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N-Nitrosoamide-Mediated N → O Nitroso Transfer to Alcohols with Subsequent Denitroxylation

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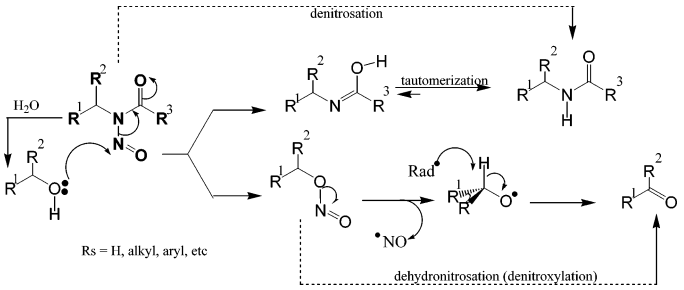

Decomposition of certain *N*-benzyl-*N*-nitrosoamides is often accompanied by small amounts of benzaldehyde whose formation was postulated to arise from in situ formation and oxidation of benzyl alcohol. Incubation of excess benzyl alcohol with thermostable *N*-benzyl-*N*-nitrosoamides at ambient temperatures in inert solvents generates benzyl nitrite, *N*-benzyl amides, and benzaldehyde as the major products. Benzyl nitrite formation appears to be linked to N → O nitroso transfer between the *N*-benzyl-*N*-nitrosoamides and benzyl alcohol, which is subject to the previously observed electronic and steric features of the acyl substituent although the former appears to play a much larger role than the latter. Benzaldehyde formation evidently arises from dehydronitrosation (denitroxylation) of the nitrite via O−N bond homolysis and H-abstraction from the resultant benzyloxy radical. Although trans-nitrosation occurs with methanol, 1°, 2°, and 3° alcohols, the reaction is evidently subject to steric effects at both the α and *β* carbons of the alcohol. Additionally, carbonyl formation only occurs with 2° alcohols and those that can derive resonance-stabilized carbonyls.

Introduction

Scientific and commercial interest in biological and medical aspects of nitric oxide and nitrosative−denitrosative phenomena, in general, have grown significantly in the last two decades.[1] NO, which is formed in vivo by the heme-based nitric oxide synthase (NOS) system, has a rich (bio)chemistry often centered around triggering the production of cGMP leading to smooth muscle relaxation,[1a,b] but diverse enough to include the physiological regulation of mitochondrial function and inhibition of cytochrome *c* oxidase.[1c] The former effect has medical implications ranging from maintaining a healthy cardiovascular system to treatment of erectile dysfunction;[1a,b] the implications of the latter effects are still under discussion.[1a−c] Several biologically active derivatives of NO appear to exist in vivo; among them are NO_2 and peroxynitrite.[1a−d] One of the more intriguing of these species, however, is nitroxyl (HNO), which "may play a significant role in biology and pharmacology, protecting the cardiovascular system [and] interacting with enzymes".[1a] Comparatively little is known about nitroxyl. It is evidently generated from nitric oxide in vivo by such species as xanthine oxidase[1e] and is more cytotoxic than NO; it also elicits biological responses analogous to those of NO and peroxynitrite.[1a−c] It is likely that nitroxyl (bio)chemistry will rise in prominence over the next decade.[1]

N-Alkyl-*N*-nitrosoamides are useful compounds that have been employed in multiple fields including organic syntheses,[2a−d] in enzyme inhibition and active site

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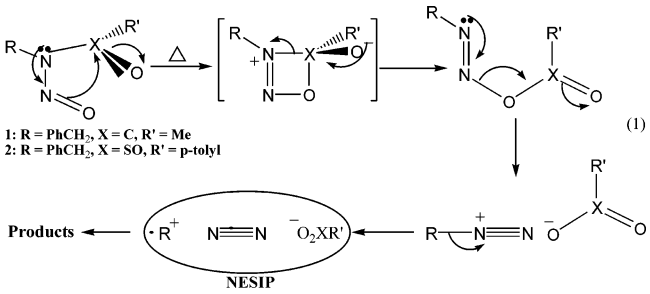
mapping,[2e] and as initiators of addition polymerization.[2f,g] Thermolysis of *N*-benzyl-*N*-nitrosoamides is a first-order reaction[3a−c] that proceeds via a metastable oxadiazetyl zwitterion,[3c] which relaxes into a *trans*-diazoester (eq 1).[3c]



