as a route to carbocations.

A comprehensive mechanistic framework has been proposed that accounts for both the observed steric and electronic effects as well as the relative stabilities of *N*-nitroso-, *N*-nitrocarboxamides, and *N*-nitrosotosylamides. In this mechanism, a high energy, strained, four-membered, charge-separated heterocyclic entity lies between the *N*-nitrosoamide and the diazotate ester in the RDS. This oxadiazetyl moiety may be an intermediate or an activated complex and indeed, its age, duration, and character may depend on the direction and extent of electron drift to or from the diazetyl nucleus and the ability of the medium to stabilize the charge separation.

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 UV−vis spectrometers.

Stability of *N*-4-R-Benzyl-*N*-nitrosopivalamides: Handling and Storage. The *N*-4-R-benzyl-*N*-nitrosopivalamides are thermolabile and unstable in the presence of acids, bases, and moisture; being photolabile they were handled in the dark. The dry, neutral oils were stored in desiccators under N_2 in capped tubes immersed in liquid nitrogen. **Caution!** Nitrosoamides should be handled with extreme care because of their possible mutagenicity[1a] and carcinogenicity (local and systemic).[1b] Efficient fume hoods and appropriate personal protection (chemical-resistant gloves, safety glasses, lab coat, etc.) are recommended when handling these compounds.

***N*-4-R-Benzylpivalamides** were prepared from the method of Heyns and von Bebenburg.[9a] ***N*-4-Methoxybenzylpivalamide** mp 88−90 °C;[9b] IR (Nujol) 3331, 1636, 1538, 1518, 1461 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.25 (s, 9H), 3.78 (s, 3H), 4.35 (d, 2H, J = 7 Hz), 5.84 (bs, 1H), 6.82−7.20 (dd, 4H). ***N*-4-Methylbenzylpivalamide** mp 94−96 °C;[9b] IR (Nujol) 3334, 1636, 1536, 1518, 1461 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (s, 9H), 2.38 (s, 3H), 4.44 (d, 2H, J = 7 Hz), 5.87 (bs, 1H), 7.20 (s, 4H). ***N*-Benzylpivalamide** mp 81−82 °C (lit.[9a] mp 81−82 °C); IR (KBr) 3309, 1689, 1510, 1390, 1375 cm^{-1}; ^1H NMR ($CDCl_3$) δ1.27 (s, 9H), 4.44 (d, 2H, J = 7 Hz), 5.90 (bs, 1H), 7.26−7.32 (m, 5H). ***N*-4-Nitrobenzylpivalamide** mp 119−121 °C;[9b] IR (Nujol) 3359, 1641, 1518, 1462, 1377 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (s, 9H), 4.54 (d, 2H, J = 7 Hz), 6.08 (bs, 1H), 6.39−8.22 (dd, 4H).

***N*-4-R-Benzyl-*N*-nitrosopivalamides (1a−d)** were prepared from the method of described in refs 1b,c. ***N*-4-Methoxybenzyl-*N*-nitrosopivalamide (1a)**. IR (Neat) 1712, 1613, 1513, 1304, 1249, 1217 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.45 (s, 9H), 3.75 (s, 3H), 4.90 (s, 2H), 6.78−7.18 (dd, 4H). ***N*-4-Methylbenzyl-*N*-nitrosopivalamide (1b)**. IR (Neat) 1714, 1505,

(8) (a) Garcia, J.; Gonzalez, J.; Segura, R.; Urpi. F.; Vilarrasa, J. *J. Org. Chem.* **1984**, *49*, 3322. (b) The molecular diameters (σ) of N_2 and N_2O are 3.681 Å and 3.879 Å, respectively. (Bird, R. B.; Stewart, W. E.; Lightfoot, E. N. *Transport Phenomena*; Wiley: Chichester, 1960; p 744). The molecular volumes (V_M) were calculated using $V_M = (4/3)\pi r^3$: $V_M(N_2) = 26.115$ Å^3; $V_M(N_2O) = 30.560$ Å^3. Thus, N_2O is ~17% larger than N_2.

(9) (a) Heyns, K.; v. Bebenburg, W. *Chem. Ber.* **1953**, *86*, 278. (b) No references to these compounds have been found.

1482, 1398, 1333, 1217 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.42 (s, 9H), 2.28 (s, 2H), 4.90 (s, 2H), 7.12−7.12 (m, 4H). ***N*-Benzyl-*N*-nitrosopivalamide (1c)**. IR (Neat) 1711, 1605, 1526, 1348, 1216 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.45 (s, 9H), 5.01 (s, 2H), 7.05−7.40 (m, 5H). UV (CH_2Cl_2) λ_{max} 275 nm (ϵ = 500), 400 nm (ϵ = 63) 394 nm (sh), 422 nm (ϵ = 66). ***N*-4-Nitrobenzyl-*N*-nitrosopivalamide (1d)**. IR (Neat) 1720, 1605, 1502, 1390, 1375 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.45 (s, 9H), 4.97 (s, 2H), 7.05−7.40 (m, 5H).

Decomposition of *N*-Nitrosoamides (1a−d). In a typical run, ∼10 mg of the appropriate *N*-nitrosoamide, **1**, was added to 750 μL of the selected solvent in an NMR tube. The sample was then loaded into the NMR probe at 18 °C and a time = 0 ^1H NMR spectrum was taken. ^1H NMR spectra were recorded at intervals,[7] and the integrals of the 4-R-benzyl pivalates and undecomposed *N*-nitrosoamide were measured (Table 1).[7] In cyclohexane-d_{12}, $CDCl_3$, and d_6-DMSO the ester and *N*-nitrosoamide were the only benzyl compounds observed. In CD_3CN low yields of SDP[1g] were observed and were incorporated in the calculation of % nitrosoamide. Most runs remained at 18.0 °C throughout; the maximal observed variation in probe temperature during runs was 0.2 °C.

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Supporting Information Available: Sample kinetic data and plots for decompositions of **1a**−**d** in chloroform and for decomposition of **1a** in various solvents. This information is available free of charge via the Internet at http://pubs.acs.org.

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