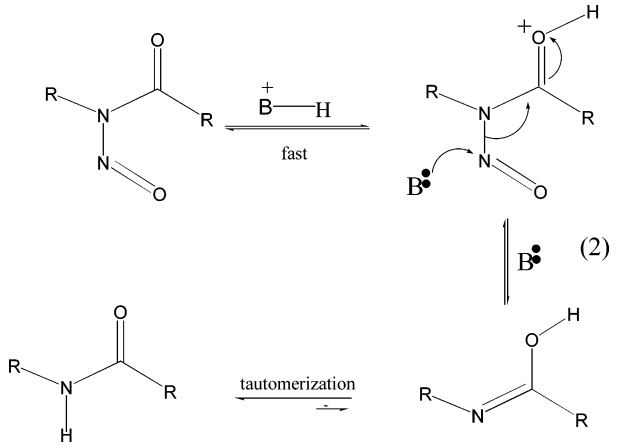
(1)

Fragmentation of the latter generates an intimate ion-pair containing a benzyldiazonium ion that dediazoniates into a nitrogenous-entity-separated ion-pair (NESIP; eq 1) the carbocation of which is extremely reactive.[3,4] The benzyl cation undergoes ion-pair collapse with its counterion when diffusion of the nitrogen molecule from the inter-ion space exposes the ions to each other.[3,4] This event may result in the clean generation of benzyl esters in the presence of inert solvents.[3d,e] If the solvent has a nucleophilicity above some threshold level (depending upon the electrophilicity of the cation), solvent-derived products (SDPs) may dominate the product mixture.[3e] During the cation's brief insulation from its counterion, cation−solvent interactions may occur resulting in the formation of as much as 80% solvent-derived product.[3f]

Trace products may arise during thermolysis; among these are *N*-benzyl amides from *N*-denitrosation.[3g] In general, the extent of *N*-denitrosation rises with the acidity of the acyl precursor of the amide (i.e., the electrophilicity of the amido unit),[3g] with decreasing bulk of the acyl group,[3g] and with increasing nucleophilicity of the denitrosating agent.[3g] Benzyl alcohol also arises during thermolyses and in organic media its formation has been traced to nitrosoamide hydrolysis by latent moisture whereas in aqueous systems it is linked to the capture of benzyl cations by water.[2b,3f]

The genesis of the present work is the hitherto unreported[3h] and unexplained formation of trace amounts of benzaldehyde during the deamination of certain *N*-benzyl-*N*-nitrosoamides.[2b] The observation of benzaldehyde in these reactions is interesting in the context that benzaldehyde formation would appear to be linked to the formation of benzyl alcohol and would require oxidation of the carbinyl carbon of the former to the carbonyl carbon of the latter. Two obvious questions arising from this sequence are the following: (1) What is the nature of the redox reaction involved especially since the oxidation does not extend to benzoic acid and (2) is the phenomenon unique to the *N*-benzyl-*N*-nitrosoamides (and presumably their benzyl alcohol hydrosylate) or does it extend to other alcohols as well?

We have previously shown that *N*-nitrosoamides undergo second-order *N*-denitrosations under near-neutral conditions in the presence of nucleophiles such as cyanide, iodide, and bromide.[3g] In this reaction, the substrate is protonated (or hydrogen bonds during electrophilic assistance) at the carbonyl-O;[3g] the oxonium ion then undergoes attack at the nitrosyl-N to derive the tautomer of the amide as well as the nitrosated nucleophile (eq 2).[3g]



(2)

To account for benzaldehyde formation in the present case, we postulated in situ nitrosation of hydrosylate benzyl alcohol to yield benzyl nitrite followed by dehydronitrosation (denitroxylation) of the latter to form benzaldehyde. The following report describes our efforts to test this hypothesis.

Results and Discussion

An obvious source of benzaldehyde is via oxidation of benzyl alcohol by dissolved oxygen present in the solvents. Thus, benzaldehyde-free benzyl alcohol was dissolved in $CDCl_3$ (undegassed) in an NMR tube and heated at 40 °C for 3 days. No reaction occurred as evidenced by the lack of any new signals in the ^1H NMR spectrum (most poignantly, no signal at δ 9.6 due to the aldehydic proton, or at ca. δ 11 due to the carboxyl-H of benzoic acid). The absence of PhCHO and/or $PhCO_2H$ under these conditions supports the notion that the alcohol to aldehyde conversion under the reaction conditions follows a less direct route than simple air-oxidation.

Benzaldehyde-free benzyl alcohol was then incubated with nitrosonium tetrafluoborate in $CDCl_3$ at 20 °C in an NMR tube and the reaction was followed by ^1H NMR

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TABLE 1. Relative Distribution of *N*-Benzyl-*N*-nitrosotoluenesulfonamide and Its Decomposition Products from Benzyl Alcohol-Promoted *N*-Denitrosation at 20 °C as a Function of Time

time (h)	relative distribution (%)					
	NTS[a]	ester[b]	amide[c]	BzONO[d]	PhCHO	$CHCl_3$
0	99.9	0.0	0.0	0.0	0.0	0.1
3	99.6	0.3	0.0	0.0	0.0	0.1
21	10.5	2.3	48.9	32.9	3.4	2.0
45	6.0	1.2	52.2	12.9	16.9	10.8
69	5.4	1.2	53.7	5.1	21.4	13.2

[a] *N*-Benzyl-*N*-nitrosotoluenesulfonamide (**2**). [b] Benzyl tosylate. [c] *N*-Benzyltoluenesulfonamide. [d] Benzyl nitrite.

spectroscopy. A rapid series of reactions occurred during which benzyl nitrite (δ 5.72) followed by benzaldehyde (δ 9.6) were observed. This result suggests that *O*-nitrosation of benzyl alcohol does in fact yield benzaldehyde via benzyl nitrite, as postulated.

Nitrosonium salts, however, are far more potent nitrosating agents than *N*-alkyl-*N*-nitrosoamides and even though the latter compounds nitrosate aggressive nucleophiles such as Br^- ($n = 5.7$),[5] CN^- ($n = 6.8$),[5] and I^- ($n = 7.4$),[5] etc.,[3g] it was still necessary to demonstrate their ability to nitrosate a relatively weak nucleophile like benzyl alcohol ($n \approx 0$).[5] The most likely N → O nitroso vectors for such a reaction would appear to be nitrosoamides with acyl groups bereft of steric bulk and with high electrophilicity.[3g] The following experiments were performed to determine the validity of this assumption and to delineate the relative importance of these two effects.

***N*-Benzyl-*N*-nitrosoamides in the Presence of Benzyl Alcohol.** *N*-Benzyl-*N*-nitrosoacetamide (**1**) was incubated in the presence of 10 equiv of benzaldehyde-free benzyl alcohol in $CDCl_3$ at 20 °C. There was no observable reaction after 3 days as illustrated by an absence of new signals in the ^1H NMR spectra. The sample was then heated to 40 °C, but there was no observable reaction after 10 days at that temperature.

This is an interesting result in the context that (1) *N*-denitrosation of *N*-nitrosoamides by nucleophiles under near-neutral conditions had been shown to depend on steric effects in the acyl portion of the substrate such that denitrosation was encouraged by small alkyl groups[3g] and (2) benzaldehyde formation was not observed when the acyl portion of the nitrosoamide possessed ^{i}Pr or ^{t}Bu groups.[3g] The absence of appreciable reaction under these circumstances suggests that either (1) our proposed model for *N*-nitrosoamide-mediated benzaldehyde formation is incorrect or that (2) the steric accessibility of the N−N=O unit may not be a major factor in *N*-denitrosation via the weakly electrophilic benzyl alcohol and that other factors (presumably electronic ones) supersede the steric advantage. To test this hypothesis, the experiment was repeated with *N*-benzyl-*N*-nitroso-*p*-toluenesulfonamide (**2**): a nitrosoamide that possessed a relatively sterically hindered but electronically active acyl group.[3g]

To this end, *N*-benzyl-*N*-nitrosotosylamide (**2**) was incubated with 10 equiv of benzyl alcohol in $CDCl_3$ and spectra were taken in intervals of several hours over the course of ~6 days. The data (Table 1) show that compound **2** (δ 4.93) decomposes to yield *N*-benzyl tosylamide (δ 4.06), benzyl nitrite (δ 5.72), and benzaldehyde (δ 9.6) as the major products; low yields of benzyl tosylate (δ 5.06) are also observed.

The virtual absence of benzyl tosylate as a reaction product (Table 1; Figure 1) is consistent with the relative thermostability of *N*-nitrosotosylamides to deamination[2b,3c] so that this mode of decomposition is not competitive at ambient temperatures. The significant yields of benzyl nitrite and benzaldehyde as well as the timing of their appearance and demise (Table 1; Figure 1) under these conditions is typical of A → B → C reaction sequences and is thus consistent with our hypothesis.

Table 1 shows that the combined yield of benzyl nitrite + benzaldehyde is roughly constant at ~34% from time = 21 h. Further, as the yield of the former falls, that of the latter rises. The implication therefore is that the nascent benzyl nitrite is transformed into benzaldehyde, as postulated. Such a reaction would require an oxidation of the carbinyl carbon of the nitrite to the carbonyl carbon of the aldehyde.

The O−N=O bond is prone to homolysis because the enhanced electronegativity of the N (sp^2-hybridized and doubly bonded to O) makes the O−N single bond relatively nonpolar. Additionally, the α-effect along this short O−N σ-bond significantly enhances the lability of this bond. The consequence of these combined factors is facile fission to yield the nitrosyl radical and the benzyloxy radical. Evidence for the formation of free radicals in the present case is the massive production of hexachloroethane (vide infra) when benzyl nitrite is allowed to decompose in $CDCl_3$.

The benzyloxy radical is then believed to undergo hydrogen abstraction by any number of free radicals in the system [trichloromethyl radicals (in $CDCl_3$) and other benzyloxy radicals] to yield benzaldehyde. The former reaction would yield protochloroform resulting in the observed increase in the integral for $CHCl_3$ in $CDCl_3$ (Table 1). The latter reaction would result in the formation of benzyl alcohol; however, presumably because the large excess of alcohol is present at time = 0, no significant change in percent benzyl alcohol is noted. There must be at least one species apart from $^\bullet CCl_3$ involved in H-abstraction from the benzyloxy radical since the yield of $CHCl_3$ is less than the yield of benzaldehyde (Table 1). It is interesting that even though an A → B → C reaction is proposed, the yield of amide does not equal the yield of nitrite + aldehyde. It is likely that the reactive nitrite undergoes another reaction in addition to dehydronitrosation. An obvious candidate is hydrolysis to benzyl alcohol (to which the reaction system is insensitive) by trace moisture in $CDCl_3$; a more likely candidate is reaction with benzyl alcohol (a much more abundant nucleophile in the system) to form benzyl ether. In support of this hypothesis, a significant amount of benzyl ether was observed as a reaction product by GC ($t_R = 15.2$ min).[6]

The Relative Impact of Steric and Electronic Factors in *N*-Denitrosation of *N*-Alkyl-*N*-nitrosoamides. The absence of benzyl nitrite/benzaldehyde

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(6) The chemical shifts of benzyl alcohol and benzyl ether in $CDCl_3$ are both δ 4.56 so NMR distinction between these two is not easy. Although benzyl ether was detected by GC ($t_R = 15.2$; vide supra) no relative response factor calculations were performed so accurate measurements of yields are not available.

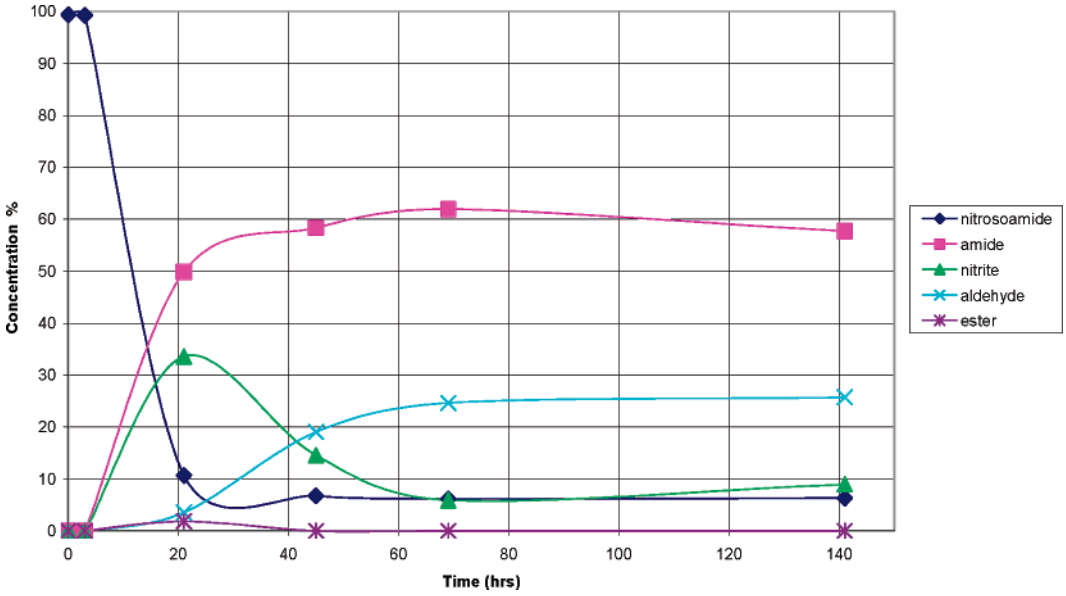

FIGURE 1. Relative distribution of *N*-benzyl-*N*-nitrosotosylamide and its decomposition products during N to O nitroso transfer to benzyl alcohol and subsequent dehydronitrosation at 20 °C.

formation during the incubation of benzyl alcohol with **1** as compared to ~34% production of that pair in the companion reaction with **2** is instructive. The implication is that the sterically accessible acetyl group lacks the minimum electrophilicity necessary to elicit N → O nitroso transfer from nitrosoamide to benzyl alcohol; conversely, the bulkier tosyl group has sufficient electrophilicity to counteract its significant bulk. Evidently, in this reaction, electronic factors outweigh steric ones. It is noteworthy that the extent of denitrosation via N → nucleophile nitroso transfer from nitrosoacetamides was 36%, 42%, and 87%, when the strongly nucleophilic Br^-, CN^-, and I^- ions, respectively were employed.[3g] Evidently, in that case the high reactivity of these nucleophiles ($n = 5.7, 6.8, 7.4$, respectively)[5] compensated for the low electrophilicity of the acetyl group.

The Role of Alcohol Type in *N*-Denitrosation of *N*-Alkyl-*N*-nitrosoamides. The question now arises concerning the generality of the "N → O nitroso transfer followed by denitroxylation" phenomenon observed for benzyl alcohol. It is reasonable that three separate reactions are necessary for the alcohol → carbonyl conversion described here: (1) preliminary N → O nitroso transfer, a necessary but perhaps insufficient step as nitrite solvolysis (and to a lesser extent hydrolysis) to ethers (and alcohols) appear to be competitive; (2) N−O homolysis, which is probably an equilibrium phenomenon necessary but insufficient for the final denitroxylation to the carbonyl compound; and (3) H-abstraction from the alkoxy species to yield the carbonyl. With respect to this first step, we postulated that the character of an unhindered alkyl portion would not likely play a large role in N → O nitroso transfer and that alcohol nitrosation would be relatively similar for MeOH, 1°, and 2° carbinols. In a similar manner, N−O homolysis is not likely to be affected by the alkyl character of the alcohol. It can be readily argued, however, that the transition state for H-abstraction from the alkoxy radical is likely to be stabilized by conjugation with the aromatic ring in the benzyl alcohol case and may be subject to other inductive and perhaps hyperconjugative effects in other cases. It could be argued that the oxidation of benzyl alcohol in the present work would be exaggerated because a large excess of the alcohol is used whereas in the normal runs, only small yields of alcohol and even smaller yields (0−2%) of aldehyde are observed. Additionally, p/p stabilization of the transition state to benzaldehyde may be operative.

TABLE 2. Relative Distribution of *N*-Benzyl-*N*-nitrosotoluenesulfonamide and Its Decomposition Products from Ethanol-Promoted *N*-Denitrosation at 40 °C as a Function of Time

time (h)	relative distribution (%)					
	NTS[a]	ester[b]	amide[c]	EtONO	ethanal	$CHCl_3$
0	100.0	0.0	0.0	0.0	0.0	0.0
1	99.6	0.4	0.0	0.0	0.0	0.0
21	38.2	1.8	35.0	25.0	0.0	0.0
45	19.5	1.4	43.7	35.4	0.0	0.0
69	11.9	1.4	48.7	38.0	0.0	0.0

[a] *N*-Benzyl-*N*-nitrosotoluenesulfonamide (**2**). [b] Benzyl tosylate. [c] *N*-Benzyltoluenesulfonamide.

To examine the generality of this phenomenon, the experiments were repeated with MeOH, unhindered 1° alcohols (EtOH, ^{n}PrOH, ^{n}BuOH), a relatively hindered 1° alcohol (^{i}BuOH), 2° alcohols (^{i}PrOH, 3-pentanol, cyclohexanol), and ^{t}BuOH.

***N*-Benzyl-*N*-nitrosotosylamide in the Presence of Selected Alcohols.** The carbonyl-free alcohol was allowed to stand for 3 days in $CDCl_3$ at 40 °C; no reaction was observed. Ten equivalents of the alcohol were then incubated with **2** for 3 days at 40 °C and integrals were taken as a function of time. Table 2 shows the time-based profile for ethanol in which ethyl nitrite (t, δ 1.35; q, δ 4.72) and *N*-benzyl tosylamide (δ 4.06) were the major species formed. Further, (1) no ethanal was generated, (2) the disappearance of **2** is somewhat slower in the ethanol case, and again (3) the yield of amide is greater than the yield of nitrite "(+ aldehyde)" indicative perhaps of nitrite hydrolysis and ethanolysis (diethyl ether was observed by GC at $t_R = 1.0$ min).

TABLE 3. Rate Constants for Nitrite and Carbonyl Formation as a Function of Alcohol from Alcohol-Promoted *N*-Denitrosation at 40 °C

	ROH									
	MeOH	EtOH	^{n}PrOH	^{n}BuOH	^{i}BuOH	BzOH[a]	^{i}PrOH	3-PeOH[b]	CxOH	^{t}BuOH
k_{NO}[c] ($\times 10^{-3}$)	8.8	6.9	8.0	9.2	5.6	5.9	5.2	6.2	4.4	5.0
k_{CO}[d]	0.0	0.0	0.0	0.0	0.0	0.15	0.13	0.08	NA	0.0

[a] Benzyl alcohol. [b] 3-Pentanol. [c] Data are averages of at least duplicate runs; maximum standard deviation = 3×10^{-4}. [d] Data are averages of at least duplicate runs; maximum standard deviation = 0.1.

In a similar fashion, **2** was incubated in the presence of the other carbonyl-free alcohols and the reactions followed by ^{1}H NMR. The rate constants for formation of the nitrite (≈rate of disappearance of **2**) and carbonyl compound (when formed) (k_{NO} and k_{CO}, respectively) are shown in Table 3.

Several features emerge from the data in Table 3. (1) There appears to be only a small sensitivity of the trans-nitrosative event upon the character of the denitrosating alcohol. Thus, the difference in rate constants for the fastest trans-nitrosation (R = ^{n}Bu) and the slowest (R = Cx) is barely a factor of 2. (2) Nonetheless there appears to be a clear though nonlinear correlation between the sterics of the alcohol and k_{NO}. Thus, in general, the smaller the alkyl group, the faster the nitroso transfer. That the less sterically crowded alcohols appear to be better denitrosative agents ostensibly arises from their ability to "dock" at the N−N=O group, which is compromised with increasing bulk. Note that the correlation is not absolute since the value of k_{NO} for R = Me is not the largest nor is that for R = ^{t}Bu the smallest (although they are not statistically different from the relevant extremes). This inconsistency may arise from inherent experimental errors (note standard deviations are on the order of 5×10^{-4}) or because a factor other than sterics may be operational. Given the dynamics of the system, it is our opinion that experimental errors may be the more likely culprit. (3) Although to a rough approximation k_{NO} decreases in the order Me ≈ 1° > 2° > 3°, it is interesting that the two 1° alcohols with bulky β-carbons (^{i}BuOH and benzyl alcohol) have k_{NO} values that mirror those of 2° alcohols. Evidently the steric effect of the alkyl group is determined by more than substitution at the α-carbon and is also influenced by the degree of alkyl substitution at the β-carbon.

Interestingly, neither MeOH nor the 1° alkanols were found to yield a carbonyl product. Carbonyls (from denitroxylation) were only observed from benzyl alcohol and the secondary alcohols. These results imply that the denitroxylation event is encouraged by molecular features that stabilize the developing carbonyl group. Thus the minimum inductive stabilization necessary for C=O formation is found in 2° alkanols (which therefore derive ketones); evidently a single +I alkyl group is unable to facilitate denitroxylation, but a lone +M group can. This result suggests that the assisted formation of the C=O π-bond plays a significant role in the formation of the carbonyl compound. Thus, the aromatic ring of the benzyloxy radical stabilizes the transition state leading to benzaldehyde by p/p overlap. Similarly, the production of ketones versus aldehydes (yield = 0%) is likely a consequence of the greater stability of ketones as compared to their isomeric aldehydes and thus the enhanced stabilization of the transition state leading to the former. Thus, the dehydronitrosative step appears to be influenced largely by enthalpic factors.

Interestingly, the absence of acetone from the reactions with ^{t}BuOH suggests that the conceivable loss of an alkyl fragment (Me$^{\bullet}$) from ^{t}BuO$^{\bullet}$ is apparently noncompetitive.

It is noteworthy that under conditions where *N*-benzyl-*N*-nitrosoamides are employed as carbocationogens,[2,4] the formation of benzaldehyde is of little consequence since under reasonably dry conditions only a small fraction of the *N*-nitrosoamides are diverted to alcohol and only a small fraction of the alcohol is oxidized to the aldehyde.[2b] Additionally, the high carbocation reactivity results in the cations reacting in a somewhat statistical manner, so that products from the cations reacting with nascent trace aldehyde have not been observed. Interestingly, benzaldehyde formation is also completely absent when the acyl portion is hindered. Thus, when the α-carbon of the acyl group is 2° or 3°, no denitrosation occurs (as is consistent with our previous observations[3g]) and consequently no benzaldehyde formation occurs.

Conclusion

Alcohols generated in situ by hydrolysis of *N*-alkyl-*N*-nitrososulfonamides are mildly active at denitrosating the *N*-nitrososulfonamides in a reaction that is dominated by the electron-withdrawing ability of the acyl moiety and electronic assistance to the formation of the π-bond of the carbonyl group. This reaction series involves initial nitrososulfonamide to alcohol trans-nitrosation followed by rapid proton transfer to yield the alkyl nitrite, which may undergo reversible homolysis of the labile O−N σ-bond to yield an alkoxy radical. H-Abstraction from the latter by other radicals including $Cl_3C^{\bullet}$ (and possibly RO$^{\bullet}$) may yield a carbonyl product if the latter is ketonic or resonance-stabilized. The overall reaction involves an *N*-nitrososulfonamide-mediated oxidation of secondary and selected primary carbinols to their respective carbonyl derivatives.

Experimental Section

Materials and Methods. All commercially available reagents were reagent grade and were used without further purification. Fresh bottles of benzyl alcohol, ethanol, and propan-2-ol were employed; they were opened, employed, and stored under an argon blanket. All moisture sensitive experiments were performed in a glovebox, which had been purged exhaustively with ultrahigh purity argon. Spectra were recorded on 300 MHz FT-NMR, FT-IR UV−vis spectrometers. In many instances, reactions were performed in evacuated sealed NMR tubes. Gas chromatography was performed on a 30 m SE-30 column at an oven temperature of 150 °C and a helium flow rate of 15 psi.

Handling and Storage of *N*-Benzyl-*N*-nitrosoamides. *N*-Nitrosoamides are thermolabile, photolabile, and unstable

in the presence of acids, bases, and moisture. They should be stored in dry vials under an inert gas, and in a cryogen dewar containing liquid nitrogen. They must be stored and handled in the dark. *N*-Nitrosoamides should be handled with extreme care due to their possible mutagenicity[7a] and carcinogenicity (local and systemic).[7b] Efficient fume hoods and appropriate personal protective equipment (chemical resistant gloves, safety glasses, lab coat, etc.) should be used when handling these types of compounds.

***N*-Benzyl-*N*-nitrosoacetamide (1)** was prepared as outlined in ref 3b: IR (neat) 1725, 1605, 1502, 1375, 1114 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.80 (s, 3H), 4.92 (s, 2H), 7.18−7.28 (m, 5H); UV (CH_3CN) λ_{max} 425 (ϵ 66), 405 (ϵ 63) 394 (sh), 422 nm (ϵ 66).

***N*-Benzyl-*N*-nitrosotosylamide (2)** was prepared as outlined in ref 8: IR (KBr) 1596, 1497, 1384, 1196, 1134 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.41 (s, 3H), 4.93 (s, 2H), 7.11−7.27 (m, 7H), 7.71−7.74 (d 2H, J = 9.0 Hz); UV (Et_2O) λ_{max} 289 (ϵ 500), 391 (ϵ 15), 391 (ϵ 15), 409 nm (ϵ 15).

Proof of Stability of Alcohols to Air Oxidation. A solution of a fresh sample of the requisite alcohol (benzyl alcohol, ethanol, propan-2-ol; 5−10 μL) in undegassed $CDCl_3$ (800 mL) was prepared in a pressure NMR tube and a ^1H NMR spectrum was run to confirm the absence of an aldehydic signal or C*H*$_3$−C=O signal in the case of propan-2-ol. The solutions of the carbonyl-free alcohols were then placed in an oven at 40 °C for 3 days after which the sample was allowed to cool and another ^1H NMR spectrum was taken. No signals due to the carbonyl compounds were observed.

Nitrosation of Benzyl Alcohol with Nitrosonium Tetrafluoroborate. To a sample of nitrosonium tetrafluoborate (5 mg) that had been dried at oil pump vacuum in an NMR tube with a PTFE valve was added a solution of fresh benzyl alcohol (10 μL) and 2,6-di-*tert*-butyl-4-methylpyridine (2 equiv) in dry $CDCl_3$ (800 μL). The suspension was shaken vigorously and ^1H NMR spectra were recorded at intervals (Table 1). Benzyl nitrite (δ 5.73) followed by benzaldehyde (δ 9.6) was observed.

Incubation of Benzyl Alcohol with *N*-Benzyl-*N*-nitrosoacetamide. To 800 μL of $CDCl_3$ in an NMR tube with PTFE valve were added *N*-benzyl-*N*-nitrosoacetamide (5 mg, 0.028 mmol) and benzyl alcohol (30.3 mg, 0. 28 mmol). The solution was then analyzed via ^1H NMR when signals consistent with only nitrosoamide and benzyl alcohol were observed. The sample was then allowed to stand for 3 days at 20 °C and then for 10 days at 40 °C. No reaction was observed.

Incubation of Alcohols with *N*-Benzyl-*N*-nitrosotosylamide. To 800 μL of $CDCl_3$ in an NMR tube with a PTFE valve were added *N*-benzyl-*N*-nitrosotosylamide (5 mg, 0.017 mmol) and 10 equiv of the requisite alcohol (0. 17 mmol). The solution was then analyzed via ^1H NMR when signals consistent with only nitrosotosylamide and the alcohol were observed. The sample was then allowed to stand for 3 days at 20 °C and ^1H NMR spectra were recorded at intervals. Signals at δ 5.73, 4.06, 5.06 due to benzyl nitrite, *N*-benzyltosylamide, and benzyl tosylate were observed in all spectra. In addition, benzaldehyde (δ 9.6) from benzyl alcohol and acetone (δ 2.4) from propan-2-ol were observed (Tables 1 and 3).

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